Prescribing Outlook
National Developments

November 2015

A resource for the NHS to help with budget setting, prescribing planning and medicines optimisation
1. GASTROINTESTINAL SYSTEM

Inflammatory Bowel disease (IBD) .................................................. 9
Diarrhoea and constipation ................................................................. 11
Dyspepsia and gastro-oesophageal reflux disease (GORD) ......................... 12
Other gastro-intestinal related conditions ........................................ 12

2. CARDIOVASCULAR DISEASE

Patent expiries ........................................................................ 15
Hypertension ............................................................................... 15
Lipid modification ............................................................................ 15
Acute coronary syndrome [ACS - unstable angina and myocardial infarction (MI)] & chest pain ............... 19
Heart failure (HF) ........................................................................ 21
Ischaemic stroke & atrial fibrillation (AF) ........................................ 22
Venous thromboembolism (VTE) ..................................................... 23
3. Respiratory System

Patent expiries ........................................................................ 24
Asthma ......................................................................................... 24
Chronic Obstructive Pulmonary Disease (COPD) ......................... 25
Drug allergy .................................................................................. 27
Other respiratory conditions ......................................................... 27

4. CENTRAL NERVOUS SYSTEM

Patent expiries ........................................................................ 29
Psychosis and schizophrenia ......................................................... 29
Hypnotics and sedation .................................................................... 30
Bipolar disorder .............................................................................. 31
Depression ..................................................................................... 31
Autism .......................................................................................... 32
Attention Deficit Disorder .............................................................. 32
Obesity .......................................................................................... 32
Pain ............................................................................................... 34
Substance dependence ....................................................................... 34
Alzheimer’s disease & dementia ....................................................... 37
Parkinson’s disease ......................................................................... 37
Eating disorders ............................................................................. 37
Other mental health and CNS related guidance ......................... 38

5. INFECTIONS

Patent expiries ........................................................................ 40
General strategy ............................................................................ 40
Infection in children ...................................................................... 42
Respiratory infections ................................................................... 43
Tuberculosis (TB) .......................................................................... 43
Pneumonia .................................................................................... 43
Hepatitis C .................................................................................... 43
Hepatic encephalopathy ................................................................. 46
Infective endocarditis ..................................................................... 47
Sepsis ............................................................................................ 47
Other infection-related developments and guidance ............... 47

6. ENDOCRINE SYSTEM

Patent expiries ........................................................................ 48
Diabetes ........................................................................................ 48
Osteoporosis .................................................................................. 54
Fertility .......................................................................................... 55
Menopause .................................................................................... 55
Autosomal dominant polycystic kidney disease (ADPKD) ............ 56

7. OBSTETRICS, GYNAECOLOGY AND URINARY TRACT DISORDERS

Patent expiries ........................................................................... 57
Incontinence .................................................................................... 57
Contraception .................................................................................. 57
Antenatal, intrapartum and postnatal care ....................................... 57
Endometriosis and menstrual disorders ...................................... 58

8. MALIGNANT DISEASE AND IMMUNOSUPPRESSION

Patent expiries ........................................................................... 59
Multiple sclerosis (MS) .................................................................. 59
Organ transplantation ...................................................................... 59
Malignant disease .......................................................................... 61
Breast cancer ................................................................................. 61
Gastrointestinal (GI) cancer ......................................................... 62
Haematological cancers ................................................................... 64
NHL and other lymphomas ............................................................ 67
Lung cancer ..................................................................................... 69
Head and neck cancers ................................................................... 71
Skin and connective tissue cancers .............................................. 71
Sarcoma .......................................................................................... 73
Urogenital and renal cancers ......................................................... 74
Ovarian cancer ................................................................................ 75
Bone cancers and metastases ......................................................... 75
Prostate cancer ............................................................................... 76
Brain cancer ................................................................................... 77

9. NUTRITION AND BLOOD

Patent expiries ........................................................................... 78
Anaemia ........................................................................................ 78
Nutrition ....................................................................................... 79
Renal .............................................................................................. 79
Metabolic disorders ........................................................................ 80

10. MUSCULOSKELETAL AND JOINT DISEASES

Patent expiries ........................................................................... 81
NSAIDs .......................................................................................... 81
Rheumatoid Arthritis (RA) ............................................................ 81
Juvenile Idiopathic Arthritis (JIA) .................................................... 83
Ankylosing spondylitis (AS) ............................................................ 83
Psoriatic Arthritis (PsA) ................................................................. 84
Systemic lupus erythematosus (SLE) ............................................ 86
Osteoarthritis (OA) ........................................................................ 88
Gout ............................................................................................... 88
Spasticity ....................................................................................... 88

11. EYE

Patent expiries ........................................................................... 90
Macular oedema ............................................................................. 90
Age related macular degeneration (AMD) ................................. 92
Cataracts ....................................................................................... 92
Dry eye disease .............................................................................. 92

13. SKIN

Patent expiries ........................................................................... 94
Psoriasis ......................................................................................... 93
Urticaria ....................................................................................... 94
Wound care .................................................................................... 95
Extemporaneous Specials ............................................................... 95

PATENT EXPRIRES .................................................................... 96
Managing new medicines

Underpinning the strategic direction for managing new medicines is the Department of Health's (DH) report *Innovation Health and Wealth, Accelerating Adoption and Diffusion in the NHS*. It sets out government support for the NHS to embrace innovation to meet current and future healthcare challenges, and outlines the importance of early adoption and uptake of clinically and cost effective innovative practices, including medicines. Horizon scanning is essential for this process at many organisational levels so new medicines that have been shown to improve patient outcomes can be planned for and adopted. Increasing financial pressure facing the NHS means it is even more important that the introduction of new medicines is actively managed.

Funding of medicines in the NHS is inextricably linked to the national tariff payment system. Monitor, in conjunction with NHS England, is responsible for the National Tariff of NHS prices which includes producing the ‘High Cost Drugs’ (HCD) list for drugs that are not funded within Tariff. This year (2015-16) two national tariff systems are operating; the Enhanced Tariff Option (ETO) and the Default Tariff Rollover (DTR) option for trusts who opted out of the ETO. This has implications for funding drugs as financial flow could differ depending on which Tariff a particular Trust is operating to; in particular, the HCD list will differ slightly. Throughout this document when it is stated a drug is a ‘Specified high cost drug’ it is the ETO HCD list 2015-16 used as reference. Those Trusts on the DTR option should refer to the 2014-15 HCD list. Many drugs on these lists are not yet available in the UK but are included so that commissioners and providers can start a dialogue about funding in advance of launch. In *Prescribing Outlook*, for medicines not listed on the ETO HCD list, an ‘educated guess’ regarding potential tariff positioning has been made.

NHS England has a strategic medicines management role and is responsible for commissioning most high cost drugs as well as all cancer chemotherapy. An updated list has recently been published (March 2015) of medicines not reimbursed through national prices that are used in the delivery of services directly commissioned by NHS England. The list outlines mechanisms for funding, highlights which drugs have been appraised by NICE, which are formally commissioned via policies and those which require an Individual Funding Request (IFR). In addition, it highlights which drugs are managed by specialist centres and which may be suitable for shared care between the specialist centre and secondary care. There is a move for CCGs to take on more commissioning of specialised services and therefore associate drug costs so the latest available list should be used.

Funding for most cancer drugs differs and involves use of the Cancer Drugs Fund (CDF) for drugs that have yet to be appraised by NICE. The CDF has undergone significant review this year and is likely to undergo further significant change following recent publication of an independent cancer taskforce report which proposes it becomes a ‘managed access’ fund that could support data collection in advance of NICE appraisal. In *Prescribing Outlook* the current CDF status is highlighted.

Inevitably, more expensive medicines will receive most attention but a comparatively cheaper drug could still have a big financial impact in the NHS if used in a large number of patients. *Prescribing Outlook* includes such drugs but quantifying their impact is difficult. However, there are other mechanisms in place at a national level to mitigate the financial impact of such drugs.

The mechanism agreed between the government and the pharmaceutical industry for setting the NHS cost of new drugs is known as the Pharmaceutical Price Regulation Scheme (PPRS). This scheme is negotiated every five years. The latest scheme *PPRS 2014* is very different to previous schemes. A question and answer document outlines how it operates. Pharmaceutical companies decide whether to join the PPRS scheme. If they decide not to join they are subject to the alternative statutory scheme which imposes a price cut on individual medicines of 15% of their NHS list price. If they join the scheme they are subject to an overall aim of limiting growth of NHS spending on branded medicines. Growth in the branded medicines bill above the agreed level will result in a ‘PPRS Payment’ being made by pharmaceutical companies back to the DH with payments based on the difference between the agreed forecast and the allowed growth level. The overall allowed growth rate in the NHS branded medicines bill is 0% for the first two years and then only a small growth rate (less than 2% per year) for the remaining three years of the current scheme. Future payments will be adjusted if actual growth is above or below the agreed forecast. There are exclusions to this; further detail is in the question and answer document. The scheme has been in operation for over a year now and, up to end of March 2015, a total of £517 million has been paid back to the DH. The rebate is divided across the home countries according to primary care spend on licensed branded medicines. In Scotland, the money will go into a New Medicines Fund, set up last year to support funding for orphan, ultra-orphan and end-of-life drugs for patients. In England, a proportion of the rebate has been allocated to NHS England.

A further mechanism for reducing the cost of new medicines to the NHS is use of a Patient Access Scheme (PAS) for those undergoing a NICE technology appraisal. This allows NICE to recommend treatments that it might otherwise not find cost effective. PAS are either cost (discounts, free stock, etc.) or outcome (price variation linked to patient outcomes) based but the finer details are confidential. A list of NICE technologies with an approved PAS can be viewed on the NICE website. In *Prescribing Outlook* current PAS schemes are highlighted if they are relevant to a new medicine in the same therapeutic area, and, although this will not give an indication of the likely cost of the new medicine, it suggests that subsequent treatment options will have to be competitive.

In addition to producing technology appraisals, NICE supports uptake of guidance and implementation of appraisal outcomes with a number of tools. In *Prescribing Outlook* there are links to a therapeutic area overview page on NICE Evidence from which all relevant tools and details of guidance and appraisals in progress can be accessed. Anticipated publication dates of NICE technology appraisals are subject to change but up-to-date information can be accessed from the overview page.

There have also been changes in regulatory processes impacting on availability of new drugs in the UK following launch of the early access to medicines scheme (EAMS). This scheme is operated by the MHRA and aims to give patients with life threatening or seriously debilitating conditions access
Prescribing Outlook – National Developments

This publication primarily aims to provide advance information to commissioners and providers about the impact on clinical practice and prescribing budgets of national guidance, mainly that issued by NICE. It is intended to inform discussions between commissioners and providers and highlight issues around implementing guidance. Access is via www.ukmi.nhs.uk. There will be additional, unquantifiable, local factors that influence implications for the NHS such as local demographics and prescribing preferences which cannot be accommodated in a national document.

As in previous editions of Prescribing Outlook, drugs with patents due to expire in the near future are highlighted. It is important that generic options are considered as part of the wider medicines optimisation agenda. This documents include an ‘educated guess’ as to which drugs have the potential for generic competition and an indication whether generic product licence applications are currently in progress in the EU. Although there are a small number of biosimilar drugs already on the market many more are in the pipeline that could have a potentially cost saving impact on medicines budgets.

Other UKMi horizon scanning resources

Prescribing Outlook – New Medicines
This publication aims to provide advance information about new medicines (and new licensed indications or formulations) with anticipated market launches in the next 18 to 24 months. The content is not comprehensive but focuses on medicines with the potential for significant clinical or financial impact on the NHS. Estimates of potential uptake, patient, service and financial implications are included where possible. Reference is made to relevant national guidance and links to in-depth independent reviews are included, where available. Access is via www.ukmi.nhs.uk.

Prescribing Outlook – Cost Calculator is an Excel spreadsheet tool to facilitate estimates of potential prescribing changes for a local population. Access is via www.ukmi.nhs.uk.

New Drugs Online (NDO) database includes information on medicines in clinical development from late phase II trials to product launch and includes links to evidence-based reviews up to one year post launch. This database is maintained by UKMi and forms the basis of the content of Prescribing Outlook – New Medicines. It is updated daily and can be used to produce reports based on a number of criteria including possible launch date, stage of clinical development or pharmaceutical company. Access is free to all with an NHS email address via www.ukmi.nhs.uk but requires individual registration. Limited access is freely available to non-registered users via Evidence search (www.evidence.nhs.uk).

VAT statement

Where the costs are available for a licensed drug, cost estimates are based on BNF or Drug Tariff prices and exclude VAT. Where the cost has been estimated – this should be taken indicatively and local interpretation is advised.
Key authors of this document:

Martin Bradley, Senior Formulary Pharmacist, Guy’s and St. Thomas’ NHS Foundation Trust (GSTT)
David Erskine, Director - London and South East Regional Medicines Information Centre, GSTT
Nicola Pocock, Senior Pharmacist - London and South East Regional Medicines Information Centre, GSTT
Hina Radia, Pharmacist - London and South East Regional Medicines Information Centre, GSTT
Devika Sennik, Senior Pharmacist - London and South East Regional Medicines Information Centre, GSTT
Yuet Wan, Principal Pharmacist - London and South East Regional Medicines Information Centre, GSTT

Acknowledgements:
We would like to thank the following people for commenting on draft versions of this document:
Nisha Shaunak, Lead Pharmacist for Oncology, GSTT and Specialised Cancer Commissioning Pharmacist, NHS England (London region)

Please direct comments on Prescribing Outlook – National Developments and the Cost Calculator to:
David Erskine or Devika Sennik, London and South East Medicines Information Centre, Guy’s and St. Thomas’ NHS Foundation Trust.
Email: david.erskine@gstt.nhs.uk; devika.sennik@gstt.nhs.uk

Please direct comments on Prescribing Outlook – New Medicines to the editor: Helen Davis, North West Medicines Information Centre. Email: helen.davis@lrippu.nhs.uk.

Please direct comments and enquiries on New Drugs Online to: London Medicines Information Service - Northwick Park. Email: nwmedinfo@nhs.net.

Horizon scanning and new medicines support materials are available via www.ukmi.nhs.uk

The information in these resources is the best available at the time of publication but is subject to significant change with time.
Table 1: High Cost Drug related PbR exclusions proposed in the 16/17 National Tariff.

Note: From 14/15, the DH is no longer responsible for PbR. Monitor is reviewing the PbR payment system therefore this list is subject to change.

Key:
Addition/amendment in 15/16
Addition/amendment proposed for 16/17
BNF category followed by a ‘>’ symbol means that only that drug or drug sub category is excluded
Drugs with ^ have been excluded for non-chemotherapy indications

<table>
<thead>
<tr>
<th>Proposed exclusions for 16/17</th>
<th>Exclusions categorised by BNF category</th>
<th>Responsible commissioner (NHSE or CCG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cykotine modulators</td>
<td>1.5.3 &gt;Drugs affecting the immune response &gt; Cytokine Modulators[^] 10.1.3 &gt; Cytokine Modulators[^] (includes Apremilast, Secukinumab, Teduglutide, Tofacitinib and Vercimon) Epratuzumab (cytokine modulator) Siltuximab Blisibimod Sarilumab</td>
<td>CCG – adults NHSE – paeds and specialist indications (see Manual)</td>
</tr>
<tr>
<td>Vasodilator antihypertensive drugs/ Primary pulmonary hypertension (PPH)</td>
<td>2.5.1 &gt; Ambrisentan 2.5.1 &gt; Bosentan 2.5.1 &gt; Iloprost 2.5.1 &gt; Sildenafil * <em>(Sildenafil excluded only when used for Pulmonary Arterial Hypertension)</em> (also includes Macitentan, Nitric Oxide, Riociguat, Sellexipag and Treprostinil sodium) Treprostinil diethanolamine 2.8.1 &gt; Epoprostenol 7.4.5 &gt; Tadalafil * <em>(Tadalafil excluded only when used for Pulmonary Arterial Hypertension)</em></td>
<td>NHSE</td>
</tr>
<tr>
<td>Fibrinolytic drugs</td>
<td>2.10.2 &gt; Alteplase ** <em>(Alteplase is dealt with as an adjustment under PbR)</em> Thrombomodulin, Recombinant Human</td>
<td>CCG TBC</td>
</tr>
<tr>
<td>Blood related products except fibrin sealants</td>
<td>2.11 &gt; Blood Products (includes Albutrepenonacog alfa, Nonacog alpha, Nonacog beta pegol, Susoctocog alfa, Trenonacog alfa)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Allergen immunotherapy</td>
<td>3.4.2 &gt; Onaluzumab (includes Mepolizumab and Reslizumab)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Allergic emergencies</td>
<td>3.4.3 &gt; Angioedema (Includes Ecallantide)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Pulmonary surfactants</td>
<td>3.5.2 &gt; Beractant 3.5.2 &gt; Poractant alpha</td>
<td>NHSE</td>
</tr>
<tr>
<td>Mucolytics</td>
<td>3.7 &gt; Dornase alfa 3.7 &gt; Ivcavator 3.7 &gt; Mannitol (when delivered via nebulisation/inhalation) 3.7 &gt; Lumacaflor with Lvcavator</td>
<td>NHSE</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>3.11 &gt; Pirfenidone</td>
<td>NHSE</td>
</tr>
<tr>
<td>Hypnotics and anxiolytics</td>
<td>4.1.1 &gt; Sodium oxybate</td>
<td>CCG – adults NHSE – paeds</td>
</tr>
<tr>
<td>Non-opioid analgesics</td>
<td>4.7.1 &gt; Ziconotide</td>
<td>NHSE</td>
</tr>
<tr>
<td>Neurodegenerative Conditions</td>
<td>4.9.1 &gt; Co-careldopa internal tube intestinal gel *** ***(Only when used as intestinal gel with internal tube) 4.9.3 &gt; Tafamidis</td>
<td>NHSE</td>
</tr>
<tr>
<td>Torsion dystonias and other involuntary movements</td>
<td>4.9.3 &gt; Riluzole 4.9.3 &gt; torsion dystonias and other involuntary movements</td>
<td>CCG</td>
</tr>
<tr>
<td>Antibacterial Drugs</td>
<td>5.1.2.3 &gt; Aztreonam Lysine**** 5.1.4 &gt; Tobramycin**** 5.1.4 &gt; Amikacin Inhalation 5.1.4 &gt; Amikacin liposomal 5.1.7 &gt; Colistimethate sodium**** 5.1.12 &gt; Levofloxacin**** ****(when delivered via nebulisation/inhalation) (includes Amikacin liposomal) 5.1 &gt; Amikacin 5.1 &gt; Bedaquiline, Delamanid, Para - Aminosalicylic acid</td>
<td>NHSE</td>
</tr>
<tr>
<td>Antifungals</td>
<td>5.2.1 &gt; Triazole antifungals &gt; Posaconazole 5.2.1 &gt; Triazole antifungals &gt; Voriconazole 5.2.3 &gt; Polyene antifungals &gt; Amphotericin &gt; lipid formulations 5.2.4 &gt; Echinocandin antifungals &gt; Anidulafungin 5.2.4 &gt; Echinocandin antifungals &gt; Caspofungin 5.2.4 &gt; Echinocandin antifungals &gt; Micafungin (includes Isavuconazole)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Proposed exclusions for 16/17</td>
<td>Exclusions categorised by BNF category</td>
<td>Responsible commissioner (NHSE or CCG)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>AIDS/HIV antiretrovirals</td>
<td>5.3.1 (includes Cobicistat, Dolutegravir, Elvitegravir, Elvitegravir + Cobicistat + Emtricitabine + Tenofovir, Elvucitabine and Vedolizumab)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td><strong>Atravenamide</strong></td>
<td>NHSE</td>
</tr>
<tr>
<td>Cyto,mevalovirus infection</td>
<td>5.3.2.2 &gt;Cytomegalovirus infection</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>Brincidofovir</td>
<td>NHSE</td>
</tr>
<tr>
<td>Viral hepatitis (B&amp;C) &amp;</td>
<td>5.3.3 (includes: Alisporivir, Asunaprevir with Daclatasvir, Daclatasvir, Faldaprevir, Motazavimab, Nitazoxanide, Simeprevir, Sofosbuvir, Sofosbuvir with Ledipasvir and Taribavirin, Ombitasvir with Paritaprevir with Ritonavir with Dasabuvir, Asunaprevir, Elbasvir, Grazoprevir, Ledipasvir, Simeprevir, Sofosbuvir, Sofosbuvir with Ledipasvir and Taribavirin)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Respiratory syncytial virus (RSV)</td>
<td>5.3.5</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Interferon alfa</td>
<td>NHSE</td>
</tr>
<tr>
<td>Endocrine</td>
<td>6.1.1 &gt;Mifepristone (for Cushing's ONLY)</td>
<td>TBC</td>
</tr>
<tr>
<td>Growth hormone &amp; growth</td>
<td>6.5.1 &gt;Anterior pituitary hormones &gt;growth hormone receptor antagonist</td>
<td>NHSE &amp; CCG NHSE</td>
</tr>
<tr>
<td>hormone receptor antagonist</td>
<td>6.5.1 &gt;Anterior pituitary hormones &gt;growth hormone</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>6.5.2 &gt;Tolvaptan</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>6.7.4 &gt;Mecasermin (includes Octreolin, Tesamorelin and Lixivaptan)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs affecting bone</td>
<td>6.6.1 &gt;Teriparatide</td>
<td>CCG</td>
</tr>
<tr>
<td>metabolism</td>
<td>Abaloparatide</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>Velcalcetide</td>
<td>TBC</td>
</tr>
<tr>
<td></td>
<td>6.6.1 &gt;Parathyroid hormone</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>6.6.1 &gt;Human Parathyroid hormone-related protein analogue</td>
<td>TBC</td>
</tr>
<tr>
<td></td>
<td>6.6.2 &gt;Odanacatib</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Ganetespib</td>
<td>TBC</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Pomalidomide</td>
<td>NHSE</td>
</tr>
<tr>
<td>Immunomodulating drugs</td>
<td>8.1 &gt;Dexrazoxane</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.3 &gt;Cladribine^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Interferon alfa&gt;interferon alfa</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Interferon beta</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Aldesleukin</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Glatiramer</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Lenalidomide^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Natalizumb</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Thalidomide^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Fingolimod (includes Dimethyl fumarate, Laquinimod, Nintedanib, Peginterferon Beta-1a, Peginterferon Lambda-1a, Rilonacept and Teriflunomide)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.4 &gt;Ganetespib</td>
<td>NHSE</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>8.1.3 &gt;Azacitidine^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.3 &gt;Decitabine^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>Rigosertib^ (no BNF category available)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Antineoplastic drugs</td>
<td>8.1.5 &gt;Bevacizumab^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Bortezomib^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Cetuximab^</td>
<td>NHSE</td>
</tr>
<tr>
<td>Protein kinase inhibitors</td>
<td>8.1.5 &gt;Protein kinase inhibitors^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>(includes Fostamatinib disodium^, Masitinib^ and Pacritinib^)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Afatinib</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Bosutinib</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Dabrafenib</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Ponatinib</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.1.5 &gt;Rogafenib</td>
<td>NHSE</td>
</tr>
<tr>
<td>Corticosteroids and other</td>
<td>8.2.2 &gt;Basiliximab</td>
<td>NHSE</td>
</tr>
<tr>
<td>immunosuppressants</td>
<td>Declizumab</td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs affecting the immune</td>
<td>8.2.3 &gt;Belatacept</td>
<td>NHSE</td>
</tr>
<tr>
<td>response</td>
<td>8.2.3 &gt;Alectuzumab^</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.2.3 &gt;Ofatumumab</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>9.1.7 &gt;Plerixafor</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>10.1.3 &gt;Belimumab</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>13.5.3 &gt;Efalizumab</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>13.5.3 &gt;Ustekinumab (includes Vedolizumab)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>Baricitinib (BNF code TBC)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>Brodalumab (BNF code TBC)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Somatostatin analogues</td>
<td>8.3.4.3 (includes Fibroblast growth factor 1 gene therapy)</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>8.3.4.4 &gt;Oteronel</td>
<td>NHSE or CCG, depends on drug</td>
</tr>
<tr>
<td>Paroxysmal nocturnal</td>
<td>9.1.3 &gt;Eculizumab</td>
<td>NHSE</td>
</tr>
<tr>
<td>haemoglobinuria</td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Platelet Disorder Drugs</td>
<td>9.1.4 &gt;Elotrombopag</td>
<td>NHSE</td>
</tr>
<tr>
<td></td>
<td>9.1.4 &gt;Romiplostim (includes Avatrombopag)</td>
<td>NHSE</td>
</tr>
<tr>
<td>Proposed exclusions for 16/17</td>
<td>Exclusions categorised by BNF category</td>
<td>Responsible commissioner (NHSE or CCG)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---------------------------------------</td>
<td>---------------------------------------</td>
</tr>
</tbody>
</table>
| Drugs used in hypoplastic, haemolytic, and renal anaemias | 8.2.2 >Antilymphocyte globulin  
9.1.3 >Antithymocyte Immunoglobulin  
9.1.3 >Iron Overload (For chronic iron overload) | NHSE |
| Drugs used in Metabolic disorders | 8.2.4 >Canakinumab  
9.4.1 >Saprapoterin  
9.8.1 >Carntine deficiency  
9.8.1 >Fabry's disease  
9.8.1 >Gaucher's disease  
9.8.1 >Mucopsonalyccharidosis  
9.8.1 >Nephropathic cystinosis  
9.8.1 >Pompe Disease  
9.8.1 >Tyrosinaemia type I  
9.8.1 >Urea cycle disorders  
9.8.1 >Homocystinuria  
9.8.1 >Other metabolic disorders (includes Alipogene Tiparvovec, Cysteamine bitartrate, Eliglustrat, Elcosulfase Alfa, Human Arginate, Sebelipase alfa and Taliglucerase alfa)  
9.8.1 >Agalsidase alfa, agalsidase beta, aglucosidase alfa  
9.8.1 >Alfafa 1 antiprtysin  
9.8.1 >Alpha-Mannosidase recombinant human  
9.8.1 >Asfotase alfa  
9.8.1 > Human Heterologous Liver Cells  
9.8.1 >Cholic acid  
9.8.1 >Glycerol phenylbutyrate | NHSE  
| Drugs used in Neutropenia | 9.1.6^ >Parenteral Nutrition (after 14 days or when the patient is receiving parenteral nutrition prior to admission) | NHSE  
| Parenteral Nutrition | 9.3 >Parenteral Nutrition (after 14 days or when the patient is receiving parenteral nutrition prior to admission) | NHSE |
| Gout and cytotoxic-induced hyperuricaemia | 10.1.4 >Hyperuricaemia associated with cytotoxic drugs  
Pegloticase (no BNF category available) | CCG |
| Neuromuscular Disorders | 10.2.1 >Amifarmpindine phosphate  
10.2.1 >Famprindine (includes Ataluren*) | NHSE |
| Enzymes | 10.3.1 >Collagenase (only when used in outpatients) | CCG |
| Eye | 11.1 >Cysteamine hydrochloride | TBC |
| Macular Oedema | 11.4.1>Dexamethasone intravitreal implant  
Flucinolone acetonide (only when used as an intravitreal implant) | CCG |
| Retinal disorders/intraocular lens replacement surgery | 11.8.2 >Ocriplasmin (includes Ketonolac with Phenylyphrine) | CCG  
| Subfoveal choroidal neovascularisation | 11.8.2 >Afiblercept  
11.8.2 >Pegaptanib  
11.8.2 > Ranibizumab  
11.8.2 > Vertimepin | CCG |
| Skin Conditions | 13.5.1 >Alitretinoin  
Afamelanotide (no BNF category available) | CCG |
| Intravenous/subcutaneous human normal immunoglobulins | 14.5 >Normal immunoglobulin>for intravenous use  
14.5 >Normal immunoglobulin>for subcutaneous use | NHSE |
| Bone morphogenetic protein | No BNF Category available (includes Dibotemin Alpha and Eptotermin alpha) | NHSE (spinal use) |
| Poisoning | Emergency treatment of poisoning >Other poisons >Ethylene glycol and methanol >Fomepizole (includes Digoxin immune fab) | CCG |
| Hypertension and heart failure | Serelaxin (no BNF category available) | TBC |
| Lipid-regulating drugs | Lomitapide (no BNF category available) | TBC |
| Hormone antagonists | 8.3.4 >Abrisatone  
8.3.4.2 >Enzalutamide | NHSE  
| Likely BNF category unclear | Drisapersen (Duchenne Muscular Dystrophy); Efroloctocog alfa (platelet disorder drugs); Efrenonacog alfa (platelet disorder drugs); Eprodisate; Forgerimodacetae; Gevozumab; Idebenone; Ixazomib; Ixekizumba; Macimorelkin Ocrolizumab; Octocog Alfa  
Tabalumab; Aganirsen; Alirocumab; Andexanet alfa; Ciproflaxacin inhalation; Ciproflaxacin liposomal; Damococog alfa pegol; Glucarpidase (poisening); Gusekumab; Mavlirumab; Metreleptin; Pegpleranib (E10030); Sirukumab; Tildrakizumab | TBC |

- Drug related device exclusions include insulin pumps and pump consumables and intrathecal drug delivery pump
- Drugs which are excluded from the tariff when used for chemotherapy may also have other purposes. When used for non-chemotherapy purposes they may or may not continue to be excluded.
### 1. Gastrointestinal system

**Patent expiries**

According to Prescribing Outlook New Medicines 2015, there are no patent expiries due within the next couple of years that may have a significant impact on prescribing costs. The patent for adalimumab expires in April 2018 and it is likely at that stage biosimilar products will be available.

**Inflammatory Bowel disease (IBD)**

- **NICE Pathway for Crohn’s disease and ulcerative colitis** available
- **NICE Quality Standard on inflammatory bowel disease**, issued Feb 2015
- **NICE Guideline on Crohn’s disease (standing update)**, expected May 2015
- **NICE Evidence Summary on budesonide multimatrix for ulcerative colitis** available (Jun 2015)

- **NICE guidance on the use of infliximab, adalimumab and golimumab for the treatment of moderately to severely active ulcerative colitis after the failure of conventional therapy**, issued Feb 2015

This is an area of moderate financial risk

This Quality Standard covers the diagnosis and management of inflammatory bowel disease (Crohn’s disease and ulcerative colitis) in adults, children and young people. There are no increased costs expected with respect to drug therapy with this Quality Standard, however there may be an increase in costs associated with an increase in specialist referrals. A commissioning support tool is also available to assist commissioners in its implementation.

This update will review the clinical and cost-effectiveness of anti-TNFs (infliximab and adalimumab) in combination with immunosuppressants compared with anti-TNFs alone following publication of evidence suggesting that the azathioprine plus infliximab was associated with significantly greater rates of remission for people with severe active Crohn’s disease than infliximab alone. This update is not expected to have a significant resource impact as treatment with azathioprine is negligible (about £50 per patient per annum) compared to anti-TNFs.

Infliximab, adalimumab and golimumab are recommended as options for treating moderately to severely active ulcerative colitis in adults whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who cannot tolerate, or have medical contraindications for, such therapies. This NICE guidance supercedes previous NICE guidance TA140 which did not recommend infliximab for subacute manifestations of ulcerative colitis, and TA262 (adalimumab for moderate to severe ulcerative colitis) which was terminated as an evidence submission was not received from the manufacturer. This NICE guidance advises that consideration may be given to the use of biosimilars with this appraisal. Two biosimilar infliximab products are available, and costs should be adjusted according to local contracts and uptake of the biosimilar infliximab products.

The NICE costing statement estimates a prevalence of ulcerative colitis of approximately 240 per 100,000 and assumes:
- 20% of patients have moderate to severe disease
- 3% of patients with ulcerative colitis are already eligible for treatment with infliximab under TA163 (infliximab for acute exacerbations of ulcerative colitis) (~7 per 100,000)
- an additional 11.5% of adults patients overall with ulcerative colitis might be eligible for treatment with infliximab, adalimumab or golimumab (~22 people per 100,000 population) following failure of standard treatment under this new guidance.

Adalimumab if used as per dosing in its SPC (40mg alternate weeks) costs around £9,200 per patient per year, golimumab costs around £9,900 per patient per year and infliximab (Remicade brand) costs around £10,900 per patient per year for the Remicade branded product (drug costs only).
### Disease or Indication:
**National targets and guidance**

#### IBD cont’d
- NICE guidance on the use of infliximab, adalimumab and golimumab for the treatment of moderately to severely active ulcerative colitis after the failure of conventional therapy, cont’d
- NICE guidance on vedolizumab for treating of moderately to severely active ulcerative colitis issued Jun 2015
- NICE guidance on vedolizumab for treating moderately to severely active Crohn’s disease after prior therapy issued Aug 2015
- Savings through the use of biosimilar versions of infliximab and etanercept

#### Epidemiology, potential financial implications for a population of 100,000 and other comments

Assuming a 30% reduction in price with biosimilar infliximab, and 50% uptake of this product, if 50% of adults eligible for anti-TNF therapy under this guidance receive infliximab, 25% receive adalimumab and 25% receive golimumab this could result in approximate additional costs of around £205,000 per 100,000 population. This cost excludes any service delivery costs and does not cover the cost of adalimumab if dosing frequency is increased to weekly in those experiencing a decrease in response.

Vedolizumab is recommended as a possible treatment for adults with moderate to severe ulcerative colitis and therefore will compete with infliximab, adalimumab and golimumab as per usage recommended in TA329. NICE has produced a costing statement for this guidance. The list price of vedolizumab is £13,325 per patient per annum, however the manufacturer has agreed an NHS-wide discounted rate which will make vedolizumab a similar cost to the current anti-TNFs and therefore no significant incremental drug costs are expected from this guidance. Vedolizumab is administered by IV infusion therefore service delivery costs will need to be considered.

Vedolizumab is recommended as an option for treating moderately to severely active Crohn’s disease if an anti-TNF has failed, is not tolerated or is contraindicated. NICE has produced a costing statement which estimates that:
- 1% of patients with Crohn’s disease have moderate to severe disease and would be appropriate for vedolizumab by virtue of failing conventional therapy but not being suitable for anti-TNF therapy
- 8% of patients with Crohn’s disease have moderate to severe disease and would be appropriate for vedolizumab by virtue of anti-TNF therapy failing

This equates to ~18 per 100,000 population. Most of these patients would however be patients with difficult to treat disease, so if 30% of those patients responded to, and were maintained on vedolizumab this would equate to 6 per 100,000. The undiscounted cost of vedolizumab is £13,325 per patient per annum, and therefore this guidance might represent a potential £80,000 per 100,000 population. As vedolizumab has an agreed NHS-wide discounted rate these costs should be reduced according to the agreed patient access scheme. Vedolizumab is administered by IV infusion therefore service delivery costs will need to be considered.

Two biosimilar infliximab products are now available. Data from the HSCIC indicates that approximately £159.6m (or ~£300,000 per 100,000 population) was spent on infliximab in 14/15 in the NHS (spend not separated by indication). Assuming a 30% reduction in price and a 50% switch to use of biosimilar, this could result in overall savings of around £45,000 per 100,000 population. Some of these savings may have already been realised as biosimilar infliximab has been available since February 2015.

#### Actions/ issues which may be considered by commissioners and providers
- Demand management through service redesign may mean more patients are treated in primary care for certain gastrointestinal conditions such as IBS using condition specific protocols instead of being referred to secondary care.
- Several cytokine modulators are recommended by NICE as options for the treatment of IBD. Agree local pathways for the use of these agents, including whether dose optimisation through antibody measurement and switching between agents will be supported.
- Cytokine modulators, such as TNF-inhibitors, are listed as exclusions in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. Drug exclusions under Payment by Results 15/16. NHS England is the responsible commissioner when cytokine modulators are used in children (aged 18 years or younger) and for some specialist indications in both adults and children. CCGs are the responsible commissioners for use of these agents in adults in non-specialist settings.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diarrhoea and constipation</strong></td>
<td></td>
</tr>
<tr>
<td>NICE pathways available for constipation and diarrhoea and vomiting in children</td>
<td>Laxatives have been retired from the key therapeutic topics (KTT) and associated comparators list for 2015/16</td>
</tr>
<tr>
<td>• Laxatives - retired from Key Therapeutic Topics 2015/16</td>
<td>Naloxegol is recommended, within its marketing authorisation, as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to at least 1 laxative used for at least 4 days over the previous 2 weeks. Approximately 32,000 people (or 60 people per 100,000 population) receive strong opioids (for cancer and non-cancer pain) in England. The prevalence of opioid induced constipation is 50% in non-cancer pain and 90% in cancer pain and 50% patients report limited to no improvement in symptoms after taking laxatives. If it is assumed that 50% of the use of strong opioids is for non-cancer pain this would equate to 42 per 100,000 population potentially being suitable for naloxegol which could result in an additional cost of £33,000 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on the use of naloxegol for opioid induced constipation issued Jul 2015</td>
<td>This NICE appraisal is suspended because the regulatory timeline has changed as the MHRA has not granted a license for the use of lubiprostone in this indication. The MHRA issued a negative opinion because of insufficient evidence of efficacy.</td>
</tr>
<tr>
<td>• NICE guidance on the use of lubiprostone for treating opioid induced constipation, expected Oct 14</td>
<td>The guidance will appraise the cost-effectiveness of methylnaltrexone, within its marketing authorisation for use in opioid induced constipation in both cancer pain and chronic non-cancer pain. Methylnaltrexone will be compared to oral laxative therapy, rectal interventions, opioid analgesic and opioid antagonist combinations (oxycodone with naloxone) and naloxegol. Methylnaltrexone is given as a subcutaneous injection, so practicalities (e.g. issues with self-administration) and patient acceptability is likely to reduce usage. The cost of methylnaltrexone is £294 per patient per month if used at the standard dose of alternate day administration, though it may be given less frequently depending on response. Approximately 32,000 people (or 60 people per 100,000 population) receive strong opioids (for cancer and non-cancer pain) in England. The prevalence of opioid induced constipation is 50% in non-cancer pain and 90% in cancer pain and 50% patients report limited to no improvement in symptoms after taking laxatives. If it is assumed that 50% of the use of strong opioids is for non-cancer pain and if 10% of patients with laxative refractory opioid induced constipation are suitable for methylnaltrexone in preference to other treatments such as naloxegol this would equate to 4 per 100,000 population and a £15,000 cost per 100,000 population per annum.</td>
</tr>
<tr>
<td>• NICE guidance on the use of methylnaltrexone for treating opioid induced constipation, expected Feb 2017</td>
<td></td>
</tr>
<tr>
<td><strong>Actions/ issues which may be considered by commissioners and providers</strong></td>
<td></td>
</tr>
<tr>
<td>• Commissioners and providers may wish to jointly review their local pathways for the management of constipation following publication of the NICE TAG on the use of naloxegol in opioid induced constipation.</td>
<td></td>
</tr>
</tbody>
</table>
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Disease or Indication</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dyspepsia and gastro-oesophageal reflux disease (GORD)</strong></td>
<td>This Quality Standard covers the investigation and management of dyspepsia and gastro-oesophageal reflux disease (GORD) symptoms in adults 18 and older. It includes the investigation of dyspepsia and GORD symptoms as a risk factor for oesophagogastric cancer but it does not include the diagnosis and management of oesophagogastric cancer because this will be covered by a separate quality standard. There are no direct drug costs associated with implementation of this Quality Standard.</td>
</tr>
<tr>
<td>- NICE Quality Standard on <a href="https://www.nice.org.uk/guidance/ng86">Dyspepsia and GORD in adults: investigation and management</a> issued Jul 2015</td>
<td></td>
</tr>
<tr>
<td>- NICE Quality Standard on <a href="https://www.nice.org.uk/guidance/ng72">GORD in children and young people</a>, expected Jan 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Other gastro-intestinal related conditions</strong></td>
<td>This guideline update provided new recommendations on dietary advice, TCAs and SSRI’s as second line treatment where laxatives, loperamide or antispasmodics have not helped (only offer SSRIs if TCAs are ineffective) and constipation. Only the recommendation for constipation in irritable bowel syndrome is anticipated to have a local resource impact as this includes linaclotide as a treatment option for use where laxatives from different classes have not helped and constipation has persisted for 12 months. IBS has a prevalence of 10% of the general population, if it is assumed that 25% of patients have predominantly constipatory symptoms (as opposed to diarrhoea or mixed symptoms), 50% of patients with symptoms consult healthcare professionals for management and 10% do not respond adequately to laxatives this represents 125 people per 100,000 population that might be considered for treatment. If maintenance treatment is suitable for 50% of this population this would represent a potential increase in costs of £33,000 per 100,000 population.</td>
</tr>
<tr>
<td><strong>Irritable bowel syndrome (IBS)</strong></td>
<td></td>
</tr>
<tr>
<td>NICE Pathway on <a href="https://www.nice.org.uk/guidance/ps87">irritable bowel syndrome</a> available</td>
<td></td>
</tr>
<tr>
<td>- NICE guideline on <a href="https://www.nice.org.uk/guidance/ps87">irritable bowel syndrome in adults</a> update, issued Feb 2015</td>
<td></td>
</tr>
<tr>
<td>Other gastro-intestinal related conditions cont’d</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>IBS cont’d</strong></td>
<td></td>
</tr>
<tr>
<td>▪ NICE Quality Standard on <a href="#">irritable bowel syndrome in adults</a>, expected Feb 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Coeliac disease</strong></td>
<td></td>
</tr>
<tr>
<td>NICE Pathway on <a href="#">coeliac disease</a> available</td>
<td></td>
</tr>
<tr>
<td>▪ NICE guideline on <a href="#">coeliac disease: recognition assessment and management</a>, issued Sep 2015</td>
<td></td>
</tr>
<tr>
<td>▪ NICE Quality Standard on <a href="#">coeliac disease: recognition assessment and management</a>, expected Aug 2015</td>
<td></td>
</tr>
<tr>
<td><strong>Gallstone disease</strong></td>
<td></td>
</tr>
<tr>
<td>NICE Pathway on <a href="#">gallstone disease</a> available</td>
<td></td>
</tr>
<tr>
<td>▪ NICE guideline on <a href="#">gallstone disease</a>, issued Oct 2014</td>
<td></td>
</tr>
<tr>
<td>▪ NICE Quality Standard on <a href="#">gallstone disease</a>, expected Dec 15</td>
<td></td>
</tr>
<tr>
<td><strong>Neonatal Jaundice</strong></td>
<td></td>
</tr>
<tr>
<td>NICE Pathway on <a href="#">neonatal jaundice</a> available</td>
<td></td>
</tr>
<tr>
<td>▪ NICE guideline on <a href="#">neonatal jaundice: diagnosis (sc update)</a>, and NICE guideline on <a href="#">neonatal jaundice: treatment (sc update)</a>, expected Apr 16</td>
<td></td>
</tr>
</tbody>
</table>

This quality standard will cover the diagnosis and management of irritable bowel syndrome in adults. No significant costs are expected, however there may be an increase in inflammatory marker testing depending on current local practice.

This guideline covers the recognition, assessment and management of coeliac disease in children, young people and adults. It covers advice on dietary management, non-responsive and refractory coeliac disease, the monitoring and review of patients with coeliac disease and referral criteria. Patients are recommended to take vitamin and mineral supplements (e.g. vitamin D and calcium) if their dietary intake is low, and prednisolone therapy is recommended as short-term treatment prior to being seen by a specialist in refractory cases. Other than these there are no other drug recommendations in the guideline and there are likely to have any significant cost implications.

This guideline provides recommendations about how gallstone disease should be identified, diagnosed and managed in adults. There is specific advice on the management of gallbladder stones and common bile duct stones and advice relates to surgical and interventional management. There are no drug recommendations in this guideline. The costing statement suggests that implementation of this guideline might be associated with an increase in costs due to an increase in the proportion of treatments offered as day case procedures.

NICE are reviewing the use of phototherapy as part of the update for CG98: Jaundice in newborn babies under 28 days. They are specifically reviewing the most appropriate phototherapy treatment modality and administration schedule. There are however no expected direct drug costs with this guideline update.
### Other gastro-intestinal related conditions cont’d

**Cirrhosis cont’d**
- NICE guideline on [assessment and management of cirrhosis](#), expected Jun 16

**Non-alcoholic fatty-acid liver disease (NAFLD)**
- NICE guideline on [liver disease (non-alcoholic fatty)[NAFLD]](#), expected Jul 16

**Abdominal Aortic aneurysm**
- NICE guideline on [abdominal aortic aneurysm: diagnosis and management](#), expected Oct 17
  
  NICE Evidence Summary on [ondansetron for management of vomiting in children and young people with gastroenteritis](#), Oct 2014

### Actions/ issues which may be considered by commissioners and providers
- Following publication of the NICE guideline on coeliac disease, organisations may wish to develop local guidelines for prescribing gluten free products on the NHS for people with coeliac disease. Recent [reports](#) in the media suggest that the NHs in England spent ~£27m (or ~£50,000 per 100,000 population) on gluten free products last year and not all prescribing may be appropriate.
**Disease or Indication:**
National targets and guidance

**Epidemiology, potential financial implications for a population of 100,000 and other comments**

## 2. Cardiovascular disease

### Patent expiries

According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: tenecteplase (Jun 2015), bivalirudin (Aug 2015), bosentan (Aug 2017), ivabradine (Sept 2017), prasugrel (Sep 2017), ezetimibe (Oct 2017), tadalfil (Nov 2017), rosvuastatin (Dec 2017)

### Hypertension

- **Key Therapeutic Topic (KTT) for renin-angiotensin system drugs**
  
  According to *QoF data for 13/14*, the raw prevalence rate for hypertension in England is 13.7%.

  **This area is unlikely to have any major cost implications for prescribing**

  A set of key therapeutic topics (KTT) and associated comparators have been developed to support NHS England's Medicines Optimisation Measurement work stream. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The renin angiotensin system (RAS) drugs comparator (number of prescriptions for ACE inhibitors as a % of the total number of prescriptions for all drugs affecting the RAS system excluding aliskiren) has been retired.

### Lipid modification

- **Key Therapeutic Topic (KTT) for lipid modifying drugs**
  
  **This is an area of high financial risk**

  According to *QoF data for 13/14*, the raw prevalence rate for CHD in England is 3.3%.

  A set of key therapeutic topics (KTT) and associated comparators have been developed to support NHS England's Medicines Optimisation Measurement work stream. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The low cost lipid modifying drugs and ezetimibe comparators have been retired. A new comparator measures the number of items for bile acid sequestrants, fibrates, nicotinic acid and omega-3 fatty acid compounds (BNF 2.12 sub-set) as a percentage of total items.

  NICE has produced a *summary* of the evidence-base on omega-3 fatty acid supplements which is a key therapeutic topic identified to support Medicines Optimisation.

  This quality standard is expected to contribute to improvements in the incidence of CVD events, mortality from CVD, and patient experience of GP services.
### Lipid modification cont’d

- NICE guideline on lipid modification (update of previous guideline), issued Jul 2014

This guideline includes recommendations on risk assessment, lifestyle modifications and the use of lipid-lowering drugs. The new recommendation reduces the threshold from 20% to a 10% risk of developing CVD before statin treatment is offered for the primary prevention of CVD and specifically states that the QRISK2 assessment tool should be used to determine the risk of developing CVD within 10 years. The previous guideline recommended simvastatin 40 mg for the primary and secondary prevention of CVD. The updated guideline changed the recommendation to using atorvastatin 20 mg for the primary prevention of CVD, and starting statin treatment in people with established CVD with atorvastatin 80 mg.

It should be noted that the analysis looked at effectiveness of treatment shown by 'high-intensity' statins as a group, as it was not possible to establish relative effectiveness of atorvastatin 20 mg, 40 mg and 80 mg using trial data. Trial data with clinical outcomes exist only for atorvastatin 80mg vs. atorvastatin 10mg.

Total cholesterol, HDL cholesterol and non-HDL cholesterol should be measured in all people who have been started on high-intensity statin treatment at 3 months of treatment. Treatment is aiming for > 40% reduction in non-HDL cholesterol and if this is not achieved, need to address adherence and timing of dose, optimise adherence to diet and lifestyle measures, consider increasing dose if started on < atorvastatin 80mg and person judged to be at higher risk because of comorbidities, risk score or using clinical judgement.

Annual medication reviews should be carried out for people taking statins. Discuss with those who are stable on a low- or middle-intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

This guidance is likely to have a significant impact on CCGs prescribing budgets for commissioners. According to the costing report, the increase in prescribing costs from decreasing the threshold for treatment with statins (NICE estimates increase in number of eligible patients for statins from just under 8000 to ~14,000 per 100,000 population) is ~ £120,000 per 100,000 population per year.

At the time of publication of guideline, rosuvastatin is the only statin still in patent. This is due to expire in Dec 2017. Many prescribing advisers are still targeting the use of rosuvastatin in their localities and its replacement by generic alternatives such as atorvastatin. Expert opinion suggests that this could reduce the future prescribing of rosuvastatin by up to 50%. Expenditure in 2013/14 in England was estimated to be £46.2m (a decrease of 5.1% on previous year). A 50% reduction in this would equate to a spend of £22.8m which approximates to a reduction of ~£42,000 per 100,000 population, although some of this cost decrease will be offset by the need to increase the use of atorvastatin.

Draft guidance recommends ezetimibe monotherapy as an option for treating primary heterozygous-familial and non-familial hypercholesterolaemia in adults, when a statin is considered inappropriate or is not tolerated, only if: they need lipid modification therapy for the primary prevention of cardiovascular disease and have both type 2 diabetes and ≥20% 10-year risk of developing cardiovascular disease according to QRISK2 risk assessment tool, OR they need lipid-modification therapy for the secondary prevention of cardiovascular disease.

According to 2007 costing statement for ezetimibe, the population prevalence of primary heterozygous-familial hypercholesterolaemia is ~ 0.2% (78,000 people). However, only 11,000 (15%) cases are likely to be diagnosed. The population prevalence of primary non-familial hypercholesterolaemia is ~4% (1.5 million people). Of these, ~ 600,000 (40%) cases are likely to be diagnosed. Although nearly all of the people with familial hypercholesterolaemia are likely to
### Lipid modification cont’d

- **NICE guidance on ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia (review of TA132), cont’d**
  - require treatment with lipid-lowering therapy, ~75% with non-familial hypercholesterolaemia are likely to require treatment (~460,000 people). Therefore, a total of just over 470,000 people could be eligible for treatment with statins. Approximately 2% of eligible patients are unable to take statins because of contraindication or intolerance thus 10,000 people could be eligible for treatment with ezetimibe monotherapy. Of those people who are able to tolerate statins, ~30% would be considered for an alternative statin or ezetimibe. Approximately 140,000 people could be eligible for treatment with ezetimibe in combination with a statin.

As ezetimibe is already in use as recommended in NICE TA132, and spend (including the simvastatin combination product) totalled ~£53.7m (or £100,000 per 100,000 population) in primary care in England in 13/14, it is unclear how the updated draft guidance which is much more restrictive (people must have both type 2 diabetes and ≥20% 10-year risk of developing cardiovascular disease) will impact on prescribing budgets.

The IMPROVE-IT trial in 18,144 patients stabilised after ACS was powered to assess a primary end point which was a composite of cardiovascular death, nonfatal myocardial infarction, unstable angina requiring rehospitalization, coronary revascularization (≥30 days after randomization), or nonfatal stroke. After a median follow-up was 6 years the Kaplan–Meier event rate for the primary end point at 7 years was 32.7% in the simvastatin–ezetimibe group, as compared with 34.7% in the simvastatin-monotherapy group (absolute risk difference, 2.0%; p=0.016). This is the first study to demonstrate that ezetimibe is associated with an improvement in clinical end-points and may lead to an increase in use.

The IMPROVE-IT trial in 18,144 patients stabilised after ACS was powered to assess a primary end point which was a composite of cardiovascular death, nonfatal myocardial infarction, unstable angina requiring rehospitalization, coronary revascularization (≥30 days after randomization), or nonfatal stroke. After a median follow-up was 6 years the Kaplan–Meier event rate for the primary end point at 7 years was 32.7% in the simvastatin–ezetimibe group, as compared with 34.7% in the simvastatin-monotherapy group (absolute risk difference, 2.0%; p=0.016). This is the first study to demonstrate that ezetimibe is associated with an improvement in clinical end-points and may lead to an increase in use.

**Evolocumab** is a monoclonal antibody, PCSK9 inhibitor, administered by S.C. injection which was licensed in the UK in July 2015 for the treatment of adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet, either in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin OR; alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated. It is also licensed to treat adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

**Draft NICE guidance (ACD)** does not recommend evolocumab, alone or in combination with lipid-lowering therapies within its marketing authorisation for treating primary hypercholesterolaemia (heterozygous-familial and non-familial) or mixed dyslipidaemia in adults.

The Appraisal Committee acknowledged that evolocumab was a first-in-class therapy with a novel mechanism of action, which consistently reduced LDL-C levels compared with placebo and ezetimibe, while also being well-tolerated by patients. However, it recalled its previous conclusion that the extent to which evolocumab could reduce CVD was a key area of uncertainty, and so it considered that equating the effect of evolocumab on CVD to that of statins, and assuming in the model that this effect would last indefinitely, was uncertain. The Committee also considered that the degree of uncertainty in the cost-effectiveness evidence was too high for it to be able to make recommendations about evolocumab.

The company estimated the following incremental cost-effectiveness ratios with the patient access scheme:

- **Non-familial hypercholesterolaemia without CVD**: £74,300 per quality-adjusted life year (QALY) gained for evolocumab plus statin compared with ezetimibe plus statin (statin-tolerant), and £78,800 per QALY gained for evolocumab compared with ezetimibe (statin-intolerant).
Lipid modification cont’d

- NICE guidance on evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia cont’d

- NICE guidance on alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia expected Jun 2016

- Non-familial hypercholesterolaemia with CVD: £46,000–50,900 per QALY gained for evolocumab plus statin with or without ezetimibe compared with ezetimibe plus statin (statin-tolerant), and from £49,300–52,800 per QALY gained for evolocumab with or without ezetimibe compared with ezetimibe (statin-intolerant).

- Heterozygous-familial hypercholesterolaemia: £22,900–24,800 per QALY gained for evolocumab plus statin with or without ezetimibe compared with ezetimibe plus statin (statin-tolerant), and £23,900–25,600 per QALY gained for evolocumab with or without ezetimibe compared with ezetimibe (statin-intolerant).

Alirocumab is a monoclonal antibody, PCSK9 inhibitor, administered by S.C. injection which is not yet marketed in the UK but it was approved in the EU in September 2015 for the treatment of adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet, either in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin OR; alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Ten phase III studies (n=5296) demonstrate efficacy vs. placebo or ezetimibe in addition to standard therapy. Studies using an up-titration regimen found a mean reduction in LDLc from baseline of 45.6 to 48.9%, whilst those studying 150mg fortnightly dosing found reductions of 60.4%. Patients on placebo had a 0.5- 4.2% increase in LDLc, whilst those using ezetimibe showed reductions of 19.3 to 22.3%.

Prescribing Outlook New Medicines 2015 notes alicrocumab is likely to be more expensive than oral lipid lowering options and costs will be additive to current treatments. It will compete with evolocumab. Use may be limited by S.C administration but it is suitable for self administration.

Using the estimates from the 2007 costing statement for ezetimibe, the population prevalence of primary heterozygous-familial hypercholesterolaemia is ~ 0.2% (78,000 people). However, only 11,000 (15%) cases are likely to be diagnosed. The population prevalence of primary non-familial hypercholesterolaemia is ~4% (1.5 million people). Of these, ~ 600,000 (40%) cases are likely to be diagnosed. Although nearly all of the people with familial hypercholesterolaemia are likely to require treatment with lipid-lowering therapy, approximately 75% of people with non-familial hypercholesterolaemia are likely to require treatment (~ 460,000 people).

Therefore, a total of just over 470,000 people could be eligible for treatment with statins. Approximately 2% of eligible patients are unable to take statins because of contraindication or intolerance (~10,000 people [19 per 100,000 population]). Of those people who are able to tolerate statins, ~30% (140,000 people [260 per 100,000]) could be eligible for combination treatment with a statin. However the NHS spent £53.7m on ezetimibe in 2014/15 which indicates that around 150,000 are taking this drug already although it is not clear if these are the appropriate patients. Uptake of PCSK9 inhibitors is hard to predict at present and thus their budgetary impact remains to be determined. Based on data from the 2007 ezetimibe costing statement, the following assumptions have been made:

- Cost of evolocumab 140mg/ml prefilled syringe = £170.10; cost per annum is £3642.60 and it is assumed that alirocumab will be similarly priced.

- If it is assumed that all people who are not eligible for statin treatment receive a PCSK9 inhibitor rather than another form of treatment, this could result in additional drug cost of ~£70,000 per 100,000 per annum.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lipid modification cont’d</strong></td>
<td>• If it is assumed that 10% of people who would be eligible for combination treatment with a statin receive a PCSK9 inhibitor rather than ezetimibe, this could result in additional drug cost of ~£94,700 per 100,000 per annum.</td>
</tr>
<tr>
<td>• NICE guidance on alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia cont’d</td>
<td>This gives a potential total of ~£165,000 per 100,000 population. Although it is possible that NICE will not approve these medicines until there is evidence that use is associated with a reduction in clinical end-points.</td>
</tr>
<tr>
<td>• Meta-analysis – PCSK9 inhibitors</td>
<td>A recent network meta-analysis of 17 RCTs (n=13,083) found PCSK9 inhibitors reduced LDL cholesterol by 57% vs. placebo and 36.1% vs. ezetimibe, and reduced all-cause mortality [OR 0.43; 95% CI, 0.22–0.82, p =0.01] vs. placebo, but they were linked to a higher rate of neurocognitive adverse events.</td>
</tr>
<tr>
<td>• NICE guidance on identification and management of familial hypercholesterolaemia, publication date to be confirmed.</td>
<td>This will be an update of CG71 (published August 2008) and is unlikely to have additional implications for prescribing budgets over and above those listed above.</td>
</tr>
<tr>
<td><strong>Actions/ issues which may be considered by commissioners and providers</strong></td>
<td>• As the PCSK9 inhibitors are likely to be listed as exclusions in the National Tariff for 16/16, a decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. It is likely that NHSE will be the responsible commissioners for use of these agents in heterozygous familial hyperlipidaemia and CCGs will be the responsible commissioners for non-familial and mixed hyperlipidaemia.</td>
</tr>
<tr>
<td><strong>Acute coronary syndrome [ACS - unstable angina and myocardial infarction (MI)] &amp; chest pain</strong></td>
<td>• As the PCSK9 inhibitors are likely to be listed as exclusions in the National Tariff for 16/16, a decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. It is likely that NHSE will be the responsible commissioners for use of these agents in heterozygous familial hyperlipidaemia and CCGs will be the responsible commissioners for non-familial and mixed hyperlipidaemia.</td>
</tr>
<tr>
<td>• NICE Quality Standard on secondary prevention after a myocardial infarction issued Sep 2015</td>
<td>This is an area of low to moderate financial risk</td>
</tr>
<tr>
<td>• NICE guidance on cangrelor for coronary heart disease has been terminated</td>
<td>There are approximately 188,000 hospital episodes attributed to myocardial infarction in the UK each year. Of the 80,724 hospital admissions recorded in the Myocardial Ischaemia National Audit Project (MiNAP), 39% were STE-segment elevation myocardial infarctions (STEMIs) and 61% were non-NSTEMIs.</td>
</tr>
<tr>
<td></td>
<td>This quality standard is expected to contribute to improvements in: life expectancy, mortality incidence of cardiovascular disease (CVD) events, health-related quality of life for people with long-term conditions, readmissions, functional ability after MI, return to employment, patient experience, and psychological wellbeing.</td>
</tr>
<tr>
<td></td>
<td>Cangrelor is a direct-acting P2Y12 platelet receptor antagonist that blocks ADP induced platelet activation and aggregation. Its short plasma half-life (platelet function is restored in &lt;60 minutes) yields a rapid loss of activity following discontinuation, which is a potentially significant safety advantage. It is administered as a 30µg/kg IV bolus followed by IV infusion at 4µg/kg/min for 2-4 hours. Cangrelor has been compared with clopidogrel in phase III trials. It is licensed for the reduction of thrombotic cardiovascular events, in combination with aspirin, for use in adult patients with coronary artery disease undergoing percutaneous coronary intervention (PCI) who have not received an oral P2Y12 inhibitor prior to the PCI procedure and in whom oral therapy with P2Y12 inhibitors is not feasible or desirable.</td>
</tr>
<tr>
<td></td>
<td>NICE is unable to make a recommendation about the use in the NHS of cangrelor for reducing atherothrombotic events in people undergoing percutaneous coronary intervention or awaiting surgery requiring interruption of anti-platelet therapy because no evidence submission was received from The Medicines Company so this is unlikely to have any cost implications.</td>
</tr>
</tbody>
</table>
### ACS [unstable angina and MI & chest pain] cont’d

- **NICE guidance on rivaroxaban for the prevention of adverse outcomes in patients after the acute management of ACS**, issued Mar 2015

  NICE recommends rivaroxaban as an option, in combination with aspirin plus clopidogrel or aspirin alone, for preventing atherothrombotic events in people who have had an acute coronary syndrome with elevated cardiac biomarkers. A new strength of rivaroxaban (2.5mg) was launched in UK in October 2014. The licensed dose for this indication is 2.5mg twice daily (continue after 12 months only if necessary).

  The costing template estimates that 149 per 100,000 population of the admissions (STEMI and NSTEMI) were eligible for secondary prevention of atherothrombotic events. It is expected that only the people currently treated with aspirin with or without clopidogrel will switch to rivaroxaban in combination with aspirin with or without clopidogrel upon the implementation of the guidance. Based on the standard assumptions in the template, the annual cost associated with implementing the guidance is estimated to be £16,100 per 100,000.

  The annual cost of rivaroxaban is £705. If as suggested by the costing template, 14% of the people on aspirin and clopidogrel also receive rivaroxaban, this could result in an additional drug cost of £14,700 per 100,000 per year. This excludes additional costs due to increased admissions from complications of treatment (e.g. bleeding) or savings from events avoided.

- **NICE guidance on vorapaxar for reducing atherothrombotic events after a myocardial infarction or in peripheral vascular disease** suspended

  Licensed in EU January 2015 for reduction of atherothrombotic events in adult patients with a history of myocardial infarction. Prescribing Outlook New Medicines 2015 notes that it is likely to be added to existing therapies but bleeding risk could affect uptake, and it is likely to be considerably more expensive than current options. NICE appraisal will be rescheduled to align with the commercial availability of the product within the UK. Therefore, NICE has decided to suspend this appraisal from its current work programme for the time being and thus it is unlikely to impact during the next financial year.

### Actions/ issues which may be considered by commissioners and providers

Agree the place in therapy locally of rivaroxaban for the secondary prevention of ACS in light of NICE guidance. A recently published systematic review found that the increase in major bleeding events associated with use of new-generation oral anticoagulants in patients receiving dual anti-platelet therapy following an ACS probably outweigh their ischaemic benefits in this setting for many patients.
### Heart failure (HF)

- **NICE clinical guideline on** [acute heart failure](#), **issued Oct 2014**
- **NICE guidance on** [sacubitril valsartan for treating heart failure with systolic dysfunction](#), **expected May 2016**
- **NICE Quality Standard on** [acute heart failure](#), **expected Dec 2015**
- **NICE Quality Standard on** [chronic heart failure in adults](#), **expected Feb 2016**

### This area is moderate to high financial risk

According to [QoF data for 13/14](#), the raw prevalence rate for HF in England is 0.7%.

This guideline covers the care of adults who have a diagnosis of acute heart failure, or have possible acute heart failure, or are being investigated for acute heart failure. [Costing template](#) notes that several recommendations were identified but assessed not to have a significant resource impact.

Sacubitril valsartan includes the nephrilysin inhibitor sacubitril and the angiotensin II receptor inhibitor valsartan. It does not currently have a marketing authorisation in the UK. It was filed in EU Feb 2015 with promising innovative medicine status for treatment of chronic heart failure, NYHA class II-IV and left ventricular ejection fraction $<40\%$. It has been studied in a clinical trial compared with enalapril in adults with heart failure (NYHA class II-IV) with a left ventricular ejection fraction (LVEF) $\leq 35\%$. It is being assessed in an ongoing trial in adults with heart failure with a preserved LVEF $\geq 45\%$, compared with valsartan.

[Prescribing Outlook New Medicines 2015](#) notes that if the observed beneficial effects on mortality and hospitalisation can be achieved in clinical practice, this fixed dose combination has the potential to displace current options (ACE inhibitors, angiotensin receptor and beta-blockers) but it is likely to be considerably more costly than generically available first-line options.

In the [costing template](#) for ivabradine, NICE estimates that there are 32 patients with NYHA Stage II-IV heart failure and an ejection fraction $\leq 35\%$ per 100,000 population. If it is assumed that this is similar to the population that would be considered eligible for this treatment, that it cost £2500 per year and that 50% of patients have this added to their regimen then this would increase costs by £40,000 per 100,000 population.

This draft quality standard is expected to contribute to improvements in: mortality rates, incidence of major cardiovascular events (non-fatal myocardial infarction, stroke), length of hospital stay, readmission rates, incidence of adverse events (withdrawal of beta-blockers and other disease-modifying drugs); and quality of life.

This draft quality standard is expected to contribute to improvements in: mortality due to heart failure, hospital admissions, ability to manage a long-term condition, quality of life, and medication safety.

### Actions/ issues which may be considered by commissioners and providers

- Many commissioners are redesigning services for HF so that more care is provided in the community through community HF clinics. Education and training requirements should be identified for practices providing community management of heart failure and appropriate protocols should be developed for medicines optimisation.
- Existing treatment pathways will need to be revisited once NICE guidance on sacubitril become available.
**Disease or Indication:** National targets and guidance

**Epidemiology, potential financial implications for a population of 100,000 and other comments**

**Ischaemic stroke & atrial fibrillation (AF)**

- NICE clinical guideline on the management of AF, issued Jun 2014

- NICE guidance on edoxaban tosylate for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation; issued Sep 2015

---

**This is an area of high financial risk**

According to *Prescribing Outlook New Medicines 2014*, the prevalence of AF is approx 1,600 per 100,000 people. Over 57% are at moderate to high risk of stroke and should be offered anticoagulation therapy. NICE estimates less than half of those with AF who need anticoagulation therapy are currently receiving it.

This guideline updates and replaces NICE clinical guideline 36 (published June 2006). Recommendations include following:

- Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist and should be offered to people with a CHA2DS2-VASc score of 2 or above, taking bleeding risk into account.
- Aspirin monotherapy should not solely be used for stroke prevention in people with atrial fibrillation.

The *costing report* notes that the recommendations considered to have the greatest resource impact nationally, and therefore require the most additional resources to implement or can potentially generate the biggest savings are:

- Do not offer aspirin monotherapy solely for stroke prevention to people with AF.
- Use the CHA2DS2-VASc stroke risk score to assess stroke risk in people with: symptomatic or asymptomatic paroxysmal, persistent or permanent AF, atrial flutter or a continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm.
- Refer people promptly at any stage if treatment fails to control the symptoms of atrial fibrillation and referral for more specialised management is needed.

There will be significant costs from implementing the recommendation to not treat patients with atrial fibrillation with aspirin to reduce risk of stroke, as alternative treatments are significantly more expensive. The alternative treatments listed in the guideline are assumed to reduce future adverse events.

The overall annual cost of implementing the recommendations to not offer aspirin to prevent strokes in people with AF and use CHA2DS2-VASc for stroke risk assessment is estimated to be £88,000 per 100,000 population.

The annual additional spend on NOACs is estimated to increase from a current spend of ~£180,000 per 100,000 population to ~£442,000 per 100,000 population i.e. an additional spend of ~£262,000 per 100,000.

NICE recommends edoxaban as an option for preventing stroke and systemic embolism in adults with non-valvular atrial fibrillation with ≥1 risk factors, including: congestive heart failure, hypertension, diabetes, prior stroke or transient ischaemic attack; or age ≥75 years. The decision about whether to start treatment with edoxaban should be made after an informed discussion about the risks and benefits of edoxaban compared with warfarin, apixaban, dabigatran etexilate and rivaroxaban. For people considering switching from warfarin, edoxaban's potential benefits should be considered against its potential risks, taking into account INR.

Because it is an alternative to rivaroxaban, dabigatran etexilate and apixaban and the four drugs are similarly priced, NICE does not anticipate a significant impact on resources as a result of implementing the guidance. Once daily dosing of edoxaban may be important for adherence (rivaroxaban is currently the only other licensed once daily NOAC).
### Disease or Indication:
#### National targets and guidance

<table>
<thead>
<tr>
<th>Ischaemic stroke &amp; atrial fibrillation (AF)</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• UKMI has produced <a href="#">common questions and answers</a> on the practical use of oral anticoagulants in non-valvular atrial fibrillation</td>
<td>The quality standard is expected to contribute to improvements in the rates of mortality, stroke and transient ischaemic attacks, and admission with a primary diagnosis of atrial fibrillation; and also in quality of life.</td>
</tr>
<tr>
<td>• NICE Quality Standard on <a href="#">atrial fibrillation</a>, issued Jul 2015</td>
<td>Organisations may want to consider carrying out some work to identify patients with AF within their localities who are currently not anticoagulated. Whilst this is likely to increase spend on oral anticoagulants, it could lead to longer term savings from a reduction in stroke events and resulting complications.</td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

<table>
<thead>
<tr>
<th>Venous thromboembolism (VTE)</th>
<th>The NOACs could have major implications on the delivery of anticoagulant services in this group of patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NOACs for the treatment and long term secondary prevention of VTE</strong></td>
<td>Dabigatran, apixaban and edoxaban will compete with rivaroxaban. The <a href="#">costing template</a> for rivaroxaban estimates cost of implementing this guidance in patients without active cancer to be ~ £17,406 per 100,000 population. As the NOACs represent a substitution of one for the other and they are priced similarly, NICE does not anticipate a significant impact on resources as a result of implementing guidance. However, edoxaban is licensed for once daily use whilst rivaroxaban is licensed for once daily use after initial 21 day BD treatment regimen, which may be a consideration where adherence to therapy is an issue.</td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">dabigatran for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism</a>, issued Dec 2014</td>
<td>Dabigatran, is recommended, within its marketing authorisation, as an option for treating and for preventing recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE) in adults.</td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism</a>, issued Jun 2015</td>
<td>Apixaban is recommended, within its marketing authorisation, as an option for treating and for preventing recurrent DVT and PE in adults.</td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism</a>, issued Aug 2015</td>
<td>Edoxaban is recommended, within its marketing authorisation, as an option for treating and for preventing recurrent DVT and PE in adults.</td>
</tr>
<tr>
<td>• Updated NICE guidance on <a href="#">management of venous thromboembolic diseases</a>, expected Nov 2015</td>
<td>This is an update of CG144 (published June 2012) however the updated recommendations that are out for consultation would seem unlikely to have significant implications for prescribing budgets</td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

| • Locally agree which agents will be used for the prophylaxis of DVT in the different patients groups covered by the updated [NICE VTE guideline](#). | |
| • It is likely that there will be significant interest in the use of the NOACs for the treatment of acute VTE and long term secondary prevention. Organisations will need to consider their place in therapy vs. parenteral anticoagulants if service redesign in this area is being discussed. Consideration should also be given to what is currently covered under existing contracts with providers as some commissioners may have block contracts in place for warfarin, which include associated services, such as phlebotomy and district nursing. | |
| • Commissioners should confirm whether local tariffs charged by providers for VTE prevention in certain patient groups, for example post surgery or in maternity patients, include LMWH. There are increasing requests for prescribing of these anticoagulants to be continued in primary care and such requests may be inappropriate. | |
| • Uptake of NOACs by CCGs is reported in the [Innovation Scorecard](#) for NICE Technology Appraisals in the NHS | |

---

Note: Links for further reading and resources are included in the text.
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

### 3. Respiratory System

#### Patent expiries

According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: tiotropium (Mar 2016), omalizumab (Aug 2017 – though we are not currently aware of any biosimilar products in development), ciclesonide (Sep 2016).

#### Asthma

NICE pathway for asthma available

- Updated [BTS/SIGN guideline](#) on asthma (Oct 2014)
- Medicines Optimisation Key Therapeutic Topic: high dose inhaled corticosteroids
- NICE clinical guideline on [diagnosis and monitoring of asthma](#), expected TBC
- NICE clinical guideline on [asthma management](#), expected Jun 2017
- NICE guidance on [mepolizumab for severe eosinophilic asthma](#), expected Jul 2016

NICE Evidence Summaries on:
- [Asthma: beclometasone/formoterol dry powder inhaler (Fostair NEXThaler)](#)
- [Asthma: tiotropium (Spiriva Respimat)](#)

---

**This is an area of low financial risk**

According to *QoF data for 14/15*, the raw prevalence rate for asthma in England is 6.0%.

There have been no significant changes to the recommendations on drug therapy. It includes reference to the use of tiotropium in the treatment of asthma (license extension granted Sep 2014), stating that its addition to ICS and salmeterol in patients who remain symptomatic despite these medications appears to be of benefit (step 4). There are however very few clinical trials in this specific patient group to guide management and this treatment is not formally recommended in the guideline.

A set of [key therapeutic topics (KTT) and associated comparators](#) have been developed to support NHS England’s Medicines Optimisation Measurement work stream. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. Although there isn’t a specific indicator for this Key Therapeutic Topic, it is recommended that organisations:

- Review the use of ICS routinely in people with asthma
- Step down the dose and use of ICS when clinically appropriate in people with asthma

This guideline will cover adults, children and young people who are being investigated for suspected asthma, or who have been diagnosed with asthma and are having their condition monitored. According to the [final scope](#), the final guideline will not discuss treatment of asthma but will consider objective tests such as spirometry/flow volume loop and peak expiratory flow variability. It will also consider the use of telehealthcare as a route for assessment, monitoring adherence and inhaler technique.

This guideline will cover the pharmacological management of chronic asthma, as well as certain non-pharmacological aspects (e.g. adherence, risk stratification, supported self management and breathing exercises). The guideline will not cover biologics (e.g. omalizumab) or comparison of drug delivery devices (i.e. inhalers) or acute asthma management by healthcare professionals.

The guidance will appraise the cost-effectiveness of mepolizumab for severe eosinophilic asthma. It is expected that mepolizumab would compete with omalizumab which has been approved by NICE for use in severe persistent confirmed allergic IgE-mediated asthma and would most likely be cost neutral.
### Actions/Issues which may be considered by commissioners and providers

- **Use of high-dose ICS** should be audited as there are concerns over excessive use. Agree local policy on the use of high dose ICS, to ensure patients are appropriately reviewed and stepped down, which could achieve savings in this area. The London Respiratory Team have produced a safety card for patients prescribed a high-dose ICS and accompanying guidance, which lists the available ICS preparations and the doses at which a safety card is required/recommended. Users may wish to consider use of these resources locally.
  - A DTB article highlighted that many healthcare professionals do not know how to use inhalers properly and are therefore not in a position to educate and counsel patients on the use of these devices. Healthcare professionals should be appropriately trained in checking inhaler technique and local guidance should also address this and promote the use of spacer devices where appropriate. These simple measures could prevent progression to more advanced treatment (e.g. LABA/ICS) and therefore be cost saving in the long run.
- Locally agree place in therapy of tiotropium (Spiriva Respimat™), the first LAMA to be licensed as an add-on maintenance treatment for asthma (license extension approved September 2014).
- There are a number of combination (ICS/LABA) inhalers now available for use in the treatment of asthma. Develop local guidelines on which combination inhalers are most appropriate for use in the treatment of asthma. Treatment pathways may need to take more account of the type of device available than the specific drug choice.
- Omalizumab is listed as an exclusion in the National Tariff for 15/16 and it is expected that mepolizumab would be excluded from tariff. The responsible commissioner for specialist asthma services in England is NHS England. **Drug exclusions under Payment by Results 15/16**

### Chronic Obstructive Pulmonary Disease (COPD)

**NICE pathway for COPD available**


**NICE Evidence Summaries on:**
- COPD: umecclidinium/vilanterol combination inhaler (Anoro Ellipta)
- COPD: umecclidinium (Incruse)
- COPD: olodaterol
- COPD: aclidinium/formoterol
- Non-cystic fibrosis bronchiectasis: long term azithromycin

This is an area of increased activity and moderate financial risk

According to [QoF data for 14/15](https://www.qof.org.uk), the raw prevalence rate for COPD in England is 1.8%.

This will update the current **COPD Quality Standard**. This quality statement covers the assessment, diagnosis and clinical management of chronic obstructive pulmonary disease (COPD) in adults. The scope of the quality standard does not include prevention, screening or case finding. The **draft update** includes quality statements on assessing inhaler technique, pulmonary rehabilitation and hospital discharge bundles.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>
| **Actions/ issues which may be considered by commissioners and providers** | ▪ The way in which COPD services are delivered is being redesigned in many areas so that more care is commissioned in the community enabling “frequent flyers” to be identified and treatment targeted appropriately. An article in the HSJ (2010) estimated that a proactive approach to care pathway management could save England over £800m (or £1.5m per 100,000 population) on COPD inpatient care alone.  
▪ It has been estimated that 40% to 50% of patients on COPD registers still smoke. Since stopping smoking is one of the single most effective interventions for COPD, the use of smoking cessation products should be prioritised locally in this population.  
▪ There is debate about the place in therapy and cost effectiveness of triple therapy (LABA + LAMA + ICS) as recommended in the revised NICE guideline for COPD vs. pulmonary rehabilitation. The London Respiratory Team value pyramid illustrates the high QALY of triple therapy when compared to other treatment strategies. A DTB review found that smoking cessation is the most effective intervention for patients with COPD, and suggests that there is insufficient evidence to show that any further benefit is gained from the use of triple therapy.  
▪ Use the commissioning guide developed by NICE on commissioning services for people with COPD when planning services for this patient group. The Department of Health also published a commissioning toolkit for COPD as a resource to help to implement the Outcomes Strategy for COPD and Asthma.  
▪ The NHS Improvement team has produced a basic guide covering ten key principles to adopt to provide good COPD care. Key principles covered within the guide include checking inhaler technique at every opportunity and ensuring clinically appropriate and cost effective prescribing of oxygen. The team has also produced a report on improving home oxygen.  
▪ Commissioners and respiratory teams should consider the good practice guide from Primary Care Commissioning for assessment and review of home oxygen as there are potential savings to be made in this area. The guide covers the development and commissioning of good assessment and review services for all home oxygen patients.  
▪ There are a number of combination inhalers now available for use in the treatment of COPD, including both ICS/LABA and LABA/LAMA. Develop local guidelines on their place in therapy and which combinations are most appropriate; treatment pathways may need to take more account of the type of device available than the specific drug choice.  
▪ It should be noted that the only licensed preparations containing corticosteroids for the treatment of COPD are the combination inhalers; not all combination inhalers are however licensed for use in COPD. |
### Disease or Indication: National targets and guidance

**Epidemiology, potential financial implications for a population of 100,000 and other comments**

<table>
<thead>
<tr>
<th>Drug allergy</th>
<th>NICE pathway for Drug allergy available</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NICE Quality Standard on <strong>Drug Allergy: diagnosis and management</strong>, Jul 2015</td>
</tr>
<tr>
<td></td>
<td>This Quality Standard covers the diagnosis and management of drug allergy in adults, young people and children. It does not cover treatment of the acute phase, including anaphylaxis, because this will be covered by a separate quality standard.</td>
</tr>
<tr>
<td></td>
<td>According to the costing statement for the drug allergy guideline, implementation may have resource implications at a local level as a result of national variation in clinical practice; costs are not however expected to be high. Organisations should evaluate their own practices against the guideline recommendations and assess costs locally. Although there may be increased costs associated with referrals, these could be offset by improved quality of care to patients and substantial short-term and longer-term resource benefits to the NHS.</td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

- Locally discuss and agree a policy on the supply of adrenaline auto injector pens to people at risk of anaphylactic reactions. The MHRA has advised that people who have been prescribed an adrenaline auto-injector because of the risk of anaphylaxis should carry two with them at all times for emergency, on-the-spot use. After every use of an adrenaline auto-injector, an ambulance should be called (even if symptoms are improving), the individual should lie down with their legs raised and, if at all possible, should not be left alone. There are currently 3 adrenaline auto-injector products available and, training on use is specific to the device. It is important that patients carry the auto-injector that they are familiar so they can use confidently if needed.

### Other respiratory conditions

**Bronchiolitis**

- NICE clinical guideline on **bronchiolitis in children**, June 2015
- NICE Quality Standard on **bronchiolitis**, expected June 2016

**Idiopathic Pulmonary Fibrosis (IPF)**

- NICE pathway available for **IPF**
- NICE Quality Standard on **IPF**

The guideline covers the diagnosis and management of children with bronchiolitis in all NHS care settings but not those with other respiratory conditions, such as recurrent viral induced wheeze or asthma. The guideline recommends that antibiotics, hypertonic saline, nebulised adrenaline, salbutamol, ipratropium and inhaled or systemic steroids should not be used to treat children with bronchiolitis. It recommends chest physiotherapy assessment in children with relevant comorbidities and oxygen supplementation if saturation is persistently less than 92% and that continuous positive airway pressure (CPAP) is considered in children with impending respiratory failure. There are no direct drug costs associated with this guideline. The costing statement indicates that there may be some costs associated with staff training and making devices available to aid diagnosis (e.g. oximeters)

This Quality Standard is at an early stage of development.

This quality standard covers the diagnosis and management of idiopathic pulmonary fibrosis in adults, from the initial suspicion of the disease to referral, supportive care and treatment. The standards indicate that patients should only be diagnosed with IPF from a consensus MDT with expertise on interstitial lung disease and that patients with the disease should have a specialist nurse available to them. There are no direct drug costs associated with this quality standard.
### Disease or Indication:
#### National targets and guidance

<table>
<thead>
<tr>
<th>Other respiratory conditions cont’d</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IPF cont’d</strong></td>
<td>The <em>draft guidance</em> currently recommends nintedanib for IPF only if the person has an FVC between 50 and 80% predicted and that treatment should be stopped if a patient has a confirmed decline of predicted FVC of 10% or more in any 12 month period. This patient cohort and usage exactly matches the NICE recommendation for pirfenidone with which nintedanib will compete. The undiscounted list price of both nintedanib and pirfenidone is £2,151 per month (30 days) and pirfenidone has a commercial in confidence patient access scheme discount. Nintedanib will also have a patient access scheme applied, so there may or may not be increased costs for commissioners depending on the magnitude of the patient access scheme discount. The <em>costing template</em> for pirfenidone suggests that this treatment is associated with £173,000 per annum cost per 100,000 population at the undiscounted rate. This update was progressed since publication of the ASCEND study which showed that patients with an FVC &gt;80% of predicted may benefit from pirfenidone treatment. The <em>costing template</em> for the original recommendation suggests that 10% of patients with IPF have an FVC &gt;80% predicted and that 60% of patients have FVC between 50% and 80% predicted. If approved for use where FVC &gt;80% predicted this would increase the patient cohort eligible for treatment by 17%. As the original cost impact was £173 per 100,000 this would equate to an increase of £30,000 per 100,000 population, at undiscounted prices (there is a patient access scheme for this treatment in place).</td>
</tr>
<tr>
<td>• NICE Guidance on nintedanib for IPF, expected Jan 2016</td>
<td></td>
</tr>
<tr>
<td>• NICE Guidance on pirfenidone for IPF (review), expected May 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Cystic Fibrosis</strong></td>
<td>This guideline will cover the diagnosis and management of cystic fibrosis in infants, children, young people and adults including management of clinical manifestations and complications of disease. In terms of pharmacological therapy this guideline will cover antimicrobial management for prevention of colonisation and treatment of acute pulmonary infection, as well as immunomodulatory treatment and the use of mucoactive or mucolytic agents. The guidance will appraise the cost-effectiveness of lumacaftor with ivacaftor for cystic fibrosis (CF) homozygous for the f508 del mutation. CF has a prevalence of around 13.5 per 100,000 population, and globally 46% of CF patients are homozygous for the f508 del mutation. If the cost of this treatment is similar to ivacaftor at £170,000 per annum and 30% of patients with this mutation were treated with this potential costs would be approximately £320,000 per 100,000 population</td>
</tr>
<tr>
<td>• NICE Guideline on cystic fibrosis, expected Aug 2017</td>
<td></td>
</tr>
<tr>
<td>• NICE Guidance on lumacaftor (with ivacaftor) for cystic fibrosis homozygous for the f508 del mutation due Jul 2016</td>
<td></td>
</tr>
<tr>
<td>NICE Evidence Summary on: <strong>Cystic fibrosis: long-term azithromycin</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

- Ivacaftor is listed as an exclusion in the National Tariff for 15/16, and it is expected that lumacaftor with ivacaftor would also be excluded from tariff. The responsible commissioner for cystic fibrosis in England is NHS England. *Drug exclusions under Payment by Results 15/16*
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

### 4. Central nervous system

#### Patent expiries

According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: palonosetron (Nov 2015), eletriptan hydrobromide (Dec 2015), frovatriptan (Dec 2015), agomelatine (Feb 2016), melatonin (Apr 2017), aprepitant (Nov 2018).

#### Anxiety

- NICE Quality Standard on [anxiety disorders](#)
- NICE pathways for [social anxiety disorder](#), [generalised anxiety disorder](#) available
- NICE Key Therapeutic Topic on [first-choice antidepressant use in adults with depression or generalised anxiety disorder](#) issued Jan 2015
- MHRA [learning module](#) on benzodiazepines

This Quality Standard covers the identification and management of anxiety disorders in primary, secondary and community care for children, young people and adults. A [commissioning support tool](#) is available to assist commissioners in its implementation.

This summarised existing guidance form NICE on the use of first-line antidepressants in these conditions and highlights the degree of prescribing variation seen.

This learning module identifies the most important hazards of benzodiazepines and informs health professionals how to anticipate, minimise and manage the risks.

#### Actions/ issues which may be considered by commissioners and providers

- Commissioners and providers should locally agree a treatment pathway for social anxiety disorder, specifying where agents fit in.

#### Psychosis and schizophrenia

- NICE [pathway](#) for psychosis and schizophrenia
- NICE [pathway](#) for psychosis with coexisting substance misuse overview
- NICE Quality Standard on [psychosis and schizophrenia in adults](#) issued Feb 2015
- NICE support for [commissioning using the quality standard for psychosis and schizophrenia in adults](#) issued Feb 2015
- MHRA [learning module](#) on antipsychotics

This guideline update is unlikely to have any significant impact on medicines spend.

This resource provides information on the key clinical, cost and service-related issues to consider during the commissioning process for psychosis and schizophrenia services. It is underpinned by NICE’s quality standard for psychosis and schizophrenia in adults.

This learning module on antipsychotics identifies their most important hazards and informs on actions health professionals can take in order to anticipate, minimise and manage the risks.
### Psychosis and schizophrenia cont’d

- NICE guideline on **severe mental illness and substance misuse (dual diagnosis) - community health and social care services** expected Nov 2016
- NICE Quality Standard on **bipolar disorder, psychosis and schizophrenia in children and young people** issued Oct 2015
- NICE guideline on **psychosis and schizophrenia in children and young people - recognition and management (update)** expected May 2016

This Guideline will focus on service provision and is unlikely to have significant impact on medicine use in this population

This is unlikely to impact significantly in terms of prescribing budgets

This is an update of the existing clinical guideline (CG 155) which was published in 2013. It is likely that this revision will include an assessment of whether olanzapine can be considered a suitable first-line treatment in this population in light of its metabolic effects. However overall it seems unlikely that this will have a significant impact on prescribing costs

### Actions/ issues which may be considered by commissioners and providers

- Develop local protocols for the use of newer antipsychotic drugs such as depot aripiprazole, paliperidone and lurasidone. Agree a place in therapy for the injectable second-generation antipsychotic formulations and monitor and audit their use. NICE new medicines evidence summaries are available for **depot aripiprazole** and **lurasidone**.
- Improving physical healthcare to reduce premature mortality in people with severe mental illness is a national CQUIN target for mental health providers. A resource to support implementation of this CQUIN is available.

### Hypnotics and sedation

- Key Therapeutic Topic area for hypnotics

A set of **key therapeutic areas** and associated **comparators** have been developed to support the QIPP medicines use and procurement workstream. The aim of the comparators is to support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation.

The following hypnotics-related comparator has been developed:

- The number of average daily quantities (ADQs) for benzodiazepines (indicated for use as hypnotics) and ‘Z’ drugs per Hypnotics (BNF 4.1.1 sub-set) ADQ based STAR-PU.

This **KTT** will be retained in 2016

- MHRA **learning module** on benzodiazepines

This learning module identifies the most important hazards of benzodiazepines and informs health professionals how to anticipate, minimise and manage the risks.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bipolar disorder</strong></td>
<td></td>
</tr>
<tr>
<td>- NICE guideline on [bipolar disorder (update)] issued Sep 2014</td>
<td>This guideline is not expected to have any significant impact on medicines spend, but local investment in psychological therapies will increase costs. This guideline covers the recognition, assessment and management of bipolar disorder in children, young people and adults. It updates and replaces NICE clinical guideline 38 (July 2006). All areas of the guideline have been updated.</td>
</tr>
<tr>
<td>- NICE pathway available</td>
<td></td>
</tr>
<tr>
<td>- NICE Quality Standard on [bipolar disorder in adults issued Jul 2015]</td>
<td>This Quality Standard is unlikely to impact significantly on prescribing budgets but emphasises the need for patients taking lithium to be monitored appropriately.</td>
</tr>
<tr>
<td>- NICE Quality Standard on [bipolar disorder, psychosis and schizophrenia in children and young people issued Oct 2015]</td>
<td>This Quality Standard includes a specific recommendation that Children and young people with bipolar disorder, psychosis or schizophrenia prescribed antipsychotic medication have their treatment monitored for side effects.</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
</tr>
<tr>
<td>- QIPP area for antidepressants</td>
<td>A set of key therapeutic areas and associated comparators have been developed to support the QIPP medicines use and procurement workstream. The aim of the comparators is to support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation.</td>
</tr>
<tr>
<td>- NICE pathway available</td>
<td>The following comparators related to antidepressants have been developed:</td>
</tr>
<tr>
<td>- NICE guidance on the use of [vortioxetine for treating major depressive disorder] issue date TBC</td>
<td>- Antidepressant (selected): ADQ/STAR-PU (ADQ based): Number of average daily quantities (ADQs) for selected antidepressant prescribing per Antidepressants (BNF 4.3 sub-set) ADQ based STAR-PU</td>
</tr>
<tr>
<td></td>
<td>- First choice % items: Number of prescription items for ‘1st choice’ generic SSRIs as a percentage of the total number of prescription items for selected ‘other antidepressants’.</td>
</tr>
<tr>
<td></td>
<td>Vortioxetine is licensed for the treatment of major depressive episodes in adults. Within the FAD NICE provisionally recommend restricting use to treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode. The NICE clinical guideline on the management of depression in adults recommends that people with moderate or severe depression should be provided with a combination of antidepressant medication and a high-intensity psychological intervention (CBT or IPT).</td>
</tr>
<tr>
<td></td>
<td>The draft scope for this guidance states that in the UK, the prevalence of major depressive disorder ranges from 5% to 10% of people seen in primary care settings and 10% to 14% of medical inpatients. Assuming that the prevalence is 10% (or 10,000 per 100,000 population), that 50% of these are considered for drug treatment (or 5,000 per 100,000 population) and that 1% (50 people per 100,000) of these are prescribed vortioxetine third line at an additional cost (vs. citalopram) of £26/month (assume cost of vortioxetine is £27/month/patient), this could result in a cost implication of around £15,600 per 100,000 per year.</td>
</tr>
</tbody>
</table>
### Depression cont’d

- NICE guideline on *depression in children and young people (update)*, updated Mar 2015
- NICE guideline on *treatment and management of depression in adults* expected May 2017.
- MHRA learning module on SSRIs

This is an update of NICE clinical guideline 28 (issued 2005), as new evidence relating to the use of computer-based CBT and the use of antidepressants in combination with psychological therapy has been identified. In terms of medicines the updated recommendations now recommend the use of fluoxetine in combination with psychological therapy as an option for initial treatment in moderate to severe depression and in patients that are unresponsive after 4-6 sessions. NICE also now state that fluoxetine should not be offered to patients with moderate to severe depression that are not also receiving psychological therapy. In terms of prescribing budgets these changes are likely to have minimal impact on expenditure.

This is an update of the Clinical Guideline published in 2009. It seems unlikely that there will be significant changes in terms of advice about use of antidepressants.

This learning module identifies the most important hazards of SSRIs and informs on actions that health professionals should take in order to minimise and manage the risks.

**Actions/ issues which may be considered by commissioners and providers**

- Revisit any treatment pathways in adults and align the place of vortioxetine in the pathway for the treatment of major depressive disorder with the final NICE Guidance once available.
- Revisit any treatment pathways describing the treatment of depression in children and adolescents and ensure that the revised guidance issued in 2015 is given due consideration.

### Autism

- NICE Quality Standard on *autism in children, young people and adults* issued Jan 2014

This Quality Standard covers autism in children, young people and adults, including both health and social care services. A commissioning support tool is available to assist commissioners in its implementation.

### Attention Deficit Disorder

NICE pathway available

- NICE guideline on *attention deficit disorder* – partial update expected Feb 2016
- NICE guideline on *attention deficit disorder* – update expected Jan 2018

This partial update will only address two specific questions relating to the use of elimination and restriction diets in children with ADHD and the case for using polyunsaturated fatty acid dietary supplements in children with ADHD. The draft advice from NICE is not to support the use of polyunsaturated fatty acid supplements and it is therefore unlikely to have significant implications for prescribing budgets.

No detail is available yet on which areas of the Guideline will be reviewed.

### Obesity

- NICE guideline on the *prevention, identification, assessment and management of overweight and obesity in children, young people and adults (update)*, issued Nov 2014

This guideline is a partial update of clinical guideline 43 (issued 2006). Recommendations on very-low-calorie diets and follow-up care packages after bariatric surgery have been updated. The updated guidelines offers the following new recommendations on the role of bariatric surgery in the management of type 2 diabetes of recent onset in people with obesity:

### Obesity cont’d
Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE guideline on the prevention, identification, assessment and management of overweight and obesity in children, young people and adults (update). cont'd</td>
<td>- Offer an expedited assessment for bariatric surgery to people with a BMI of 35 or over who have recent-onset type 2 diabetes* as long as they are also receiving or will receive assessment in a tier 3 service (i.e. multi-disciplinary team interventions or equivalent).</td>
</tr>
<tr>
<td>NICE pathway available</td>
<td>- Consider an assessment for bariatric surgery for people with a BMI of 30–34, who have recent-onset type 2 diabetes* as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent).</td>
</tr>
<tr>
<td>NICE Quality Standard expected Jan 2016</td>
<td>- Consider an assessment for bariatric surgery for people of Asian family origin who have recent-onset type 2 diabetes* at a lower BMI than other populations as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent).</td>
</tr>
<tr>
<td>NICE Quality Standard on obesity in children, issued Jul 2015</td>
<td>*The guideline development group considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10-year time frame.</td>
</tr>
<tr>
<td>Statistics on Obesity, Physical Activity and Diet England 2014</td>
<td>Within the costing template available for this guideline, it is estimated that the recommendations above will increase the number of people receiving bariatric surgery from 2410 per year in England to 7955 and therefore any ongoing prescribing post bariatric surgery (e.g. vitamins) will also increase. However, these are likely to be offset by reduced type 2 diabetes and complications arising from type 2 diabetes.</td>
</tr>
<tr>
<td>NICE guidance on naltrexone-bupropion prolonged release, in addition to diet and physical activity, for managing people with obesity or overweight with risk factors issue date TBC</td>
<td>Recommendations on pharmacological interventions have not been updated, and this is therefore unlikely to have any further significant impact on medicines spend.</td>
</tr>
<tr>
<td>Actions/ issues which may be considered by commissioners and providers</td>
<td>This Quality Standard covers public health strategies to prevent overweight and obesity, and interventions for lifestyle weight management, in children and young people aged under 18 years.</td>
</tr>
<tr>
<td>A report from a working group of NHS England/Public Health England on joined up clinical pathways for obesity, discusses issues relating to the obesity care pathway. The report defines tier 3 services as comprising of a multi-disciplinary team of specialists, led by a clinician and typically including: a physician (consultant or GP with a special interest); specialist nurse; specialist dietician; psychologist or psychiatrist; and physiotherapist/physical activity specialist/physiology. The report notes that provision of tier 3 services is variable, with the absence of such services in many areas.</td>
<td>This annual report presents a range of information on obesity, physical activity and diet, from a variety of sources. Drug items prescribed for treating obesity in 2012 (392,000) fell by 56% from 2011 (898,000), and by 47% compared to 2002 (737,000). This decrease may be due to supply problems experienced with orlistat in 2012. Almost all of the prescription items in 2012 for obesity drugs were for orlistat.</td>
</tr>
<tr>
<td>The role of naltrexone-bupropion will need to be defined in terms of existing disease pathways once NICE Guidance is available.</td>
<td>Naltrexone-bupropion has been licensed for the treatment of adults with a BMI of ≥ 30 or ≥ 27 with the presence of one additional weight-related risk factor. However it has not yet been launched in the UK, it is expected to be launched in 2016 and there is as yet no indication on cost. The license is broadly similar to orlistat. In 2014 the NHS in England spent just over £15m on orlistat supplied on prescription, however in 2009 the spend on this drug class was closer to £50m although there were a few more options available. It therefore seems reasonable to assume that a new agent launched at a similar price might increase expenditure back to those levels again.</td>
</tr>
</tbody>
</table>

*The guideline development group considered that recent-onset type 2 diabetes would include those people whose diagnosis has been made within a 10-year time frame.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

### Pain
- NICE guideline on [headaches: diagnosis and management of headaches in young people and adults (update on CG 150)](update on CG 150) expected Nov 2015

There are only minor changes proposed to migraine prophylaxis regimens in the draft version of the updated guidance. These would not be expected to impact significantly on prescribing budgets.

### Actions/ issues which may be considered by commissioners and providers
- Locally agree the approach to the management of neuropathic pain, including the role of pregabalin – based on the revised guideline, there are opportunities for cost savings in this area.
- Generic versions of pregabalin became available in the first half of 2015. However, these do not currently cover all licensed indications of the branded version. Commissioners and providers should consider this and ongoing legal cases when developing local guidelines.

### Substance dependence

#### Smoking Cessation
- NICE pathways available for: [Smokeless tobacco cessation in South Asian communities](Smokeless tobacco cessation in South Asian communities)
- [Smoking](Smoking)
- [Smoking cessation in secondary care](Smoking cessation in secondary care)
- [Smoking – tobacco harm reduction processes](Smoking – tobacco harm reduction processes)
- Quality standards
  - [Smoking harm reduction](Smoking harm reduction)
  - [Smoking – reducing and preventing tobacco use](Smoking – reducing and preventing tobacco use)
  - [Smoking – supporting people to stop](Smoking – supporting people to stop)
- NICE Guideline on [smoking cessation interventions and services](on smoking cessation interventions and services) expected Oct 2017

NICE has published a [commissioning guide](commissioning guide) to support implementation of the Quality Standard for smoking: reducing tobacco use. Within that document it is stated that if an intervention costs less than £200 for each 1% of people who quit smoking, it is likely to be cost effective. For example, if an intervention has a quit rate of 4% it needs to cost less than £800 (4x£200) to be cost effective. Likewise, an intervention needs to cost less than £100 per smoking 'reducer' in order to be cost effective. For example, if an intervention has a 'reduce' rate of 7%, it will need to cost less than £700 to be cost effective.

There is no documentation available as yet on the scope of the Guideline but it would seem unlikely that it will impact significantly on current practice unless it addresses the prescribability of e-cigarettes (see below).

This report estimates that e-cigarettes may be 95% less harmful to health than smoking cigarettes. This report has been criticised in terms of the robustness of the science that underpins this claim but it is clear from this report that e-cigarettes are being used extensively (an estimated 2.6m users) and that licensed versions that will be prescribable as medicines may become available within the next 1-2 years (one is currently going through the licensing process and Voke – a nicotine inhaler but not a e-cigarette has been licensed but not launched).

Also within the report it is estimated that there are currently 1.8m prescription items dispensed each year which relate to smoking cessation (of which about 50% are nicotine replacement therapies). If a prescribable e-cigarette became available at a cost of £60 per year and was prescribed to 1 million people on an ongoing basis (about 40% of current e-cigarette users) – it would increase prescribing costs by £600m or about £1.1m per 100,000 population per year. There would be probably some costs offset by reduced use of NRT but these are likely to be insignificant in comparison. This cost would double if just 15% of non-e-cigarette using tobacco smokers also converted to a prescribable e-cigarette to give a total cost of £2.2m per 100,000 population. Unlike current smoking cessation products e-cigarettes are aimed at reducing harm rather than facilitating nicotine withdrawal and therefore are potentially a life-long treatment.
### Alcohol Use Disorders

- NICE Quality Standard on [preventing harmful alcohol use in the community](https://www.nice.org.uk/guidance/qs176), issued Mar 2015
- NICE pathway available
- NICE guidance on [nalmefene for reducing alcohol consumption in people with alcohol dependence](https://www.nice.org.uk/guidance/qs81), issued Nov 2014

This Quality Standard covers the prevention of harmful alcohol use in the community amongst children young people and adults.

NICE support the use of nalmefene within its marketing authorisation, as an option for reducing alcohol consumption, for people with alcohol dependence who have a high drinking risk level (defined as alcohol consumption of >60g/day for men and >40g/day for women) without physical withdrawal symptoms, and who do not require immediate detoxification. The marketing authorisation states that nalmefene should **only** be prescribed in conjunction with continuous psychosocial support focused on treatment adherence and reducing alcohol consumption, and be initiated only in patients who continue to have a high drinking risk level 2 weeks after initial assessment.

Naltrexone plus psychosocial intervention is not considered to be part of established treatment for the reduction of alcohol consumption, and therefore was not considered to be an appropriate comparator for nalmefene. Nalmefene plus psychosocial intervention was therefore compared to psychosocial intervention alone, and found to be a cost-effective use of NHS resources in this setting (ICER likely to be less than £5200 per QALY gained).

According to clinical experts consulted during guideline development, psychosocial intervention is the standard first-line treatment in England for people with alcohol dependency who have a high or very high drinking risk level without physical withdrawal symptoms and who do not require immediate detoxification. The NICE clinical guideline on the [diagnosis, assessment and management of harmful drinking and alcohol dependence](https://www.nice.org.uk/guidance/cg115) (CG115) recommends that the goal of treatment for most people with alcohol dependence is abstinence. However, for those with harmful drinking or mild dependence, without significant comorbidity, and with adequate social support, moderation of drinking may be appropriate. For those with mild alcohol dependence*, pharmacological treatment should only be considered when psychosocial intervention has not helped, or when specifically requested. Most patients with mild alcohol dependency will be treated in the primary care setting.

*The inclusion criteria for the nalmefene studies reflected the definition in NICE CG115 for mild alcohol dependence, according to clinical experts*

The AWMSG also recommends nalmefene as an option for reducing alcohol consumption in line with its marketing authorization and appear to have used a similar costing model to NICE. The advice includes the following assumptions on the eligible Welsh population made by the company (converted to per 100,000 population):

- After accounting for alcohol-related mortality, the estimated number of patients for the specific indication is 1420 per 100,000 population in year 1
- 6% of eligible patients receive treatment in year 1, rising to 14% in year 5
- The uptake of nalmefene is 20% in year 1, increasing to 60% in year 5

The number of patients treated with nalmefene can be estimated as 26 per 100,000 population in year 1, increasing to 179 per 100,000 in year 5.
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Substance dependence cont’d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol Use Disorders cont’d</strong></td>
</tr>
<tr>
<td>- NICE guidance on nalmefene for reducing alcohol consumption in people with alcohol dependence, cont’d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs misuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>- NICE pathways available for:</td>
</tr>
<tr>
<td>- Drug misuse</td>
</tr>
<tr>
<td>- Needle and syringe programmes</td>
</tr>
<tr>
<td>- Psychosis with co-existing substance misuse</td>
</tr>
<tr>
<td>- Reducing substance misuse among children and young people</td>
</tr>
<tr>
<td>- NICE guideline on drug misuse prevention expected Jan 2017</td>
</tr>
<tr>
<td>- NICE guideline on severe mental illness and substance misuse (dual diagnosis) - community health and social care services expected Nov 2016</td>
</tr>
</tbody>
</table>

### Epidemiology, potential financial implications for a population of 100,000 and other comments

If it is assumed that nalmefene is taken for an average of 127 days each year (annual cost of around £385 per person) and that the withdrawal rate is 17.5% (as per AWMSG advice), then the introduction of nalmefene may be associated with initial costs of £5,500 per 100,000 population in year 1, increasing to £38,000 per 100,000 population by year 5 (drug costs only).

Nalmefene is likely to have considerable service delivery costs, due to the requirement for continuous psychosocial support; these costs have not been included here but are estimated by NICE to be £951 per patient per year which is approximately three times higher than the drug cost. The associated reduction in drinking will however be associated with longer-term benefits and potential cost-savings.

There are no details available as yet on scope but it would seem unlikely that this will impact significantly on prescribing budgets.

### Actions/ issues which may be considered by commissioners and providers

- Local authorities now commission services for substance misuse. Health and social care will need to work together to implement NICE recommendations. Health and Wellbeing boards are ideally placed to ensure this occurs.
- The Tobacco Return on Investment Tool developed by NICE and Brunel University will help support commissioners and policy makers count the cost of tobacco-related harm in their communities and estimate the longer-term cash savings that they can expect by putting tobacco control strategies in place.
- The NCSCT have produced a Needs analysis- toolkit for commissioners to assist commissioners in assessing what level of stop smoking provision is needed for their local population. Organisations may wish to use this resource to assist them in assessing the resource impact of implementing NICE guidance on smoking cessation in secondary care.
- NICE has published a Health Technologies adoption programme to support the uptake of their guidance on Nalmefene. This indicates that there is some prescribing happening in about 80% of CCGs some 12 months after publication with defined daily doses ranging from 2 to about 190 in those CCGs were there is evidence of use. There is very limited prescribing outside of CCG-funded services. The document provides top tips to support implementation.
**Alzheimer’s disease & dementia**

- NICE [Key Therapeutic Topics](#) includes use of low dose antipsychotics in people with dementia published Jan 2015
- NICE pathway available
- NICE Quality Standard on [delirium](#), issued Jul 2014
- NICE guideline on [dementia - assessment, management and support for people living with dementia and their carers](#) expected Sept 2017
- NICE guideline on [dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset](#) issued Oct 2015.

**Actions/ issues which may be considered by commissioners and providers**

- Users may wish to refer to the NICE [tool](#) providing support for commissioners of dementia care (2013).
- Commissioners and providers should consider developing local integrated pathways for the management of dementia that include initiation of treatment by GPs to reduce referrals. Appropriate education, training and guidelines/protocols will need to be developed to support this.

**Parkinson’s disease**

- NICE guideline on [Parkinson’s disease (update)](#), expected Oct 2016
- NICE pathway available

**Actions/ issues which may be considered by commissioners and providers**

- Co-careldopa intestinal gel (Duodopa) is listed as an exclusion in the National Tariff for 15/16. [Drug exclusions under Payment by Results 15/16](#). NHS England is the responsible commissioner for this drug in line with the Clinical Commissioning Policy issued in July 2015.

**Eating disorders**

- Update NICE guideline on [eating disorders: recognition and treatment](#) expected Apr 2017

**Actions/ issues which may be considered by commissioners and providers**

- This update will include a review of pharmacological treatment since the Guideline was last updated in 2004 and at that time restricted recommended medicines to SSRIs (specifically fluoxetine) in bulimia nervosa and binge eating disorder. It is unlikely that this review will have significant implications for prescribing budgets.
### Disease or Indication: National targets and guidance

#### Other mental health and CNS related guidance

- NICE clinical guideline on *antenatal and postnatal mental health (update)*, issued Dec 2014
- NICE pathway available

- NICE clinical guideline on *challenging behaviour and learning disabilities: prevention and interventions for people with learning disabilities whose behaviour challenges* issued May 2015

- NICE Quality Standard on *challenging behaviour with learning disability*, issued Oct 2015

- The *Winterbourne Medicines Programme* issued July 2015

- NICE Medicines Practice Guide on the *safe use and management of controlled drugs*, expected Mar 2016

### Epidemiology, potential financial implications for a population of 100,000 and other comments

This is a partial update of *Antenatal and postnatal mental health* (NICE clinical guideline 45; first issued 2007). It covers the care of women who have, or are at risk of, mental health disorders during pregnancy and the postnatal period, in the same healthcare settings as the original NICE guideline. Treatments covered include psychological and pharmacological interventions, electroconvulsive therapy and combined interventions, and the balance of risk and benefit for the mother, foetus and baby.

The guidance includes advice on use of the following drugs during pregnancy and the postnatal period, which may be useful for commissioners developing local treatment pathways:

- TCAs, SSRIs and SNRIs
- Benzodiazepines
- Antipsychotic medication
- Anticonvulsants (valproate, carbamazepine and lamotrigine)
- Lithium

This guideline provides recommendations on prevention and interventions for adults, young people and children with learning disabilities whose behaviour challenges. The interventions covered in the guideline include environmental, psychosocial and pharmacological. It is noted that medication (e.g. antipsychotics) is the most common intervention used to manage behaviour that challenges. Although it may be effective for some people, it is considered overused by most professionals, and there is a danger that it may simply sedate and lead to polypharmacy. This guideline may lead to a reduction in the use of antipsychotics in this group of people; it is however at an early stage of development and it is therefore difficult to assess its impact.

This Quality Standard reiterates the key points outlined above and includes the following two statements that impact on the use of medicines:

- People with a learning disability and behaviour that challenges only receive antipsychotic medication as part of treatment that includes psychosocial interventions.
- People with a learning disability and behaviour that challenges have a multidisciplinary review of their antipsychotic medication 12 weeks after starting treatment and then at least every 6 months

These resources were published as a result of three separate reviews that showed that people with learning disabilities were being over-prescribed psychotropic medicines. It is estimated that on an average day in England, between 30,000 and 35,000 adults with a learning disability are being prescribed an antipsychotic, an antidepressant or both without appropriate clinical indications (psychosis or affective disorder). This is 16.2% of the adult population known to their GP as having a learning disability.

This site provides access to a number of resources including example pathways and guidance intended to support healthcare professionals to address the issues outlined above.

This guide will provide recommendations for good practice in this area. A *draft version* is now out for consultation.
Other mental health and CNS related guidance cont’d

- NICE guideline on the mental health of people in prison, expected Nov 2016
- NICE guideline on mental health problems in people with learning disability, expected Sep 2016
- NICE guideline on children’s attachment: attachment in children and young people who are adopted from care, in care or at high risk of going into care, expected Nov 2015
- NICE guideline on violence and aggression (update), issued Apr 2015
- NICE Quality Standard on personality disorders (borderline and antisocial), issued Jun 2015

**Actions/ issues which may be considered by commissioners and providers**

- Users may wish to refer to the NICE commissioning guide for stepped care for people with common mental health disorders
- Commissioners need to develop local pathways to ensure that when people with learning disabilities are prescribed psychotropic medicines that that prescribing is indicated and is reviewed in line with NICE Quality Standards
5. Infections

Patent expiries

According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: lopinavir/ritonavir (Dec 2015); emtricitabine (Jan 2016); linezolid (Jan 2016); oseltamivir (Feb 2016); telithromycin (Jul 2016); voriconazole (Jun 2016); adefovir dipivoxil (Sep 2016); valganciclovir (Mar 2017); caspofungin (Apr 2017); entecavir (Apr 2017); ertapenem (Apr 2017); tigecycline (Aug 2017).

General strategy

- Key Therapeutic Topic (KTT) – antibiotics

A set of key therapeutic topics (KTT) and associated comparators have been developed to support NHS England’s Medicines Optimisation Measurement work stream. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The following antibiotic-related comparators have been developed:
  - Antibacterial items/STAR PU (number of prescription items for antibacterial drugs per oral antibacterials ITEM based STAR-PU)
  - Co-amoxiclav, cephalosporins and quinolones % items (number of prescription items for co-amoxiclav, cephalosporins and quinolones as a percentage of the total number of prescription items for selected antibacterial drugs)
  - 3 day courses of antibiotics: ADQ/item (number of ADQs per item for trimethoprim 200mg tablets, nitrofurantoin 50mg capsules/tablets, nitrofurantoin 100mg m/r capsules etc [include pivmecillinam]). This is being introduced as an interim comparator whilst an alternative (3 day courses of antibiotics: % items) is being developed. It will be available up to and including Q4 (2015/16) as a minimum.
  - Minocycline ADQ/1000 patients (total number of average daily quantities for minocycline per 1000 patients)

The following comparators have been retired as of Q1 2015/2016:
  - “3 days trimethoprim ADQ/item”
  - “Cephalosporins and quinolones % items”

The number of antibacterial items dispensed in the community in 2014 increased slightly (by 0.1 million, or 0.2% since 2013); costs have however increased more significantly (by £5.6 million; 2.9%). The largest increase in cost was for nitrofurantoin, due to changes in preparations being used (fall in use of proprietary capsules and generic nitrofurantoin 50mg tablets [combined reduction of £7.4m]; use of two new generic preparations [50mg and 100mg capsules, cost of £12.0m]); 140% increase in use of modified-release 100mg capsules [cost of £1.7m]. The largest decrease in use was for amoxicillin and the largest increases were for doxycycline hyclate and clarithromycin.

Broad-spectrum penicillins are the most commonly prescribed antibacterial; use gradually increased from 2004 but has dropped over the past two years. Antibiotic prescribing has generally increased since 2004 except for the cephalosporins, quinolones and more recently metronidazole and tinidazole. Use of medicines for UTI, tetracyclines and sulfonamides and trimethoprim continues to rise. Prescribing of clindamycin also continues to rise, along with the ‘some other antibiotics’ group – this group consists largely of colistimethate sodium formulations used to treat cystic fibrosis.

Prescriptions dispensed in the community: England 2004-14, issued Jul 2015
### General strategy cont’d

- **UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018**, issued Sep 2013

- **The 2014 English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)**

- **Antimicrobial prescribing and stewardship competencies**, issued Oct 2013

- **Start Smart - Then Focus: Antimicrobial Stewardship Toolkit for English Hospitals** (updated Mar 2015)

- **2015-2016 Antibiotic Quality Premium**

### Epidemiology, potential financial implications for a population of 100,000 and other comments

This cross-government UK strategy aims to slow the development and spread of antimicrobial resistance by focusing activities around 3 strategic aims: (i) improve knowledge and understanding of antimicrobial resistance; (ii) conserve & steward the effectiveness of existing treatments; (iii) stimulate development of new antibiotics, diagnostics and novel therapies. The first annual progress report sets out the work that is underway and some of the key achievements in the first year of the strategy. A further report includes details of the initial antimicrobial prescribing quality measures that will be used in England from 2015.

This report found that from 2010 to 2013, the total use of antibiotics increased by 6%; within general practice use increased by 4%, while hospital prescribing increased by 12% and other community prescriptions (e.g. dental prescriptions) increased by 32%.

The DH and PHE have published these competencies for all independent prescribers to help improve the quality of prescribing practice. There are 5 overarching competencies:

- Infection prevention and control
- Antimicrobial resistance and antimicrobials
- Prescribing antimicrobials
- Antimicrobial stewardship
- Monitoring and learning

Actions that independent prescribers can take for each competency are outlined within the document.

This toolkit provides an outline of evidence-based antimicrobial stewardship in the secondary healthcare setting. It was originally published in 2011 and has been updated to take into account recommendations from a number of sources, including the UK Five Year Antimicrobial Resistance Strategy and the ESPAUR report. It also acknowledges the NICE antimicrobial stewardship guideline (which was draft at the time of its publication).

The aim of this Quality Premium measure is to reduce overuse and inappropriate use of antibiotics in order to reduce the spread of antimicrobial resistance. It is a composite consisting of three parts:

a) Reduction in the number of antibiotic prescriptions/STAR-PU by ≥1%
b) Reduction in the proportion of broad spectrum antibiotics (cephalosporins, quinolones & co-amoxiclav) by 10% from the 2013-14 baseline or to stay below the England median value (11.3%)c) Secondary care providers with 10% or more of their activity being commissioned by the relevant CCG have validated their total antibiotic prescribing data as certified by PHE
**General strategy cont’d**

- Public Health England’s *Management of common infection guidance for primary care* (reviewed Nov 2014)
- TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) toolkit
- NICE guideline on *antimicrobial stewardship*, issued Aug 2015
- NICE guideline on *antimicrobial resistance: changing risk-related behaviours*, expected Mar 2016
- NICE Quality Standard on *effective antimicrobial stewardship*, expected April 2016

**Actions/ issues which may be considered by commissioners and providers**

- Review and, where appropriate, revise current prescribing practice and use implementation techniques to ensure prescribing is in line with guidance from Public Health England and in line with the Department of Health Strategy.
- Benchmark and review the total volume of antibiotic prescribing and the prescribing of quinolones, cephalosporins, trimethoprim and minocycline against local and national data.

**Infection in children**

- NICE guideline on *bronchiolitis in children*, issued June 2015
  
  NICE pathway available

- NICE Quality Standard on *bronchiolitis* expected Jun 2016

- NICE Quality Standard on *antibiotics for neonatal infection*, issued Dec 2014
  
  NICE pathway available.

This guidance for managing common infections, including upper respiratory, lower respiratory and urinary tract infections, can be adapted for local use.

This antibiotics toolkit from the RCGP aims to help influence prescribers’ and patients’ personal attitudes, social norms and perceived barriers to optimal antibiotic prescribing.

This guideline covers the effective use of antimicrobials in children, young people and adults. It aims to change prescribing practice to help slow the emergence of antimicrobial resistance and ensure that antimicrobials remain an effective treatment for infection. The recommendations cover antimicrobial stewardship programmes, antimicrobial prescribing and introducing new antimicrobials.

This public health guideline will cover interventions to change people’s behaviour to help reduce antimicrobial resistance, by making the public aware of the importance of using antimicrobials correctly and the dangers associated with their overuse. The draft guideline includes recommendations on national and local campaigns, national and local interventions to prevent and stop the spread of infections (e.g. handwashing; food hygiene), and interventions to reduce inappropriate antimicrobial demand and use. Specific recommendations are made for childcare settings, schools, universities and healthcare settings.

This Quality Standard will cover reducing emergence of antimicrobial resistance through effective antimicrobial stewardship in all publicly funded health and social care settings.

This guideline covers the diagnosis and management of bronchiolitis in children. The recommendations discuss the appropriate use of fluids and oxygen supplementation, but no drug therapy is recommended (the following should not be used: antibiotics, hypertonic saline, nebulised adrenaline, salbutamol, montelukast, ipratropium, inhaled or systemic corticosteroids, or the combination of systemic corticosteroids and nebulised adrenaline). The costing statement notes that the guideline may have additional costs but also additional savings at a local level as a result of variation in clinical practice across the country. Potential areas for additional costs and cost savings are highlighted and organisations are encouraged to assess this locally. None of the highlighted areas are related to medicines use and the guideline is therefore unlikely to result in any significant financial impact on medicines spend.

This Quality Standard is at an early stage of development.

This Quality Standard covers the use of antibiotics to prevent and treat infection in newborn babies (both term and preterm) from birth to 28 days in primary (including community) and secondary care. It includes antibiotics that are given to newborn babies or to mothers during intrapartum care to prevent neonatal infection (antibiotic prophylaxis).
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory infections</strong></td>
<td>This guideline will cover the prevention, diagnosis and management of latent and active TB, including both drug-susceptible and drug-resistant forms of the disease. It will update and replace previous guidance in this area (2011) and incorporates and adapts the public health guideline (PH37) on 'Identifying and managing tuberculosis among hard-to-reach groups' (2012). With respect to the treatment of active TB, the guideline makes recommendations on when treatment should deviate from the 'standard recommended regimen', taking into account factors such as the site and severity of the disease, and individual patient characteristics including age and the presence of co-morbidities such as HIV, renal or liver disease and drug dependency. Identification and treatment of multi-drug resistant (MDR) TB and treatment of latent TB infection will also be included. The draft recommendations are available and new ones have been added for the diagnosis, treatment, monitoring and support of people with TB, as well as the prevention of the transmission of infection, and on the organisation of TB services. It is unlikely that this guideline will have any significant financial impact on medicines spend.</td>
</tr>
<tr>
<td><strong>Tuberculosis (TB)</strong></td>
<td>This guideline will cover the prevention, diagnosis and management of latent and active TB, including both drug-susceptible and drug-resistant forms of the disease. It will update and replace previous guidance in this area (2011) and incorporates and adapts the public health guideline (PH37) on 'Identifying and managing tuberculosis among hard-to-reach groups' (2012). With respect to the treatment of active TB, the guideline makes recommendations on when treatment should deviate from the 'standard recommended regimen', taking into account factors such as the site and severity of the disease, and individual patient characteristics including age and the presence of co-morbidities such as HIV, renal or liver disease and drug dependency. Identification and treatment of multi-drug resistant (MDR) TB and treatment of latent TB infection will also be included. The draft recommendations are available and new ones have been added for the diagnosis, treatment, monitoring and support of people with TB, as well as the prevention of the transmission of infection, and on the organisation of TB services. It is unlikely that this guideline will have any significant financial impact on medicines spend.</td>
</tr>
<tr>
<td>• NICE guideline on TB (update), expected Dec 2015 NICE Pathway available.</td>
<td></td>
</tr>
<tr>
<td><strong>Pneumonia</strong></td>
<td>This guideline covers the diagnosis and management of community-acquired pneumonia and hospital-acquired pneumonia in adults. The recommendations cover diagnostic and microbiological investigations, use of severity assessment tools, pharmacological treatment (antibiotics [choice, when to start, duration of therapy] and glucocorticoids), safe discharge and the provision of patient information. The guideline recommends considering the use of point of care CRP testing to guide antibiotic prescribing in cases where a diagnosis of pneumonia has not been made after clinical assessment. The costing statement notes that although this recommendation will lead to costs associated with purchasing point of care test analysers (around £700 each) and recurrent costs associated with testing (around £13.50 per test), improvement in identifying appropriate treatment regimes could lead to a reduced use of antibiotics. Appropriate use of delayed antibiotic prescriptions should also reduce unnecessary use of antibiotics and there may be efficiency savings in primary care because of reduced numbers of repeat appointments. Improved targeting of antibiotics supports the Department of Health’s ‘Start smart, then focus’ antimicrobial stewardship guidance to help reduce the growing threat of antibiotic resistance. This Quality Standard will cover adults with a suspected or confirmed diagnosis of community-acquired pneumonia or hospital-acquired pneumonia.</td>
</tr>
<tr>
<td>• NICE guideline on Pneumonia - including community acquired issued Dec 2014</td>
<td></td>
</tr>
<tr>
<td>• NICE Quality Standard on pneumonia in adults; expected Jan 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>NICE has taken the decision to pause the development of the clinical guideline for Hepatitis C until NICE technology appraisals evaluating new pharmacological therapies have published. The final scope is not yet available. The guideline is at an early stage of development; however it is unlikely to have an additional significant resource impact on medicines use in this area, as many of the medicines related aspects are already being implemented. Note: Although the drugs being considered within this guideline are now commissioned through NHS England, the guideline’s content will be useful for CCGs and hospital Trusts.</td>
</tr>
<tr>
<td>• NICE clinical guideline on hepatitis C, expected date TBC</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>NICE has taken the decision to pause the development of the clinical guideline for Hepatitis C until NICE technology appraisals evaluating new pharmacological therapies have published. The final scope is not yet available. The guideline is at an early stage of development; however it is unlikely to have an additional significant resource impact on medicines use in this area, as many of the medicines related aspects are already being implemented. Note: Although the drugs being considered within this guideline are now commissioned through NHS England, the guideline’s content will be useful for CCGs and hospital Trusts.</td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>NICE has taken the decision to pause the development of the clinical guideline for Hepatitis C until NICE technology appraisals evaluating new pharmacological therapies have published. The final scope is not yet available. The guideline is at an early stage of development; however it is unlikely to have an additional significant resource impact on medicines use in this area, as many of the medicines related aspects are already being implemented. Note: Although the drugs being considered within this guideline are now commissioned through NHS England, the guideline’s content will be useful for CCGs and hospital Trusts.</td>
</tr>
</tbody>
</table>
Hepatitis C cont’d

- NICE guidance on simeprevir for chronic hepatitis C, issued Feb 2015

- NICE guidance on simeprevir in combination with sofosbuvir for chronic hepatitis C, expected June 2016

- NICE guidance on sofosbuvir for chronic hepatitis C, issued Feb 2015

NICE recommends the use of simeprevir in combination with peginterferon alfa and ribavirin, within its marketing authorisation, as an option for treating genotype 1 and 4 chronic hepatitis C in adults. A 12-week course of simeprevir costs approximately £22,400, excluding the cost for ribavirin and peginterferon and ribavirin. The costing statement estimates that implementation of this guidance will be associated with a cost of £4 million for England (£7420 per 100,000). This includes savings from onward transmissions avoided of £3 million (£5,565 per 100,000) and resources released from reduced treatment periods of £3 million (£5,565 per 100,000). The population eligible for treatment is approximately 13,200 people per year in England (25 per 100,000 population).

The effectiveness of simeprevir in combination with sofosbuvir was initially to be considered in TA331. It was decided however to develop recommendations in separate guidance, to await the availability of mature observational data (including data on people who cannot tolerate of are not eligible for interferon treatment) before making a decision on the use of this combination. NICE will be combining this with an appraisal of a new indication considered through the topic selection process - sofosbuvir and simeprevir for the treatment of chronic hepatitis C virus infection in adult patients. The guidance is at an early stage of development.

NICE recommends use of sofosbuvir in combination with peginterferon alfa and ribavirin for the following patient groups:
- Adults with genotype 1 HCV (any treatment history)
- Adults with genotype 3 HCV – all treatment-experienced patients (i.e. those who have not adequately responded to interferon-based treatment) and treatment-naive patients who have cirrhosis
- Adults with genotype 4, 5 or 6 HCV – any treatment history but only when cirrhosis present
[Not licensed for use in genotype 2 infection]

Sofosbuvir in combination with ribavirin is recommended for the following:
- Adults with genotype 2 HCV – treatment-naive patients who are intolerant to or ineligible for interferon; all treatment-experienced patients
- Adults with genotype 3 HCV - only recommended for people with cirrhosis who are intolerant to or ineligible for interferon

This combination is not recommended for those with genotype 1, 4, 5 or 6 HCV

A course of sofosbuvir is approximately £35,000-£70,000 depending on length (12-24 weeks), excluding the cost for ribavirin and peginterferon alfa. The costing statement estimates that implementation of this guidance will be associated with a cost of £106 million for England (£196,660 per 100,000). This includes savings from onward transmissions avoided of £10 million (£18,550 per 100,000) and resources released from reduced treatment periods of £10 million (£18,550 per 100,000).

NHS England has issued interim commissioning guidance for sofosbuvir in combination with daclatasvir or ledipasvir (via compassionate use programmes) for patients with hepatitis C. Patients eligible for treatment are those with significant risk of death or irreversible damage within the next 12 months, irrespective of genotype. The scheme will treat ~500 patients at an estimated cost of £34,983 per patient for sofosbuvir with an additional estimated £2,400 for ribavirin required for the full 12 week treatment course.
### Hepatitis C cont’d

- NICE guidance on [ledipasvir-sofosbuvir for chronic hepatitis C](#), expected Nov 2015

This guidance will consider the clinical and cost effectiveness of ledipasvir-sofosbuvir (Harvoni®), within its licensed indication for treating chronic hepatitis C. In the final appraisal determination, NICE recommends its use for the following groups:

- Genotype 1 without cirrhosis: untreated (8 week course); previously treated (12 week course)
- Genotype 4 without cirrhosis: previously treated (12 weeks)
- Genotype 1 or 4 with compensated cirrhosis: untreated (12 week course); previously treated patients, only when the following criteria are met: Child-Pugh class A; platelet count of 75,000/mm3 or more; no features of portal hypertension; no history of an HCV-associated decompensation episode; not previously treated with a NS5A inhibitor

Ledipasvir-sofosbuvir plus ribavirin is not recommended for genotype 3 (not licensed for genotype 1 or 4).

- NICE guidance on [daclatasvir for chronic hepatitis C](#), expected Nov 2015

This guidance will consider the clinical and cost effectiveness of daclatasvir in combination with other medicinal products within its licensed indication for treating chronic hepatitis C. In the final appraisal determination, the use of daclatasvir is recommended in the following patient groups:

- Genotype 1 without cirrhosis: in combination with sofosbuvir for 12 weeks only in those with significant fibrosis (any treatment history)
- Genotype 4 without cirrhosis: in combination with sofosbuvir for 12 weeks, only in those who have been previously treated or who are interferon-ineligible or intolerant
- Genotype 1 or 4 with compensated cirrhosis: in combination with sofosbuvir (± ribavirin) for 24 weeks in those who are interferon-ineligible or intolerant
- Genotype 3 without cirrhosis: in combination with sofosbuvir for 12 weeks, only in those who are interferon-ineligible or intolerant, who have significant fibrosis
- Genotype 3 with compensated cirrhosis: in combination with sofosbuvir and ribavirin for 24 weeks in those who are interferon-ineligible or intolerant
- Genotype 4: in combination with peginterferon alfa and ribavirin for 24 weeks in untreated or previously treated patients who have significant fibrosis or compensated cirrhosis

- NICE guidance on [ombitasvir/paritaprevir/ritonavir with or without dasabuvir for chronic hepatitis C](#), expected Nov 2015

This guidance will consider the clinical and cost effectiveness of the fixed-dose combination of paritaprevir/ritonavir/ombitasvir (Viekirax®), with or without dasabuvir, within its licensed indication for treating chronic hepatitis C. The final appraisal determination recommends the following treatment regimens, provided the company provides the medicine at the same price or lower than that agreed with the Commercial Medicines Unit:

- Ombitasvir-paritaprevir-ritonavir (OPR) + dasabuvir – for those with genotype 1b HCV without cirrhosis (12 weeks)
- OPR + dasabuvir + ribavirin: genotype 1b with compensated cirrhosis (12 weeks); genotype 1a without cirrhosis (12 weeks)
- OPR + ribavirin: genotype 4 without cirrhosis who have been previously treated (12 weeks)
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis C cont’d</strong></td>
<td>NICE is unable to make a recommendation about the use in the NHS of simeprevir in combination with sofosbuvir for treating genotype 1 or 4 chronic hepatitis C because no evidence submission was received from Janssen for the technology. Overall if it is assumed that 10,000 patients with hepatitis C are identified for treatment or retreatment each year and the regimens used are £30,000 more per course than existing treatments (which will vary depending on course length), this could increase costs by at least £300 million (or £556,500 per 100,000 population). There is also potential for treatment of a backlog of patients who may have been delaying treatment in anticipation of an interferon-free regimen becoming available. If we assume that there are 5000 patients waiting (50% of those identified each year) there would also be a one-off catch up cost of ~£280,000 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on <a href="https://www.nice.org.uk/guidance/ta265">simeprevir in combination with sofosbuvir for treating genotype 1 or 4 chronic hepatitis C</a> terminated Oct 2015</td>
<td>NICE recommends that access to the drugs used to treat hepatitis C is managed through the specialised commissioning programme put in place by NHS England with prescribing decisions made by multidisciplinary teams/centres to ensure that treatment is prioritised for patients with the highest unmet clinical need.</td>
</tr>
<tr>
<td>• Treatment of chronic Hepatitis C in patients with cirrhosis: <a href="https://www.icpd.nhs.uk/wp-content/uploads/2016/01/HP-15-008-ICPD-Interim-Clinical-CMP.pdf">Interim Clinical Commissioning Policy Statement</a>, issued June 2015</td>
<td>This policy statement sets out the hepatitis treatments that will be routinely commissioned by NHS England for the treatment of chronic hepatitis in patients with cirrhosis and with advanced liver disease. It also sets out how access to treatments will be organised with the setting up of Operational Delivery Networks from August 2015 and arrangements in the interim.</td>
</tr>
<tr>
<td>• Public Health England report on <a href="https://www.gov.uk/government/publications/hepatitis-c-in-the-uk">hepatitis C in the UK</a>, 2015</td>
<td>This report estimates that around 214,000 individuals are chronically infected with HCV in the UK. Most of this infection (~90%) is genotype 1 and genotype 3. Over the last decade (2004-2013), there has been a 2.8-fold increase in hospital admissions from HCV-related end stage liver disease and hepatocellular carcinoma, and deaths from these indications have more than doubled. There has been an overall increase in registrations for liver transplants for post-hepatitis C cirrhosis, with 15% of all liver transplants carried out between 1996 and 2014 in patients with hepatitis C-related disease. Injecting drug use continues to be the most important risk factor for HCV infection in the UK.</td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

| • Drugs for hepatitis B and C are listed as exclusions in the National Tariff for 15/16. The responsible commissioner for hepatitis B drugs in England is NHS England. [Drug exclusions under Payment by Results 15/16](https://www.gov.uk/government/publications/drug-exclusions-under-payment-by-results-15-16) |

**Hepatic encephalopathy**

| • NICE guidance on [rifaximin for preventing episodes of overt hepatic encephalopathy](https://www.nice.org.uk/guidance/ta249) issued Mar 2015 | NICE recommends the use of rifaximin, within its marketing authorisation, as an option for reducing the recurrence of episodes of overt hepatic encephalopathy (HE) in people aged 18 years or older. The costing report notes that the population eligible for treatment is expected to be approximately 11,950 people in England (22 per 100,000 population), based on an estimated prevalence of cirrhosis of 76 per 100,000 population, with HE occurring in 37.5% of these. The estimated cost of implementing this guidance from year 3 onwards (at which time costs are assumed to remain constant) is £8.2 million for England (£15,200 per 100,000 population). This assumes uptake in 40% of the treated population (rising from current use of 21%), with lactulose co-administration in 91% of these, and that 91% will opt for future treatment. Expert opinion suggests rifaximin is effective in reducing the recurrence of HE; other potential savings may be realised if treatment reduces hospital admission rates, length of stay and improves quality of life (data are not available to quantify these potential savings). |
### Infective endocarditis
- **NICE guideline on prophylaxis against infective endocarditis** (Standing Committee A update), issued Sep 2015

Following the publication of new research showing an increase in the incidence of infective endocarditis in the UK, NICE launched an immediate review of this guideline. New evidence has been taken into account but was considered insufficient to warrant a change to the existing recommendations; those in the original guideline (2008) therefore remain in place. This update will therefore have no impact on medicines spend in this area.

### Sepsis
- **NICE guideline on sepsis**, expected Jul 2016
- NICE Pathway available

This guideline will provide recommendations for recognising and treating sepsis in any person in any clinical environment, linking to other relevant existing NICE guidance. This guideline will not replicate the existing critical care guidelines for sepsis in children or adults.

### Other infection-related developments and guidance
- **NICE Quality Standard on urinary tract infection**; issued June 2015
- **NICE Quality Standard on healthcare-associated infections**; expected Feb 2016

NICE Pathway on urinary tract infections in children available

This Quality Standard covers the management of suspected community-acquired bacterial urinary tract infection in adults aged 16 years and over.

This Quality Standard will cover the organisational factors in preventing and managing healthcare-associated infections in secondary care settings.
## 6. Endocrine system

### Patent expiries

According to [Prescribing Outlook New Medicines](#), the following patent expiries (which may have a significant impact on prescribing costs) are due within the next few years: strontium ranelate (Aug 2015), tolvaptan (Apr 2016), dutasteride (Jul 2017), insulin determir (Nov 2018)

### Diabetes

- NICE pathways available for diabetes, preventing type 2 diabetes and diabetes in pregnancy
- NICE Quality Standards under development for diabetes in children and young people, expected Jun 2016 and (ii) diabetes in pregnancy, expected Jan 2016
- Key Therapeutic Topic (KTT) – diabetes

This is an area of major financial risk depending on rate of uptake of newer therapies and the anticipated rise in the number of cases over the next few years.

According to [QoF data for 12/13](#), the raw prevalence rate of diabetes in England is 6% (based on patients aged over 17 years old).

This quality standard covers the clinical management of diabetes in adults excluding children, young people and pregnant women

The Quality Standard on diabetes in children and young people is under development. The Quality standard on diabetes in pregnancy is currently in draft and undergoing consultation.

A set of key therapeutic topics (KTT) and associated comparators have been developed to support NHS England's Medicines Optimisation Measurement work stream. These areas and comparators originally supported the DoH’s QIPP medicines and procurement medicines work stream but have been renamed Medicines Optimisation KTT Comparators. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The following diabetes related comparators have been developed:

- Prescribing of metformin and sulfonylureas in line with the NICE guideline. This indicator measures the number of prescriptions for metformin and sulfonylureas as a % of the total number of prescriptions for all antidiabetic drugs.
- Prescribing of long acting insulin analogues. The indicator measures the number of prescriptions for the long acting human analogue insulins detemir, glargine and degludec as a percentage of the total number of prescription items for all long acting and intermediate acting insulins excluding biphasic insulins.
- Self monitoring of blood glucose (SMBG): although this area does not currently have a defined KTT comparator available, this is an identified area for the NHS QIPP programme. It is recommended that organisations review and, where appropriate, revise local use of SMBG in type 2 diabetes mellitus to ensure that it is in line with NICE recommendations, which have been updated in the draft NICE guideline for type 2 diabetes (see later).

Current [DVLA](#) medical guidelines should also be considered when organisations are developing guidance for self monitoring of blood glucose. The DVLA guidelines contain recommendations on monitoring for different categories of patients with type 2 diabetes (e.g. those on agents which carry a risk of hypoglycaemia) by driver group.

The National Diabetes Audit (NDA) programme is commissioned by The Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit programme (NCA) and presents findings about the quality of care for people with diabetes in England and Wales. This report covers the provision of core diabetes care for everyone with diabetes (all types) and presents findings on care processes and treatment target achievement rates from 2012-2013. Overall, in 2012-13:

- National Diabetes Audit: Report 1 – Care processes and treatment targets, published Oct 2014
## Diabetes

- NICE guidance on the use of *empagliflozin in type 2 diabetes*, issued Mar 2015
  
  Empagliflozin (Jardiance℠) is the most recently licensed sodium-glucose cotransporter-2 (SGLT-2) inhibitor. NICE supports use of emapagliflozin in dual and triple therapy regimens and in combination with insulin in adults with type 2 diabetes where glycaemic control is inadequate despite other measures. The costing statement for this guidance notes that the guidance is not expected to have a significant impact on NHS resources. Empagliflozin provides an additional treatment option for people with type 2 diabetes alongside other treatment options which have similar costs and outcomes.

- NICE guidance on the use of *buccal insulin for the management of type 1 diabetes*, expected date TBC
- Review of NICE clinical guideline on *the management of type 2 diabetes in adults*, expected Oct 2015

<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Completion of eight care processes was 59.9 per cent, compared to 60.5 per cent in 2011–2012 and 60.6 per cent in 2010–2011.</td>
<td></td>
</tr>
<tr>
<td>- Concurrent achievement of all three NICE recommended glucose, blood pressure and serum cholesterol levels remains at 35.9 per cent (35.9 per cent in 2011-2012; 33.7 per cent in 2010-2011)</td>
<td></td>
</tr>
<tr>
<td>- NICE recommended glucose control (HbA1c &lt;58mmol/mol) was recorded in 27.3 per cent of people with Type 1 diabetes and 64.8 per cent of people with Type 2 diabetes</td>
<td></td>
</tr>
<tr>
<td>- Very few people with diabetes are recorded as having been offered structured education and even fewer people with diabetes are recorded as attending structured education.</td>
<td></td>
</tr>
</tbody>
</table>

This report presents statistics about diabetes outcomes including diabetic ketoacidosis (DKA), chronic kidney disease and treatment of end stage kidney disease (renal replacement therapy), lower limb amputations, heart disease and stroke.

A recently published placebo-controlled *RCT* that assessed the impact of empagliflozin in 7020 patients with Type 2 diabetes and high risk of cardiovascular disease showed that after a median follow-up of 3.1 years a primary outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke showed that empagliflozin was associated with an absolute risk reduction of 1.6%. This is the first study to show a reduction a reduction in clinical outcomes in patients with Type 2 diabetes for any medicine other than metformin and may lead to a more rapid uptake of this medicine than might have been anticipated.

According to the UKMi New Drugs Online database, buccal insulin (spray formulation) is currently in phase III trials and a predicted UK launch date is not yet available. This guidance is therefore at an early stage of development and is not expected to impact significantly in the next financial year.

This guideline will update and replace the existing guideline published in 2009. The *draft version* includes recommendations on:

- Individualised care
- Patient education
- Dietary advice
- Blood pressure management – the recommendations are largely the same as in the previous version of the guideline.
- Antiplatelet therapy – the guideline now recommends that antiplatelet (aspirin or clopidogrel) therapy should not be offered for adults with type 2 diabetes without cardiovascular disease. Readers are also referred to the NICE guidelines on lipid modification and myocardial infarction (secondary prevention) for guidance on the primary and secondary prevention of CVD in adults with type 2 diabetes.
Diabetes cont’d

- Review of NICE guideline on the management of type 2 diabetes in adults, cont’d

- NICE guideline on the diagnosis and management of diabetes (type 1 and type 2) in children and young people, published Aug 2015

- Blood glucose management – this section has a number of new recommendations, including:
  - When HbA1c should be measured
  - Targets for HbA1c
  - Self monitoring of blood glucose. The guideline advises that DVLA requirements should be taken into account when offering self monitoring. The guideline also recommends that self-monitoring of blood glucose should not be routinely offered unless caveats outlined in the guideline apply. It also outlines the circumstances under which self monitoring may be considered on a short term basis. Patients who are self monitoring should have a structured assessment at least annually.

- Drug treatment of blood glucose
  - A list of criteria against which to base the choice of drug treatment(s) is included within the guideline, these include consideration of the person’s clinical circumstances and their preferences/needs. If 2 drugs in the same class are appropriate, the option with the lowest acquisition cost should be chosen.
  - Rescue therapy with either insulin or a sulfonylurea is recommended where there is symptomatic hyperglycaemia
  - If a person’s HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions, metformin is recommended as the first line standard treatment option in all patients. Where metformin is contraindicated or not tolerated initial drug treatment with either a sulfonylurea or a DPP-4 inhibitor or pioglitazone or repaglinide
  - If initial drug treatment with metformin has not continued to control HbA1c to below the person’s individually agreed threshold for first intensification, consider metformin in a dual therapy regimen with either pioglitazone or a sulfonylurea or a DPP-4 inhibitor.
  - Where metformin is contraindicated or not tolerated, for first intensification of treatment dual therapy should be considered as follows: pioglitazone and a sulfonylurea, or pioglitazone and a DPP-4 inhibitor, or sulfonylurea and a DPP-4 inhibitor.
  - The guideline also notes that treatment with combinations of medicines including the SGLT-2 inhibitors may be appropriate for some people with type 2 diabetes
  - Further detail on 2nd intensification of therapy and insulin based treatment is also provided within the draft guideline. Unless the patient meets caveats outlined in the guideline, human insulin remains the first line insulin where insulin is considered appropriate.

The guideline also includes sections on the management of complications of type 2 diabetes.

The revised version of the guideline supports first line monotherapy with either pioglitazone, a DPP-4 inhibitor or repaglinide where metformin is contraindicated. It also states that the combination use of insulin and a GLP-1 mimetic should only be offered with specialist care advice and ongoing support. These are new recommendations and may result in increased costs, although the practice is already occurring and it is therefore difficult to quantify their impact.

This guideline updates recommendations for children and young people in NICE guideline CG15 (published July 2004). The guideline includes recommendations on diagnosis, education and management; recognition, diagnosis, referral for and treatment of diabetic ketoacidosis and diabetes service provision. The guideline recommends strict targets for blood glucose control to reduce the long-term risks associated with diabetes. The costing statement discusses recommendations that could potentially present a resource issue and this includes:

- increasing the number of diabetes units achieving the diabetes best practice tariff
- a recommendation encouraging the use of continuous glucose monitoring for children and young people with type 1 diabetes. The costing statement notes that the number of children and young people who might need continuous
### Diabetes cont’d

- NICE guideline on the [diagnosis and management of diabetes (type 1 and type 2)](https://www.nice.org.uk/guidance/ng10) in children and young people, cont’d

- NICE guideline on the [diagnosis and management of type 1 diabetes in adults](https://www.nice.org.uk/guidance/ng10-1), published Aug 2015

---

**Epidemiology, potential financial implications for a population of 100,000 and other comments**

- Glucose monitoring is not expected to rise significantly above current levels. NICE also estimate there will be savings generated through preventing 960 episodes of severe hypoglycaemia and the associated emergency hospital admissions, which they estimate could result in potential savings of £0.3–1.5 million.

- The guideline recommends that children and young people with type 1 diabetes should be offered blood ketone testing strips and a meter, and they or their family members or carers (as appropriate) should be advised to test for ketonaemia if they are ill or have hyperglycaemia. The costing statement highlights that this recommendation represents a significant change in practice because there would need to be a shift from using urine ketone detection strips to using blood ketone detection strips. The cost of urine detection strips ranges from £2.25 to £3.06 for a pack of 50 (4 packs needed per year), and the cost of blood ketone detection strips ranges from £20.84 to £21.04 for a pack of 10 (3 packs needed per year). Therefore the estimated minimum annual cost is £9 per patient using urine strips and £62 per patient using blood ketone strips. The national cost of this would be up to £1.3 million (or ~£2500 per 100,000 population). However, for each hospital admission avoided for diabetic ketoacidosis NICE estimate there is a potential saving of £1,000–1,400, which would offset the additional cost from use of ketone strips (based on a reduction of around 1100 admissions).

- This guideline covers the care and treatment of adults (aged 18 and over) with type 1 diabetes. Key priorities for implementation to improve care for adults with type 1 diabetes identified in the guideline that are likely to result in increased prescribing costs include:
  - Aim for a target HbA1c level of 48 mmol/mol (6.5%) or lower, to minimise the risk of long-term vascular complications. The previous guideline suggested a target HbA1c level of below 58.5 mmol/mol, (7.5%) for long-term blood glucose control. The costing statement notes that there might be an increase in the use of insulin pump therapy to help achieve better HbA1c control. Currently about 6% (approximately 16,900) of adults with type 1 diabetes use an insulin pump. If the total number of adults with type 1 diabetes using insulin pump therapy increased from 6% (costing approximately £45.2 million) to 7% (costing approximately £50.2 million), this would result in a cost impact of £5 million for England or £10,000 per 100,000 population.

  - Supporting adults with type 1 diabetes to test at least 4 times a day, and up to 10 times a day if caveats outlined in the guideline apply (includes DVLA requirements). The costing statement estimates a cost impact of between £6m and £19m (or £11,000 and £35,000 per 100,000 population) in England if half of the 90% of people currently self monitoring their blood glucose 4 times a day increased testing to between 5 and 7 times a day. The recommendation should encourage the most cost-effective prescribing of blood glucose testing strips. The costing statement notes that savings are possible through reduced hospital/emergency admissions, GP appointments and ambulance call outs for hypoglycaemia.

  - Offer multiple daily injection basal–bolus insulin regimens, rather than twice-daily mixed insulin regimens, as the insulin injection regimen of choice for all adults with type 1 diabetes. Although not highlighted in the key priorities, the guideline recommends that adults with type 1 diabetes should be offered twice-daily insulin detemir as basal insulin therapy. Cost estimates are not provided for this recommendation in the NICE costing resource but this recommendation makes it difficult to promote the biosimilar version of insulin glargine to new patients and the difference in cost between the branded versions of insulin detemir and insulin glargine is marginal. In 14/15, a total of £40.3m was spent on insulin detemir (700K scripts) and ~£70m on insulin glargine (1.4m scripts) in primary care.

  - The guideline also recommends that real-time continuous glucose monitoring should not be offered routinely to adults with type 1 diabetes. Where it is considered appropriate (in line with criteria set out in the guideline) it should be provided by a centre with expertise in its use.
### Diabetes cont’d

- NICE guideline on the management of diabetes in pregnancy, published Feb 2015
- NICE guideline on prevention and management of foot problems in people with diabetes, published Aug 2015
- NICE guidance on the use of canagliflozin, dapagliflozin and empagliflozin for the monotherapy treatment of type 2 diabetes, expected May 2016
- MHRA Drug Safety update: High strength, fixed combination and biosimilar insulin products: minimising the risk of medication error, issued Apr 2015
- Potential savings from the availability of biosimilar insulin glargine

<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes cont’d</td>
<td>This guideline offers advice on managing diabetes and its complications in women who are planning pregnancy and those who are already pregnant. The guideline focuses on areas where additional or different care should be offered to women with diabetes and their newborn babies.</td>
</tr>
<tr>
<td></td>
<td>This guideline offers best practice advice on the care of adults, young people and children with type 1 or type 2 diabetes with, or at risk of developing, diabetic foot problems. A key priority for implementation includes the recommendation that all hospital, primary care and community settings should have antibiotic guidelines covering the care pathway for managing diabetic foot infections that take into account local patterns of resistance.</td>
</tr>
<tr>
<td></td>
<td>The draft updated NICE guideline on the management of type 2 diabetes recommends metformin as the first line standard treatment option in all patients. Where metformin is contraindicated or not tolerated initial drug treatment with either a sulfonylurea or a DPP-4 inhibitor or pioglitazone or repaglinide is recommended. If NICE approves the use of the SGLT2 inhibitors as monotherapy, they would also be a treatment option at this point. The costs are difficult to quantify as it is likely that there is already some use of all the agents concerned in this way.</td>
</tr>
<tr>
<td></td>
<td>Serious and life-threatening cases of DKA have been reported in patients taking SGLT2 inhibitors. The MHRA has advised that patients being treated with these agents who have acidosis symptoms should be tested for raised ketones, even if plasma glucose levels are near-normal. One third of the cases involved off-label use in patients with type 1 diabetes. The MHRA reminds prescribers that none of the available SGLT2 inhibitors are licensed for the treatment of type 1 diabetes. The EMA has started a review of these medicines to evaluate the risk of diabetic ketoacidosis.</td>
</tr>
<tr>
<td></td>
<td>Several new high strength insulin products are now on the market. This draft guidance summarises ways to minimise the risk of medication errors with high strength, fixed combination and biosimilar insulin products already on the market.</td>
</tr>
<tr>
<td></td>
<td>As biosimilars will likely be available at lower costs than the originator, they have the potential to reduce treatment costs, expand market competition and increase patient accessibility. Abasaglar® (biosimilar insulin glargine) is available at a cost of £35.28 for 5x3mL (for both the cartridges and the prefilled pens). This compares to a cost of £41.50 for the equivalent pack of Lantus®. As an example, the difference between the two in annual cost for one patient at a dose of 40 units daily would be around £60.</td>
</tr>
<tr>
<td></td>
<td>In 2014/15, the total spend on insulin glargine (Lantus®) in primary care in England was ~£70m. If a 50% switch to the biosimilar version is assumed, this could result in savings of approximately £5.25 million, or ~£10,000 per 100,000 population.</td>
</tr>
</tbody>
</table>
### Disease or Indication: National targets and guidance  

<table>
<thead>
<tr>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

#### Actions/ issues which may be considered by commissioners and providers

- A redesign of diabetes services has been undertaken in many CCGs so that more care is provided in the community setting instead of referral into secondary care. Ensure that the medicines related aspects are included in any redesign - this may include insulin and GLP-1 agonist start groups, for which agreed protocols should be developed.

- Ensure local policy not only provides guidance on when to initiate the newer treatments (such as SGLT2 inhibitors, gliptins and GLP-1 agonists) for type 2 diabetes in line with the NICE recommendations, but also when to stop them. This should be audited to ensure NICE criteria for stopping treatments are being followed. Many specialists are approaching the SGLT2 inhibitors with caution in view of adverse effects observed in clinical trials, such as urinary tract and genital infections (which have been linked to the drug’s mechanism of action).

- Develop local guidance on self-monitoring of blood glucose by patients with type 2 diabetes. A UKMi Medicines Q&A document summarises the available data in this area. The revised NICE guideline for type 2 diabetes is also likely to contain updated recommendations in this area once published.

- Consider developing a locally approved list of preferred meters and strips for monitoring blood glucose levels. Some CCGs have developed guidance on choice of meters and strips and some have implemented switch programmes to help achieve better value for money in this area.

- Commissioners and providers should work together to discuss and agree local key messages for biosimilar insulin glargine, including whether switching is supported and the recommendation to prescribe by brand to reduce the risk of errors. The UKMi in use product safety assessment report and FAQ briefing sheet will help support these discussions.

- Commissioners and providers may want to work with public health to develop local policy on the use of the continuous glucose monitoring system, which has limited evidence of efficacy in certain patient groups.

- Insulin pumps and consumables are listed as an exclusion in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these for indications outside NICE recommendations. Drug exclusions under Payment by Results 15/16. Commissioners and providers should agree local prices for insulin pumps and consumables, and choice of pump and put in place local arrangements for monitoring activity. It should be noted that NHS England is the responsible commissioner for paediatric insulin pumps.

- Organisations may find a comparative table of insulin pumps (2015) produced by the LMEN helpful. The document aims to inform commissioners about insulin pumps available in the UK, their features, and the cost of the pump and associated consumables. A “How to Why to” guide from the NHS Technology Adoption Centre (NTAC, archived content) might also be useful when setting up an insulin pump service.

- Commissioners and providers should ensure that pathway work for diabetes encompasses all aspects of diabetes care, not just blood glucose control - for example cardiovascular and renal.
### Osteoporosis

- NICE Quality Standard on [falls in older people](#), Mar 2015

- NICE guideline on the [assessment and management of complex fractures](#), expected Feb 2016. NICE guideline on the [diagnosis, management and follow up of fractures](#) (non-complex), expected Feb 2016

- NICE guidance on [bisphosphonates for preventing osteoporotic fragility fractures](#) (including a partial update of NICE technology appraisal guidance 160 and 161), expected Nov 2015

NICE [pathway](#) available

### This is an area of low financial risk

This quality standard covers assessment after a fall and preventing further falls (secondary prevention) in older people living in the community and during a hospital stay.

These two guidelines are part of 5 being developed by NICE relating to trauma. With respect to prescribing, both will discuss pain relief (opioids and non-opioids). The complex fractures guideline will also discuss wound management of open fractures (including dressings). These guidelines are unlikely to have additional significant impact on medicines spend.

This guidance will assess the clinical and cost effectiveness of bisphosphonates (alendronate, ibandronate, risedronate and zoledronate) within their licensed indications for preventing osteoporotic fragility fractures. No drafts of the guidance were available at time of writing.

The [final scope](#) for the guidance notes that following a stakeholder workshop, NICE decided a multiple technology appraisal (MTA) was needed to align NICE technology appraisal guidance on treatment with the NICE clinical guideline on risk assessment, to include new prices, to include other bisphosphonates for which guidance is needed, and to include guidance for treatment in men. This MTA will also develop the framework to link absolute fracture risk with intervention thresholds, based on cost effectiveness.

Whilst the guideline is unlikely to result in significant financial impact on medicines spend, it could result in increased use of parenteral bisphosphonates over oral, which could impact on service delivery costs.

### Actions/ issues which may be considered by commissioners and providers

- Health and Social Care organisations should consider working together to develop local integrated falls prevention services.
- The [costing statement](#) for the NICE denosumab guidance suggests that the initial prescribing will be started in secondary care via a hospital outpatient appointment. It will subsequently be delivered almost exclusively in primary care. However, it is acknowledged that GPs may be cautious about administering a new therapy, particularly a monoclonal antibody, in a primary care setting following initiation in secondary care. If denosumab is not administered in primary care after the initial dose, commissioners will have recurring costs due to additional outpatient activity. Develop appropriate protocols for denosumab to enable GPs to take on continued prescribing in the primary care setting (e.g. shared care), with appropriate education and training. A [DTB](#) article (2012) reviewed the evidence base for the use of denosumab in postmenopausal osteoporosis.
- The patent for zoledronic acid expired in May 2013 and generic preparations are now available. Savings are possible in this area and commissioners should ensure any tariffs that include this drug have taken any price reductions/discounts into account.
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

#### Fertility
- NICE Quality Standard on fertility problems, Oct 2014
  - NICE pathway available
- Legal ruling relating to fertility guideline, May 2014

**This is an area of moderate financial risk**

This quality standard covers the assessment and treatment of fertility problems in people:
- with explained or unexplained infertility
- who are preparing for cancer treatment who may wish to preserve their fertility.

A court ruling, relating to funding of oocyte cryopreservation before beginning chemotherapy, determined that CCGs cannot choose not to follow NICE guidance because they merely disagree with it, even where there is no statutory duty to do so. The updated NICE fertility guideline gave stronger support for the effectiveness of oocyte cryopreservation. The CCG refused funding on the basis that no exceptionality had been established. Whilst CCGs do not have a legal duty to comply with NICE guidelines, the court ruled that the CCG was under an obligation in public law to have regard for the NICE guideline and to provide clear reasons for any general policy that does not follow NICE guidance. The judge noted that the CCG could have found other reasons, on the basis of exceptionality, for not following the guidance. It had not done so and mere disagreement was insufficient. The policy was therefore unlawful.

### Actions/ issues which may be considered by commissioners and providers
- Commissioners and providers should agree on choice of gonadotrophin products locally. A biosimilar version of follitropin alfa (Ovaleap®) has been approved and is expected to launch in 2015. This is likely to result in some cost savings in this area (up to 30%). As these drugs are tariff bundled, commissioners and providers should work together to ensure that the tariffs charged reflect the cost of the biosimilar where it is in use.
- Readers may wish to refer to the support for commissioning for fertility problems tool developed by NICE, which provides information on key clinical, cost and service-related issues to consider during the commissioning process for fertility services.

#### Menopause
- NICE guideline on the diagnosis and management of menopause, issued Nov 2015
  - NICE pathway available

**This is an area of low financial risk**

This guideline addresses the diagnosis and management of menopause. It covers women in the perimenopause and postmenopause, and the particular needs of women with premature ovarian insufficiency and women with hormone-sensitive cancer (for example, breast cancer). The guideline concentrates on the clinical management of menopause-related symptoms, considers both pharmaceutical and non-pharmaceutical treatments, includes a health economic analysis, and reviews the benefits and adverse effects of HRT used for up to 5 years. It also quantifies the long-term benefits and risks of HRT in terms of impact on venous thromboembolism, cardiovascular disease, Type 2 diabetes, breast cancer, osteoporosis, dementia and muscle mass/strength and advocates preferential use of transdermal formulations in women at increased risk of DVT.

The guideline is unlikely to result in additional significant impact on medicines spend in this area but may result in some increase as it is perhaps more positive than recent national guidance in this area from bodies like the MHRA.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>
| **Autosomal dominant polycystic kidney disease (ADPKD)** | NICE recommend tolvaptan as an option for treating ADPKD in adults to slow the progression of cyst development and renal insufficiency only if:  
• they have chronic kidney disease stage 2 or 3 at the start of treatment  
• there is evidence of rapidly progressing disease and  
• the company provides it with the discount agreed in the patient access scheme  
ADPKD affects as many as 1 in 1,000 individuals. It accounts for about 10% of people on dialysis. There are currently no therapies that modify the disease course and slow the rate of decline in renal function. Current management options include anti-hypertensives, dialysis and renal transplantation.  
The number of patients eligible for therapy and uptake is difficult to estimate. The HSRIC estimates that ADPKD is one of the most common hereditary disorders, with a prevalence of 1.0-1.3 per 1,000 population (at least 60,000 people in the UK or ~94 per 100,000 population). In the costing statement, NICE estimate that there are 2,300 people in England that meet the criteria for this treatment (which approximates to 4 per 100,000 population). Tolvaptan is licensed at total daily doses of 60-120mg for ADPKD. Based on information in the FAD, tolvaptan is available as 15 mg, 30 mg, 60 mg and 90 mg tablets, in 28-day packs of split-dose tablets, at a flat net price of £1208.20, equating to £43.15 per day, regardless of dose. The annual cost of tolvaptan is estimated by the company to be £15,750 per person (based on list price rather than PAS price, which is commercial in confidence).  
NICE estimate that between 1.67 and 50% of eligible patients will receive this drug over the next 5 years – if we assume that 10% of the prevalent population (0.4 people per 100,000 population) access it in the next year, this could result in a cost impact of around £6,000 per 100,000 population ultimately increasing to £31,500 based on a 50% uptake (estimate based on list price rather than PAS price). |
| Actions/ issues which may be considered by commissioners and providers | Tolvaptan is listed as an exclusion in the National Tariff for 15/16. Drug exclusions under Payment by Results 15/16. NHS England is the responsible commissioner for this drug when used in SIADH. CCGs are likely to be the responsible commissioners for the use of tolvaptan in ADPKD (as CCGs commission services for people with stage 2 and 3 CKD). |
### 7. Obstetrics, gynaecology and urinary tract disorders

#### Patent expiries
According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: darifenacin (Mar 2015); norelgestromin (Aug 2017).

#### Incontinence
- **NICE Quality Standard on urinary incontinence in women**, issued Jan 2015

This Quality Standard covers the management of urinary incontinence in women aged 18 years and over.

#### Contraception
- **Health & Social Care Information Centre annual report on Sexual and Reproductive Health Services**, Oct 2015
- **NICE local government briefing on contraceptive services**, issued Mar 2014
- **NICE Quality Standard on contraceptive services** expected Jul 2016

This annual report covers activity taking place in the community at dedicated Sexual and Reproductive Health (SRH) services between April 2014 to March 2015, including family planning services, community contraception clinics, integrated GUM and SRH services and young people’s services e.g. Brook advisory centres. A total of 941,169 women contacted SRH services for reasons of contraception. Oral contraception remains the most commonly used primary method (45% of women attending); however use of LARC has continued to increase (37%). The number of emergency contraception items provided to women by both SRH and at other locations in the community was approximately 318,000 in 2014/15; this has fallen steadily over the past ten years (from 521,000 in 2004/05; 39% decrease). This is possibly due to the reclassification of EHC in 2001 which made it possible for women aged 16 and over to buy it at pharmacies without a prescription. In addition nurses and pharmacists can supply EHC to women of all ages under a PGD.

This briefing summarises some of NICE’s recommendations for local authorities and their partner organisations on contraceptive services (in particular, for under-25s) and on the general use of long-acting reversible contraception. It is particularly relevant to health and wellbeing boards. The national cost-impact report for NICE clinical guideline 30 notes that for every £1 spent on switching from oral contraception to long acting reversible contraception, £9 is saved by the health economy from the prevention of unintended pregnancies.

This Quality Standard is at an early stage of development.

#### Actions/ issues which may be considered by commissioners and providers
- Local authorities are now the commissioners of sexual health services, including contraception. Health and social care will need to work together to implement NICE recommendations.

#### Antenatal, intrapartum and postnatal care
- **NICE guideline on intrapartum care for healthy women and babies**, issued Dec 2014

This guideline offers advice on the care of healthy women (at low risk of intrapartum complications) and their babies during labour and immediately after birth. It is a partial update of NICE clinical guideline 55 (issued 2007), which it replaces. New recommendations have been added in a number of areas, including choosing place of birth, care during the latent first stage of labour, transfer of care, foetal assessment and monitoring during labour and management of the third stage of labour.

The costing statement outlines the potential areas for additional costs and for savings, and the potential resource implications should be evaluated locally. Although the updated guideline covers some pharmacological interventions (such as pain control and the use of oxytocin), it is unlikely to have a significant financial impact on medicines spend.

A standing committee update of this guideline is now underway (expected in Nov 2016) which will review recommendation 1.7.3 (regarding use of team midwifery), in light of new evidence from a Cochrane review.
### Antenatal, intrapartum and postnatal care cont’d

- NICE guideline on post-natal care (update), issued Dec 2014
- NICE guideline on pre-term labour and birth, expected Nov 2015
- NICE guideline on intrapartum care for high risk women expected Jan 2017
- NICE Quality Standard on intrapartum care expected Dec 2015
- NICE Quality Standard on premature birth and premature labour expected Oct 2016

New recommendations on reducing the risk of sudden infant death syndrome (SIDS) have been added to clinical guideline 37, following the publication of new information on the association between co-sleeping and SIDS in 2013. The aim of the recommendations is to ensure that parents and carers are fully informed for any decision-making and the update is therefore unlikely to have any resource impact.

This guideline will address the additional antenatal care and intrapartum care required for women at risk of, or in suspected or diagnosed preterm labour, in order to improve outcomes for women and preterm babies. Although the draft guideline includes a number of recommendations on pharmacological interventions (e.g. tocolytics and progesterone/progestogens to improve outcomes of preterm labour; antenatal antibiotic prophylaxis; interventions to improve neonatal outcomes [e.g. maternal corticosteroids for lung maturation]), it is unlikely to result in a significant financial impact on medicines spend.

This guideline, which will sit alongside clinical guideline 190 (intrapartum care for healthy women and babies), will cover aspects of intrapartum care for women who are identified before or during labour as being at high risk of adverse outcomes because of a medical condition affecting the woman or an obstetric complication. The guideline is at an early stage of development.

This Quality Standard will cover the care of women who go into labour at term (37+0 weeks to 41+6 weeks) and their babies during labour and immediately after birth. It covers both women who go into labour at low risk of intrapartum complications and women who go on to develop complication.

This Quality Standard is at an early stage of development.

### Endometriosis and menstrual disorders

- NICE guideline on endometriosis expected May 2017
- NICE guideline on heavy menstrual bleeding (update) expected April 2016

This guideline will make recommendations on the diagnosis and management of endometriosis, in all settings in which NHS-commissioned healthcare is provided. Pharmacological treatments to be considered include analgesics, hormonal therapies and neuro-modulators, and their combination with surgical treatments. The guideline is at an early stage of development.

This will be a partial update of clinical guideline 44 (published January 2007). New evidence on progesterone receptor modulators (specifically mifepristone and ulipristal acetate) has been identified and the review will be looking at the clinical and cost effectiveness of this medical treatment for fibroids greater than 3cm in diameter. The guideline update is at an early stage of development.

### Actions/ issues which may be considered by commissioners and providers

- NICE has published a support for commissioning document which encourages commissioners to work with clinicians and managers to commission high-quality evidence-based care for women with heavy menstrual bleeding. This should be used in conjunction with the related quality standard (2013) and clinical guideline (2007; currently being updated).
## 8. Malignant disease and Immunosuppression

### Patent expiries

According to *Prescribing Outlook – New Medicines 2015*, the following patent expiries may have a significant impact on prescribing costs: Sirolimus (Sept 2015), pemetrexed (Dec 2015).

### Multiple sclerosis (MS)

- DH risk share scheme for MS treatments remains in place.
- NHS England Clinical Commissioning Policy: Disease Modifying Therapies for Patients with Multiple Sclerosis (MS) updated May 2014.
- NICE is developing a Quality Standard for multiple sclerosis expected Jan 2016.

This is an area of moderate financial risk as although NICE Guidance on the more recently launched oral agents and alemtuzumab has been in place for over 12 months there might be incremental increases in use over a number of years.

In 2011 the DH re-iterated that this scheme remains in place. It covers Avonex, Betaferon, Rebif and Copaxone (glatiramer) but not beta-interferon 1b prescribed as Extavia, fingolimod, alemtuzumab, dimethyl fumarate, tentiflunomide or natalizumab. At present 10-year patient data are being collected in the 72 centres participating in this scheme, and the 8-year data have been made available for analysis. The **6-year data** indicate that the drugs are being prescribed in a cost effective manner for the NHS and produce an estimated cost utility of about £36k per QALY.

This document describes the starting and stopping criteria that NHS England use to commission Beta interferon, glatiramer acetate, natalizumab and fingolimod for the management of Multiple Sclerosis (MS)

NICE did not revisit the use of immunomodulatory treatments as these are currently covered by the relevant technology appraisals, however they do state that Sativex should not be used to treat spasticity in people with MS nor fampridine to treat lack of mobility in people with MS. NICE also do not support the use of pregabalin in treating spasticity but advocate gabapentin and baclofen alone or in combination and then dantrolene or tizanidine as second-line choices. In terms of acute treatment of relapses NICE support the use of 5-day courses of oral methyprednisolone and suggest that this may lead to some cost reductions in centres which use IV courses of corticosteroid (either in hospital or administered in the patient’s home).

A recently published non-inferiority study provided additional evidence that oral methyprednisolone was non-inferior to IV courses in the treatment of acute exacerbations.

This review is unlikely to lead to any major changes in clinical practice.

### Actions/ issues which may be considered by commissioners and providers

- Drugs for multiple sclerosis are listed as exclusions in the National Tariff for 15/16. The responsible commissioner for multiple sclerosis drugs in England is NHS England. [Drug exclusions under Payment by Results 15/16](#).
- Local guidance/ pathways may be needed to help inform management of neuropathic pain and spasticity associated with multiple sclerosis.

### Organ transplantation


This is an area of low financial risk – there are no significant new drugs and a few key drugs have come off patent within the last few years which may still lead to significant cost reductions.

When NICE last assessed this area of practice in 2006 they recommended basiliximab, daclizumab, tacrolimus, mycophenolate mofetil and sirolimus as options for immunosuppressive therapy for kidney transplant in children and young people. Since that time some of the recommended treatments have become available as generic products, the
Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Organ transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE guidance on immunosuppressive therapy for renal transplantation in children and adolescents (review of existing guidance 99)</td>
</tr>
<tr>
<td>• NICE guidance on kidney transplantation (adults) - immunosuppressive therapy (Review of TA 85)</td>
</tr>
<tr>
<td>• NICE guidance on belatacept in treatment of kidney transplantation rejection</td>
</tr>
<tr>
<td>• NICE guidance on everolimus in prevention of kidney transplantation rejection</td>
</tr>
<tr>
<td>• NICE guidance on everolimus in cardiac transplantation rejection, expected date TBC</td>
</tr>
<tr>
<td>• NICE guidance on everolimus for the prevention of organ rejection in allogeneic liver transplantation, published Jul 2015</td>
</tr>
</tbody>
</table>

**Actions/ issues which may be considered by commissioners and providers**

- **NHS England** announced that from April 2014 it is expected that all post-transplant immunosuppressants will be commissioned directly from trusts; patients receiving these treatments via GPs in primary care should be repatriated to secondary care. However with problems ensuring continuity of homecare services this timescale may slip.
<table>
<thead>
<tr>
<th>Malignant disease</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Malignant disease</strong></td>
<td>The Cancer Drugs Fund (or Interim predecessor) has now been in place for over 4 years in England. Originally a figure of £200m per year was made available to fund cancer medicines which were not routinely available on the NHS – this equates to a sum of around £400,000 per 100,000 population (actually £320,000 per 100,000 population once the VAT has been excluded). Although this figure was increased to £280m there has been a significant delisting of products during 2015/16 to mitigate against a projected overspend. As a consequence there has been a major revision of evidence to support the drugs currently funded to ensure that ongoing funding is justified and NHS England will work more closely with NICE to align their assessment processes moving forward into 2016/17.</td>
</tr>
</tbody>
</table>

| **Breast cancer** | This is an area of low financial risk as the only outstanding decisions from NICE have been funded via the CDF for the last year. |

| NICE pathway for advanced breast cancer | This is unlikely to have a significant financial impact |

| NICE pathway for early and locally advanced breast cancer | Progress with this guidance has been delayed because NICE estimate that this medicine would not be cost effective even if it had zero cost. They estimate the incremental £ per QALY gained to exceed £125,000 and the manufacturer has stated that it is not possible to set a price that meets current acceptability criteria for cost effectiveness. In the meantime pertuzumab is currently available via the CDF for first-line treatment of locally advanced or metastatic breast cancer patients provided certain additional criteria are met. |

| NICE Quality Standard for breast cancer, published Sep 2011 | NICE estimate that the annual incidence of women presenting with advanced breast cancer in England is 11,384 (2013 presenting at that stage and 9371 presenting following disease progression) – this equates to an incidence of 21 cases per 100,000 population. If we assume that 70% are eligible for chemotherapy and that 25% are HER2 positive and would receive a trastuzumab-based regimen this would equate to about 4 patients per 100,000 population per year. If 50% of these received pertuzumab then potentially an uptake of 2 patients per 100,000 is feasible. |

| Revised Quality Standard for breast cancer expected Jun 2016 | If 50% of these received pertuzumab then potentially an uptake of 2 patients per 100,000 is feasible. If we assume that the treatment costs £2400 per cycle, and that patients get treated for 18 months, then this drug could increase drug budgets by £125,000 per 100,000 population. There is likely to also be prolonged use of trastuzumab because of the extended duration of disease-free progression which could add an additional £12,000 per patient, to give an overall incremental cost of £137,000 per 100,000 population. There will also be service implications associated with giving an additional infusion every 3 weeks. |

| NICE guidance on pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer, which has not been previously treated, or has relapsed after adjuvant therapy – expected date TBC | Draft Guidance from NICE outlined in a FAD indicates that they do not recommend the use of trastuzumab emtansine within its marketing authorisation. This decision was based on evidence showing that although the drug was associated with a 3.2 month increase in PFS, a 5.8 month increase in OS and some evidence of improvement in QoL it was unlikely represent a cost effective use of NHS resources. |

| NICE guidance on trastuzumab emtansine for treating unresectable metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane – expected date TBC | This provisional advice was appealed against on the basis that NICE did not take the 2014 PPRS agreement into account when estimating incremental cost effectiveness. NICE recently published a statement outlining their reasoning on why |
### Breast cancer cont’d

- NICE guidance on trastuzumab emtansine for treating unresectable metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane, cont’d

- NHS England support use of subcutaneous trastuzumab – issued Sept 2013

- PPRS should not be taken into account and cost-effectiveness analyses should be based on list prices or prices available via approved PAS schemes. Now that this decision has been published it is not clear when NICE will publish their final guidance on trastuzumab emtansine. Trastuzumab emtansine remains available via the CDF provided certain criteria are met. Based on the assumptions outlined above – if we assume that 3 patients per 100,000 population receive trastuzumab for metastatic or recurrent breast cancer and that 1.5 progress and are eligible for consideration for trastuzumab emtansine at a cost of £90,000 per treatment course, this would equate to an additional expenditure of £135,000 per 100,000 population.

- NHS England supports the use of subcutaneous trastuzumab as a means of improving patient experience and reducing waste and overall drug costs. The SMC accepted the findings of a manufacturer-authored cost minimisation analysis which estimated that for the overall analysis (medicine and non-medicine costs) there were cost savings per early breast cancer patient of £3,454 over a full 1-year treatment, and for metastatic breast cancer patients of £3,162 over a full 1-year treatment. If restrict analysis to medicine costs only, the cost savings per patient per year are £1,441 and £1,239 for EBC and MBC respectively. These results may no longer be valid once we have access to biosimilar versions of trastuzumab – when decreases of over 25% of list price of branded product may be anticipated, however a biosimilar version of trastuzumab is not anticipated in the next 18 months.

### Gastrointestinal (GI) cancer

#### Colorectal/ anal cancer

- NICE colorectal cancer quality standard – issued Aug 2012

- NICE guidance on cetuximab (review of TA176) and panitumumab (partial review of TA240) for the first line treatment of metastatic colorectal cancer – expected Apr 2016

- This is an area of low financial risk

- NICE currently support the use of cetuximab in combination with FOLFIRI or FOLFOX as a first-line treatment in patients whose primary tumour has been resected or is potentially operable and whose metastatic disease is confined to the liver and is currently unresectable but the patient is fit enough to undergo surgery should the tumour become resectable. NICE were unable to recommend panitumumab for this indication previously as the manufacturer did not provide an evidence submission. In this review NICE are restricting the evaluation to safety and efficacy in patients with wild-type KRAS status. In draft guidance outlined in the ACD NICE do not support the use of either cetuximab or panitumumab in this population.

- Cetuximab and panitumumab are currently available via the CDF for patients who do not meet NICE criteria for 1st line therapy provided they have wild-type KRAS. This guidance is therefore not expected to impact significantly in the next financial year and may reduce costs if this advice remains unchanged and they are removed from the CDF.
<table>
<thead>
<tr>
<th>Disease or Indication:</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI cancer cont’d</td>
<td>This drug was launched in the UK in 2013 but NICE has terminated the appraisal and is therefore unable to make a recommendation as the manufacturer is unable to provide an evidence base which compares regorafenib with existing clinical practice in the UK. The drug is not currently available via the CDF for this indication.</td>
</tr>
<tr>
<td>Colorectal/ anal cancer cont’d</td>
<td>This update was restricted to a review of the evidence to support stents to reduce GI obstruction and the management of early rectal cancer and is therefore not expected to impact significantly on drugs budgets</td>
</tr>
<tr>
<td>- NICE guidance on regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease - terminated Feb 2015</td>
<td><strong>NICE</strong> has recommended the My5-FU assay only for use in research for guiding changes to the 5-FU dose given during chemotherapy. <strong>NICE</strong> recommends that more evidence on its use in NHS clinical practice is needed</td>
</tr>
<tr>
<td>- Update on NICE Clinical guideline on colorectal cancer – issued Dec 2014.</td>
<td><strong>NICE</strong> do not support the use of paclitaxel as albumin-bound particles in combination with gemcitabine for this indication. This recommendation seems to be based on findings that this formulation of paclitaxel plus gemcitabine was less effective than FOLFIRINOX and similarly effective to capcitabine plus gemcitabine but potentially less well tolerated. The calculated ICER over gemcitabine alone was estimated to be between £72,500 and £78,500. Albumin-bound paclitaxel was removed from the CDF for the first-line treatment of pancreatic cancer in November 2015.</td>
</tr>
<tr>
<td>- NICE guidance on fluorouracil plasma monitoring: the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion issued Dec 2014</td>
<td>This drug has not yet been submitted for license despite the key Phase III trial being completed over two years ago and showing a 12% difference in overall rate at 12 months when given in combination with gemcitabine versus gemcitabine alone (but not a significant difference in median overall survival). It is therefore unlikely to impact in the next financial year.</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>NICE do not support the use of paclitaxel as albumin-bound particles in combination with gemcitabine for this indication. This recommendation seems to be based on findings that this formulation of paclitaxel plus gemcitabine was less effective than FOLFIRINOX and similarly effective to capcitabine plus gemcitabine but potentially less well tolerated. The calculated ICER over gemcitabine alone was estimated to be between £72,500 and £78,500. Albumin-bound paclitaxel was removed from the CDF for the first-line treatment of pancreatic cancer in November 2015.</td>
</tr>
<tr>
<td>- NICE pathway for pancreatic cancer</td>
<td>This drug has not yet been submitted for license despite the key Phase III trial being completed over two years ago and showing a 12% difference in overall rate at 12 months when given in combination with gemcitabine versus gemcitabine alone (but not a significant difference in median overall survival). It is therefore unlikely to impact in the next financial year.</td>
</tr>
<tr>
<td>- NICE guidance on paclitaxel as albumin-bound nanoparticles in combination with gemcitabine for previously untreated metastatic pancreatic cancer issued Oct 2015</td>
<td>This drug has not yet been submitted for license despite the key Phase III trial being completed over two years ago and showing a 12% difference in overall rate at 12 months when given in combination with gemcitabine versus gemcitabine alone (but not a significant difference in median overall survival). It is therefore unlikely to impact in the next financial year.</td>
</tr>
<tr>
<td>- NICE guidance on nimotuzumab for the first line treatment of metastatic pancreatic cancer expected date TBC</td>
<td>NICE support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
<tr>
<td>- NICE guidance on liposomal cisplatin in combination with gemcitabine for untreated locally advanced or metastatic pancreatic cancer expected date TBC</td>
<td><strong>NICE</strong> support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumours (GIST)</td>
<td><strong>NICE</strong> support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
<tr>
<td>NICE pathway for GIST available</td>
<td><strong>NICE</strong> support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
<tr>
<td>- NICE Quality Standard for sarcoma published Jan 2015</td>
<td><strong>NICE</strong> support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
<tr>
<td>- NICE guidance on imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196) issued Nov 2014</td>
<td><strong>NICE</strong> support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.</td>
</tr>
</tbody>
</table>
**Disease or Indication:** National targets and guidance

<table>
<thead>
<tr>
<th>GI cancer cont’d</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oesophageal cancer</strong></td>
<td>This is unlikely to impact significantly in the next 18 months</td>
</tr>
<tr>
<td>• NICE guideline on <a href="#">oesophago-gastric cancer</a> expected Jan 2018</td>
<td>Ramucirumab in combination with paclitaxel is licensed for the treatment of adult patients with advanced gastric cancer or gastro–oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy and as a monotherapy for the patients in whom treatment in combination with paclitaxel is not appropriate. Within the <strong>ACD</strong> provisional guidance from NICE indicates that they do not support its use within these indications. This decision seems to reflect evidence that although ramucirumab prolongs median overall survival in two trials (by 1.4 and 2.3 months respectively) the calculated ICER is over £400,000 per QALY gained when used in combination with paclitaxel and over £180,000 when used as a monotherapy. It is estimated that to treat a patient with 7 cycles of ramucirumab costs about £42,000. NICE state that there are around 4000 deaths from gastric cancer every year in England – if we assume that 20% of these patients might have been considered suitable for ramucirumab then this would increase costs by £33.6m which equates to about £64,600 per 100,000 population. However at this estimated level of cost effectiveness it seems unlikely that NICE will approve this medicine.</td>
</tr>
<tr>
<td><strong>Stomach cancer</strong></td>
<td></td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma after chemotherapy</a> expected Jan 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Haematological cancers</strong></td>
<td>This is an area of moderate to high financial risk</td>
</tr>
<tr>
<td>• NICE guideline on <a href="#">improving outcomes in haematological cancers</a> update expected May 2016</td>
<td>This update will not revisit current recommendations on treatments for specific types of haematological cancer, management of complications of chemotherapy or high-dose treatment and when the revised Guideline is published these sections of the existing guideline will be removed.</td>
</tr>
<tr>
<td><strong>Chronic myeloid leukaemia</strong></td>
<td></td>
</tr>
<tr>
<td>No new guidance available or in progress</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic lymphocytic leukaemia</strong></td>
<td></td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia</a> issued Jun 2015</td>
<td><strong>NICE</strong> support the use of obinutuzumab in combination with chlorambucil for adults with untreated chronic lymphocytic leukaemia who have comorbidities that make full-dose fludarabine-based therapy unsuitable for them but only if bendamustine is unsuitable and the company provides obinutuzumab with the discount agreed in the PAS. Within the costing statement <strong>NICE</strong> estimate that 550 patients in England will be eligible to receive either this treatment or ofatumumab (as outlined below) within 5 years and that it will cost £6.8m in England – this equates to about £14,000 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on <a href="#">ofatumumab for treating previously untreated chronic lymphocytic leukaemia</a> issued Jun 2015</td>
<td><strong>NICE</strong> support the use of ofatumumab in combination with chlorambucil as an option for untreated chronic lymphocytic leukaemia only if the person is ineligible for fludarabine-based therapy and bendamustine is not suitable and the company provides ofatumumab with the discount agreed in the PAS. The cost impact is outlined above for obinutuzumab which is approved for use in the same patient cohort.</td>
</tr>
</tbody>
</table>
### Haematological cancers cont’d

#### Chronic lymphocytic leukaemia cont’d
- NICE guidance on *ofatumumab for maintenance treatment of relapsed chronic lymphocytic leukaemia* expected Sep 2016
- NICE guidance on *idelalisib for treating chronic lymphocytic leukaemia* issued Oct 2015
- NICE guidance on *ibrutinib for treating chronic lymphocytic leukaemia* expected Jun 2016

#### Multiple myeloma
- NICE guideline on *diagnosis and management of myeloma* expected Feb 2016
- NICE guidance on *lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib (part-review of TA171)* currently suspended

---

Ofatumumab may get licensed for this indication in mid-2016. Interim results of a phase III study indicate that when given as an 8 weekly treatment to patients that responded to treatment after relapse it prolonged progression free survival compared to patients that were randomised to observation only (28.6 months vs 15.2 months). NICE estimate that there are around 1140 patients with CLL that relapse and receive treatment each year. If we assume that 30% of these were to receive 10 cycles of ofatumumab costing £38,000 that would increase costs by around £13m which equates to £25,000 per 100,000 population.

NICE support the use of idelalisib in combination with rituximab in adults with untreated CLL and a 17p deletion or TP53 mutation and in adults when the disease has been treated but has relapsed within 24 months. The product is actually licensed for use in untreated adults who meet the criteria above and adults who have received at least one prior therapy, so the proposed approval criteria are a restricted subgroup.

NICE state that there are around 1325 patients that present each year in England with newly diagnosed CLL that are suitable for treatment. If we assume that 7% of the patients that present have the genetic mutations that merit treatment with this drug and that 1100 patients also present with recurrent disease in any year of whom 20% might be considered for this treatment then 340 patients per year might be expected to be treated with this drug. Again if we assume that the average patient with newly diagnosed disease remains on treatment for 3 years and the average patient with recurrent disease remains on treatment for 18 months then expenditure would increase from about £12.9m (or £25,000 per 100,000 population) to £26.7m (or £49,500 per 100,000 population). This is substantially higher than the SMC estimate which ranges from £6300 in Year 1 to £19,000 in Year 5 but do not provide any insight into the assumptions made to derive that figure. Over the first 3 months that this drug was available on the CDF in England there were an average of 60 applications per month across England although that may reflect a backlog of eligible patients awaiting availability. NICE has not provided any indicative cost estimates as this drug is commissioned by NHS England and there is a PAS in place which remains commercial in confidence. This remains available via the CDF route until it moves to baseline funding.

Ibrutinib is licensed for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy i.e. the same patient cohort as idelalisib (discussed above). Therefore this medicine is likely to compete with idelalisib and the overall cost implications will be reflected in the figure estimated above. This is currently available via CDF route.

The draft guideline does not revisit existing NICE guidance on specific treatments for myeloma and therefore it seems unlikely that there will be any significant cost implications from a medicines perspective.

In current guidance described in TA171 NICE support the use of lenalidomide as an option in patients who have received two or more prior therapies. In this ACD the preliminary advice from NICE is that this should not be extended to patients who have received one prior treatment with bortezomib and for whom thalidomide is not appropriate. However NICE has suspended the appraisal to give the manufacturers an opportunity to submit additional evidence. This indication for lenalidomide has been funded via the CDF, but this indication has now been removed in Nov 2015.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>
| **Haematological cancers cont’d**  
**Multiple myeloma**  
- NICE guidance on *panobinostat for treating multiple myeloma in people who have received at least one prior therapy* expected Jan 2016  
- NICE guidance on *lenalidomide for the treatment of newly diagnosed multiple myeloma* currently suspended  
- NICE guidance on *pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib* issued Mar 2015  
- NICE guidance on *carfilzomib for treating multiple myeloma in people who have received at least 1 prior therapy* expected Sept 2016  
Draft guidance from NICE outlined in the ACD indicates that panobinostat in combination with bortezomib and dexamethasone is not supported for use in treating multiple myeloma, that is, for ‘adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent. This guidance reflects the actual licensed indication which differs from the title of the TA itself. The decision seems to be primarily based on concerns that NICE could not adequately determine the clinical and cost effectiveness against alternative regimens used to treat patients that have received at least two prior lines of therapy.

This drug is licensed and is expected to be launched in the latter part of 2015. In trials it has been tested in combination with bortezomib and dexamethasone in patients with relapsed or refractory MM. In the PANORAMA study it is reported that median progression-free survival was significantly longer in the panobinostat group than in the placebo group (11.9 months vs 8.08 months). It is likely that if eventually approved this intervention would compete with lenalidomide which is already approved by NICE for use in this patient cohort and it is might be considered unlikely that it would be approved if it proves to be significantly more expensive than the capped course of lenalidomide.

In this TA, NICE will assess the use of lenalidomide instead of a thalidomide or bortezomib-based regimen in the first-line treatment setting. The cost implications in this setting are probably insignificant as it involves relatively small numbers of patients (maybe 1 per 100,000 population) treated for short periods of time and if used lenalidomide would be displacing similarly costly medicines. At present work is suspended because the manufacturer has requested that a PAS needs to be agreed with the DH in advance of making an evidence submission to NICE. As work has not commenced on this, it is unlikely to impact significantly in the next financial year.

NICE do not support the use of pomalidomide for this indication and as such this guidance is unlikely to have any significant cost implications. This drug has been available via the CDF for this indication but has been removed in Nov 2015.

Carfilzomib has recently received approval for use in combination with lenalidomide and dexamethasone to treat adults with multiple myeloma who have received at least one prior therapy and is expected to be launched before the end of 2015. At present the therapies approved for use by NICE after one prior therapy is bortezomib or thalidomide, and lenalidomide is approved for use in patients that have received 2 or more previous lines of treatment. The efficacy of carfilzomib was demonstrated in a Phase III study involving 792 patients with relapsed multiple myeloma who were randomly assigned to receive carfilzomib combined with lenalidomide and dexamethasone or lenalidomide and dexamethasone. The study found that patients who received the carfilzomib combination had an average increase of 8.7 months during which their disease did not progress compared with lenalidomide and dexamethasone (26.3 months versus 17.6 months). Given previous decisions in this area it seems likely that NICE will restrict assessment to comparing clinical and cost effectiveness of the combination of carfilzomib and lenalidomide with lenalidomide monotherapy in patients that have received at least two prior lines of treatment.

When NICE approved lenalidomide in this patient group it was estimated that there were around 650 patients that would qualify for treatment and that the average patient would remain on treatment for almost 14 months and that 17% would qualify for free lenalidomide after 2 years. If we assume that the current lenalidomide PAS scheme remains in place but the percentage of patients taking the combination means that the average patient remains on treatment for two years at an additional cost of £40,000 and that carfilzomib is costs £6000 per cycle and is taken for 25 cycles – this would increase the treatment cost per patient treated by £190,000. If we assume that 500 patients receive this treatment that would equate to a total cost of £95m or £180,000 per 100,000 population.
### Myelodysplastic syndrome

- NICE guidance on lenalidomide for the treatment of myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality – issued Sep 2014.

NICE support the use of lenalidomide as an option for treating transfusion-dependent anaemia caused by low or intermediate-1 risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate, with the proviso that the manufacturer provides the drug free of charge to patients that have been taking it for more than 26 cycles. This indication for lenalidomide is currently funded via the CDF.

NICE estimate that there are around 200 patients per year that meet suggested criteria for receiving this medicine and that it will cost £5.6m in Year 1 decreasing to £3m in Year 2 to implement. – this equates to £10,600 per 100,000 population in Year 1 dropping to £5600 in Year 2. NICE do not provide any insight into how these estimates were derived.

Previous estimates in this resource were based on an estimated incidence of 1993 patients developing MDS each year and that the 5q cytogenetic abnormality occurs in between 16 and 28%. If we assume that 22% of patients have the cytogenetic abnormality, 50% are transfusion dependent and 50% of those receive treatment with lenalidomide (costing £48,000/year), and that they typically receive treatment for 2 years, then potentially there could be 110 patients receiving treatment. This equates to an expenditure of about £20,000 per 100,000 population.

### Non-Hodgkin’s lymphoma (NHL) and other lymphomas

- NICE guideline on diagnosis and management of non-Hodgkin’s lymphoma – expected August 2016

This is an area of high financial risk

This guideline will cover a wide-range of issues including the following – but is unlikely to impact significantly in terms of costs in the next financial year.

- The most effective first-line treatment for early-stage follicular lymphoma.
- The role of autologous and allogeneic transplantation in people with follicular lymphoma.
- The role of immediate compared with deferred chemotherapy (watch and wait) in treating advanced asymptomatic follicular lymphoma.
- The most effective first-line treatment for people with MALT lymphoma, including the role of antibiotic therapy, radiotherapy and chemo-immunotherapy.
- The most effective first-line treatment for people with mantle cell lymphoma, including the choice of first-line treatment, the role of consolidation of high-dose therapy with stem cell support and the role of maintenance treatment.
- The most effective first-line treatment for peripheral T-cell lymphoma.
- The most effective first-line treatment for Burkitt’s lymphoma.
- The initial treatment of composite/discordant and transformed follicular lymphoma.
- The most appropriate salvage strategies, including indication for autologous and allogeneic transplantation, for people with diffuse large B-cell lymphoma.
- Indications and methods for central nervous system prophylaxis for people with diffuse large B-cell lymphoma.
### NHL and other lymphomas cont’d

- **NICE guidance on bendamustine in combination with rituximab for the first-line treatment of advanced indolent non-Hodgkin’s lymphoma** - issue date TBC

- **NICE guidance on bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma** currently suspended

- **NICE guidance on lenalidomide for treating relapsed or refractory mantle cell lymphoma** expected Jun 2016

- **NICE guidance on ibrutinib for treating relapsed or refractory mantle cell lymphoma** expected Dec 2016

### Epidemiology, potential financial implications for a population of 100,000 and other comments

It is expected that bendamustine will be licensed for this indication in the near future. Data from an RCT suggest that the combination is associated with a 20-month prolongation of PFS compared with the current standard of treatment R-CHOP. When NICE evaluated maintenance rituximab they estimated that around 1000 cases of NHL per year might be considered for chemotherapy of whom 73% might be suitable. If we assume that 90% of these patients would now be considered suitable for the addition of bendamustine and that the regimen (bendamustine plus rituximab) is £5000 more expensive than existing regimens – then this regimen would increase treatment costs by £6,600 per 100,000 population. It is not clear if adoption would lead to a reduction in the use of maintenance rituximab. Bendamustine is currently available via the CDF for this indication.

There has been no progress with this appraisal since 2013 and therefore it seems unlikely it will impact significantly in the next financial year. In the scope NICE estimate that there are around 670 new cases of mantle cell lymphoma diagnosed each year in England and Wales. In a Phase 3 comparative study this combination was shown to be associated with a 38 month improvement in median PFS compared with the current standard of treatment R-CHOP (69.5 versus 31.2 months). If we assume that 90% of these patients receive chemotherapy and that 90% receive this regimen and it costs £5000 more than R-CHOP – then this regimen could increase costs by £4800 per 100,000 population. This drug is currently available via the CDF for this indication.

Lenalidomide was filed for use in patients with relapsed or refractory MCL after prior therapy that included bortezomib and chemotherapy/rituximab in late 2014 and might be expected to be licensed in late 2015/ early 2016. A, phase II randomized trial compared lenalidomide with investigators’ choice (IC) in patients with relapsed/refractory (MCL) (MCL-002 SPRINT) has been presented at conference. 250 patients were randomized 2:1 to receive either lenalidomide (n=170) or single agent cytarabine, rituximab, gemcitabine, fluorarabine or chlorambucil (n=84). The study demonstrated a statistically significant reduction in the risk of disease progression or death for lenalidomide over investigator’s choice in patients with relapsed/refractory MCL. At a median follow-up of 15.9 months, median PFS, the primary endpoint of the study, was 8.7 months for patients receiving lenalidomide vs. 5.2 months for IC. Median overall survival for patients receiving lenalidomide was 27.8 months vs 21.2 months.

If it is assumed that 500 patients present each year with relapsed disease and that 70% of them are eligible for lenalidomide and take it for 8 cycles at a cost of £4000 more per cycle than alternative treatments then this would increase costs by £11.2m which equates to a cost of about £21,500 per 100,000 population.

The appraisal is scheduled to begin in April 2016 when the results of a Phase III trial become available (a head-to-head comparison with temsirolimus). This product was licensed and marketed for this indication in late 2014 and has is available via the CDF for patients who have received at least one but no more than five previous lines of treatment. A Phase II study indicates that treatment is associated with a median progression-free response duration of 13.9 months. If we assume that the population is as described above for lenalidomide and the average patient receives treatment for 12 months costing £75,000 per year this would increase costs by £26.25m which equates to a cost of about £50,000 per 100,000 population. It is likely that if approved this medicine would be competing with lenalidomide for the same patient cohort.
### NHL and other lymphomas cont’d
- NICE guidance on bortezomib for untreated mantle cell lymphoma expected Feb 2016
- NICE guidance on idelalisib for treating follicular lymphoma that is refractory to two previous treatments terminated Dec 2014

### Lung cancer
**Non-small cell lung cancer (NSCLC)**
- NICE pathway for lung cancer
- NICE guidance on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175) issue date TBC

### This is an area of moderate financial risk
A review of the existing guidance is underway again after a delay caused by an error in the economic model and NICE deliberations on the relevance of PPRS in the assessment of cost effectiveness. Within existing guidance NICE currently support the use of erlotinib as an alternative to docetaxel in the second line treatment of NSCLC provided the overall treatment cost is the same (however this was published before docetaxel became available as a generic medicine). It is not recommended for use in patients in whom docetaxel is considered unsuitable or as a third-line treatment option. Conversely NICE were unable to support the use of gefitinib as the manufacturer did not provide an evidence submission.

### Disease or Indication: National targets and guidance
### Epidemiology, potential financial implications for a population of 100,000 and other comments
There is no provisional NICE guidance available yet. Bortezomib was launched for use in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation. A Phase III study (n=487) was published showing that VR-CAP (R-CHOP regimen, but replacing vincristine with bortezomib was more effective than R-CHOP in patients with newly diagnosed mantle cell lymphoma who were ineligible or not considered for stem-cell transplantation (median PFS: 24.7 vs. 14.4 months.

The SMC accepted that this license extension represented a cost-effective use of NHS resources. They estimated that there were 28 patients per year eligible for this treatment in Scotland and that 75% might receive it. If these figures are extrapolated to England then we might expect around 200 patients per year to receive this treatment and the SMC estimate this would increase medicines costs by around £3.7m taking the cost of drugs displaced into account. This equates to a figure of around £7000 per 100,000 population.

The SMC approved this drug for use in adult patients with relapsed or refractory CD30+ Hodgkin lymphoma following autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. The former group was approved on the basis of an open-label, single arm Phase II study indicating an objective response rate of 75% and a median duration of response of 6.7 months. The latter group was on the basis of case reports. This decision was made using the SMC framework for assessment of ultra-orphan medicines. The SMC estimate that based on trial evidence the median number of cycles received per patient is about 9 and it costs £7500 per cycle – this equates to a treatment cost of £67,500 per patient. They also accept that there about 8 patients per year in Scotland that would be eligible for treatment and that 80% of these would receive treatment. This equates to 0.12 patient per 100,000 population and an additional cost of around £8000 per 100,000 population. This medicine is available through the CDF.

This guidance was terminated by NICE as they did not receive a submission from the manufacturer. As such it means there is unlikely to be any cost implications within the next financial year.

There is no provisional NICE guidance available yet. Bortezomib was launched for use in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation. A Phase III study (n=487) was published showing that VR-CAP (R-CHOP regimen, but replacing vincristine with bortezomib was more effective than R-CHOP in patients with newly diagnosed mantle cell lymphoma who were ineligible or not considered for stem-cell transplantation (median PFS: 24.7 vs. 14.4 months.

The SMC accepted that this license extension represented a cost-effective use of NHS resources. They estimated that there were 28 patients per year eligible for this treatment in Scotland and that 75% might receive it. If these figures are extrapolated to England then we might expect around 200 patients per year to receive this treatment and the SMC estimate this would increase medicines costs by around £3.7m taking the cost of drugs displaced into account. This equates to a figure of around £7000 per 100,000 population.
### Lung cancer cont’d

#### NSCLC cont’d

- **NICE guidance on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175), cont’d**

- **NICE guidance on ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer - expected Jan 2016**

- **NICE guidance on nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer** issued Jul 2015

- **NICE guidance on paclitaxel albumin-bound nanoparticles with carboplatin for untreated non-small-cell lung cancer** terminated Oct 2015

- **NICE guidance on ramucirumab for treating metastatic non-small-cell lung cancer after platinum-based chemotherapy** expected Aug 2016

Within the ACD, draft guidance from NICE indicates that this is unlikely to change significantly in that EGFR status is now assessed routinely and if mutation positive a targeted treatment (erlotinib or gefitinib) is given first line. In the revised guidance erlotinib is provisionally recommended as an option for patients that have progressed after non-targetted chemotherapy provided it is now known to be EGFR-TK mutation positive or there is reason to suspect it is. Gefitinib remains unapproved for the treatment of EGFR-TK positive NSCLC that has progressed. This revised guidance is likely to have minimal cost implications.

Ceritinib is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib. At present NICE do not recommend crizotinib for people with a type of advanced non-small-cell lung cancer that is ‘ALK-positive’ and has been treated before but it is available via the CDF. Provisional guidance from NICE within the ACD suggests that NICE are not supportive of making this medicine available as although they accept it was likely to prolong life, it was unclear on the extent of treatment benefit and judged it not to be cost-effective.

It has previously been estimated by LCNDG that around 0.5 cases per 100,000 population might be eligible for crizotinib. If we assume that these patients are accessing that medicine via the CDF and that 60% would be eligible for a 3rd line treatment and that it costs £40,000 per treatment course then this drug could increase costs by around £14,000 per 100,000 population.

NICE support the use of nintedanib in combination with docetaxel as an option for treating locally advanced, metastatic or locally recurrent non-small-cell lung cancer of adenocarcinoma histology that has progressed after first-line chemotherapy but only if the company provides nintedanib with the discount agreed in the patient access scheme.

NICE estimate that there are 600 patients per year that would be eligible for this treatment in England and that expenditure will increase from £0.2m to £2.4m over the course of 4 years (without taking the PAS into account). They do not provide any further details of how this estimate has been derived but if we assume that the average patient receives four cycles this would approximate to about 25 patients receiving treatment in Year 1 rising to about 280 by Year 5. This equates to a cost of between £400 and £4600 per 100,000 population.

NICE is unable to make a recommendation about the use in the NHS of paclitaxel as albumin-bound nanoparticles with carboplatin for adults with untreated non-small-cell lung cancer when potentially curative surgery or radiation therapy or both are unsuitable, because no evidence submission was received from Celgene technology. Therefore this is unlikely to impact significantly in the next financial year.

Ramucirumab has been approved to treat patients with metastatic non-small cell lung cancer in combination with docetaxel in the US but is not expected to be approved in the UK until 2016. A Phase III trial published in the Lancet (n=1253) showed that the combination of ramucirumab and docetaxel was associated with a 1.4 month survival advantage over docetaxel alone (10.5 vs 9.1 months).

In the past NICE has estimated that there are 33,450 new cases of lung cancer diagnosed each year of which about 85% are NSCLC. Of these 25% get first-line chemotherapy and about 30% of these get second-line chemotherapy – If we assume that 50% would be eligible for a course of ramucirumab and it costs £40,000 per treatment course this would equate to about 1000 patients in England or 2 patients per 100,000 population and would increase costs by around £80,000. However with this level of survival gain it would seem unlikely that it would meet NICE thresholds for cost effectiveness unless there is a substantial discount offered within any PAS scheme.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung cancer cont’d</strong></td>
<td>Nivolumab is not yet licensed for the treatment of metastatic non-squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adults and it is not clear when that license is expected. According to the NICE scope it is likely that this agent will be competing with docetaxel for use in this particular patient cohort. However it would be included in the patient cohort calculated above for ramucirumab and it is likely that any cost implications would be included in that figure.</td>
</tr>
<tr>
<td><strong>NSCLC cont’d</strong></td>
<td>Nivolumab (branded as Nivolumab BMS) is licensed for the treatment of locally advanced or metastatic squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adults. Results of a Phase III study published in NEJM in patients with non-small-cell lung cancer (n=272) and randomised to receive nivolumab two weeks or docetaxel every three weeks show that median overall survival was 9.2 months with nivolumab versus 6.0 months (95% CI, 5.1 to 7.3) with docetaxel. This medicine is likely to compete with nintedanib and ramucirumab in the treatment pathway for patients that have relapsed after first-line chemotherapy and is therefore unlikely to have any significant cost implications over and above those outlined above for ramucirumab.</td>
</tr>
<tr>
<td>• NICE guidance on nivolumab for treating metastatic, non-squamous, non-small-cell lung cancer after chemotherapy expected Sep 2016</td>
<td>This drug has not yet been filed for regulatory approval and is therefore unlikely to impact significantly within the next financial year.</td>
</tr>
<tr>
<td>• NICE guidance on nivolumab for treating metastatic, squamous, non-small-cell lung cancer after chemotherapy expected May 2016</td>
<td></td>
</tr>
<tr>
<td>• NICE guidance on liposomal cisplatin in combination with chemotherapy for treating inoperable advanced non-small cell lung cancer issue date TBC</td>
<td></td>
</tr>
<tr>
<td><strong>Head and neck cancers</strong></td>
<td>The draft guideline is available for consultation and the recommendations made in relation to chemotherapy treatment seem unlikely to carry significant implications in terms of existing clinical practice</td>
</tr>
<tr>
<td>• NICE guideline on upper airways tract cancers: assessment and management of upper airways tract cancers expected Feb 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Skin and connective tissue cancers</strong></td>
<td>This is an area of moderate to high financial risk</td>
</tr>
<tr>
<td>NICE pathway on preventing skin cancer available</td>
<td>NICE has published a clinical guideline on the assessment and management of malignant melanoma. Amongst the medicine-related issues addressed are the following:</td>
</tr>
<tr>
<td>NICE pathway on melanoma available</td>
<td>• The most effective treatment for in-transit melanoma metastases.</td>
</tr>
<tr>
<td>• NICE Quality Standard on skin cancer expected Aug 2016</td>
<td>• The role of systemic anti-cancer therapy in the treatment of metastatic melanoma (for example, dacarbazine and temozolomide).</td>
</tr>
<tr>
<td>• NICE guideline on the assessment and management of melanoma published Jul 2015</td>
<td>• The role of measuring vitamin D levels and of supplementation in people who have been diagnosed with melanoma.</td>
</tr>
<tr>
<td></td>
<td>• The role of imiquimod in the treatment of melanoma.</td>
</tr>
</tbody>
</table>
Skin and connective tissue cancers

- NICE guideline on the assessment and management of melanoma published Jul 2015
- NICE guidance on dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma published Oct 2014
- NICE guidance on dabrafenib and trametinib for treating advanced unresectable or metastatic BRAFV600 mutation-positive melanoma expected Aug 2016
- NICE guidance on ipilimumab for the adjuvant treatment of completely resected high risk stage III or IV melanoma issue date TBC
- NICE guidance on pembrolizumab for treating advanced melanoma after disease progression with ipilimumab issued Oct 2015

The guideline does not revisit existing or upcoming TAs relating to specific treatments for melanoma nor does it address immunotherapy.

NICE support the use of dabrafenib as an option for the treatment of unresectable or metastatic BRAF V600 mutation-positive melanoma provided the manufacturer make the drug available with the discount agreed in the patient access scheme. In the costing statement NICE state that they expect about 100 patients (ie about 0.2 per 100,000 population) to be considered eligible for this drug but overall it might be considered cost neutral as dabrafenib will be competing with the similarly priced vemurafenib (which was approved by NICE in Dec 2012).

Trametinib is licensed for use as monotherapy or in combination with dabrafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation. A phase III study comparing dabrafenib plus trametinib with dabrafenib monotherapy published in the Lancet showed that median overall survival was 25.1 months in the dabrafenib and trametinib group versus 19.7 months in the dabrafenib only group. Overall survival was 74% at 1 year and 51% at 2 years in the dabrafenib and trametinib group versus 68% and 42%, respectively, in the dabrafenib only group. Median progression-free survival was 11.0 months in the dabrafenib and trametinib group and 8.8 months in the dabrafenib only group. If we assume that an average treatment course of trametinib costs £30,000 and that it is added to the 90% of the patients NICE estimate would be eligible for dabrafenib monotherapy this would increase costs by about £5200 per 100,000 population.

Data have been presented at conference showing that ipilimumab [10 mg/kg (n=475)] significantly improved recurrence-free survival vs. placebo (n=476) for patients with stage 3 melanoma who are at high risk of recurrence following complete surgical resection. At three years, an estimated 46.5% of patients treated with ipilimumab were free of disease recurrence compared to an estimated 34.8% of patients on placebo. The median RFS was 26.1 months for ipilimumab vs. 17.1 months for placebo, with a median follow-up of 2.7 years. The manufacturer has not yet applied for license so this is unlikely to impact in the next financial year. NICE will confirm appraisal dates once regulatory timelines are known. However NICE estimate that there are 10,600 people diagnosed with malignant melanoma in England every year – if we assume that 10% of them receive an adjuvant course of ipilimumab costing £50,000 this would increase costs by £53m which equates to about £102,000 per 100,000 population

NICE support the use of pembrolizumab as an option for treating advanced (unresectable or metastatic) melanoma in adults only:after the disease has progressed with ipilimumab and, for BRAF V600 mutation-positive disease, a BRAF (vemurafenib or dabrafenib) or MEK inhibitor (trametinib) and provided the company provides pembrolizumab with the discount agreed in the PAS. NICE has not publically quantified the cost impact of this guidance as the PAS scheme is commercial in confidence. If we assume there are 700 patients per year that are treated with a first-line/second-line agents as described and that 40% of them go on to become eligible for treatment with pembrolizumab at a cost of £30,000 per treatment course this would increase costs by around £16,000 per 100,000 population.
### Skin and connective tissue cancers cont’d

- **NICE guidance on** cobimetinib in combination with vemurafenib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma expected Jun 2016

- **NICE guidance on** nivolumab for treating advanced, unresectable or metastatic melanoma expected May 2016

- **NICE guidance on** nivolumab with ipilimumab for untreated, advanced, unresectable, metastatic melanoma expected Sep 2016

- **NICE guidance on** talimogene laherparepvec for treating metastatic melanoma expected Jul 2016

This medicine has been recommended for approval to be licensed use in combination with vemurafenib for treatment of adults with unresectable or metastatic melanoma with a BRAF V600 mutation and is expected to be launched in early 2016. A Phase III study has shown that the combination is associated with a median progression-free survival of 9.9 months compared with 6.2 months in the control group. The combination of vemurafenib plus cobimetinib will compete with the combination of dabrafenib plus trametinib and therefore the cost implications are likely to be reflected in the estimate provided for trametinib discussed above.

Nivolumab is licensed as monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults. It is currently unclear where this drug will sit in the treatment pathway but is likely to primarily compete with ipilimumab and may therefore be cost neutral. However in Phase III trials it was compared with chemotherapy and if it is used as an additional line of treatment it would perhaps compete with pembrolizumab and again might be cost neutral.

It is not clear when this license extension is expected to be approved. In a Phase III trial comparing nivolumab plus ipilimumab with ipilimumab alone in untreated patients (n=945) with unresectable stage III/IV melanoma. It was reported that patients randomised to receive the combination had a median PFS of 11.5 months compared with 2.9 months for ipilimumab alone. The combination regimen comprised 1 mg/kg of nivolumab plus 3 mg/kg of ipilimumab every 3 weeks for four doses followed by 3 mg/kg of nivolumab every 2 weeks. If we assume that the average course of nivolumab given as part of a combination regimen costs £45,000 and this is additional to the ipilimumab which would have been given already and is NICE approved and that 500 patients per year receive this treatment this would increase costs by £22.5m which equates to about £43,000 per 100,000 population.

Talimogene laherparepvec is an oncolytic immunotherapy designed to selectively replicate in tumour tissue and to initiate a systemic anti-tumour immune response. It is administered by intratumoral injection. The product was filed for licensing in Sept 2014 and assuming no issues are raised may expect to be licensed in late 2015 or early 2016. It has been recommended for approval in the US. In a published comparison with subcut, GMCSF median overall survival was assessed as a secondary outcome and it was shown that it was 23.3 months with talimogene vs 18.9 months with GM-CSF (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; P = .051). There is no insight yet into cost or place in disease pathway but it would seem to be unlikely that it would receive full NICE approval on the strength of the current evidence base available to support it.

### Sarcoma

- **NICE Quality Standard on sarcoma published Jan 2015**

This is not expected to have any significant cost implications.
### Urogenital and renal cancers

**NICE pathway for bladder cancer** available

- NICE Quality Standard on bladder cancer expected Dec 2015
- NICE guidance on axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment published Feb 2015
- NICE guidance on axitinib (review of TA333), everolimus (review of TA219), sorafenib and sunitinib (partial review of TA178) and nivolumab for treating advanced renal cell carcinoma after systemic treatment expected Apr 2017.
- NICE Guideline on the diagnosis and management of bladder cancer published Feb 2015

### This is an area of low financial risk

**NICE** support the use of axitinib as an option for treating adults with advanced renal cell carcinoma after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine, but only if the company provides axitinib with the discount agreed in the patient access scheme. **NICE** estimate that around 1500 people in England will be eligible to receive axitinib as it is the only agent approved for second-line use and that this will increase costs by around £14m. This equates to about 3 patients and a cost of around £27,000 per 100,000 population.

The above recommendation is strictly only applicable to use of axitinib after the use of sunitinib within the terms of product license. This review will seek to revisit all existing guidance on treatment of renal carcinoma after failure of approved first-line treatments. If we assume that this review leads to the approval of an alternative agent to axitinib and this increases the potential patient population by another 500 people this could increase costs by around £4.5m or £6800 per 100,000 population. Everolimus is currently available on the CDF for the treatment of patients for whom axitinib is unsuitable.

This Guideline is currently out for consultation and draft medicine-related recommendation include the following:

- Offer people with suspected bladder cancer a single dose of intravesical mitomycin C given at the same time as transurethral resection of the bladder tumour (TURBT).
- Offer the choice of intravesical BCG (Bacille Calmette-Guérin) or cystectomy to people with high-risk non-muscle-invasive bladder cancer, and base the choice on a full discussion with the person, the clinical nurse specialist and a urologist who performs both intravesical BCG and cystectomy.
- Offer neoadjuvant chemotherapy using a cisplatin combination regimen before radical cystectomy or radical radiotherapy to people with newly diagnosed muscle-invasive urothelial cancer of the bladder for whom cisplatin-based chemotherapy is suitable.
- Offer a choice of cystectomy or chemoradiotherapy to people with muscle-invasive bladder cancer for whom radical therapy is suitable.

**NICE** has identified that the first of these recommendations may represent a significant change in practice and estimate that it affects about 5200 patients per year and adds £80 per patient in terms of drug costs. This equates to £460,000 or less than £1000 per 100,000 population.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovarian cancer</strong></td>
<td>This is an area of moderate financial risk</td>
</tr>
<tr>
<td>- NICE ovarian cancer quality standard – published May 2012</td>
<td></td>
</tr>
<tr>
<td>- NICE pathway for ovarian cancer</td>
<td></td>
</tr>
<tr>
<td>- NICE guidance on topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for advanced ovarian cancer (for recurrent disease only) (Review of TA 91 &amp; TA 222)</td>
<td>This is a review of two TAs – NICE currently support the use of topotecan, pegylated liposomal doxorubicin hydrochloride (PDLH) and paclitaxel, but not the use of trabectedin for the treatment of recurrent advanced disease. They have not considered the merits of the case for use of gemcitabine before. An appeal against the preliminary advice outlined in a FAD which is no longer available on the website has been upheld and the appraisal has been referred back to the appraisal committee. It seems unlikely that any revised guidance that arises from this revision will impact significantly on clinical practice.</td>
</tr>
<tr>
<td>- NICE guidance on olaparib for the maintenance treatment of BRCA 1 or 2 mutated, relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people whose relapsed disease has responded to platinum-based chemotherapy expected Jan 2016</td>
<td>Within the ACD2 NICE are provisionally minded not to recommend olaparib as maintenance treatment for adults with relapsed, platinum-sensitive ovarian, fallopian tube or peritoneal cancer who have BRCA1 or BRCA2 mutations and whose disease has responded to platinum-based chemotherapy, only if they have had 3 or more courses of platinum-based chemotherapy. Also they do not support as maintenance treatment if they have had fewer than 3 previous lines of platinum-based chemotherapy. A study published in The Lancet Oncology (n=162) showed that PFS was significantly longer in the olaparib plus chemotherapy group (median 12.2 months than in the chemotherapy alone especially in patients with BRCA mutations (HR 0.21 p=0.0015). If we assume there are around 300 women per year that are eligible for this treatment (around 15% carry the BRCA mutation and around 4000 women die each year from this form of cancer), that the average patient would take it for 12 months at a cost of £50,000 per year then this would increase costs by around £29,000 per 100,000 population.</td>
</tr>
<tr>
<td>- NICE guidance on bevacizumab for treating relapsed, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer published Aug 2015</td>
<td>NICE terminated this appraisal and are unable to make a recommendation as Roche Pharmaceuticals did not provide an evidence submission for this technology. As such it is unlikely that this will have any cost implications for the NHS and it was removed from the CDF in Mar 2015.</td>
</tr>
<tr>
<td><strong>Bone cancers and metastases</strong></td>
<td>This is an area of low financial risk</td>
</tr>
<tr>
<td>No relevant developments</td>
<td></td>
</tr>
</tbody>
</table>
### Disease or Indication: National targets and guidance

#### Prostate cancer
- NICE prostate cancer quality standard

NICE prostate cancer pathway available

- NICE guidance on abiraterone acetate in combination with prednisolone for the treatment of metastatic, castrate-resistant prostate cancer in people who have not been previously treated with chemotherapy currently suspended

- NICE guidance on Degarelix depot for treating advanced hormone dependent prostate cancer issue date TBC

- NICE guidance on radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases expected Jan 2016

- NICE guidance on Sipuleucel-T for the first line treatment of metastatic hormone relapsed prostate cancer published Feb 2015

### Epidemiology, potential financial implications for a population of 100,000 and other comments

**This is an area of high financial risk**

This appraisal is suspended whilst NICE await a revised submission from the manufacturer which will include an amended patient access scheme. In the FAD NICE do not support the use of abiraterone for this indication primarily on grounds of cost-effectiveness. This drug remains available on the CDF for this indication.

Results of a Phase III study (COU-AA-302) comparing abiraterone plus prednisolone with prednisolone alone have been published in *NEJM*. These indicate that abiraterone is associated with a statistically significant prolongation of PFS (16.5 vs 8.3 months) and also in overall survival (median not reached vs 27.2 months). In this trial patients received a median 15 cycles of abiraterone.

In their costing model for 2nd-line use of abiraterone NICE estimate that there are around 13 patients per 100,000 population that might be considered for first line treatment and of these 7 currently get treated with docetaxel. If we assume that approval of abiraterone would lead to 5 patients per 100,000 receiving it instead of docetaxel at an average cost per patient of £45,000 (ie to take account of cost of docetaxel offset), then this could increase costs by around £225,000 per 100,000 population. In the longer term it is likely that abiraterone will be used in either first-line or second-line setting but in the short-term there will be patients in each group that may receive this form of treatment.

In the ACD2 provisional advice from NICE indicates that they do not recommend the use of degarelix for the treatment of advanced hormone dependent prostate cancer. Previously in the FAD which was withdrawn following appeal NICE indicated that they were supportive of use in adults with spinal metastases who present with signs or symptoms of spinal cord compression. NICE has also stated that it has received additional evidence from the manufacturer which it will now take into consideration. Depending on the outcome of the re-evaluation it is likely that between 500 and 3500 patients will be eligible for Degarelix depot per year. If we assume that the average patient stays on treatment for 6 years and that Degarelix costs £600 more per year than existing treatments then this will increase costs by between £600 and £4200 per 100,000 population in Year 1 rising to between £6,600 and £25,000 per 100,000 at steady state.

In the ACD3 provisional advice from NICE is that they recommend Radium-223 dichloride as an option for treating adults with hormone-relapsed prostate cancer, symptomatic bone metastases and no known visceral metastases but only if they have had treatment with docetaxel and the company provides radium-223 dichloride with the discount agreed in the patient access scheme. NICE state that it costs around £24,000 to treat a patient with a 6-month course of radium-223. NICE estimate that there are around 4 patients per 100,000 population that might be considered eligible for abiraterone in the 2nd-line treatment setting and it would expect an uptake of 3 patients per 100,000 population. If this drug is used instead of abiraterone then it is cost neutral, if however it is used in addition to abiraterone in 50% of eligible patients then it would increase costs by £36,000 per 100,000 population. This medicine has been available via the CDF but this indication is currently subject to appeal outcome from the November delisting process.

This guidance was withdrawn after the product was withdrawn from the market in May 2015. NICE had already stated that this product would not be recommended for use in the NHS
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate cancer cont’d</strong></td>
<td>Enzalutamide will be competing with abiraterone for this indication (which is discussed above) and as the two drugs are similarly priced this guidance is unlikely to have significant cost implications over and above those described above. NICE are currently assessing additional evidence submitted by the manufacturer before progressing to a FAD. Enzalutamide is available via the CDF for this indication.</td>
</tr>
<tr>
<td>• NICE guidance on enzalutamide for treating metastatic hormone-relapsed prostate cancer not previously treated with chemotherapy issue date TBC</td>
<td>When NICE last appraised cabazitaxel for this indication in 2012 they did not support its use. However it is available via the CDF for use in patients who have previously received a docetaxel-based regimen. If we assume that the NICE estimate that 7 patients per 100,000 population receive treatment with docetaxel and that 30% would go on to receive cabazitaxel at a cost of £22,000 per patient treated then this would increase costs by £44,000 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on cabazitaxel for hormone-relapsed metastatic prostate cancer previously treated with a docetaxel-containing regimen (review of TA255) expected May 2016</td>
<td></td>
</tr>
<tr>
<td><strong>Brain cancer</strong></td>
<td>Dinutiximab is licensed for the treatment of high-risk neuroblastoma in patients aged 12 months to 17 years, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and ASCT. It is administered in combination with GM-CSF, interleukin-2 and isotretinoin. Approval was based on demonstration of improved event-free survival (EFS) and overall survival (OS) in a multicentre, open-label, randomised trial in which 226 pts were randomised to receive either the dinutiximab/13-cis-retinoic acid (RA) arm or the RA alone arm. Pts in each arm received six cycles of treatment. EFS was 66% among pts receiving dinutiximab immunotherapy plus isotretinoin vs. 48% in pts receiving isotretinoin alone (p = 0.033) although this difference did not reach formal statistical significance according to the pre-specified plan for interim analyses. The three-year estimates of OS were 80% vs. 67% among pts receiving dinutiximab immunotherapy plus isotretinoin and isotretinoin alone, respectively. The five-year estimates of OS were 74% for dinutiximab immunotherapy compared to 57% for isotretinoin alone. NICE estimate that there are 90 children each year that are diagnosed with neuroblastoma and that 40% of them might be considered high risk. No cost information is available at this stage but it is likely to be very expensive on an individual patient basis. However on an indicative basis even if it was marketed at £200,000 per course and 40 patients per year received treatment – it would increase treatment costs by £10m which equates to ~ £15,400 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on dinutiximab for treating high-risk neuroblastoma expected Apr 2016</td>
<td></td>
</tr>
</tbody>
</table>
## Disease or Indication: 
National targets and guidance

### 9. Nutrition and blood

#### Patent expiries

According to [Prescribing Outlook New Medicines 2015](#), the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: darbepoetin alfa (Jun 2016); agalsidase alfa (Aug 2016); agalsidase beta (Aug 2016); pegfilgrastim (Aug 2017); velaglucerase alfa (Jan 2017); nitisinone (Jun 2017).

#### Anaemia

- NICE clinical guideline on [anaemia management in people with chronic kidney disease (CKD)](#), issued Jun 2015
- NICE guidance on [erythropoiesis-stimulating agents (epoetin and darbepoetin) for cancer-treatment induced anaemia](#), issued Nov 2014

This is an area of low financial risk

This guideline updates and replaces NICE guideline CG114 (published Feb 2011). It offers advice on diagnosing and managing anaemia of chronic kidney disease (CKD). New recommendations have been added on diagnosis and management, including the detection and management of erythropoietic stimulating agents (ESAs)-resistant anaemia. Savings are anticipated nationally because of decreased testing costs, and more accurate diagnosis and treatment of anaemia in people with CKD, avoiding the need for hospital admissions. The guideline might have resource implications at a local level as a result of variation in clinical practice across the country. NHS organisations are advised to assess the resource implications of this guidance locally.

Note: Although NHS England is now the responsible commissioner for erythropoietins in CKD, the guideline’s content will be useful for CCGs and hospital Trusts.

This guidance updates TA 142 (issued 2008). NICE recommends the use of ESAs (epoetin alfa, beta, theta and zeta, and darbepoetin alfa), within their marketing authorisations, as options for treating anaemia in people with cancer who are having chemotherapy. If different ESAs are equally suitable, the product with the lowest acquisition cost for the course of treatment should be used.

Based on the following assumptions, the annual cost associated with implementing this recommendation is estimated as £132,000 for a population of 100,000 (taking into account a potential saving of around £17,000 per 100,000 population as a result of the reduction in blood transfusions and the number of units of blood transfused):

- Current practice assumes an estimated 20% of people who have chemotherapy will have a red blood cell transfusion, around 1% have ESA’s and, in the remaining 79%, the disease can be managed with either chemotherapy dose adjustment or iron supplements.
- Future practice assumes that 50% of people who develop anaemia will have a haemoglobin level of less than 100 g per litre and would have treatment with ESA’s.
- ESA’s reduce the number of blood transfusions needed by 37%
- ESA’s reduce the number of units of blood transfused by 0.87

Data from the [HSCIC](#) show total spend on ESAs across primary and secondary care was approximately £86.4m in 2014-15 (approx £163,000 per 100,000 popn) with darbepoetin accounting for over £50m of that spend – it is not possible to ascertain how much that use is associated with oncology treatment but overall there has not been much increase in overall expenditure seen in the last year.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

### Nutrition
- NICE guideline on [intravenous fluids therapy in children](#), expected Dec 2015
- NICE Pathway available (adults)
- NICE guideline on [assessment for and management of blood transfusion](#), issued Nov 2015

**No significant changes in practice are expected in this area**

The draft guideline includes recommendations about general principles for managing IV fluids in babies born at term, children and young people, and will apply to a range of conditions and different hospital settings. This guidance represents a major opportunity to improve patient safety for children receiving intravenous fluid therapy in hospital.

Key issues addressed include:
- Assessment, monitoring and reassessment of fluid and electrolyte status
- IV fluid therapy for fluid resuscitation; routine maintenance; replacement and redistribution
- Management of hypernatraemia and hyponatraemia that develops during IV fluid administration
- Skills needed for adequate training and education of healthcare professionals

This guidance is not expected to have a significant additional impact on prescribing budgets.

This guideline focuses on the general principles of transfusion and the appropriate use of blood. The detailed management of specific clinical conditions is not considered. The key clinical in terms of medicines include:

The guideline includes recommendations on:
- alternatives to transfusion for patients having surgery (oral and IV iron, recombinant EPO, tranexamic acid as an adjunct to minimise transfusion, cell salvage therapy)
- thresholds, targets and doses for red blood cells, platelets, fresh frozen plasma, cryoprecipitate, and prothrombin complex concentrate
- patient safety
- patient information

NICE do not support the routine use of EPO unless there are religious or other reasons not to have a transfusion but do support the use of iron supplements (oral and parenteral), tranexamic acid and intraoperative cell salvage therapy in specific circumstances.

In terms of costs, NICE estimate that it costs £1.51 to treat a patient with oral iron, £79.70 to treat with intravenous iron (plus a day-care tariff) and between £0.60 and £1.19 to treat a patient with tranexamic acid. However, it is estimated that it costs between £146 and £689 to give a patient a blood transfusion. NICE do not quantify the overall cost impact of implementing this guidance.

### Renal
- NICE Quality Standard on [acute kidney injury](#), issued Dec 2014
- NICE Quality Standard on [renal replacement therapy services](#), issued Nov 2014

This quality standard covers the prevention, detection and management of non-traumatic acute kidney injury up to the point of renal replacement therapy in adults, young people and children older than 1 month. It does not cover the management of acute kidney injury in people with renal transplants or in pregnant women, but does include when to involve nephrology services for people with renal transplants.

This quality standard covers renal replacement therapy services for kidney failure in adults, young people and children.
### Metabolic disorders

<table>
<thead>
<tr>
<th>Disease or Indication:</th>
<th>National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE guidance on elosulfase alfa for mucopolysaccharidosis (type IVA), expected Dec 2015</td>
<td>Preliminary NICE guidance recommends elosulfase alfa within its marketing authorisation, as an option for treating mucopolysaccharidosis type IVA (MPS IVA) only in the context of a managed access agreement, and provided that the company makes elosulfase alfa available with the discount agreed in the patient access scheme.</td>
<td>NICE estimates that the average cost per year for elosulfase alfa is £394,680 per patient (based on the recommended dosage of 2 mg/kg/week and an average body weight of 25.3 kg). The company has proposed a patient access agreement, in which elosulfase alfa would be provided at a discounted cost; the discount is commercial in confidence.</td>
</tr>
<tr>
<td>NICE guidance on eliglustat for Gaucher disease (Type 1), suspended</td>
<td>It is estimated that 88 people are living with mucopolysaccharidosis type IVA (MPS IVA) in England, and about 3 new diagnoses made per year. About 74–77 people are anticipated to be eligible for enzyme replacement therapy and may want treatment with elosulfase alfa. This equates to 0.14 patient per 100,000, costing £56,383 per 100,000 population.</td>
<td>NICE has suspended this Highly Specialised Technology and the topic evaluation will be rescheduled to align with the commercial availability of the product within the UK.</td>
</tr>
</tbody>
</table>

### Actions/issues which may be considered by commissioners and providers

- Drugs used in metabolic disorders are listed as exclusions in the National Tariff for 15/16. Link: [Drug exclusions under Payment by Results 15/16](#). NHS England is the responsible commissioner for these agents.
### 10. Musculoskeletal and joint diseases

#### Patent expiries

According to the CMU, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: etanercept (Jul 15, biosimilar expected Feb 2016)

#### NSAIDs

- QIPP area – NSAIDs

A set of **key therapeutic topics** (KTT) and associated **comparators** have been developed to support NHS England's Medicines Optimisation Measurement work stream. These areas and comparators originally supported the DoH’s QIPP medicines and procurement medicines work stream but have been renamed Medicines Optimisation KTT Comparators. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The following diabetes related comparators have been developed:

The therapeutic area on NSAIDs offers the following options for implementation:

(i) review the appropriateness of NSAID prescribing widely and on a routine basis, especially in people who are at higher risk of both gastrointestinal and cardiovascular morbidity and mortality (for example, older people)

(ii) If an NSAID is needed, use ibuprofen (1200 mg per day or less) or naproxen (1000 mg per day or less).

(iii) Review and, if appropriate, revise prescribing of etoricoxib to ensure it is in line with [MHRA advice](https://www.mhra.gov.uk) and the NICE clinical guideline on [osteoarthritis](https://www.nice.org.uk/guidance/CG172).

(iv) Co-prescribe a proton pump inhibitor with NSAIDs for people with osteoarthritis, rheumatoid arthritis or low back pain (for people over 45 years), in accordance with NICE clinical guidelines.

The following comparators are available for this QIPP area:

- **ADQ/STAR-PU**: the total number of average daily quantities (ADQs) of all NSAIDs prescribed per Specific Therapeutic Group Age-sex weightings Related Prescribing Unit (STAR-PU).

- **Ibuprofen & naproxen % items**: the total number of ibuprofen and naproxen items prescribed as a percentage of the total number of all NSAID prescription items.

An [EU review](https://www.mhra.gov.uk) has confirmed that the cardiovascular risk of high-dose ibuprofen (≥2400mg/day) is similar to COX 2 inhibitors and diclofenac. The MHRA has issued advice to healthcare professionals to help mitigate these risks.

#### Rheumatology

- A list of all NICE guidance relating to rheumatology/musculoskeletal can be found at the NICE [arthritis webpage](https://www.nice.org.uk/guidance).

- **Rheumatoid Arthritis (RA)**

  - **NICE Quality Standard** in RA, issued Aug 2013

  - **NICE pathway** available

  - **Biologics – general**

This is an area of moderate financial risk

This quality standard covers the diagnosis and management of rheumatoid arthritis in adults (16 years and older).

Several biologics are approved for use in RA where:

1. the disease has responded inadequately to conventional DMARDs only, including methotrexate and/or
### Rheumatology

**RA cont'd**

- Biologics – general cont’d

- NICE guidance on the use of [adalimumab](https://www.nice.org.uk/guidance/ta130), [etanercept](https://www.nice.org.uk/guidance/ta186), [infliximab](https://www.nice.org.uk/guidance/ta224), [certolizumab pegol](https://www.nice.org.uk/guidance/ta234), [golimumab](https://www.nice.org.uk/guidance/ta225), [abatacept](https://www.nice.org.uk/guidance/ta247) and [tocilizumab](https://www.nice.org.uk/guidance/ta225) for the treatment of rheumatoid arthritis for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247), expected date TBC.


### Epidemiology, potential financial implications for a population of 100,000 and other comments

2. for the treatment of RA in adults whose RA has responded inadequately to other DMARDs, including a TNF inhibitor - i.e. sequential use, where rituximab is not appropriate – that is response is inadequate, or it is contraindicated/not tolerated

As usage is likely to be a substitution of one agent for another, **it is unlikely that there will be a significant impact on spend in this area** (as long as NICE criteria for initiating and stopping the drug are being adhered to). However, if NICE support earlier use of biologics in RA, there could be some additional cost impact. Organisations should agree which agents will be preferred based on locally negotiated discounts. The service delivery costs of intravenously administered biologics should also be considered along with savings achievable through the use of biosimilars.

This guidance reviews previous sets of guidance in this area. The FAD for this guidance makes the following recommendations:

(i) The agents listed, all in combination with methotrexate, are recommended as options for treating RA only if:
   - disease is severe, that is, a disease activity score (DAS28) greater than 5.1 and
   - disease has not responded to intensive therapy with a combination of conventional DMARDs
   - the companies provide certolizumab pegol, golimumab, abatacept and tocilizumab with the discount agreed in their patient access schemes.

(ii) Adalimumab, etanercept, certolizumab pegol or tocilizumab can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance where the criteria above are met.

(iii) Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy.

(iv) After initial response within 6 months, withdraw treatment if a moderate EULAR response is not maintained.

(v) Start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may need to be varied for some people because of differences in the mode of administration and treatment schedules.

The guidance does not specify when the DAS readings should be taken or how many DMARDs should be tried and for how long (which current existing guidance does).

The FAD is under appeal. The details of the appeal have not been published on NICE website at time of writing, but may relate to use of the biologics in patients not previously treated with DMARDs. If the guidance stays as it is, it is unlikely to have a significant additional cost impact on medicines spend in this area. See also savings from biosimilars section.

This guideline will update the guideline issued in 2009. A draft was issued in September 2015 for consultation and includes two new recommendations on hand exercise programmes for adults with RA. The recommendations on pharmacological management of RA do not appear to have changed in the update.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Juvenile Idiopathic Arthritis (JIA)</strong></td>
<td>This is an area of low financial risk</td>
</tr>
<tr>
<td>- NICE guidance on the use of abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (JIA) (including review of TA35), expected Feb 2016</td>
<td>The FAD for this guidance recommends:</td>
</tr>
<tr>
<td></td>
<td>(i) The agents listed, within their marketing authorisations, as options for treating polyarticular JIA, including polyarticular-onset, polyarticular-course and extended oligoarticular JIA. That is:</td>
</tr>
<tr>
<td></td>
<td>• for abatacept, people 6 years and older whose disease has responded inadequately to other DMARDs, including at least 1 TNF inhibitor</td>
</tr>
<tr>
<td></td>
<td>• for adalimumab, people 2 years and older whose disease has responded inadequately to 1 or more DMARD</td>
</tr>
<tr>
<td></td>
<td>• for etanercept, people 2 years and older whose disease has responded inadequately to, or who are intolerant of, methotrexate</td>
</tr>
<tr>
<td></td>
<td>• for tocilizumab, people 2 years and older whose disease has responded inadequately to previous therapy with methotrexate.</td>
</tr>
<tr>
<td></td>
<td>Abatacept and tocilizumab are recommended only if the companies provide them with the discounts agreed in the patient access schemes for these technologies.</td>
</tr>
<tr>
<td></td>
<td>(ii) Adalimumab and etanercept are recommended, within their marketing authorisations, as options for treating enthesitis-related JIA, that is, for people 6 years and older (adalimumab) and 12 years and older (etanercept) whose disease has responded inadequately to, or who are intolerant of, conventional therapy.</td>
</tr>
<tr>
<td></td>
<td>(iii) Etanercept is recommended, within its marketing authorisation, as an option for treating psoriatic JIA, that is, in people aged 12 years and over whose disease has responded inadequately to, or who are intolerant of, methotrexate.</td>
</tr>
<tr>
<td></td>
<td>(iv) When more than 1 technology is suitable (taking into account extraarticular manifestations) treatment should be started with the least expensive technology, taking into account administration costs, the dose needed and the product cost per dose.</td>
</tr>
<tr>
<td></td>
<td>As this is a review of previous guidance and the newer agents are already being used in practice to treat JIA, it is unlikely that this guidance will have a significant impact on medicines spend in this area. However, as the responsible commissioner for these agents changes from NHSE to CCG for patients with JIA transferring from child to adult services, CCGs will need to ensure there are locally agreed pathways in place to manage this transition.</td>
</tr>
<tr>
<td></td>
<td>This Quality Standard has been referred to NICE and is at an early stage of development.</td>
</tr>
<tr>
<td></td>
<td>The FAD for this guidance makes the following recommendations:</td>
</tr>
<tr>
<td></td>
<td>(i) Adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are recommended, within their marketing authorisations, as options for treating severe active AS in adults whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs. Infliximab is recommended only if treatment is started with the least expensive infliximab product. People currently receiving infliximab should be able to continue treatment with the same infliximab product until they and their NHS clinician consider it appropriate to stop.</td>
</tr>
<tr>
<td></td>
<td>(ii) Adalimumab, certolizumab pegol and etanercept are recommended, within their marketing authorisations, as options for treating severe non-radiographic axial spondyloarthritis in adults whose disease has responded inadequately to, or who cannot tolerate, NSAIDs.</td>
</tr>
<tr>
<td><strong>Ankylosing spondylitis (AS)</strong></td>
<td>This Quality Standard has been referred to NICE and is at an early stage of development.</td>
</tr>
<tr>
<td>- NICE Quality Standard on seronegative arthropathies, expected date TBC</td>
<td>The FAD for this guidance makes the following recommendations:</td>
</tr>
<tr>
<td>- NICE guidance on TNF-alpha inhibitors for AS and non-radiographic axial spondyloarthritis (including review of previous guidance - TA143 and TA233), expected date TBC</td>
<td>(i) Adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are recommended, within their marketing authorisations, as options for treating severe active AS in adults whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs. Infliximab is recommended only if treatment is started with the least expensive infliximab product. People currently receiving infliximab should be able to continue treatment with the same infliximab product until they and their NHS clinician consider it appropriate to stop.</td>
</tr>
<tr>
<td></td>
<td>(ii) Adalimumab, certolizumab pegol and etanercept are recommended, within their marketing authorisations, as options for treating severe non-radiographic axial spondyloarthritis in adults whose disease has responded inadequately to, or who cannot tolerate, NSAIDs.</td>
</tr>
</tbody>
</table>
Rheumatology
AS cont’d

- NICE guidance on TNF-alpha inhibitors for AS and non-radiographic axial spondyloarthritis (including review of previous guidance - TA143 and TA233), cont’d

Psoriatic Arthritis (PsA)

- NICE guidance on the use of ustekinumab for treating active psoriatic arthritis, issued Jun 2015

- NICE guidance on the use of apremilast for treating active PsA, expected date TBC

(iii) The choice of treatment should be made after discussion between the clinician and the patient about the advantages and disadvantages of the treatments available. This may include considering associated conditions such as extra-articular manifestations. If more than 1 treatment is suitable, the least expensive (taking into account administration costs and patient access schemes) should be chosen.

(iv) The response to treatment should be assessed 12 weeks after the start of treatment. Treatment should only be continued if there is clear evidence of response, defined as:

- a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and
- a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more.

(v) Treatment with another TNF-alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to, treatment with the first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response.

(vi) When using BASDAI and spinal pain VAS scores, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the questionnaires, and make any adjustments they consider appropriate.

As this is a review of previous guidance, this is unlikely to have further additional significant impact on medicines spend in this area.

There are no drafts are currently available for this guideline, which will cover pharmacological interventions for articular symptoms (for example, antibiotics for reactive arthritis, NSAIDs, corticosteroids, standard DMARDs, and biological agents). It will also include switching and sequencing of pharmacological interventions.

This is an area of low to moderate financial risk

Previous guidance issued in May 2014 has been reviewed and NICE now supports use of ustekinumab as an option alone or in combination with methotrexate, in line with existing NICE guidance on the use of etanercept, infliximab and adalimumab and separate guidance on the use of golimumab for the treatment of psoriatic arthritis. The costing statement estimates that the guidance is not expected to have a significant impact on NHS resources as ustekinumab is an alternative option for treating active psoriatic arthritis and other options are similarly priced. Additionally The number of people affected by the change in practice is expected to be small.

Apremilast is an orally active agent that inhibits multiple pro-inflammatory mediators including, TNF-alpha, interleukins 6, 17 & 23, and interferon-gamma. It is licensed, alone or in combination with DMARDs, for the treatment of active PsA in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy.

Apremilast is likely to be used after conventional systemic therapies, but as an oral preparation, it may be used before parenteral biological therapies.

The FAD does not recommend the use of apremilast alone or in combination with DMARDs, within its marketing authorisation for treating adults with active PsA that has not responded to prior DMARD therapy, or such therapy is not tolerated.
The FAD is under appeal. If the appeal does not result in a change to the guidance then it will not have additional impact on medicines spend in this area. However, if the appeal is upheld and results to a change in the guidance so that apremilast is supported:

NIHR HSC suggests about 60,000 people in England are affected, other estimates suggest up to 1% of the population may be affected. The recommended dosage is 30 mg twice daily after an initial titration schedule and according to the FAD, the price of apremilast is £265.18 for a 14-day treatment initiation pack (4×10 mg tablet; 4×20 mg tablet; 19×30 mg tablet) and £550.00 for a 28-day-treatment standard pack (56×30 mg; excluding VAT. If it is used in place of parenteral biologics then cost of administration will be reduced.

The costing statement for the golimumab guidance notes:
- an estimated prevalence of PsA in England of 0.15% (or 60,353 people)
- an incidence of 0.017% (or 6,840 people)
- The number of people PsA estimated as eligible for treatment with a biologic (prevalence population only) is given as 2.4% (1448 people or ~3 people per 100,000 population)
- Of these, 1,248 people in England annually will respond to and continue TNF-alpha inhibitor therapy (or 2.5 per 100,000 population)

The NIHR HSC review, however, estimates that 25% of people with PsA will discontinue their first anti-TNF treatment within the first year (9.5% discontinue due to inefficacy and 10% due to adverse events) and 30% don’t respond to anti-TNF treatment (overall 55% of patients may therefore require alternative therapy).

If it is assumed that:
- treatment with apremilast costs ~ £7140 per patient per year
- it is used prior to anti-TNF agents (ranging from 0.5 to 1.5 people per 100,000 population) i.e. as an additional treatment step

This could result in an additional cost implication of between ~ £3500 to £11,000 per 100,000 population. This is based on the list price and does not account for any locally negotiated discounts/patient access schemes.

Data from the HSCIC indicates that approximately £159.6m (or ~£300,000 per 100,000 population) was spent on infliximab in 14/15 in the NHS and £229.2m (or ~£425,000 per 100,000 population) on etanercept. This spend is not separated out by indication.

For infliximab, assuming a 30% reduction in price and a 50% switch to use of biosimilar, this could result in overall savings of around £45,000 per 100,000 population. Some of these savings may have already been realised as biosimilar infliximab has been available since February 2015.

For etanercept, assuming a 30% reduction in price and an 80% switch to the biosimilar, this could release overall savings of around £102K per 100,000 population. A biosimilar version of etanercept is due to be launched in Q4 15/16.
**Actions/ issues which may be considered by commissioners and providers**

- Cytokine modulators, such as TNF-inhibitors and apremilast are listed as exclusions in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these indications outside NICE recommendations. **Drug exclusions under Payment by Results 15/16**. NHS England is the responsible commissioner when cytokine modulators are used in children (aged 18 years or younger) and for some specialist indications in both adults and children. CCGs are the responsible commissioners for use of these agents in adults in non-specialist settings.
- Several biologics have been approved by NICE for the treatment of RA. Commissioners and providers should locally agree a treatment pathway in these patients, including preferred choices for 1st and sequential line use. Similarly, locally agree treatment pathway for JIA (in particular when patients transfer between commissioners from child to adult services), AS and PsA including use of biologic agents.
- Some organisations have included the use of sub-cutaneous methotrexate prior to progressing to biologics in their treatment pathways as this step could delay the need for cytokine modulators in some patients and therefore reduce costs.
- Locally agree principles for the use of biosimilar versions of infliximab and etanercept, including whether switching existing patients will be supported and whether any time limited gain share arrangements will be implemented.
- Commissioners may wish to refer to the commissioning guide produced by NICE for the use of biologic drugs for the treatment of inflammatory disease in rheumatology, dermatology and gastroenterology to aid these decisions. NICE has also produced a guide for **Support for Commissioning for RA**
- Trusts should audit this area of prescribing to ensure that any variations to the drug regimens recommended in the NICE guidance are appropriate.

**Systemic lupus erythematosus (SLE)**

- NICE guidance on the use of belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus, expected Apr 2015

**This is an area of moderate financial risk**

Belimumab is a monoclonal antibody approved in Europe in July 2011 and launched in the UK in September 2011. It is the first human monoclonal antibody specifically licensed to treat SLE. The drug is licensed as add-on therapy in adult patients with active, autoantibody-positive SLE with a high degree of disease activity (e.g. positive anti-dsDNA and low complement) despite standard therapy. The monoclonal antibody rituximab has also been used in the treatment of SLE (and is supported for this indication by NHS England within criteria set out in the NHSE interim commissioning policy), although it is not licensed for this indication.

Belimumab is available as a 120 mg or 400 mg powder for intravenous infusion in solution. The recommended dose regimen is 10 mg/kg belimumab on days 0, 14 and 28, and at 4 week intervals thereafter. The SPC states that discontinuation of treatment with belimumab should be considered if there is no improvement in disease control after 6 months of treatment. The list price of belimumab is £121.50 for a 120 mg vial and £405 for a 400 mg vial.

A **FAD** for this guidance was published in April 2012 in which NICE did not recommend belimumab for use as per the licensed indication. The NICE Appraisal Committee noted that for the comparison of belimumab compared with standard care, the incremental cost effectiveness ratio (ICER) with the patient access scheme applied remained above the threshold range usually considered as an acceptable use of NHS resources. For the comparison of belimumab compared with rituximab the Committee concluded that there was no sound case presented to it on the cost effectiveness of belimumab compared with rituximab. The FAD was appealed against and this was upheld by the appeal panel in Sept 2012 on two grounds:
**Systemic lupus erythematosus (SLE)**

- NICE guidance on the use of belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus, cont’d

<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

(i) The Appraisal Committee’s decision to reject GlaxoSmithKline’s proposal that discontinuation of treatment with belimumab after week 24 should be considered if there was no improvement in a patient’s SELENASLEDAI score of 6 points or more is not explained

(ii) The Committee’s findings in relation to the clinical and cost effectiveness of belimumab compared with rituximab are unreasonable in the context of the available evidence and the licence status of rituximab.

The appraisal was remitted back to the appraisal committee and a second ACD was developed (July 2013), which did not recommend belimumab. The company has since submitted further evidence and analyses been submitted by the company, which are being reviewed by the evidence review group. The manufacturer of belimumab has agreed a patient access scheme with the Department of Health, in which a discount on the list price of belimumab is offered. The size of the discount is commercial-in-confidence.

An archived LNDG review on belimumab for SLE notes that only prednisolone, azathioprine and hydroxychloroquine are licensed for the treatment of SLE. Other treatments include NSAIDs and immunosuppressants. The review adds that about 15,000 people in England and Wales have SLE, with ~2000 people diagnosed each year.

The incidence of SLE varies among ethnic groups. In the UK, 1 in 5000 white women, 1 in 1000 women of Chinese origin and 1 in 625 Afro-Caribbean women will develop SLE. According to the company, as belimumab will be used in patients with high disease activity, who are not well controlled on standard therapy, they estimate this to be 4,151 patients across England and Wales, or 7.5/100,000 population.

Based on this, if it assumed that the drug is used in a 70kg patient for 6 months, the cost would be ~£6,160 (drug only, exc. VAT). Using belimumab in the population estimated by the company for 6 months would result in a total cost of £46,200 per 100,000 population. If it is further assumed that 50% of patients will respond positively to treatment and therefore continue for another 6 months, this could add another £17,300 per 100,000 population.

Therefore the total cost implication for belimumab in SLE could result in additional costs of ~£63,500 per 100,000 population per year. This cost represents the cost of the drug only and does not include associated service costs, such as in/outpatient attendance, fluids, pre-medication and other associated IV drug administration costs.

The SMC issued advice in April 2012 not recommending belimumab for use within its licensed indications in NHS Scotland.

**Actions/ issues which may be considered by commissioners and providers**

- Belimumab is listed as exclusion in the National Tariff for 15/16. NHS England is the responsible commissioner for this drug. [Drug exclusions under Payment by Results 15/16](#).
- NHS England has set out criteria for use of rituximab in SLE in an [interim policy](#).
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Disease or Indication</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osteoarthritis (OA)</strong></td>
<td>This guidance is unlikely to impact over the next year</td>
</tr>
<tr>
<td>NICE Quality Standard on OA, published Jun 2015</td>
<td>This Quality Standard topic has been referred to NICE and is at an early stage of development.</td>
</tr>
<tr>
<td>NICE pathway available</td>
<td>Diacerein is not currently licensed in the UK. It acts differently from traditional NSAIDs which inhibit prostaglandin synthesis, leading to adverse gastrointestinal effects. In November 2013 the EMA’s PRAC recommended suspension of diacerein in the EU following concerns over gastro-intestinal side effects (severe diarrhoea) and liver toxicity. This decision was reviewed in March 2014 and the PRAC recommended that diacerein remains available in Europe but with restrictions to manage the risks of severe diarrhoea and effects on the liver. This guidance is therefore not expected to have a significant impact on medicines spend in the NHS.</td>
</tr>
<tr>
<td>NICE guidance on the use of diacerein for the treatment of OA, expected date TBC</td>
<td></td>
</tr>
<tr>
<td><strong>Gout</strong></td>
<td>This area could have a moderate financial impact</td>
</tr>
</tbody>
</table>
| Lesinurad for treating chronic hyperuricaemia in people with gout, expected Nov 2016 | Lesinurad is a first in class, orally administered selective urate transporter-1 (URAT-1) inhibitor, which blocks the reabsorption of urate within the renal proximal tubule. A licence application has been filed for the drug in Europe and it is expected to be launched in Q1 2016. The licence application covers the treatment of gout second-line in combination with a xanthine-oxidase inhibitor. According to Prescribing Outlook, New Medicines, the estimated UK population with gout eligible for urate-lowering therapy is 472,000 (or 736 people per 100,000 population). Up to 25% of these may not achieve desired urate-lowering with tolerated doses of current drugs. As a further treatment option, lesinurad will be additional to current costs. If it is assumed that:  
- 184 people per 100,000 population may not achieve desired urate lowering with tolerated doses of current drugs  
- 20% of these may be suitable for treatment with lesinurad (37 people per 100,000 population)  
- The treatment costs around £35 per patient per month  
This could result in an additional cost impact of ~£15,500 per 100,000 population. |
| **Spasticity**         |                                                                                                  |
| NICE guidance on the use of collagenase clostridium histolyticum for treating Dupuytren's contracture, expected date TBC | Collagenase clostridium histolyticum (Xiapex®) is licensed for the treatment of Dupuytren’s contracture in adult patients with a palpable cord. Treatment with collagenase clostridium histolyticum seeks to restore hand function - surgery is widely used and can be an effective treatment for hand impairment. Collagenase clostridium histolyticum is a fixed ratio mixture of two purified collagenolytic enzymes isolated from the bacterium Clostridium histolyticum. The collagenase breaks up the collagen fibres, which weakens and disrupts the cord, sometimes with the help of finger extension procedures. It is administered as a 580mcg intralesional injection into the palpable cord and costs £780 per injection (inc. VAT). If necessary this can be repeated at intervals of approximately 4 weeks, maximum of 3 injections per cord. Only one cord may be treated at a time. Clinical study experience with collagenase is currently limited to up to 3 injections per cord and up to 8 injections in total. The health technology assessment report (May 2014) produced to support development of this NICE guidance concludes that based on the current evidence base, amongst people considered to be suitable candidates for surgery, collagenase does not appear to be the most cost-effective option to manage moderate to severe Dupuytren’s contracture. A second FAD was issued for this guidance in September 2015 which did not recommend collagenase clostridium histolyticum in this setting, except in the context of research. The FAD is under appeal. If the appeal is rejected and final |
### Spasticity cont’d

- NICE guidance on the use of [collagenase clostridium histolyticum](https://www.nice.org.uk/guidance/cg115) for treating Dupuytren’s contracture, cont’d

  guidance remains as per the second FAD, this guidance will not impact on medicines spend in the NHS.

  However, if the appeal is upheld and final guidance supports use:

  The final scope for the guidance notes that in the UK, the prevalence of Dupuytren’s disease ranges from 0.2-30%, varying widely with geographical location possibly due to genetics, environment, or a combination of both. It is more common in men than women, and is most commonly found in people of northern European descent. About 1 in 6 men in the UK over the age of 65 have some degree of Dupuytren’s contracture.

  Hospital episode statistics data show that on average there were approximately 13,000 admissions for Dupuytren’s contracture per year between April 2003 and March 2008 in England and Wales (or 23 per 100,000 population per year).

  A NETAG review (legacy website) for collagenase states that it is likely to be considered as an alternative treatment option to surgical intervention for moderate to severe Dupuytren’s contracture. Evidence from clinical studies indicates that patients require an average of two injections per case.

  If collagenase is used in 25% of cases (or 6 patients per 100,000 population) and two injections are used per case, this would result in a drug cost of £9,360 per 100,000 population. The NETAG note that collagenase will incur outpatient admission costs for administration and subsequent digital extension. The cost is therefore estimated at nearly £2,000 per case when this is factored in. However, collagenase (when used at 2 injections or less) could result in savings vs. surgery. If 3 or more injections are used then collagenase is likely to be less cost-effective than surgery. The net cost impact of collagenase could be optimised by directing treatment at patients who will be expected to require fewer injections, for example patients with only one or two affected joints.

  In May 2012 the SMC accepted collagenase for restricted use in NHS Scotland for use as an alternative to limited fasciectomy in adult patients with Dupuytren’s contracture of moderate severity (as defined by the British Society for Surgery of the Hand [BSSH]), with a palpable cord and up to two affected joints per hand, who are suitable for limited fasciectomy, but for whom percutaneous needle fasciotomy is not considered a suitable treatment option. Based on an estimated uptake of 16% (21 patients) in year 1 and 80% (104 patients) in year 5, the total impact on the Scottish medicines budget was estimated at £25k in year 1 (or £500 per 100,000 population) and £124k (or £2,500 per 100,000 population) in year 5.

### Spasticity cont’d

- NICE guidance on the use of [botulinum toxin type A](https://www.nice.org.uk/guidance/cg85) for treating upper or lower limb focal spasticity associated with stroke, expected date TBC

  Work on this appraisal is not expected to start until late January 2017 to align with the latest regulatory expectations. A draft scope for the guidance notes that it will include the three brands of botulinum toxin A (Botox, Dysport and Xeomin). Botox is licensed for focal spasticity post stroke in both upper limb spasticity (wrist and hand disability) and lower limb spasticity (ankle disability). Dysport and Xeomin are currently only licensed for use in upper limb spasticity. According to UKMI New Drugs online, licence applications have been submitted for both Dysport and Xeomin for use in lower limb disability post stroke. The exact botulinum toxin A dose and number of injection sites are tailored to the individual based on the size, number and location of muscles involved, the severity of spasticity, the presence of local muscle weakness, and the patient response to previous treatment. Repeat courses are determined on a case by case basis. For example, for Botox, if it is deemed appropriate by the clinician, the patient should be considered for re-injection when the clinical effect of the previous injection has diminished. Re-injections should occur no sooner than 12 weeks after the previous injection.

  This guidance is not expected to impact in 16/17.

### Actions/ issues which may be considered by commissioners and providers

- Collagenase (when used in outpatients) and botulinum toxin are listed as exclusions in the National Tariff for 15/16. CCGs are the responsible commissioners for these agents. [Drug exclusions under Payment by Results 15/16](https://www.gov.uk/government/publications/national-tariff-drug-exclusions-2015-16)
### Patent expiries

According to *Prescribing Outlook New Medicines 2015*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: travoprost (Nov 2016); bimatoprost (Mar 2017); olopatadine (May 2017).

### Macular oedema

- **NICE guidance on the use of aflibercept for the treatment of diabetic macular oedema (TA346), issued Jul 2015**

  **This is an area of major financial risk**

  Aflibercept is recommended as an option for the treatment of diabetic macular oedema if the eye has a central retinal thickness of 400 micrometres or more at the start of treatment and the company provides aflibercept with the discount agreed in the patient access scheme.

  Aflibercept is given as a single 2 mg intravitreal injection every month for 5 consecutive months, followed by 1 injection every 2 months with no requirement for monitoring between visits. After the first 12 months, the treatment interval may be extended based on visual and anatomic outcomes. The schedule for monitoring should be determined by the treating physician. The total cost for treating a patient in the first year is £6936 (based on 8.5 aflibercept injections). The company has agreed a patient access scheme with the Department of Health which provides a simple discount to the list price of aflibercept, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.

  The **costing report** estimates that implementation of this guidance will be associated with an additional annual cost of £48,407 per 100,000 over and above current expenditure on ranibizumab in this population, or a total of £26million for England, based on an eligible population of 12 per 100,000, or a total of 6,205 people in England.

  The annual cost associated with implementing the guidance is estimated at £26 million in England after 5 years, based on the following assumptions:

  - 10% (620) will receive laser treatment, 55% (3,413) will receive aflibercept monotherapy, 25% (1,551) will receive ranibizumab monotherapy, 5% (310) will receive combination therapy with laser and aflibercept, 2% (125) will receive combination therapy with laser and ranibizumab, and 3% (186) will receive no active treatment.
  - It is estimated that 19% of the eligible population will receive aflibercept in year 1, which will increase to 69% in year 5. By the same token, the 81% of population receiving ranibizumab will reduce to 31% in year 5.
  - 53.5% of people will need treatment in one eye and 46.5% of people will need treatment in both eyes.
  - All treatment and monitoring appointments will be shared when both eyes are treated.
  - A treatment period of up to three years
  - Some people will have diabetic macular oedema that will not respond to treatment. It is assumed that they will only have 3 injections in each eye treated before moving to laser treatment as monotherapy in year 2. It is estimated that 8% (440) of people treated with aflibercept monotherapy, ranibizumab monotherapy or combination therapy will not respond.

  Dexamethasone intravitreal implant is recommended as an option for treating both chronic and non-chronic diabetic macular oedema if the implant is to be used in an eye with an intraocular (pseudophakic) lens and the diabetic macular oedema does not respond to non-corticosteroid treatment, or such treatment is unsuitable.
<table>
<thead>
<tr>
<th>Macular oedema cont’d</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE guidance on <a href="https://www.nice.org.uk/guidance/ctsu15">dexamethasone intravitreal implant for diabetic macular oedema</a>, cont’d</td>
</tr>
<tr>
<td>• NICE guidance on the use of <a href="https://www.nice.org.uk/guidance/ctsu15">aflibercept for visual impairment due to macular oedema secondary to branch retinal vein occlusion</a>, expected Oct 2016</td>
</tr>
</tbody>
</table>

**Epidemiology, potential financial implications for a population of 100,000 and other comments**

The costing report for this guidance estimates that 595 people in England may be eligible for dexamethasone intravitreal implant each year. The annual total cost of implementing this guidance for the incident population is estimated at £4 million in England (equating to 1 person per 100,000 population and a cost of £7,845 per annum) assuming unilateral treatment.

The costing report also suggests that there will be a non-recurring cost for treating the prevalent population not previously treated with fluocinolone, estimated to be implemented over 3 years at a cost of £17 million in year 1 (which equates to ~£32,000 per 100,000 population, £17 million in year 2 and £15 million in year 3.

The following assumptions have been made:

- In future practice, it is assumed that 10% of people with both chronic and non-chronic diabetic macular oedema will receive watching and waiting only.
- For the remaining 90% with chronic diabetic macular oedema, treatment is split 75:25 between dexamethasone and fluocinolone.
- For the remaining 90% with non-chronic diabetic macular oedema treatment is with dexamethasone.

For bilateral treatment with a corticosteroid, 2 separate administration appointments are needed 75% of the time and just one is needed for the remaining 25%. This produces an average of 1.75 appointments for bilateral treatment with a steroid. NICE adds that there is uncertainty around the current level of use of fluocinolone acetonide intravitreal implant, and how practice will change following implementation of the guidance.

This guidance is at an early stage of development and no information on impact is currently available.

The Scottish Medicines Consortium has accepted for use in NHS Scotland, aflibercept ([Eylea®](https://www.nice.org.uk/guidance/ctsu15)) for the treatment of visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO) in adults. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of aflibercept. Current treatment options for patients with macular oedema secondary to BRVO are intravitreal ranibizumab which, like aflibercept, is administered monthly, or intravitreal dexamethasone which is administered as a single implant, although retreatment is allowed if required.

Based on data submitted to the SMC, it would be expected that 19 patients per 100,000 population would be eligible for treatment in year 1, rising to 94 patients per 100,000 in year 5 with an assumed uptake rate of 50% in each year and a small proportion of discontinuations. As other medicines were assumed to be displaced, the net budget impact would be estimated to be £6,000 per 100,000 population in year 1 and £11,730 in year 5. Note that these figures are based on the list price for both aflibercept (£816 per dose) and ranibizumab.
<table>
<thead>
<tr>
<th>Disease or Indication:</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>National targets and guidance</td>
<td></td>
</tr>
<tr>
<td><strong>Age related macular degeneration (AMD)</strong></td>
<td>This guideline is at an early stage of development and no information on impact is currently available. The guideline will cover the following interventions of interest for late &quot;wet&quot; AMD: anti-angiogenic therapies (aflibercept, bevacizumab [aliquoted for use in the eye], pegaptanib sodium, ranibizumab), intravitreal steroids (dexamethasone, fluocinolone acetonide, triamcinolone acetonide), laser photocoagulation, photodynamic therapy, psychological therapies and reablement services. NICE specifies that while bevacizumab will be included in the evaluations carried out to develop the guideline, and information on its properties and use may be included in the final guideline, no recommendation for its use will be made in any case where there is a licensed alternative.</td>
</tr>
<tr>
<td>• NICE guideline on the diagnosis and management of age related macular degeneration, date expected Aug 2017</td>
<td></td>
</tr>
<tr>
<td><strong>Cataracts</strong></td>
<td>This guideline is at an early stage of development and no information on impact is currently available. However, it is unlikely to have a significant financial impact.</td>
</tr>
<tr>
<td>• NICE clinical guideline on the management of cataracts, date expected June 2017</td>
<td></td>
</tr>
<tr>
<td><strong>Dry eye disease</strong></td>
<td>Draft guidance outlined in the FAD supports the use of ciclosporin (Ikervis®) for treating severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. The acquisition cost of a monthly course of ciclosporin is £72 (excluding VAT). The Scottish Medicines Consortium (SMC) has accepted the use of ciclosporin 1mg/mL (0.1%) eye drops emulsion (Ikervis®) within NHS Scotland for the treatment of severe keratitis in adults with dry eye disease, which has not improved despite treatment with tear substitutes. Based on data submitted to the SMC, it would be estimated that there are around 70,000 people in England that would be eligible for treatment in England. Assuming an estimated uptake rate of 10% in year 1 (7000 patients) and 66% (40,000 patients) in year 5, the gross impact on the medicines budget would be estimated to be £6.1m in year 1 and £34m in year 5. This equates to a cost of around £11,000 rising to £64,000 per 100,000 population. However the SMC feel that this estimate may be overstated as the eligible population may be lower than stated and if this licensed formulation is used instead of unlicensed formulations the cost impact will be reduced.</td>
</tr>
<tr>
<td>• NICE guidance on the use of ciclosporin for dry eye disease expected Dec 2015</td>
<td></td>
</tr>
<tr>
<td><strong>Actions/ issues which may be considered by commissioners and providers</strong></td>
<td>• Locally agreed pathways for various ophthalmology indications. For example, there are now 3 agents approved by NICE for use as options in macular oedema. Work should be undertaken to understand local pathways and agree place in therapy of these drugs (including whether sequential use will be accepted). A pathway for the management of dry eye and glaucoma, which defines lines of therapy and the role of preservative-free eye drops may also need to be considered. • Aflibercept, bevacizumab, dexamethasone intravitreal implant, fluocinolone intravitreal implant, ketorolac with phenylephrine, ocriplasmin, pegaptanib, ranibizumab and verteporfin are listed as exclusions in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. Drug exclusions under Payment by Results 15/16. CCGs are the responsible commissioners for use of these drugs. • Commissioners may wish to refer to the commissioning guide produced by NICE on commissioning a service for people at risk of developing glaucoma. • Commissioners and providers should review the ophthalmology specials list developed by the Royal College of Ophthalmologists and agree on a local formulary for these agents based on this guidance. The list was recently updated (June 2015).</td>
</tr>
</tbody>
</table>
Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
</table>

### 13. Skin

<table>
<thead>
<tr>
<th>Patent expires</th>
</tr>
</thead>
</table>

#### Psoriasis

- NICE guidance on [apremilast for moderate to severe plaque psoriasis](#), expected Oct 2015

- NICE guidance on [secukinumab for moderate to severe plaque psoriasis](#), issued Jul 2015

Apremilast is a first-in-class oral type 4 cyclic nucleotide phosphodiesterase 4 inhibitor, which downregulates the inflammatory response by modulating the expression of inflammatory and anti-inflammatory cytokines and mediators associated with psoriasis.

Draft guidance does not recommended apremilast within its marketing authorisation for treating adults with moderate to severe chronic plaque psoriasis that has not responded to systemic therapy, or systemic therapy is contraindicated or not tolerated.

According to the [costing statement](#) for TA360 (secukinumab), the prevalence of psoriasis in adult population is 1.75% (1356 per 100,000) and an estimated 2.55% (35 per 100,000) may be eligible for biological treatment. If the cost of apremilast is assumed to be similar to that of biologicals, then its use would not be expected to have any significant impact on drug costs during the first year. There may however be additional future costs as it represents an additional treatment option for patients failing anti-TNF treatment. If it is assumed that 20% of patients discontinue such treatment (7 per 100,000) and apremilast is offered as alternative then this equates to cost of ~ £49,000 per 100,000.

Secukinumab, a first-in-class monoclonal anti-human interleukin-17A (IL-17A) antibody of the IgG1/kappa isotype, is recommended, within its marketing authorisation, as an option for treating adults with plaque psoriasis only when: the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of ≥10 and a Dermatology Life Quality Index (DLQI) > 10; the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA, or these treatments are contraindicated or the person cannot tolerate them; AND the company provides secukinumab with the discount agreed in the patient access scheme.

Standard licensed doses: 300mg by subcutaneous injection, repeated once weekly at weeks 1, 2 and 3 then monthly starting at week 4. Cost of 150mg injection in pre-filled pen or syringe: 2=£1218.78.

According to the [costing statement](#), the prevalence of psoriasis in adult population is 1.75% (1356 per 100,000) and an estimated 2.55% (35 per 100,000) may be eligible for biological treatment. Secukinumab is an alternative to available biologics as it targets a different immunological mediator. Expert clinical opinion estimates uptake may be up to 20% of the eligible population (7 per 100,000 which equates to cost of ~£64,000 per 100,000 when used as first line biological). In this scenario, the costing template assumes that secukinumab is cost neutral.

However if secukinumab is used as a second or third line biological following failure of TNFi(s), the following assumptions are made:

- 50% of patients do not respond to the first anti-TNF (18 per 100,000)
- 100% of these (18 per 100,000) receive a second anti-TNF and
- 50% fail 2nd line treatment and therefore receive secukinumab (9 per 100,000)

This could result in an additional cost of ~ £82,300 per 100,000
### Psoriasis cont’d

- **Savings through the use of biosimilar versions of infliximab and etanercept**

  Data from the [HSCIC](https://www.hscic.gov.uk) indicates that approximately £159.6m (or ~£300,000 per 100,000 population) was spent on infliximab in 14/15 in the NHS and £229.2m (or ~£425,000 per 100,000 population) on etanercept. This spend is not separated out by indication.

  For infliximab, assuming a 30% reduction in price and a 50% switch to use of biosimilar, this could result in overall savings of around £45,000 per 100,000 population. Some of these savings may have already been realised as biosimilar infliximab has been available since February 2015.

  For etanercept, assuming a 30% reduction in price and an 80% switch to the biosimilar, this could release overall savings of around £102K per 100,000 population. A biosimilar version of etanercept is due to be launched in Q4 15/16.

### Actions/ issues which may be considered by commissioners and providers

- Cytokine modulators, such as TNF-inhibitors and apremilast are listed as exclusions in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these for indications outside NICE recommendations. [Drug exclusions under Payment by Results 15/16](https://www.england.nhs.uk/wp-content/uploads/2020/12/PBR1516-1.pdf). NHS England is the responsible commissioner when cytokine modulators are used in children (aged 18 years or younger) and for some specialist indications in both adults and children. CCGs are the responsible commissioners for use of these agents in adults in non-specialist settings.

- Several biologics have been approved by NICE for the treatment of psoriasis. Commissioners and providers should locally agree a treatment pathway in these patients, including preferred choices for 1st line and sequential line use.

### Urticaria

- **NICE guidance on omalizumab for previously treated chronic spontaneous urticaria, issued Jul 2015**

  Omalizumab is recommended as an option as add-on therapy for treating severe chronic spontaneous urticaria in adults and young people aged 12 years and over only if:

  - the severity of the condition is assessed objectively, for example, using a weekly urticaria activity score of 28 or more
  - the person’s condition has not responded to standard treatment with H1-antihistamines and leukotriene receptor antagonists
  - omalizumab is stopped at or before the fourth dose if the condition has not responded
  - omalizumab is stopped at the end of a course of treatment (6 doses) if the condition has responded, to establish whether the condition has gone into spontaneous remission, and is restarted only if the condition relapses
  - omalizumab is administered under the management of a secondary care specialist in dermatology, immunology or allergy
  - the company provides omalizumab with the discount agreed in the patient access scheme.

  The commissioner for this technology is NHS England. According to [costing statement](https://www.england.nhs.uk/wp-content/uploads/2020/12/CostingStatement_Urticaria_Omalizumab.pdf), the estimated cost of implementing the guidance is £20.3m for the population of England (~£38,000 per 100,000). This cost is before taking into account the discount available in the patient access scheme. The additional population receiving omalizumab is estimated to be 3900 people per year in England (7 per 100,000) from year 5 following implementation.
### Urticaria cont’d

**NICE guidance on adalimumab for treating moderate to severe hidradenitis suppurativa**, expected Jun 2016

Adalimumab has a marketing authorisation in the UK for treating active moderate to severe hidradenitis suppurativa (HS) in adults whose disease has not responded to conventional systemic therapy.

There are approximately 90,000 people with HS in England (~170 per 100,000). If it is assumed that 10% require treatment with adalimumab, this could result in additional drug cost of ~£288,000 per 100,000.

### Actions/ issues which may be considered by commissioners and providers

- Adalimumab and omalizumab are listed as exclusions in the National Tariff for 15/16. A decision on funding will need to be agreed locally for these for indications outside NICE recommendations. **Drug exclusions under Payment by Results 15/16**. NHS England is the responsible commissioner for the use of these agents in the settings outlined above.

### Wound care

**Key Therapeutic Topic (KTT) for wound care products**

A set of **key therapeutic topics (KTT) and associated comparators** have been developed to support NHS England’s Medicines Optimisation Measurement work stream. The comparators support organisations and prescribers to review the appropriateness of prescribing, revise prescribing where appropriate and monitor implementation. The wound care products comparator (Cost [NIC] per item) has been retired.

The quality standard is expected to contribute to improvements in incidence of category 2 -4 pressure ulcers, health-related quality of life, length of hospital stay and discharge destination (such as a patient's home or care home).

### Extemporaneous Specials

**British Association of Dermatologists (BAD) specials list**

This is an area in which significant cost savings may be realised

The British Association of Dermatologists (BAD) has published an updated rationalised list of dermatology specials (2014) that may be manufactured for the treatment of dermatological conditions. The abbreviated list includes 40 preferred Specials agreed by the Specials Working Group (established in 2013). It is hoped that adherence to the list will allow patients easier access to these treatments, at less cost to the NHS.

This is an update of NPC/NICE resource first published in 2011. The guidance aims to support all prescribers with the safe and appropriate prescribing of Specials in all patients for whom no suitable licensed medicine is available.

**Royal Pharmaceutical Society – draft guidance for the prescribers of Specials**

**Actions/ issues which may be considered by commissioners and providers**

- Demand management through service redesign may mean more patients are treated in primary care for simple dermatological conditions using condition specific protocols instead of being referred to secondary care.
- Locally agree principles for the use of biosimilar versions of infliximab and etanercept, including whether switching existing patients will be supported and whether any time limited gain share arrangements will be implemented.
- Review use of wound care products locally and develop local guidelines, including community nursing services. This has the potential for releasing savings through a reduction in the inappropriate use of dressings, such as silver dressings.
- Commissioners and providers should jointly review the updated BAD specials list and agree which areas should be included within local formularies.
Generic medicines have a significant impact on prescribing budgets and can offset, to some extent, costs associated with the introduction of new medicines. Generic products can be marketed once the patent on the original product has expired although manufacturers may apply for a Supplementary Protection Certificate (SPC) to extend the effective patent life by up to 5 years (5½ years if it includes a Paediatric Investigation Plan, see below). Expiry dates in the table below take account of the SPC and any paediatric extension. The table also indicates where a licence for a generic/biosimilar product is in the latter stages of the EU licensing process or is already available in the EU. However, it does not follow that a generic/biosimilar product will be available in the UK as patent issues differ between countries. Patent legislation is complex and the information below should be used as a guide only.

On 26 January 2007, regulation (EC) No. 1901/2006 came into force. This provides the legislative framework to promote development of medicines for use in children. An incentive is the possibility of an extension to the duration of a SPC covering a marketed product. Before this regulation came into force, the maximum duration of an SPC was five years. Now, an SPC covering a product may be extended by six months beyond the term that would otherwise apply. This extension of the term applies to all authorised indications for the product (including the non-paediatric indications). Drugs with a granted paediatric extension are indicated.

Note that patent expiries are subject to change when new extensions (SPC or paediatric) are granted or if court decisions alter the patent status of a drug. In addition, the patent expiries listed only cover the basic, manufacturing patent. Additional patents on formulations and uses can influence when a generic or biosimilar becomes available commercially.

### Drug

<table>
<thead>
<tr>
<th>Drug</th>
<th>BNF</th>
<th>Patent expiry date</th>
<th>Date includes paediatric extension</th>
<th>Generic or biosimilar available/ in development</th>
<th>Commissioning route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>1.5.3/10.1.3</td>
<td>2015 Feb</td>
<td>Yes</td>
<td>Yes</td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Sevelamer HCl</td>
<td>9.5.2.2</td>
<td>2015 Feb</td>
<td></td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>7.4.2</td>
<td>2015 Mar</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Paricalcitol</td>
<td>9.6.4</td>
<td>2015 Mar</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Clofarabine</td>
<td>8.1.3</td>
<td>2015 May</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Glatiramer acetate (copolymer)</td>
<td>8.2.4</td>
<td>2015 May</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>6.1.1.2</td>
<td>2015 May</td>
<td>Yes</td>
<td>Yes</td>
<td>CCG</td>
</tr>
<tr>
<td>Insulin aspart biphasic</td>
<td>6.1.1.2</td>
<td>2015 Jun</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>8.2.2</td>
<td>2015 Jun</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Tenecteplase</td>
<td>2.10.2</td>
<td>2015 Jun</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Etanercept</td>
<td>10.1.3</td>
<td>2015 Jul</td>
<td>Yes</td>
<td></td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Rasburicase</td>
<td>10.1.4</td>
<td>2015 Jul</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>2.8.1</td>
<td>2015 Aug</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Strontium ranelate</td>
<td>6.6.2</td>
<td>2015 Aug</td>
<td></td>
<td></td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Nateglinide</td>
<td>6.1.2.3</td>
<td>2015 Sep</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Alitretinoin</td>
<td>13.5.1</td>
<td>2015 Oct</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Palonosetron</td>
<td>4.6</td>
<td>2015 Nov</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Pimecrolimus</td>
<td>13.5.3</td>
<td>2015 Nov</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Eletriptan HCl</td>
<td>4.7.4</td>
<td>2015 Dec</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Frovatriptan succinate</td>
<td>4.7.4</td>
<td>2015 Dec</td>
<td></td>
<td>Yes</td>
<td>CCG</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>5.3.1</td>
<td>2015 Dec</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Pemetrexed disodium</td>
<td>8.1.3</td>
<td>2015 Dec</td>
<td></td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Drug</td>
<td>BNF</td>
<td>Patent expiry date</td>
<td>Date includes paediatric extension</td>
<td>Generic or biosimilar available/ in development</td>
<td>Commissioning route</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----</td>
<td>-------------------</td>
<td>-----------------------------------</td>
<td>--------------------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Botulinum toxin Type B</td>
<td>4.9.3</td>
<td>2016 Jan</td>
<td></td>
<td>Depends on indication</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>5.3.1</td>
<td>2016 Jan</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>5.1.7</td>
<td>2016 Jan</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Agomelatine</td>
<td>4.3.4</td>
<td>2016 Feb</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>5.3.4</td>
<td>2016 Feb*</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Tiotropium</td>
<td>3.1.2</td>
<td>2016 Mar</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Bexarotene</td>
<td>8.1.5</td>
<td>2016 Apr</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Tolvaptan</td>
<td>6.5.2</td>
<td>2016 Apr</td>
<td>Yes</td>
<td>Depends on indication</td>
<td></td>
</tr>
<tr>
<td>Darbepoetin alfa</td>
<td>9.1.3</td>
<td>2016 Jun</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Telithromycin</td>
<td>5.1.5</td>
<td>2016 Jul</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>5.2.1</td>
<td>2016 Jul</td>
<td>Yes</td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Adefovir dipivoxil</td>
<td>5.3.3.1</td>
<td>2016 Sep</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>3.2</td>
<td>2016 Sep</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Imatinib mesylate</td>
<td>8.1.5</td>
<td>2016 Dec</td>
<td>Yes</td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Rupatadine</td>
<td>3.4.1</td>
<td>2017 Jan</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Telmisartan/hydrochlorothiazide</td>
<td>2.5.5.2</td>
<td>2017 Jan</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Velaglucerase alfa</td>
<td>9.8.1</td>
<td>2017 Jan</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Olmesartan medoxomil</td>
<td>2.5.5.2</td>
<td>2017 Feb</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Bimatoprost</td>
<td>11.6</td>
<td>2017 Mar</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Valganciclovir</td>
<td>5.3.2.2</td>
<td>2017 Mar</td>
<td>Yes</td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>5.2.4</td>
<td>2017 Apr</td>
<td>Yes</td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Entecavir</td>
<td>5.3.3.1</td>
<td>2017 Apr</td>
<td>Yes</td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>5.1.2.2</td>
<td>2017 Apr</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Melatonin</td>
<td>4.1.1</td>
<td>2017 Apr</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Parecoxib</td>
<td>15.1.4.2</td>
<td>2017 Apr*</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Tramadol/paracetamol</td>
<td>4.7.2</td>
<td>2017 Apr</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Olopatadine</td>
<td>11.4.2</td>
<td>2017 May</td>
<td></td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Peginterferon alfa</td>
<td>8.2.4</td>
<td>2017 May*</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Tegafur/gimeracil/oteracil</td>
<td>8.1.3</td>
<td>2017 May</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Travoprost</td>
<td>11.6</td>
<td>2017 May</td>
<td>Yes</td>
<td>Yes</td>
<td>CCG</td>
</tr>
<tr>
<td>Nitrisinone</td>
<td>9.8.1</td>
<td>2017 Jun</td>
<td></td>
<td>NHS England</td>
<td></td>
</tr>
<tr>
<td>Dutasteride</td>
<td>6.4.2</td>
<td>2017 Jul</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Etoricoxib</td>
<td>10.1.1</td>
<td>2017 Jul*</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Pregabalin</td>
<td>4.8.1</td>
<td>2017 Jul*</td>
<td>Yes</td>
<td>CCG</td>
<td></td>
</tr>
<tr>
<td>Bosentan</td>
<td>2.5.1</td>
<td>2017 Aug</td>
<td>Yes</td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Drug</td>
<td>BNF</td>
<td>Patent expiry date</td>
<td>Date includes paediatric extension</td>
<td>Generic or biosimilar available/ in development</td>
<td>Commissioning route</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
<td>---------</td>
<td>--------------------</td>
<td>-------------------------------------</td>
<td>-------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Estradiol/drospirenone</td>
<td>6.4.1.1</td>
<td>2017 Aug*</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Norelgestromin</td>
<td>7.3.1</td>
<td>2017 Aug</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Omalizumab</td>
<td>3.4.2</td>
<td>2017 Aug</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Pegfilgrastin</td>
<td>9.1.6</td>
<td>2017 Aug</td>
<td></td>
<td>Yes</td>
<td>NHS England</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>5.1.3</td>
<td>2017 Aug</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Ivabradine</td>
<td>2.6.3</td>
<td>2017 Sep</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>2.9</td>
<td>2017 Sep</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>2.12</td>
<td>2017 Oct</td>
<td></td>
<td>Yes</td>
<td>CCG</td>
</tr>
<tr>
<td>Mycophenolate mofetil E/C</td>
<td>8.2.1</td>
<td>2017 Oct</td>
<td></td>
<td>Depends on indication</td>
<td></td>
</tr>
<tr>
<td>Pegvisomant</td>
<td>6.5.1</td>
<td>2017 Nov</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>2.5.1/7.4.5</td>
<td>2017 Nov</td>
<td></td>
<td>Yes</td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Abatacept</td>
<td>10.1.3</td>
<td>2017 Dec</td>
<td></td>
<td>Yes</td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Retigabine</td>
<td>4.8.1</td>
<td>2017 Dec</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Rosuvastatin calcium</td>
<td>2.12</td>
<td>2017 Dec</td>
<td></td>
<td>Yes</td>
<td>CCG</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>8.3.4.2</td>
<td>2018 Mar</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Anidulafungin</td>
<td>5.2.4</td>
<td>2018 Mar</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>1.5.3 / 10.1.3</td>
<td>2018 Apr</td>
<td></td>
<td>Yes</td>
<td>Depends on indication</td>
</tr>
<tr>
<td>Enfuvirtide</td>
<td>5.3.1</td>
<td>2018 Apr</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Everolimus</td>
<td>8.1.5</td>
<td>2018 Jul</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Varicella-zoster vaccine</td>
<td>14.4</td>
<td>2018 Jul</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Human papilloma virus vaccine (Cervarix)</td>
<td>14.4</td>
<td>2018 Sep</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Vardenafil HCl</td>
<td>7.4.5</td>
<td>2018 Oct*</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Aprepitant</td>
<td>4.6</td>
<td>2018 Nov</td>
<td></td>
<td></td>
<td>NHS England</td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>6.1.1.2</td>
<td>2018 Nov</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Oxycodone/naloxone</td>
<td>4.7.2</td>
<td>2018 Dec*</td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Solifenacin succinate</td>
<td>7.4.2</td>
<td>2018 Dec</td>
<td></td>
<td>Yes</td>
<td>CCG</td>
</tr>
</tbody>
</table>