Prescribing Outlook

National Developments

2014

A resource for the NHS to help with budget setting, prescribing planning and medicines management
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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 the Government’s support for the NHS to embrace innovation to meet current and future healthcare challenges and outlines the importance of early adoption and uptake diffusion of clinically and cost effective innovative practices, including medicines. Horizon scanning is essential for this process at many organisational levels so new medicines that improve patient outcomes can be planned for and adopted. Recently, the Medicines and Healthcare Products Regulatory Agency (MHRA) launched the early access to medicines scheme. This scheme aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a licence when there is a clear unmet medical need. It will not replace the normal licensing systems but will mean that a small number of medicines will be available to patients earlier than normally anticipated.

Since April 2013, NHS England Area Teams have a strategic medicines management role and are responsible for commissioning the majority of high cost drugs as well as all cancer chemotherapy. An updated list has recently been published (August 2014) of medicines not reimbursed through national prices and are directly commissioned by NHS England. Other useful documents published by NHS England that outline various mechanisms for the managed entry and funding of drugs include:

- **Individual funding requests (IFRs)**
- **Implementation and funding of NICE guidance**
- **Experimental and unproven treatments**
- **On-going treatment following a NHS England funded trial**
- **On-going treatment following non-commercially funded clinical trials**
- **On-going access to treatment following a trial of treatment**
- **On-going access to treatment following industry sponsored clinical trials or funding**
- **Specialised commissioning - Clinical commissioning policies**
- **Manual for Prescribed Specialised Services 2013/14**
- **Drugs funded by the Cancer Drug Fund**

Much of the above guidance focuses on the most expensive medicines, but how are prices set for medicines and what are the mechanisms for reducing the cost to the NHS?

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 now being implemented and the approach is very different to previous schemes. A **question and answer** document outlines how it operates. Pharmaceutical companies decide whether to join the PPRS scheme or not. 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 the 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 agreed allowed growth rate in the NHS branded medicines bill is 0% for the next 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.

For high cost new medicines in the NICE work programme manufacturers have the option to submit a proposal for a Patient Access Scheme (PAS). This allows NICE to recommend treatments that it might otherwise not find to be cost effective. PAS are either cost (discounts, free stock etc) or outcome (price variation linked to patient outcomes) based. A Cost PAS is for medicines which require a higher cost than the NHS can afford. A Outcome PAS is for medicines which, in addition to the normal cost effectiveness criteria, require specific outcomes linked to cost effectiveness. For high cost new medicines in the NICE work programme manufacturers have the option to submit a proposal for a Patient Access Scheme (PAS). This allows NICE to recommend treatments that it might otherwise not find to be cost effective. PAS are either cost (discounts, free stock etc) or outcome (price variation linked to patient outcomes) based. A Cost PAS is for medicines which require a higher cost than the NHS can afford. A Outcome PAS is for medicines which, in addition to the normal cost effectiveness criteria, require specific outcomes linked to cost effectiveness.

NICE now has a role to provide support for implementing NICE guidance. The NICE website has recently been redeveloped and support tools including commissioning guidance, quality standards and costing templates are accessible from a single page that contains all relevant documents in a therapeutic area. This year, links to this overview page, rather than links to the individual support tools are included in monographs in Prescribing Outlook where relevant.

As of April 2013 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. There are a few changes to the list this year (2014/15 HCD list - see ‘Detailed HCDs’ for the full list). Many drugs on this list are not yet available in the UK but are listed so that commissioners and providers can start a dialogue about funding in advance of launch. In Prescribing Outlook for those medicines not listed on the latest HCD list an ‘educated guess’ as to the potential tariff positioning for them has been made.

For the pharmaceutical industry, the cost of bringing a new drug to the market is high. It is inevitable that more effort is being put into looking for new uses for, or new formulations of, currently licensed products. Applications for licence extensions are processed through licensing systems faster than those for new drugs as less safety and technical data are required. Horizon scanning for licence extensions or new formulations is more difficult as there is often less publicity than for new molecular entities being launched for their first indication. These often receive a lower priority in terms of managed entry into the NHS as there is precedent with the first indication. However, licence extensions can have a significant financial impact, especially for orphan conditions, when there will usually be a different brand name and pricing structure.
drugs for orphan indications are often more expensive than for other indications, orphan status is highlighted in Prescribing Outlook.

Biosimilars are also driving the development of new formulations. Unlike traditional generic drugs these are more costly to develop and take longer to licent. However, as biological drugs are expensive and many are nearing the end of their patent protection the potential for competition is increasing. It is estimated about 50% of the current UK market for biological medicines spend may be subject to biosimilar competition by 2019. Unlike chemical generic drugs biosimilars are not exactly interchangeable with the originator product and therefore need to be more actively managed into the NHS. Prescribing Outlook highlights which biosimilars are in development and when the originator patent expires so that managed entry can be planned.

Anon. What are biosimilars and are they important? Drug and Therapeutics Bulletin 2013; 51(5): 57-60.

About Prescribing Outlook publications

The aim of the annually published Prescribing Outlook series produced by UK Medicines Information (UKMi) is to assist NHS organisations plan, implement and budget for new medicines or licence extensions and national guidance. It provides support to commissioners and providers by highlighting new medicines and service developments that may have financial and operational resource implications. The Prescribing Outlook series is produced for primary and secondary care NHS organisations and has a national perspective. The content and presentation of the series has evolved over the years following consultation with users.

This document is the first in the series that comprises Prescribing Outlook - New Medicines and Prescribing Outlook - National Developments, and is supported by an electronic Cost Calculator. These are all available at www.ukmi.nhs.uk. The component documents of the Prescribing Outlook series are published each autumn in line with annual budget planning timeframes and key outputs from NICE. Updates on the progress of individual medicines at other times throughout the year can be found on the UKMi New Drugs Online database.

Further specialist medicines information not included in the series can also be obtained from local and regional medicines information centres. See www.ukmi.nhs.uk.

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.
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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, nwh-tr.medinfo@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 in the 14/15 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.

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<thead>
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<th>Exclusions for 14/15</th>
<th>Exclusions categorised by BNF category</th>
<th>Existing NICE guidance?</th>
<th>Future NICE guidance?</th>
<th>Responsible commissioner (NHSE or CCG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cykotine inhibitors</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 Vercinorn)</td>
<td>✓</td>
<td>✓</td>
<td>CCG – adults NHSE - paeds</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;Illoprost <em>2.5.1 &gt;Sildenafil</em> <em>(Sildenafil excluded only when used for Pulmonary Arterial Hypertension)</em> 2.8.1 &gt;Epoprostenol 7.4.5 &gt;Tadalafil* <em>(Tadalafil excluded only when used for Pulmonary Arterial Hypertension)</em> (includes Macitentan, Nitric Oxide, Riociguat, Selexipag and Treprostinil sodium)</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Fibrinolytic drugs</td>
<td>2.10.2 &gt;Alteplase** *(Alteplase is dealt with as an adjustment under PbR)</td>
<td>✓</td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Blood related products</td>
<td>2.11&gt; Blood Products</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Allergen immunotherapy</td>
<td>3.4.2&gt;omalizumab *(includes Mepolizumab and Reslizumab)</td>
<td>✓</td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Pulmonary surfactants</td>
<td>3.5.2&gt;Beractant 3.5.2&gt;Poractant alpha *(Includes Ecallantide)</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Mucolytics</td>
<td>3.7&gt;Dornase alfa 3.7&gt; Ivacator 3.7&gt;Mannitol (when delivered via nebulisation/inhalation)</td>
<td>✓</td>
<td>✓</td>
<td>NHSE</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>3.11&gt;Pirenidone</td>
<td>✓</td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Hypnotics and anxolytics</td>
<td>4.1.1&gt;Sodium oxybate</td>
<td></td>
<td></td>
<td>CCG – adults NHSE - paeds</td>
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<tr>
<td>Non-opioid analgesics</td>
<td>4.7.1&gt;Ziconotide</td>
<td></td>
<td></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)</td>
<td></td>
<td></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>✓</td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Antibacterial Drugs</td>
<td>5.1.2.3&gt;Aztreonam Lysine**** 5.1.4&gt;Tobramycin**** 5.1.7&gt;Colistimethate sodium**** 5.1.12&gt;Levofloxacin**** *(when delivered via nebulisation/inhalation) *(includes Amikacin Liposomal)</td>
<td></td>
<td></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></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>AIDS/HIV antiretrovirals</td>
<td>5.3.1 *(includes Cobicistat, Dolutegravir, Elvitegravir, Elvitegravir + Cobicistat + Emtricitabine + Tenofovir, Ertcubatine and Viciriviro)</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Cytomegalovirus infection</td>
<td>5.3.2.2&gt;Cytomegalovirus infection</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Viral hepatitis (B&amp;C) &amp; Respiratory syncytial virus (RSV)</td>
<td>5.3.3 5.3.5 8.2.4&gt;Interferon alfa *(includes Alisporivir, Asunaprevir with Daclatasvir, Faldaprevir, Motavizumab, Nitazoxanide, Simeprevir, Sofosbuvir, Sofosbuvir with Ledipasvir and Taribavir)</td>
<td>✓</td>
<td>✓</td>
<td>NHSE</td>
</tr>
<tr>
<td>Exclusions for 14/15</td>
<td>Exclusions categorised by BNF category</td>
<td>Existing NICE guidance?</td>
<td>Future NICE guidance?</td>
<td>Responsible commissioner (NHSE or CCG)</td>
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<tr>
<td>Growth hormone &amp; growth hormone receptor antagonist</td>
<td>6.5.2 &gt;Tolvaptan  6.5.1 &gt;Anterior pituitary hormones&gt;growth hormone receptor antagonist  6.5.1 &gt;Anterior pituitary hormones&gt;growth hormone  6.7.4 &gt;Mecasermin <em>(includes Octreolin, Tesamorelin and Lixivaptan)</em></td>
<td>✓</td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs affecting bone metabolism</td>
<td>6.6.1 &gt;teriparatide  6.6.1 &gt;Parathyroid hormone</td>
<td>✓</td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Immunomodulating drugs</td>
<td>8.3.4.3 <em>(includes Fibroblast growth factor 1 gene therapy)</em></td>
<td>✓</td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>8.1.3 &gt;Azacitidine^  8.1.3 &gt;Decitabine^  Rigosertib^ <em>(no BNF category available)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Antineoplastic drugs</td>
<td>8.1.5 &gt;Bevacizumab^  8.1.5 &gt;Bortezomib^  8.1.5 &gt;Gefitinib^-  8.1.5 &gt;Cetuximab^  8.1.5 &gt;Aldesleukin  8.1.5 &gt;Glatiramer  8.1.5 &gt;Lenalidomide^  8.1.5 &gt;Natalizumab  8.1.5 &gt;Thalidomide^  8.1.5 &gt;Fingolimod <em>(includes Dimethyl fumarate, Laquinimod, Nintedanib, Peginterferon Beta-1a, Peginterferon Lambda-1a, Rilonacept^ and Teriflunomide)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Corticosteroids and other immunosuppressants</td>
<td>8.2.2.2 &gt;Basiliximab  Daclizumab <em>(no BNF category available)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs affecting the Immune response</td>
<td>8.2.3.3 &gt;Belatacept  8.2.3.3 &gt;Alemtuzumab^  9.1.7.3 &gt;Plerixafor  10.1.3.3 &gt;Belimumab  13.5.3 &gt;Efalizumab  13.5.3 &gt;Ustekinumab <em>(includes Vedolizumab)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Somatostatin analogues</td>
<td>8.3.4.3 <em>(includes Fibroblast growth factor 1 gene therapy)</em></td>
<td></td>
<td></td>
<td>NHSE or CCG, depends on drug</td>
</tr>
<tr>
<td>Paroxysmal nocturnal haemoglobinuria</td>
<td>9.1.3 &gt;Eculizumab</td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Platelet Disorder Drugs</td>
<td>9.1.4.1 &gt;Eltrombopag  9.1.4.1 &gt;Romiplostim <em>(includes Avatrombopag)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs used in hypoplastic, haemolytic, and renal anaemias</td>
<td>8.2.2 &gt;Antilymphocyte globulin  9.1.3 &gt;Antithymocyte Immunoglobulin  9.1.3 &gt;Iron Overload <em>(For chronic iron overload)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs used in Metabolic disorders</td>
<td>8.2.4 &gt;Canakinumab  9.4.1 &gt;Sapropetin  9.8.1 &gt;Lipefilgrastim^ <em>(includes Lipefilgrastim^)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Drugs used in Neutropenia</td>
<td>9.1.6.1 &gt;Lipefilgrastim^ <em>(includes Lipefilgrastim^)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Parenteral Nutrition 9.3</td>
<td>&gt;Parenteral Nutrition <em>(after 14 days or when the patient is receiving parenteral nutrition prior to admission)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
</tr>
<tr>
<td>Gout and cytotoxic-induced hyperuricaemia</td>
<td>10.1.4 &gt;Hyperuricaemia associated with cytotoxic drugs <em>(Pegloticase (no BNF category available))</em></td>
<td></td>
<td></td>
<td>CCG</td>
</tr>
<tr>
<td>Neuromuscular Disorders</td>
<td>10.2.1 &gt;Amifampridine phosphate  10.2.1 &gt;Fampridine <em>(includes Ataluren)</em></td>
<td></td>
<td></td>
<td>NHSE</td>
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<td>Exclusions for 14/15</td>
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</tr>
<tr>
<td>Enzymes</td>
<td>10.3.1 &gt;Collagenase (only when used in outpatients)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Macular Oedema</td>
<td>11.4.1 &gt;Dexamethasone intravitreal implant Flucinolone acetonide (only when used as an intravitreal implant)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Retinal disorders/ intraocular lens replacement surgery</td>
<td>11.8.2 &gt;Ocriplasmin (includes Ketrarolac with Phenylephrine)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Macular Oedema</td>
<td>11.4.1 &gt;Dexamethasone intravitreal implant Flucinolone acetonide (only when used as an intravitreal implant)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Subfoveal choroidal neovascularisation</td>
<td>11.8.2 &gt;Aflibercept 11.8.2 &gt;Pegaptanib 11.8.2 &gt;Ranibizumab 11.8.2 &gt;Verteporfin</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Skin Conditions</td>
<td>13.5.1 &gt;Alitretinoin Afamelanotide (no BNF category available)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Intravenous/subcutaneous human normal immunoglobulins</td>
<td>14.5 &gt;Normal immunoglobulin for intravenous use 14.5 &gt;Normal immunoglobulin for subcutaneous use</td>
<td>✓</td>
<td>✓</td>
<td>NHSE</td>
</tr>
<tr>
<td>Bone morphogenetic protein</td>
<td>No BNF Category available (includes Diboterminal Alpha and Eptotermin alpha)</td>
<td>✓</td>
<td>✓</td>
<td>NHSE (spinal use)</td>
</tr>
<tr>
<td>Poisoning</td>
<td>Emergency treatment of poisoning &gt;Other poisons &gt;Ethylene glycol and methanol &gt;Fomepizole (includes Digoxin immune fab)</td>
<td>✓</td>
<td>✓</td>
<td>CCG</td>
</tr>
<tr>
<td>Hypertension and heart failure</td>
<td>Serelaxin (no BNF category available)</td>
<td>✓</td>
<td>✓</td>
<td>TBC</td>
</tr>
<tr>
<td>Lipid-regulating drugs</td>
<td>Lomitapide (no BNF category available)</td>
<td>✓</td>
<td>✓</td>
<td>TBC</td>
</tr>
<tr>
<td>Hormone antagonists</td>
<td>8.3.4 &gt;Abiraterone 8.3.4.2 &gt;Enzalutamide</td>
<td>✓</td>
<td>✓</td>
<td>NHSE</td>
</tr>
</tbody>
</table>

- 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 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: Infliximab patent has now expired and infliximab biosimilars are expected in Feb 2015.

#### Inflammatory Bowel disease (IBD)

- **NICE Quality Standard on inflammatory bowel disease**, expected Sept 2014
- **NICE guidance on vedolizumab for the second line treatment of moderate to severe active Crohn’s disease** expected Jun 2015
- NICE Pathway on Crohn’s disease and ulcerative colitis available.
- **NICE guidance on the use of infliximab, adalimumab and golimumab for the second line treatment of moderately to severely active UC** expected Jan 2015

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

This quality standard will cover the diagnosis and management of inflammatory bowel disease (Crohn’s disease and ulcerative colitis) in adults, children and young people. No significant costs are expected, although there may be a small increase in referrals into assessment which has been quantified as costing around £3,300 per 100,000 population.

NICE will appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active Crohn’s disease in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy. Vedolizumab will compete with infliximab and adalimumab and the cost is likely to be a substitution. The manufacturer has agreed an NHS-wide discounted rate which will make vedolizumab cost neutral. Vedolizumab is administered by IV infusion therefore service delivery costs will need to be considered.

This guidance will provide recommendations on the treatment of severely active UC after the failure of conventional therapy. Draft recommendations do not recommend the routine use of infliximab, adalimumab or golimumab to treat moderate to severe ulcerative colitis.

**TA140** did not recommend infliximab for sub-acute manifestations of UC and **TA262** (adalimumab for moderate to severe UC) was terminated as an evidence submission was not received from the manufacturer. All three biologics are licensed for the treatment of moderate to severe UC in adults who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.

The NICE guideline on UC states that the condition has an incidence in the UK of approximately 10 per 100,000 people annually, and a prevalence of approximately 240 per 100,000. This amounts to around 146,000 people in the UK (or 231 people per 100,000 population) with a diagnosis of UC. The costing template for this guideline assumes 85% of adults have mild to moderate disease, therefore if it is assumed that:

- 15% of adults have moderate to severe disease (or 35 people per 100,000 population)
- 50% of these might be eligible for treatment with infliximab, adalimumab or golimumab (~18 people per 100,000 population) following failure of standard treatment
- Adalimumab if used as per dosing in its SPC (40mg alternate weeks) costs around £10,900 per patient per year and infliximab costs around £13,400 per patient per year (drug costs only). The dosing for golimumab has not been updated in its SPC but the cost is likely to be comparable to adalimumab.
- 50% of patients receive adalimumab or golimumab and 50% receive infliximab
<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>IBD cont’d</strong></td>
<td>This could result in additional costs of around £220,000 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.</td>
</tr>
<tr>
<td>- NICE guidance on the use of <strong>infliximab, adalimumab and golimumab for the second line treatment of moderately to severely active ulcerative colitis</strong> cont’d</td>
<td>NICE will appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active UC in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy. Vedolizumab will compete with infliximab, adalimumab and golimumab (which are also being appraised) and the cost is likely to be a substitution. The manufacturer has agreed an NHS - wide discounted rate which will make vedolizumab cost neutral. Vedolizumab is administered by IV infusion therefore service delivery costs will need to be considered.</td>
</tr>
<tr>
<td>- NICE guidance on <strong>vedolizumab for the second line treatment of moderate to severe active UC</strong> expected Apr 2015</td>
<td></td>
</tr>
<tr>
<td><strong>Actions/ issues which may be considered by commissioners and providers</strong></td>
<td><strong>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.</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Cytokine modulators, such as TNF-inhibitors, are listed as exclusions in the National Tariff for 14/15. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. Drug exclusions under Payment by Results 14/15.</strong> As of April 2013, NHS England is the responsible commissioner when these agents are used in children (aged 18 years or younger). CCGs are the responsible commissioners for use of these agents in adults.</td>
</tr>
<tr>
<td></td>
<td><strong>New commissioning arrangements from April 2013 mean that these drugs are commissioned nationally by NHS England for paediatrics and locally commissioned by CCGs for adults. Ensure that any local policies for children are in line with national guidance.</strong></td>
</tr>
</tbody>
</table>
Diarrhoea and constipation

- QIPP indicator for laxative use
- NICE guidance on the use of lubiprostone for treating chronic idiopathic constipation, issued Jul 2014
- NICE guidance on the use of lubiprostone for treating opioid induced constipation, terminated appraisal
- NICE guidance on the use of naloxegol for opioid induced constipation, expected Jul 2015
- NICE Quality Standard on constipation in children and young people, issued May 2014. A commissioning support tool is also available to assist commissioners in its implementation.
- NICE Quality Standard on faecal incontinence, issued Feb 2014. A commissioning support tool is also available to assist commissioners in its implementation.

A set of comparators has 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 "laxatives" comparator considers the total number of average daily quantities (ADQs) for laxatives per STAR-PU.

NICE recommends lubiprostone for treating chronic idiopathic constipation, in adults for whom treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and for whom invasive treatment for constipation is being considered.

The NICE costing statement suggests that implementation of this guidance will not have a significant national resource impact, because lubiprostone is an additional treatment option and the cost is not significantly different from that of prucalopride which is currently recommended by NICE at a position in the treatment pathway that is alongside that proposed for lubiprostone. According to the costing report, the number of eligible patients, estimated at 25,550 is not expected to increase. Clinical opinion also suggests that upon implementation of the guidance, it is likely there will be an equal proportion of patients receiving treatment with either prucalopride or lubiprostone. There is an annual cost saving of approximately £80 if lubiprostone is used as an alternative to prucalopride 2 mg dosage, and an additional cost of £193 if lubiprostone is used as an alternative to prucalopride 1 mg dosage. (Note: prucalopride is only licensed in women.)

NICE is unable to recommend the use in the NHS of lubiprostone for treating opioid induced constipation because the regulatory timeline has changed due to the MHRA not granting a license for this indication. The MHRA issued a negative opinion because of insufficient evidence of efficacy.

The guidance will appraise the clinical and cost effectiveness of naloxegol within its licensed indication for treating opioid-induced constipation. Naloxegol does not currently hold a UK marketing authorisation for treating opioid-induced constipation but is expected to provide an additional treatment option for this group. The prevalence of opioid-induced constipation is not known, however the draft scope for lubiprostone states that approximately 32,000 people (or 60 people per 100,000 population) receive strong opioids (for cancer and non-cancer pain) in England. If it is assumed that:
- 50% of this use is for non-cancer pain (or 30 people per 100,000 population)
- 50% try at least two other laxatives and fail (or 15 people per 100,000 population) and therefore might be eligible for naloxegol.

This could result in an additional cost of ~£7,000 per 100,000 population.

This Quality Standard covers the diagnosis and management of idiopathic constipation in children and young people (from birth to 18 years). Potential costs re training to undertake a full assessment to diagnose constipation, increased prescribing of oral macrogols and ensuring appropriate continence services for children and young people exist. Potential reduction in referrals to secondary care for diagnosis and treatment of constipation and savings from inappropriate use of secondary care services.

The quality standard covers the management of faecal incontinence, defined as any involuntary loss of faeces that is a social or hygiene problem, in adults (18 years and older) in the community (at home and in care homes) and in hospital (all departments).
### Dyspepsia and gastro-oesophageal reflux disease (GORD)

- NICE guideline on the [management of dyspepsia and GORD](#), issued Sep 2014.
- NICE Pathway on dyspepsia and GORD available.

- NICE guideline on the [management of GORD in children and young people](#), expected Jan 2015.
  - NICE Pathway on irritable bowel syndrome available.

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

- A recent [DTB article](#) comments that it has been 10 years since publication of the NICE guideline on assessment and management of dyspepsia. It advises that healthcare professionals should review their current practice and assess whether it is in line with the revised recommendations.

This Quality Standard is at an early stage of development.

This partial update of CG 17 makes new recommendations about investigation and referral, Helicobacter pylori eradication therapy, specialist management, and surveillance of Barrett's oesophagus in people with dyspepsia. The [costing statement](#) states that implementing guidance will not have a significant national resource impact because many of the recommendations are embedded in current standard practice. However, NHS organisations are advised to assess the resource implications of the guidance locally and evaluate their own practices against the recommendations in the NICE guideline.

This guideline will cover the recognition, diagnosis and management of GORD in children and young people. This guideline will focus on symptoms and interventions of GORD. Commonly observed events, such as infant regurgitation, are covered as well as much rarer but potentially more serious problems, such as apnoea. It is unlikely that the guideline will have a significant financial impact on medicines spend.
### Other gastro-intestinal related conditions

- NICE guideline on [irritable bowel syndrome](#), expected (date TBC)
- NICE guideline on [coeliac disease](#), expected Sep 2015
- NICE [Pathway](#) available
- NICE guideline on [gallstone disease](#), expected Oct 2014
- NICE evidence summary on [colesevelam for bile acid malabsorption](#) available
- NICE evidence summary on [rifaximin for pouchitis](#) available
- The following Quality Standards have been referred to NICE (expected date TBC):
  - Diverticular disease
  - Irritable bowel syndrome
  - Pancreatitis

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

- NICE has issued a [Commissioning Guide](#) for faecal continence services. NICE estimates that the standard benchmark rate for a referral into a faecal continence service is 0.1%, or 100 per 100,000, of the adult population (aged 15 years or older) per year. For a standard primary care trust population of 250,000 (around 200,000 people are aged 15 years or older), the average number of people requiring referral into a faecal continence service would be 200 per year.
- NICE has issued a [Commissioning Guide](#) for the upper GI endoscopy service. NICE estimates that the benchmark endoscopy rate should be 0.75%, or 750 endoscopies per 100,000 population per year. This includes all diagnostic endoscopies and follow-up endoscopies. For a standard primary care trust population of 250,000, the number of endoscopies required would be expected to be 1875 per year.
- Commissioners and providers may wish to jointly review their local pathways for chronic constipation and the place in therapy of prucalopride and lubiprostone.
### 2. Cardiovascular disease

<table>
<thead>
<tr>
<th>Patent expiries</th>
<th>According to <em>Prescribing Outlook New Medicines 2014</em>, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: bivalirudin (August 2015)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>According to <em>QoF data for 12/13</em>, 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 comparators has 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 renin angiotensin system (RAS) drugs comparator measures the number of prescriptions for ACE inhibitors as a % of the total number of prescriptions for all drugs affecting the RAS system excluding aliskiren. This Quality Standard topic has been referred to NICE and is at an early stage of development.</td>
</tr>
<tr>
<td>Lipid modification</td>
<td>This is an area of low financial risk - the patent for atorvastatin expired in May 2012. According to <em>QoF data for 12/13</em>, the raw prevalence rate for CHD in England is 3.3%. The percentage prevalence for primary prevention of CVD increased from 1.7% in 11/12 to 2.2% in 12/13. 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. Two comparators relating to lipid modifying drugs have been developed which cover prescribing of ezetimibe and high-cost statins to ensure it is in line with NICE guidance: (i) Number of prescription items for generic statin preparations listed under category M in part VIII of the Drug Tariff as a percentage of the total number of prescription items for all statins, plus the total number of prescription items for combination of simvastatin/ezetimibe, plus total number of prescription items for ezetimibe alone. (ii) Number of items for ezetimibe and ezetimibe/simvastatin combinations as a percentage of the total number of prescription items for all statins, plus the total number of prescription items for combination of simvastatin/ezetimibe, plus total number of prescription items for ezetimibe alone. This comparator relates to the number of ADQs for omega-3 fatty acid compounds per omega-3 fatty acid compounds (BNF 2.12 sub-set) ADQ based STAR-PU. This Quality Standard topic has been referred to NICE and is at an early stage of development.</td>
</tr>
</tbody>
</table>

- **QIPP indicator for ACEi**
- **NICE Quality Standard on secondary care management of malignant hypertension, expected date TBC**
- **QIPP indicator for lipid modification drugs**
- **QIPP indicator for omega-3 fatty acid supplements**
- **NICE Quality Standard on lipid modification, expected Sep 2015**
<table>
<thead>
<tr>
<th>Lipid modification cont’d</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE guideline on lipid modification (update of previous guideline), issued Jul 2014</td>
<td>This guideline includes new and updated 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.</td>
</tr>
<tr>
<td>• Reviewing use of ezetimibe</td>
<td>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 exists only for atorvastatin 80mg vs. atorvastatin 10mg.</td>
</tr>
<tr>
<td>• NICE guidance on ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia (review of TA132), expected May 2016</td>
<td>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 &gt; 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 &lt; atorvastatin 80mg and person judged to be at higher risk because of comorbidities, risk score or using clinical judgement.</td>
</tr>
</tbody>
</table>

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 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 on patent. This is due to expire in 2016. Many prescribing advisers are targeting the inappropriate 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%. The sensitivity analysis showed that such a reduction (and replacement with atorvastatin) could lead to additional savings of £32,000 per 100,000 population. |

A DTB editorial questioned the NHS spend on ezetimibe and highlighted that the evidence on its effectiveness is based largely on surrogate outcomes and there is a lack of published data to show that it reduces mortality or morbidity. Ezetimibe spend (including the simvastatin combination product) totalled ~£54m (or £102,000 per 100,000 population) in primary care in England in 13/14 if this could be reduced by 25%, this could result in savings of approximately £25,000 per 100,000 population. |
### Disease or Indication:
**National targets and guidance**

<table>
<thead>
<tr>
<th>Actions/ issues which may be considered by commissioners and providers</th>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three statins are available generically. Organisations should review prescribing of lipid modifying agents in line with the QIPP comparators.</td>
<td>Three statins are available generically. Organisations should review prescribing of lipid modifying agents in line with the QIPP comparators.</td>
</tr>
<tr>
<td>Establish local agreement on pathway to achieve suggested cholesterol levels in patients with established CHD.</td>
<td>Establish local agreement on pathway to achieve suggested cholesterol levels in patients with established CHD.</td>
</tr>
<tr>
<td>Number of additional people who would be eligible to take statins is calculated using the QRISK2 assessment tool. If organisations are using a different assessment tool, the eligible population should be adjusted at a local level.</td>
<td>Number of additional people who would be eligible to take statins is calculated using the QRISK2 assessment tool. If organisations are using a different assessment tool, the eligible population should be adjusted at a local level.</td>
</tr>
<tr>
<td>The NICE costing model assumes implementation is spread equally over 5 years and additional GP appointments can be managed within existing resources; CCGs may wish to review this at a local level.</td>
<td>The NICE costing model assumes implementation is spread equally over 5 years and additional GP appointments can be managed within existing resources; CCGs may wish to review this at a local level.</td>
</tr>
<tr>
<td>CCGs may wish to explore at a local level the current prescribing of rosuvastatin to seek assurance that it is appropriate</td>
<td>CCGs may wish to explore at a local level the current prescribing of rosuvastatin to seek assurance that it is appropriate</td>
</tr>
<tr>
<td>Use of ezetimibe should be reviewed</td>
<td>Use of ezetimibe should be reviewed</td>
</tr>
</tbody>
</table>

### Acute coronary syndrome [ACS - unstable angina and myocardial infarction (MI)] & chest pain

<table>
<thead>
<tr>
<th>NICE Quality Standard on acute coronary syndromes (including MI), issued Sep 2014.</th>
<th>This is an area of moderate financial risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE Quality Standards expected Sep 2015 on:</td>
<td>This is expected to contribute to improvements in: deaths from cardiovascular diseases, length of hospital stay adverse effects of interventions (for example, bleeding and stroke) and incidence of further heart attacks. A commissioning support tool is also available to assist commissioners in its implementation.</td>
</tr>
<tr>
<td>Secondary prevention of MI and cardiac rehabilitation, Risk assessment of modifiable cardiovascular risk factors</td>
<td>These Quality Standard topics are in development.</td>
</tr>
<tr>
<td>NICE clinical guideline on Secondary prevention in primary and secondary care for patients following a myocardial infarction, issued Nov 2013</td>
<td>In England and Wales in 2011/12, there were approximately 110,000 myocardial infarctions. Of the 79,000 hospital admissions recorded in the Myocardial Ischaemia National Audit Project (MINAP) 41% were ST-segment elevation myocardial infarctions (STEMIs) and 59% were non-ST segment elevation myocardial infarctions (NSTEMIs).</td>
</tr>
<tr>
<td>Clopidogrel in combination with aspirin is recommended as a treatment option for up to 12 months in people who have had an NSTEMI, regardless of treatment or in people who have had a STEMI and received a bare-metal or drug-eluting stent.</td>
<td>Clopidogrel in combination with aspirin is recommended as a treatment option for up to 12 months in people who have had an NSTEMI, regardless of treatment or in people who have had a STEMI and received a bare-metal or drug-eluting stent.</td>
</tr>
<tr>
<td>Prasugrel and ticagrelor were introduced as alternatives to clopidogrel in NICE technology appraisals in October 2009 (TA182) and October 2011 (TA236) respectively, and are used as recommended as part of current practice. This guideline incorporates guidance on ticagrelor but that on prasugrel has not been incorporated because it was being updated at the time. As prasugrel and ticagrelor are alternatives to clopidogrel, the recommendations relating to their use are expected to result in only a minor increase in drug cost where these had not been fully implemented, the additional annual cost is approximately £650 per person.</td>
<td>Prasugrel and ticagrelor were introduced as alternatives to clopidogrel in NICE technology appraisals in October 2009 (TA182) and October 2011 (TA236) respectively, and are used as recommended as part of current practice. This guideline incorporates guidance on ticagrelor but that on prasugrel has not been incorporated because it was being updated at the time. As prasugrel and ticagrelor are alternatives to clopidogrel, the recommendations relating to their use are expected to result in only a minor increase in drug cost where these had not been fully implemented, the additional annual cost is approximately £650 per person.</td>
</tr>
<tr>
<td>The updated guideline no longer supports prescribing Omega 3 supplements. This is not anticipated to have a significant resource impact for commissioners, as typically these are purchased ‘over-the-counter’. Any staff time spent providing information to patients on this topic would be delivered as part of wider lifestyle advice.</td>
<td>The updated guideline no longer supports prescribing Omega 3 supplements. This is not anticipated to have a significant resource impact for commissioners, as typically these are purchased ‘over-the-counter’. Any staff time spent providing information to patients on this topic would be delivered as part of wider lifestyle advice.</td>
</tr>
</tbody>
</table>
## ACS & chest pain cont’d

- NICE clinical guideline on [Secondary prevention in primary and secondary care for patients following a myocardial infarction](https://www.nice.org.uk), cont’d

- NICE support for commissioning for acute coronary syndromes (including myocardial infarction), issued Sep 2014

- NICE guidance on [prasugrel with percutaneous coronary intervention for treating acute coronary syndromes](https://www.nice.org.uk), (review of technology appraisal guidance 182), issued Jul 2014

- NICE guidance on [cangrelor for coronary heart disease](https://www.nice.org.uk), expected Aug 2015

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

According to **costing statement**, drug therapy for secondary prevention is effectively applied nationally, but new findings on antithrombotic therapy, the efficacy of omega-3 fatty acid supplementation, and how ACE inhibitors and beta-blockers are used have also contributed to a need for the 2007 guideline to be updated and this might have resource implications at a local level as a result of variation in clinical practice across the country. Organisations should evaluate their own practices against the recommendations in the guideline and assess costs locally; potential areas for additional costs are: cardiac rehabilitation services, drug therapy; and potential savings are avoiding future non-elective admissions.

This resource addresses quality improvement through provision of information on key clinical, cost and service-related issues to consider during the commissioning process and signposting other implementation support tools.

Prasugrel 10 mg in combination with aspirin is recommended as an option within its marketing authorisation, for preventing atherothrombotic events in adults with acute coronary syndrome (unstable angina [UA], non-ST segment elevation myocardial infarction [NSTEMI] or ST segment elevation myocardial infarction [STEMI]) having primary or delayed percutaneous coronary intervention.

In 2012, 75,217 (0.14%) of people in England had percutaneous coronary intervention. It is estimated that approximately 1,200 people in England equivalent to approximately 2 per 100,000 population, will be affected by this decision each year. According to **costing statement**, the guidance is unlikely to result in a significant change in resource use in the NHS because prasugrel is an alternative treatment option to clopidogrel or ticagrelor and the population affected is small: if all patients were treated with prasugrel instead of clopidogrel or ticagrelor, the cost nationally would be below £1 million.

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 <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 not yet licensed but the European Medicines Agency accepted for review a marketing authorisation application in Dec 2013, for use in patients undergoing percutaneous coronary intervention for stable angina or acute coronary syndrome.

NICE guidance will address the use of cangrelor for reducing atherothrombotic events in people with coronary heart disease undergoing percutaneous coronary intervention and in people awaiting surgery requiring interruption of antiplatelet therapy.

According to **NHSC briefing**, for percutaneous transluminal balloon angioplasty with insertion of stent (OPCS-4 K75) and transluminal balloon angioplasty of coronary artery (OPCS4 K49), there were 52,290 and 2,872 hospital admissions, respectively, accounting for a total of 156,764 bed days.

**Prescribing Outlook New Medicines 2014** notes that if licensed, cangrelor may displace current options in this patient group, but as an i.v. infusion is likely to be more expensive. If it is assumed that cost of bolus and 4 hour infusion would be ~£600 and if 50% of the 60,000 hospital admissions for angioplasty were to receive cangrelor, this would result in additional cost of ~£34,000 per 100,000 as cost of existing antiplatelet therapy is negligible.
### ACS & chest pain cont’d

- **NICE guidance on rivaroxaban for the prevention of adverse outcomes in patients after the acute management of ACS**, expected Mar 2015
- **NICE Evidence Summary** available on rivaroxaban for secondary prevention in acute coronary syndrome

A new strength of rivaroxaban (2.5mg) was launched in UK in October 2014. The licensed indication for rivaroxaban 2.5mg twice daily is use in combination with aspirin alone or with aspirin plus clopidogrel or ticlopidine for the prevention of atherothrombotic events in adult patients after an ACS with elevated cardiac biomarkers.

**Prescribing Outlook New Medicines 2014** notes cost will be in addition to existing therapy in this population. The cost of 1 month’s treatment (2.5mg BD) is £58.80. Extension of treatment beyond 12 months should be done on an individual patient basis as experience up to 24 months is limited. The annual cost of rivaroxaban is ~ £700. Using epidemiology data from the costing template for NICE guidance on ticagrelor; if it is assumed there are 455 ACS patients per 100,000 population each year and a third receive rivaroxaban, this could result in an additional drug cost of £107,000 per 100,000 population per year. This excludes additional costs due to increased admissions from complications of treatment (e.g. bleeding) or savings from events avoided.

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

- There are now three antiplatelet agents recommended by NICE post ACS. Commissioners and providers should agree locally on the place in therapy for each of these (i.e. generic clopidogrel vs. prasugrel vs. ticagrelor) and the duration of therapy for audit purposes. This information should be communicated appropriately across the interface.
- Audit and monitor use of prasugrel and ticagrelor locally. Agree local policy on the use of these drugs for unlicensed indications not covered by the NICE guidance, for example, use in patients with “clopidogrel resistance” or intolerance, or use in combination with PPIs, as these will increase the cost implications.
- Agree the place in therapy locally of rivaroxaban for the secondary prevention of ACS. A [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.
- Users may wish to refer to the NICE Commissioning Guides on [Integrated Commissioning for the prevention of cardiovascular disease](#) (May 2012) and [Cardiac Rehabilitation](#) (October 2011).

### Heart failure (HF)

- **National Heart Failure Audit**, results, Apr 2012 - Mar 2013
- **NICE clinical guideline on acute heart failure**, issued Oct 2014

This area is unlikely to have any major cost implications

According to **QoF data for 12/13**, the raw prevalence rate for HF in England is 0.7%.

Findings from the 6th report indicate a reduction both in-hospital and one-year mortality for people admitted to hospital with acute heart failure during the 2012/13 audit cycle, when compared with the same outcomes for the 2011/12 cohort. This improvement reflects better treatment and management of heart failure, including improved prescribing rates of disease modifying therapies, and higher levels of specialist input. Prescription rates for disease modifying treatments have increased slightly since last year, although rates of exception reporting have also increased. Most (85%) patients with LVSD, and without a stated contraindication, were prescribed an ACE inhibitor or an ARB and 82% were prescribed a mineralocorticoid receptor antagonist, which is recommended as a second-line treatment. Only 39% of patients with LVSD were prescribed all three of the above treatments.

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.
<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>Heart failure (HF)</td>
<td>Eplerenone’s licence was extended in April 2012 to cover the treatment of adults with NYHA class II chronic HF and left ventricular systolic dysfunction (LVEF 30%) in addition to standard optimal therapy. The licence extension is based on the results of the EMPHASIS-HF study, which found that the addition of eplerenone (up to 50mg daily) to standard therapy reduces the risk of death and hospitalisation among patients with systolic HF and mild symptoms. It is unknown whether substituting spironolactone would produce similar results in these patients (at significantly lower cost). The manufacturer estimates that approximately 230,000 patients in the UK (or 370 patients per 100,000 population) may fall within NYHA class II and that half that number could be eligible for eplerenone for this indication. However, based on previous uptake of the drug, it anticipates only a small proportion of patients may be prescribed it.</td>
</tr>
</tbody>
</table>

- Licence extension for eplerenone –NYHA class II HF (not currently included in the NICE work plan) |
- NICE Quality Standard on acute heart failure, expected Dec 2015 |

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

- Commissioners may wish to refer to the guide developed by NICE on commissioning services for people with chronic HF. |
- 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. |

Ischaemic stroke & atrial fibrillation (AF) |

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

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. |
### Ischaemic stroke & AF cont’d

- NICE clinical guideline on the [management of AF](#), cont’d

- NICE guidance on [edoxaban tosylate for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation](#); expected Sep 2015

- UKMI has produced [common questions and answers](#) on the practical use of oral anticoagulants in non-valvular atrial fibrillation

- NICE guidance on [self-monitoring coagulation status using point-of-care coagulometers](#) (the CoaguChek XS system and the INRatio2 PT/INR in people atrial fibrillation and heart valve disease), issued Sep 2014

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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.

Edoxaban is not yet licensed but was filed for approval in the EU in Jan 2014. According to [Prescribing Outlook New Medicines 2014](#), edoxaban will be a competitor to rivaroxaban, dabigatran and apixaban, and hence the cost is likely to be a substitution, and unlikely to have any additional cost implications over those outlined above. Once daily dosing of edoxaban may be important for adherence (rivaroxaban is currently the only licensed once daily NOAC).

The CoaguChek XS and InRatio2 PT/INR system are recommended for self-monitoring coagulation status in adults and children on long-term vitamin K antagonist therapy who have AF or heart valve disease if: the person prefers this form of testing and the person or their carer is both physically and cognitively able to self-monitor effectively. Although there is greater uncertainty of clinical benefit for the InRatio2 PT/INR monitor than for the CoaguChek XS system, the evidence indicates that the precision and accuracy of both monitors are comparable to laboratory-based INR testing.

Of the estimated 450,000 people in England who may be eligible for coagulometers, the number who prefer, or are considered able to self-monitor is unknown.
### Disease or Indication: National targets and guidance

#### Ischaemic stroke & AF cont’d

- NICE guidance on self-monitoring coagulation status using point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR in people atrial fibrillation and heart valve disease, cont’d

- Patient self-testing and self-management of oral anticoagulation with vitamin K antagonists: guidance from the British Committee for Standards in Haematology, issued Aug 2014


- NICE Quality Standard on AF expected Jul 2015

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

According to costing template:

- The initial (year 1) cost of self-testing in primary and secondary care with Coagucheck XS is estimated to be about £620 and £720, respectively (purchase of device, training and management costs). Annual recurrent costs are ~ £230 and 250, respectively. Costs for self-management are respectively ~ £606, £786, £128 and £148.
- Self-monitoring allows greater frequency of INR monitoring, and so more appropriate dosage of oral anticoagulants. This can reduce rates of adverse events such as stroke or major haemorrhages, and therefore future treatment costs. As the costs of treating adverse events are considerably higher than those of self-monitoring, avoiding a small number of high-cost adverse events has the potential to make the initial investment cost-saving.
- Where self-monitoring leads to decreased demand for services such as anti-coagulation clinics there may be savings for both CCGs and NHS England. The annual cost of anti-coagulation monitoring within a primary or secondary care setting has been estimated to be approximately £250 per person.
- The cost of the device and consumables could affect CCGs where the service is provided through secondary care or community services, and/or NHS England where the service is provided in primary care.

A pack of 48 CoaguChek XS test strips costs £133.26. If 5% of estimated 450,000 people in England who may be eligible for coagulometers self tested once a week, the additional cost resulting from use of strips would be ~ £6000 per 100,000 population.

This guideline notes that:

- Patient self-testing and patient self-management (PST/PSM) in selected motivated patients can improve anticoagulation control and decrease the number of thrombotic events but has little effect on rates of major bleeding.
- The cost-effectiveness of PST/PSM depends on the cost and quality of usual care. For many patients in the UK it will not be cost-effective but for selected patients it is likely to be cost-effective, particularly if time saved by the patient is taken into account.

This found that evidence indicates point of care (POC) INR technologies are generally precise and accurate when INR values are in the commonly targeted therapeutic range. They can improve anticoagulation control by increasing the time INR values are within therapeutic range however, discordances in INR values of a magnitude that would alter clinical management occur in some patients. The review did not demonstrate a significant difference in the risk of hemorrhagic or thromboembolic events between POC and standard laboratory testing methods; however, previous reviews have shown statistically significant differences favouring POC INR testing on these outcomes, as well as on mortality. There was a lack of evidence on the comparative effectiveness between different POC INR technologies, and for PST versus PSM.

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

- Rather than the purchase of coagulometers being funded by patients, the initial investment in training, the device and the consumables may be provided by CCGs or NHS England area teams, depending on how the service is commissioned. Commissioners should collaborate with providers to ensure that self-monitoring services are appropriately funded.
- A NICE Commissioning guide is available to support commissioners to review how anticoagulation therapy is currently initiated, provided, monitored and reviewed in their local area with particular consideration to the introduction of the novel oral anticoagulants.
### Peripheral arterial disease (PAD)

- **NICE Quality Standard on peripheral arterial disease:** issued Jan 2014

- **MHRA advice – cilostazol – indication restricted,** Apr 2013

- **NICE guidance on rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis:** issued Mar 2014

This is an area of low financial risk but has been given more prominence as indicators for PAD are now included in the QOF. The indicators include the use of antiplatelets and blood pressure & cholesterol control

This covers the diagnosis and management of lower limb PAD in adults aged 18 years and over. It does not cover acute ischaemia of the lower limb. A commissioning support tool also available to assist commissioners in its implementation.

A review of the benefits and risks of cilostazol was triggered by reports of adverse reactions (mainly cardiac and haemorrhagic), and by the potential for drug interactions. As a result, cilostazol is now restricted to second-line use in patients for whom life-style modifications and other appropriate interventions have failed to sufficiently improve their symptoms. Additionally, cilostazol is now contraindicated in patients with any of the following: (i) Unstable angina, recent myocardial infarction or coronary intervention (within 6 months) (ii) a history of severe tachyarrhythmia (iii) those receiving two or more other antiplatelet or anticoagulant treatments

Rituximab taken with glucocorticoids is recommended as a possible treatment for certain people with anti-neutrophil cytoplasmic antibody-associated vasculitis (that is, severely active granulomatosis with polyangiitis [also known as Wegener's granulomatosis] and microscopic polyangiitis).

The costing statement estimates that guidance will cost approximately £1.1 million per annum. However, because rituximab is already routinely funded by NHS England for most people for whom this technology is recommended by the NICE guidance, costs are not expected to be significant.

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

- Rituximab for rheumatoid vasculitis is listed as an exclusion in the National Tariff for 14/15. The responsible commissioner for this drug is NHS England.
<table>
<thead>
<tr>
<th>Disease or Indication: National targets and guidance</th>
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</table>

### VTE cont’d

- NICE guidance on dabigatran for the treatment and secondary prevention of DVT and/or PE, expected Dec 2014
- NICE guidance on apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism, expected Jun 2015
- NICE guidance on edoxaban tosylate for treatment, secondary prevention of deep vein thrombosis and pulmonary embolism; expected Oct 2015
- SMC guidance on dabigatran etexilate for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults, issued Oct 2014

A FAD issued in Oct 2014 recommends use, within its marketing authorisation, as an option for treating and for preventing recurrent DVT and PE in adults.

Edoxaban is not yet licensed but was filed for approval in the EU in Jan 2014. According to *Prescribing Outlook New Medicines 2014*, edoxaban will be a competitor to rivaroxaban, dabigatran and apixaban. Like rivaroxaban, it is also dosed once daily which may be a consideration in terms of adherence. The cost of edoxaban tosylate is not yet known but it would seem unlikely that it would be too dissimilar to current licensed NOACs.

Dabigatran was accepted for use within NHS Scotland for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults. The economic case was based on evidence relating to a maximum of 18 months treatment so the cost-effectiveness of longer term use is uncertain.

The company estimated there to be 26,022 patients eligible for treatment with dabigatran in Scotland each year, to which an estimated uptake rate was applied. The net medicines budget impact was estimated to be £43k in year 1 and £553k in year 5 (~£800 and £10,400 per 100,000, respectively).

### 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.
- A NICE Commissioning guide is available to support commissioners to review how anticoagulation therapy is currently initiated, provided, monitored and reviewed in their local area with particular consideration to the introduction of the novel oral anticoagulants.
### 3. Respiratory System

#### Patent expiries

According to *Prescribing Outlook New Medicines 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: icatibant (Nov 2014), tiotropium (Sep 2015); ciclesonide (Sep 2016)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Respiratory System</strong></td>
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<tr>
<td><strong>Patent expiries</strong></td>
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<td>According to <em>Prescribing Outlook New Medicines 2014</em>, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: icatibant (Nov 2014), tiotropium (Sep 2015); ciclesonide (Sep 2016)</td>
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<tr>
<td><strong>Asthma</strong></td>
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<tr>
<td>- Updated BTS/SIGN guideline on asthma (October 2014)</td>
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<tr>
<td>- QIPP area for high dose inhaled corticosteroids</td>
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<tr>
<td>- NICE clinical guideline on diagnosis and monitoring of asthma, expected Jun 2015</td>
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<tr>
<td>- The National Review of Asthma Deaths report, May 2014</td>
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</table>

#### Asthma

*This is an area of low financial risk*

According to *QoF data for 13/14*, the raw prevalence rate for asthma in England is 5.9%.

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. There are however very few clinical trials in this specific patient group to guide management.

A set of *comparators* has 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. Although there isn’t a specific indicator for this comparator, 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 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 analysis of asthma deaths occurring between Feb 2012 and Jan 2013 found that personal asthma action plans were provided to only 23%, and 43% had no evidence of an asthma review in general practice within the previous year. There was evidence of excessive prescribing of reliever medication, under-prescribing of preventer medication, and inappropriate prescribing of LABA (14% prescribed a single-component LABA bronchodilator at the time of death, and at least 3% were on LABA monotherapy without ICS preventer treatment).

The report makes a number of key recommendations; those regarding medicines include:

- All asthma patients who have been prescribed more than 12 short-acting reliever inhalers in the previous 12 months should be invited for urgent review of their asthma control, with the aim of improving their asthma through education and change of treatment if required.
- An assessment of inhaler technique to ensure effectiveness should be routinely undertaken and formally documented at annual review, and also checked by the pharmacist when a new device is dispensed.
- Non-adherence to preventer ICS is associated with increased risk of poor asthma control and should be continually monitored.
- The use of combination inhalers should be encouraged. Where LABA bronchodilators are prescribed for people with asthma, they should be prescribed with an ICS in a single combination inhaler.
### 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).

- 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.

### Chronic Obstructive Pulmonary Disease (COPD)

- Systematic review and meta-analysis - tiotropium Respimat® inhaler in COPD, Oct 2012

This is an area of increased activity and moderate financial risk

According to QoF data for 13/14, the raw prevalence rate for COPD in England is 1.8%.

A systematic review and meta-analysis published in Thorax found a possible increased risk of all-cause mortality and death from cardiovascular causes associated with tiotropium administered with the Respimat device, when compared with placebo and other inhaled treatments for COPD. These increased risks were not present in all analyses and not seen with tiotropium administered by the HandiHaler device. In contrast a LABA plus ICS combination, tiotropium HandiHaler and LABAs had relatively safer profiles, with LABA-ICS having the lowest risk of overall death in patients with COPD. The higher risk was derived from doses that were higher than the currently licensed doses of Respimat. The MHRA provided information and advice for healthcare professionals in 2010 advising that patients with COPD who use tiotropium should be reminded not to exceed the recommended once-daily dose. The MHRA also advised that Respimat should be used with caution in patients with known cardiac rhythm disorders.

The TIOSPIR study has since been published and this failed to find any increased risk of mortality associated with the Handihaler (18 microg) when compared with two doses of tiotropium via the Respimat (2.5 microg and 5.0 microg) in over 17,000 patients with COPD.

### 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.
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th>Actions/ issues which may be considered by commissioners and providers cont’d</th>
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<tbody>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>• 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.</td>
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### Drug allergy

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<th>Actions/ issues which may be considered by commissioners and providers</th>
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<tbody>
<tr>
<td>• NICE guideline on drug allergy, issued Sep 2014</td>
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</table>

This clinical guideline covers the diagnosis and management of drug allergy in adults, children and young people. It makes recommendations on assessment, documentation and sharing of information with other healthcare professionals, provision of information to patients, non-specialist management and referral to specialist services.

According to the costing statement, implementation of this guideline 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.

<table>
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<tr>
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<tr>
<td>• Locally discuss and agree a policy on the supply of adrenaline auto injector pens to people at risk of anaphylactic reactions. The MHRA has recently 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.</td>
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<tr>
<td>Disease or Indication: National targets and guidance</td>
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<tr>
<td><strong>Other respiratory conditions</strong></td>
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<tr>
<td>Bronchiolitis</td>
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<tr>
<td>• NICE clinical guideline on the diagnosis and management of bronchiolitis in children, expected May 2015</td>
</tr>
</tbody>
</table>
| Idiopathic Pulmonary Fibrosis (IPF)               | • Follow TA 282 guidance on pirfenidone  
• Do not use any of the following to modify disease progression: ambrisentan; azathioprine; bosentan; co-trimoxazole; mycophenolate mofetil; prednisolone; sildenafil; warfarin  
• Advise the person that oral N-acetylcysteine is used for managing IPF but its benefits are uncertain  
• If people with IPF are already using prednisolone or azathioprine, discuss the potential risks and benefits of discontinuing, continuing or altering therapy  

The guideline also makes recommendations on best supportive care, including symptom relief with benzodiazepines and/or opioids if the person is breathless at rest; use of opioids for debilitating cough and thalidomide for intractable cough, pulmonary rehabilitation, lung transplantation and ventilation. |
<p>| • NICE clinical guideline on IPF, issued Jun 2013 | The costing report identifies three key recommendations that are likely to be associated with the most significant cost impact – none of these are related to medicines use. Any potential savings from a decrease in the use of the listed disease-modifying therapies are not expected to be significant as they are either not used in current practice or have a low cost per person. The guideline is therefore not expected to have any significant impact on medicines spend. |</p>
<table>
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<th>Other respiratory conditions cont’d</th>
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<tr>
<td><strong>IPF cont’d</strong></td>
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<tr>
<td>• NICE guidance on <a href="#">pirfenidone for treating idiopathic pulmonary fibrosis</a>, issued Apr 2013</td>
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</table>

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<tr>
<th>Epidemiology, potential financial implications for a population of 100,000 and other comments</th>
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<tbody>
<tr>
<td>NICE recommends pirfenidone as an option for treating IPF only if the person has a FVC 50-80% predicted and the manufacturer provides it with the discount agreed in the patient access scheme. Treatment should be discontinued if there is evidence of disease progression (a decline in predicted FVC of 10% or more within any 12-month period).</td>
</tr>
</tbody>
</table>

The costing template estimates that implementation of this guidance will be associated with an annual cost of £173,000 per 100,000 (based on list price; excluding the PAS). This is based on the following assumptions:

- A prevalence of IPF of 0.0227% (23 per 100,000 population), with 12 per 100,000 eligible for pirfenidone and continuing treatment
- Uptake of pirfenidone in 8 per 100,000 population, with the remaining eligible 4 per 100,000 population receiving NAC monotherapy or best supportive care/other treatment options
- A cost of current treatment of £1,000 per 100,000 (triple therapy [prednisolone, azathioprine and NAC], NAC monotherapy, or best supportive care)
- An average annual cost of ongoing pirfenidone treatment of £22,245.96 (based on an average dosage of 7.65 capsules per day in the clinical trials)
- A future proportion of eligible patients treated with pirfenidone of 67.5%

The costs are based on the estimated maximum uptake of pirfenidone, which could take around four years to reach. Uptake in the first year is likely to be highest as patients already known are started on pirfenidone, with uptake in subsequent years likely to be slower as uptake will apply to the new incident population each year. Although clinical opinion is that pirfenidone treatment may lead to increased telephone contact with nurse specialists due to side-effects and the need for dose titration, and that there is a possibility that more clinic visits will be required (depending on the severity of side-effects), the potential cost impact is not anticipated to be significant.

This Quality Standard will cover the diagnosis and management of idiopathic pulmonary fibrosis in adults, from the initial suspicion of the disease to referral, supportive care and treatment.
### 4. Central nervous system

**Patent expiries**

According to Prescribing Outlook New Medicines 2014, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: escitalopram oxalate (May 2014), paliperidone (Oct 2014), almotriptan (Dec 2014), palonosetron (Nov 2015), eletriptan hydrobromide (Dec 2015), frovatriptan (Dec 2015), and agomelatine (Feb 2016).

<table>
<thead>
<tr>
<th><strong>Anxiety</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE Quality Standard on <a href="#">anxiety disorders</a>, issued Feb 2014</td>
</tr>
<tr>
<td>NICE pathways for <a href="#">social anxiety disorder</a> and <a href="#">generalised anxiety disorder</a> available</td>
</tr>
</tbody>
</table>

**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.

<table>
<thead>
<tr>
<th><strong>Schizophrenia</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE guideline on <a href="#">psychosis and schizophrenia in adults</a>, issued Feb 2014</td>
</tr>
<tr>
<td>NICE pathway available</td>
</tr>
<tr>
<td>• MHRA <a href="#">learning module</a> on antipsychotics</td>
</tr>
<tr>
<td>• NICE Quality Standards on psychosis and schizophrenia in i) <a href="#">adults</a> (expected Feb 2015) and ii) <a href="#">children and young people</a> (expected Oct 2015)</td>
</tr>
</tbody>
</table>

**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

- QIPP area for hypnotics
- MHRA [learning module](#) on benzodiazepines

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

### Bipolar disorder

- NICE guideline on [bipolar disorder (update)](#), issued Sep 2014
- NICE [pathway](#) available

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.

The [costing statement](#) notes that there has been a change from the previous guideline (published in 2006) in the drugs recommended for bipolar depression. The main recommendations regarding drug choice in this setting are as follows:

- If a person develops moderate or severe bipolar depression and is not taking a drug to treat their bipolar disorder, offer fluoxetine combined with olanzapine, or quetiapine on its own, depending on preference and previous response to treatment.
- If the person prefers, consider either olanzapine (without fluoxetine) or lamotrigine on its own.
- If there is no response to fluoxetine combined with olanzapine, or quetiapine, consider lamotrigine on its own.
- The same additional drug treatments are recommended for patients who develop moderate or severe bipolar depression who are already taking lithium (if limited response despite optimisation of plasma level) or valproate (if limited response despite use of maximum tolerated dose).

The new recommendations are not anticipated to lead to a significant change in costs because the drugs are very similar in price. Organisations may wish to review at a local level whether there is any impact from a change in the cost of monitoring the effects of these drugs (monitoring recommendations are included in section 1.10).

Overall the guideline is not expected to result in any short-term benefits or cost savings; it may however lead to more efficient use of resources and thus long-term savings and benefits. Due to variation in clinical practice across the country, organisations are encouraged to evaluate their own practices against the recommendations and assess costs locally.

This Quality Standard is at an early stage of development.

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

- Commissioners and providers may need to work together to establish psychological therapy services for bipolar disorder.
### Depression

- **QIPP area for antidepressants**

- **NICE guidance on the use of vortioxetine for treating major depressive disorder**, expected Sep 2015

- **NICE pathway available**

- **NICE guideline on depression in children and young people (update)**, expected Mar 2015

- **MHRA learning module** on SSRIs

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 comparators related to antidepressants have been developed:

- 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
- 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’.

Vortioxetine is a bimodal oral antidepressant that is thought to work through a combination of reuptake inhibition of serotonin and modulation of serotonin receptor activity. It is licensed in the UK but has not yet been launched (due Q1 2015). The NHSC briefing for the drug notes that it is intended for the treatment of major depressive disorder as a first line treatment, a substitute in patients with no or an inadequate response to SSRIs or SNRIs, and for patients who are difficult to treat using existing pharmacological options. The comparators for vortioxetine in the clinical trials include duloxetine, agomelatine, venlafaxine and placebo. It is administered orally, once daily as monotherapy.

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). 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 first line at an additional cost (vs. citalopram) of £29/month (assume cost of vortioxetine will be £30/month/patient), this could result in a cost implication of around £17,000 per 100,000 per year. Use as a sequential antidepressant agent will have further cost implications – these have not been modelled here.

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. The guideline is at an early stage of development and no information on its likely cost impact is available.

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.

### 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.
### Disease or Indication: National targets and guidance

<table>
<thead>
<tr>
<th><strong>Obesity</strong></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), issued Nov 2014</td>
</tr>
<tr>
<td>NICE pathway available</td>
</tr>
<tr>
<td>• NICE Quality Standard on obesity in children, expected Dec 2014</td>
</tr>
<tr>
<td>• NICE public health guidance on lifestyle weight management services for managing overweight and obesity among adults (issued May 2014) and children and young people (issued Oct 2013)</td>
</tr>
<tr>
<td>NICE pathway available</td>
</tr>
<tr>
<td>• Statistics on Obesity, Physical Activity and Diet England 2014</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Epidemiology, potential financial implications for a population of 100,000 and other comments</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>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:</td>
</tr>
<tr>
<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>- 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>- 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>*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. Although a costing template is not currently available for this guideline, the recommendations above will increase the number of people receiving bariatric surgery and therefore any ongoing prescribing post bariatric surgery (e.g. vitamins). However, these are likely to be offset by reduced type 2 diabetes and complications arising from type 2 diabetes. It is estimated that an additional 5,000 weight loss surgeries will be carried out each year if the guidance is fully implemented.</td>
</tr>
<tr>
<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>
</tbody>
</table>

This Quality Standard will cover public health strategies to prevent overweight and obesity, and interventions for lifestyle weight management, in children and young people aged under 18 years.

NICE has published two guidelines on lifestyle weight management services for overweight and obese i) adults and ii) children and young people. Although the guideline recommendations do not cover drug therapy of any kind and a significant impact on medicines spend is not expected, over time they may lead to reduced medicines spend on this and other areas linked to obesity e.g. CVD, diabetes.

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.

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

- 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 dietitian; 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.
### Pain

- Update of clinical guideline on the [pharmacological management of neuropathic pain](https://www.nice.org.uk/guidance/ng90) in adults in non-specialist settings, issued Nov 2013
- [NICE pathway](https://www.nice.org.uk/guidance/ng90) available.

In March 2010, NICE published a [clinical guideline](https://www.nice.org.uk/guidance/ng90) on the management of neuropathic pain conditions in adults in primary and secondary care, in non-pain specialist settings. This recommended pregabalin or amitriptyline (unlicensed use) as options for first-line treatment, except in the case of painful diabetic neuropathy, where duloxetine should be offered (or amitriptyline if this is contra-indicated).

Due to concerns about the cost-effectiveness of some of the recommended treatment options, NICE conducted a full update of this guideline. This has now been published and recommends the following drug treatment for neuropathic pain (excluding trigeminal neuralgia):

- Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment
- If the initial treatment is not effective or not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second or third drugs tried are also not effective or not tolerated
- Consider tramadol only if acute rescue therapy is needed
- Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments

The guideline does not recommend the use of cannabis sativa extract, capsaicin patch, lacosamide, lamotrigine, levetiracetam, morphine, oxcarbazepine, topiramate, tramadol (long-term use) or venlafaxine for the treatment of neuropathic pain in non-specialist settings.

For the treatment of trigeminal neuralgia, the guideline recommends that carbamazepine be offered for initial treatment. If this is not effective or not tolerated, or is contra-indicated, expert advice and early referral to a specialist pain service or a condition-specific service should be considered.

Although the updated guideline recommends two further first-line options for the treatment of neuropathic pain (duloxetine and gabapentin), the costing statement notes that the costs of these further options are similar to existing practice. Implementation of the guideline is therefore not expected to have a significant impact on NHS resources. The addition of gabapentin may reduce the use of more expensive treatment options. Organisations are advised to check local prescribing practice to ascertain the resource impact of any changes in prescribing at a local level.

The [costing statement](https://www.nice.org.uk/guidance/ng90) lists the annual prescribing costs associated with the different drug treatments for neuropathic pain, ranging from £10.95 for amitriptyline to £839.50 for pregabalin (£127.75 for gabapentin at a dose of 1.8g daily in divided doses).

The DTB published a two-part ([part 1](https://www.dtb.nhs.uk/) and [part 2](https://www.dtb.nhs.uk/)) update on the treatment of neuropathic pain in October and December 2012 reviewing the available evidence for antiepileptics, antidepressants, opioids, tramadol, and topical agents. The author notes current guidance recommending a tricyclic antidepressant, gabapentin or pregabalin first-line, and concludes that the lowest cost agents should be used first, due to the absence of overwhelming evidence of superiority of one drug over another.

### 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 could become available in the first half of 2015. However, whether these will cover all licensed indications of the branded version is currently uncertain. Commissioners and providers should consider this when developing local guidelines.
<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>Nausea and vomiting</td>
<td>The EMA completed a review into the benefits and risks of metoclopramide, following concerns over side effects and efficacy. The review confirmed the well known risks of neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia, and concluded that these risks outweigh the benefits in long-term or high-dose treatment. This review has resulted in a number of restrictions to indication, dose and duration of use; these are summarised in a Drug Safety Update article.</td>
</tr>
<tr>
<td>• EMA review – metoclopramide and risk of neurological effects, Aug 2013</td>
<td></td>
</tr>
<tr>
<td>• MHRA: Restricted use of domperidone following EMA review, Apr 2014</td>
<td>In April 2014, the MHRA announced revised advice on the use of domperidone, following a European review of its safety. The review confirmed a small risk of serious cardiac effects, particularly in those aged &gt;60 years, those taking doses of &gt;30mg per day, and those taking QT-prolonging medicines or CYP3A4 inhibitors. The indication has now been restricted to the relief of nausea and vomiting only, and new recommendations regarding dosing, treatment duration, cautions and contra-indications have been made. The recommendations are summarised in a Drug Safety Update article. As of 4th September 2014, domperidone is only available as a prescription-only medicine.</td>
</tr>
<tr>
<td>Substance dependence</td>
<td>This guidance aims to support smoking cessation, temporary abstinence from smoking and smokefree policies in all secondary care settings. It supersedes a number of recommendations made in the public health guidance on smoking cessation services, where they apply to secondary care, and it complements (but does not replace) NICE guidance on stopping smoking. Recommendations include:</td>
</tr>
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</table>
| Smoking Cessation                                    | • Identify people who smoke and refer offer to help them stop  
• Provide intensive support for people using acute and mental health services, and maternity services  
• Provide information and advice for carers, family, other household members and hospital visitors  
• Advise on and provide stop smoking pharmacotherapies  
• Adjust drug dosages (e.g. clozapine; olanzapine; theophylline; warfarin) for people who have stopped smoking  
• Make stop smoking pharmacotherapies available in hospital  
| • NICE public health guidance on smoking cessation in secondary care - acute, maternity and mental health services, issued Nov 2013 | There are additional recommendations relating to provision of leadership on stop smoking support, the development and communication of smokefree policies, staff support and training, and commissioning of smokefree secondary care services. As there is variation in current practice, organisations are encouraged to evaluate their own practices against the recommendations and assess the potential local costs. The following potential costs are highlighted in the costing statement: |
| NICE pathway available for tobacco harm reduction approaches and smoking cessation in secondary care | • Support for users of secondary care services to deal with temporary abstinence (including provision of pharmacotherapy)  
• Intensive support for mental health users  
• Smoking cessation training for healthcare staff  
• Costs incurred to achieve a smoke-free environment  

The costs of implementation will be higher in areas where stop smoking services have not yet been developed, especially mental health settings. Despite these costs, the guidance will lead overall to long-term benefits and savings, as a reduction in the number of people smoking is likely to reduce the number of smoking-related illnesses and associated costs. |
### Disease or Indication: National targets and guidance

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

#### Substance dependence cont’d

**Smoking Cessation cont’d**

- NICE public health guidance on smoking cessation in secondary care - acute, maternity and mental health services, cont’d
- NICE public health guidance on smoking cessation (update), expected date TBC
- NICE Quality Standard on smoking – harm reduction, expected Jul 2015
- Statistics on Smoking, England 2014

#### Alcohol Use Disorders

- NICE Quality Standard on preventing harmful alcohol use in the community, expected Dec 2014
- NICE pathway available
- NICE guidance on nalmefene for reducing alcohol consumption in people with alcohol dependence, expected Nov 2014

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Healthcare costs, sickness absence rates and time lost for smoking breaks, and length of stay for surgical patients (reduced post-op complications and wound healing times). In addition as smoking can reduce the effect of antipsychotics, the guidance is expected to reduce antipsychotic drug cost. The RPC estimates that smoking increases psychotropic drug costs in the UK by up to £40 million (approximately £72,000 per 100,000 population).

This guidance is at an early stage of development but will update previous public health guidance (2006) in this area.

This Quality Standard is at an early stage of development.

Latest statistics from the HSCIC for England show:

- In 2013/14, there were nearly 1.8 million prescription items to help people stop smoking (a decrease since last year when there were there were over 2.2 million prescription items). Of these, 1.1 million were for NRT, 697,000 were for varenicline, and 22,000 were for bupropion.
- The Net Ingredient Cost (NIC) of all prescription items used to help people quit smoking was £48.8 million (decrease of 16% on last year).
- In 2012/12 there were approximately 1.6 million admissions (4,400 per day) for adults aged 35 and over with a primary diagnosis of a disease that can be caused by smoking.
- Around 460,900 admissions in this age group were estimated to be attributable to smoking (4% of all admissions in this age group). This represents a decrease of 18% since last year (559,800 admissions).

According to this report, the number of community pharmacies commissioned to provide stop smoking services rose from 2522 in 2005-06 to 5747 in 2012-13.

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

This guidance will consider the clinical and cost effectiveness of nalmefene for reducing alcohol consumption in adults with alcohol dependence. A NICE evidence summary (ESNM29) notes that nalmefene is an opioid receptor modulator, which exhibits antagonist activity at μ and δ receptors and partial agonist activity at κ receptors. It is dosed ‘as needed’, with one tablet taken on each day the patient perceives a risk of drinking alcohol, preferably 1-2 hours prior to the anticipated time of drinking. Nalmefene is the first medicine to be granted a licence for the reduction of alcohol consumption in people with alcohol dependence, although there is limited evidence for using other treatments off-label for this indication.
Substance dependence cont’d

Alcohol Use Disorders cont’d

- NICE guidance on nalmefene for reducing alcohol consumption in people with alcohol dependence, cont’d

The Final Appraisal Determination recommends 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 (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 costing template for CG115 estimates that a prevalence of alcohol dependence in people aged 16 years and over of 3.082 per 100,000 (2.588 with mild, 431 with moderate and 62 with severe dependence). The AWMSG recommends nalmefene as an option for reducing alcohol consumption in line with its marketing authorisation. 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.

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).
### Substance dependence cont’d

#### Alcohol Use Disorders cont’d

- NICE guidance on nalmefene for reducing alcohol consumption in people with alcohol dependence, cont’d

#### Drugs misuse

- NICE public health guideline on needle and syringe programmes, issued Mar 2014 NICE pathway available
- NICE public health guideline on needle and syringe programmes, cont’d

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Nalmefene is likely to have considerable service delivery costs, due to the requirement for continuous psychosocial support; these costs have not been quantified here. The associated reduction in drinking and will however be associated with longer-term benefits and cost-savings.

According to this report, the number of community pharmacies commissioned to provide local enhanced services for needle and syringe exchange increased from 1061 in 2005-06 to 2122 in 2012-13 (-0.4% from 2011-12).

This guidance makes recommendations on needle and syringe programmes, including those provided by pharmacies and drugs services for adults and young people (including those under 16) who inject drugs, including image- and performance-enhancing drugs. It updates and replaces NICE public health guideline 18 (published February 2009), and now also includes young people aged under 18 (including those under 16) and users of image- and performance-enhancing drugs.

The costing statement notes that no new economic evidence has been considered in the update of this guidance (PH18 economic evidence indicated that needle and syringe programmes were cost-effective and likely to achieve a return on investment). It is estimated that for a relatively small investment, around £200 per annum for a person who injects drugs, there is the potential to avoid significant future healthcare costs estimated to be between £10,000 and £42,000 per individual, per annum (these are the estimated costs of treating HIV or hepatitis C). In addition there may savings in wider societal costs.

Due to the variation in current local provision, the likely cost impact of implanting this guidance should be estimated locally.

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

- 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.
- 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.
### Alzheimer's disease & dementia

- QIPP area for low dose antipsychotics in people with dementia
- NICE pathway available
- Acute trust CQUIN schemes – dementia and delirium
- NICE Quality Standard on delirium, issued Jul 2014

A set of comparators has 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. Although no specific comparator is available for this area, organisations are advised to review and, if appropriate, revise prescribing of low-dose antipsychotics in people with dementia, in accordance with the NICE/Social Care Institute for Excellence (SCIE) clinical guideline and the NICE quality standard on dementia, and the Alzheimer's Society best practice guide.

Dementia and delirium is a national Commissioning for Quality and Innovation (CQUIN) target that applies to acute service providers. It aims to: incentivise the identification of patients with dementia and delirium, alone and in combination alongside their other medical conditions, prompt appropriate referral and follow up after they leave hospital, and ensure that hospitals deliver high quality care to people with dementia and support their carers.

This Quality Standard covers the prevention, diagnosis and management of delirium in adults in hospital or long-term care settings. A commissioning support tool is available to assist commissioners in its implementation.

### Parkinson's disease

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

According to the draft scope, this guideline will consider the diagnosis and management of Parkinson’s disease in primary and secondary care. It is a partial update of clinical guideline 35 (published 2006); areas to be updated include initial pharmacological management (monotherapy), drugs to be used with levodopa (as adjuvants) in the later stages of disease, pharmacological treatment of non-motor symptoms (sleep disturbance; psychosis; autonomic disturbances), pharmacological treatment of dementia associated with Parkinson’s disease, non-pharmacological management and deep brain stimulation. A number of new areas will also be considered, including transdermal dopamine patches and Duodopa® (levodopa and carbidopa) intestinal gel. Recommendations in the current guideline regarding monoamine oxidase B inhibitors, co-enzyme Q10, dopamine agonists and vitamin E for neuroprotection will not be updated. The guideline is at an early stage of development and no information on potential cost impact is available.

### Other mental health and CNS related guidance

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

This will be a partial update of Antenatal and postnatal mental health (NICE clinical guideline 45; issued 2007). It will cover 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 to be 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 draft 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:
### Other mental health and CNS related guidance

- NICE clinical guideline on [antenatal and postnatal mental health (update)](update), cont’d
- NICE clinical guideline on [head injury](head), issued Jan 2014
- NICE [pathway](pathway) available
- NICE Quality Standard on [head injury](head), issued Oct 2014
- NICE clinical guideline on [challenging behaviour and learning disabilities](learning), expected May 2015
- NICE Quality Standard on [challenging behaviour with learning disability](learning), expected Oct 2015
- CQC annual report for 2013 on the [safer management of controlled drugs](controlled), Aug 2014
- NICE Medicines Practice Guide on the [safe use and management of controlled drugs](management), expected Mar 2016

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

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

No information on the likely cost impact is currently available. However as this is a review of existing guidance, there is unlikely to be a significant additional impact on medicines spend.

This guideline covers the triage, assessment, investigation and early management of adults, young people and children presenting with a suspected or confirmed head injury. It updates and replaces NICE clinical guideline 56 (issued 2007).

The [costing report](costing) estimates that implementation of this guidance will result in a cost of £3,940 per 100,000 population; £1,180 of which is attributed to a new recommendation that all patients with head injury who are having warfarin treatment have a CT head scan performed within 8 hours of the injury. Although this recommendation will increase the number of people who will receive a CT head scan (an estimated 0.8% absolute increase), it is expected to reduce the number of people receiving delayed treatment for an intracranial bleed, and therefore reduce the use of NHS resources and lead to potential savings due to improved outcomes for these patients (the potential savings could not however be quantified). A [costing template](template) is available for organisations to assess the local impact of implementing this guideline.

This guideline will provide recommendations on prevention and interventions for adults, young people and children with learning disabilities whose behaviour challenges. The interventions covered in the guideline will include environmental, psychosocial and pharmacological. The [final scope](scope) notes 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 them 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 guideline covers the assessment, early management and rehabilitation following head injury in children, young people and adults.

This is the seventh annual report from the CQC covering the regulation of controlled drugs in England, relating to the year ending 31 December 2013. It describes developments in managing the risks associated with handling and using controlled drugs and looks at the prescribing patterns for controlled drugs over the past year. This is the first report under the amended regulations for the supervision and management of controlled drugs, which came into force in England on 1 April 2013.

This guide will provide recommendations for good practice in this area. It is at an early stage of development.
Other mental health and CNS related guidance cont’d

- NICE guideline on the [mental health of people in prison](https://www.nice.org.uk/guidance), expected Nov 2016
- NICE guideline on [mental health problems in people with learning disability](https://www.nice.org.uk/guidance), expected Sep 2016
- NICE guideline on [children’s attachment](https://www.nice.org.uk/guidance), expected Oct 2015
- NICE guideline on [violence and aggression (update)](https://www.nice.org.uk/guidance), expected Apr 2015
- NICE Quality Standard on [antisocial behaviour and conduct disorders in children and young people](https://www.nice.org.uk/guidance), issued Apr 2014
- NICE Quality Standard on [mental wellbeing of older people in care homes](https://www.nice.org.uk/guidance), issued Dec 2013

This guideline will consider the identification and management of mental health problems of people in prison. It is at an early stage of development and no information on the likely cost impact is available.

This guideline will cover identification of people at risk, recognition of mental health problems, diagnosis and assessment, interventions to prevent, reduce and manage mental health problems, service accessibility, transition between services, service structures, and interventions, training and support of family and carers. The most common intervention used to manage mental health problems in people with learning disabilities is psychotropic medication, and around 50% of adults are prescribed such drugs. The guideline is at an early stage of development and no information on the likely cost impact is available.

This guideline will cover attachment in children and young people (aged 0-18 years) who are adopted from care, in care or at high risk of going into care. The [final scope](https://www.nice.org.uk/guidance) states that the key issues to be covered include prediction, identification and assessment, prevention and management (psychosocial and pharmacological interventions) of attachment and attachment disorders. The guideline is unlikely to have any significant impact on medicines spend.

This guideline will provide recommendations on the short-term management of violent and physically threatening behaviour in mental health, health and community settings. It is an update of [clinical guideline 25](https://www.nice.org.uk/guidance), and is being undertaken due to the availability of new evidence about service users’ views on the use of physical intervention and seclusion and the effectiveness, acceptability and safety of available drugs and their dosages for rapid tranquilisation. The guideline is unlikely to have a significant impact on medicines spend.

This Quality Standard covers the recognition and management of antisocial behaviour and conduct disorders in children and young people (aged under 18 years). A [commissioning support tool](https://www.nice.org.uk/guidance) is available to assist commissioners in its implementation.

This Quality Standard covers the mental wellbeing of older people (65 years and over) receiving care in all care home settings, including residential and nursing accommodation, day care and respite care. A [commissioning support tool](https://www.nice.org.uk/guidance) is available to assist commissioners in its implementation.

This Quality Standard will cover the treatment and management of borderline and antisocial personality disorders.

- Tafamidis is an orphan drug licensed in the UK for the treatment of transthyretin familial amyloid polyneuropathy (TTR-FAP) in adults with stage 1 symptomatic polyneuropathy to delay peripheral neurological impairment. According to a [NHSC briefing](https://www.nice.org.uk/guidance), the prevalence of FAP is estimated to be <1 per 100,000 and liver transplantation is currently the only treatment option. Although tafamidis is expensive (£130,000 per year excluding VAT), it may prevent or delay liver transplantation. Tafamidis is listed as an exclusion in the National Tariff for 14/15. Currently the responsible commissioner would be CCGs although in view of the specialist nature of the condition, this may change. [Drug exclusions under Payment by Results 14/15](https://www.nice.org.uk/guidance)
5. Infections

### Patent expiries

According to *Prescribing Outlook New Medicines 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: efavirenz (Nov 2013); nelfinavir mesylate (Oct 2014); lopinavir/ritonavir (Dec 2015); adefovir (Sep 2016); entecavir (Oct 2016); linezolid (Jan 2016); oseltamvir (Feb 2016); rotonavir/lopinavir (Mar 2016); valganciclovir (Jul 2016);

### General strategy

- **QIPP area – antibiotic prescribing**

- **National Antibiotic Charts**

- **Prescriptions dispensed in the community: England 2002-13**

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

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

A set of comparators has 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 antibacterial prescribing QIPP comparators are available:

- “Antibacterial items/STAR PU” (number of prescription items for antibacterial drugs (BNF 5.1) per STAR-PU)
- “Cephalosporins and quinolones % items” (number of prescription items for cephalosporins and quinolones as a percentage of the total number of prescription items for selected antibacterial drugs).
- “3 days trimethoprim ADQ/item” (total number of average daily quantities per item for trimethoprim 200mg tablets)
- Minocycline ADQ/1000 patients (total number of average daily quantities for minocycline per 1000 patients)

These show that antibiotic prescribing in general practice in England over the last 5 years has broadly remained constant in relation to breakdown of different antibiotic prescribing. However, the overall use of antibiotics has steadily increased over several years. The most common antibiotic group prescribed is penicillins, followed by tetracyclines and macrolides. Broad-spectrum penicillins comprised 36% of all antibacterial prescribing in 2012-13. However, the prescription and use of cephalosporin antibiotics has declined following initiatives to reduce prescribing.

This bulletin notes ‘The BNF Section with the largest increase in cost between 2011 and 2012 was Antibacterial Drugs, where costs rose by £25.1 million (14.8%) to £195.4 million. The number of items dispensed increased by 2.5 million, (6.1%) to 43.3 million.’

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 (eg 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.
### General strategy cont’d

- [UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018](http://www.gov.uk), issued Sep 2013
- NICE guideline on [antimicrobial stewardship](http://www.nice.org.uk), expected May 2015
- NICE guideline on [antimicrobial resistance: changing risk-related behaviours](http://www.nice.org.uk), expected Mar 2016

This quick reference guidance, based on the best available evidence, can be adapted for local use.

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.

This medicines practice guideline will consider the evidence for effective interventions in antimicrobial prescribing, in particular for changing prescriber and patient behaviour when using antimicrobials and for minimising antimicrobial resistance.

This public health guideline will focus on the importance of the using antimicrobials correctly; the dangers associated with their overuse and misuse and the changes in behaviour that can avert the problems associated with the misuse of antimicrobials, such as infection prevention measures.

### 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](http://www.nice.org.uk), expected May 2015
- NICE Pathway on [antibiotics for early-onset neonatal infection](http://www.nice.org.uk) available.
- NICE Quality Standard on [antibiotics for neonatal infection](http://www.nice.org.uk), expected Dec 2015

This quality standard covers the assessment and initial management of unexplained feverish illness in infants and children (from birth to 5 years). A [commissioning support tool](http://www.nice.org.uk) is also available to assist commissioners in its implementation.

This guideline will cover the diagnosis and management of bronchiolitis in children.

This quality standard will cover 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 will include antibiotics that are given to newborn babies or to mothers during intrapartum care to prevent neonatal infection (antibiotic prophylaxis).
### Respiratory Infections

#### Tuberculosis (TB)
- NICE guideline on TB (update), expected Oct 2015
- NICE Pathway available.

#### Pneumonia
- NICE guideline on Pneumonia - including community acquired expected Dec 2014

This guideline will cover the clinical diagnosis and management of TB, and measures for its prevention and control. It will update and replace previous guidance in this area (2011). With respect to the treatment of active TB, the guideline will consider 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. It is unlikely that this guideline will have further significant resource implications.

This guideline will cover the diagnosis and management of community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) in adults. Its purpose will be to determine evidence-based, cost-effective best practice to reduce mortality and morbidity from pneumonia and maximise resources. Topics to be covered include diagnostic and microbiological investigations, use of severity assessment tools, pharmacological treatment (antibiotics [choice, when to start, duration of therapy] and glucocorticoids), gas exchange management, monitoring of response, safe discharge and the provision of patient information.

The guideline applies to adults only and will not consider the management of those with ventilator-associated pneumonia, pneumonia acquired in intensive care, cases where pneumonia is considered a terminal event, and immunocompromised patients. It will also not consider the management of specific identified pathogens, prevention strategies (e.g. vaccination), or other management strategies such as complementary and alternative treatments, statins, or G-CSF.

#### Hepatitis B
- NICE Quality Standard on hepatitis B, issued Jul 2014
- NICE Pathways available for chronic hepatitis B and hepatitis B and C testing
- NICE Pathway on hepatitis B and C testing available

This quality standard covers testing, diagnosis and management of hepatitis B in children (from birth), young people and adults. A commissioning support tool also available to assist commissioners in its implementation.

- Drugs for hepatitis B are listed as an exclusion in the national Tariff for 14/15. From April 2013, the responsible commissioner for the hepatitis B drugs in England is NHS England. Drug exclusions under Payment by Results 14/15

#### Hepatitis C
- NICE clinical guideline on hepatitis C, expected date TBC

This guideline will provide advice and recommendations on the diagnosis and management of hepatitis C. The guideline will cover treatment and monitoring of peginterferon with ribavirin or in combination with boceprevir or telaprevir. It will cover:
- Peginterferon alfa-2a with ribavirin versus peginterferon alfa-2b with ribavirin
- When to start or delay hepatitis C treatment
- Monitoring of treatment efficacy and how to guide treatment duration (response-guided therapy)
- Defining a sustained virologic response
- When to stop treatment
### Hepatitis C cont’d

- NICE clinical guideline on [hepatitis C](#), cont’d

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

- NICE guidance on [sofosbuvir for chronic hepatitis C](#), expected Nov 2014

- NICE guideline on [faldaprevir for chronic hepatitis C](#), suspended

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The guideline is at an early stage of development, however as many of the medicines related aspects are already being implemented, it is unlikely to have an additional significant resource impact on medicines use in this area. 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.

Simeprevir does not currently hold a UK marketing authorisation for treating chronic hepatitis C. In [draft guidance](#), NICE has recommended simeprevir in combination with peginterferon alfa and ribavirin, within its marketing authorisation, as an option for treating genotype 1 chronic hepatitis C. It has not recommended simeprevir, in combination with peginterferon alfa and ribavirin, for treating genotype 4 chronic hepatitis C because of uncertain effectiveness evidence. It has also not recommended simeprevir, in combination with sofosbuvir (with or without ribavirin) for treating genotype 1 or 4 chronic hepatitis C because it was not considered cost effective.

Current treatment options for people genotype 1 chronic hepatitis C include boceprevir or telaprevir (both plus peginterferon alfa and ribavirin). For people with genotype 4 HCV, peginterferon alfa plus ribavirin or watchful waiting are currently the main treatment options. Simeprevir is expected to be used in the same point in the treatment pathway for both groups.

This guidance will appraise the clinical and cost effectiveness of sofosbuvir within its licensed indication for treating chronic hepatitis C. [Draft recommendations](#) do not recommend sofosbuvir within its marketing authorisation for treating chronic hepatitis C because robust decisions could not be made based on the current clinical and cost-effectiveness analyses of sofosbuvir.

NICE estimate that around 9,000 patients are identified for treatment or retreatment each year. If we assume that 80% of these are switched to a regimen based on sofosbuvir (or simeprevir) and it costs £30,000 more than existing treatments, this could increase costs by up to £360,000 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 is 5000 patients waiting (50% of those identified each year) there would also be a one-off catch up cost of ~£380,000.

NHS England has issued [interim commissioning guidance for sofosbuvir](#) in combination with other direct acting antiviral drugs (specifically 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 ribivirin required for the full 12 week treatment course. This is less than the cost will be post a positive NICE TA publication when the required combination drugs will no longer be free of charge.

Boehringer Ingelheim decided not to proceed with the development of faldaprevir for treating hepatitis C as there is no longer an unmet medical need that would be filled with its faldaprevir interferon-based regimen.
<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>This report estimates that around 215,000 individuals are chronically infected in the UK. Most of this infection (~90%) is genotype 1 and genotype 3. Hospital admissions from HCV-related end stage liver disease and hepatocellular carcinomas are continuing to rise and there has been an overall increase in registrations for liver transplants for post-hepatitis C cirrhosis. Injecting drug use continues to be the most important risk factor for HCV infection. The number of people who inject drugs in England receiving drug treatment increased from 84,216 in 2005/06 to 109,396 in 2012/13 and that most of these people attend needle and exchange programmes.</td>
</tr>
<tr>
<td>• HPA report on hepatitis C, 2014</td>
<td>• Drugs for hepatitis C are listed as exclusions in the National Tariff for 14/15. From April 2013, the responsible commissioner for the hepatitis C drugs in England is NHS England. <strong>Drug exclusions under Payment by Results 14/15</strong></td>
</tr>
<tr>
<td><strong>Hepatic encephalopathy</strong></td>
<td>Draft guidance did not recommend its use as further analyses were requested from the manufacturer. If final NICE guidance is positive, the SMC estimates the cost of 6 months treatment to be around £1,685 per person. Using a 5-year time horizon, the manufacturer estimated the population eligible for treatment to be 1,102 (or 21 people per 100,000 population) in all 5 years, with an estimated uptake rate of 8% in year 1 and 40% in year 5. As no other drugs were assumed to be displaced, the net medicines budget impact is expected to be £298k (or ~£6,000 per 100,000 population) in year 1 and £1.489m (or ~£29,000 per 100,000 population) in year 5. The estimated prevalence of hepatic encephalopathy in the UK in 2008 was 1.4 per 100,000.</td>
</tr>
<tr>
<td>• NICE guidance on rifaximin for hepatic encephalopathy, expected date TBC</td>
<td><strong>Sepsis</strong></td>
</tr>
<tr>
<td><strong>Other infection-related developments and guidance</strong></td>
<td>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.</td>
</tr>
<tr>
<td>• NICE Quality Standard on surgical site infection, issued Oct 2013</td>
<td><strong>Other infection-related developments and guidance</strong></td>
</tr>
<tr>
<td>• NICE Quality Standard on infection prevention and control.</td>
<td>This Quality Standard covers the prevention and treatment of surgical site infection for adults, children and young people undergoing surgical incisions through the skin, in all healthcare settings. A <a href="#">commissioning support tool</a> is also available to assist commissioners in its implementation.</td>
</tr>
<tr>
<td>• NICE Pathway on urinary tract infections in children available</td>
<td>This Quality Standard covers the prevention and control of infection for people receiving healthcare in primary, community and secondary care settings. Implementing the quality standard is unlikely to incur costs but could help avoid costs of future healthcare associated infections. A <a href="#">commissioning support tool</a> is also available to assist commissioners in its implementation.</td>
</tr>
</tbody>
</table>
### 6. Endocrine system

#### 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: strontium ranelate (Aug 2015), tolvaptan (Oct 2015), dutasteride (Jul 2017).

#### Diabetes

- **NICE pathways available for diabetes, preventing type 2 diabetes and diabetes in pregnancy**
- **NICE Quality Standard on diabetes in adults, March 2011**
- **QIPP area – 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.

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 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 degludenc 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 QIPP comparator available, this is an identified area for the 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 guidance. The former NHS Diabetes published a report (now archived) on SMBG, including recommendations on self-monitoring for all people with Type 2 diabetes. 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.

These Quality Standard topics have been referred to NICE and are at an early stage of development.

NaDIA 2013 was carried out by diabetes teams in acute hospitals in England and Wales on a nominated day between 16 and 20 September 2013. For 8.1% of inpatients with diabetes, diabetes or a diabetic complication was the main reason for their admission to hospital, whereas 66.3% of inpatients with diabetes were admitted for other medical reasons and 25.6% were admitted for non-medical (i.e. surgical) reasons. People in hospital with diabetes were older than other patients; the median age of 75 years for inpatients with diabetes compared to 68 years for all inpatients. Those admitted to hospital as an emergency had a longer median length of stay (8 nights) than patients admitted electively (6 nights).

Findings from this year's audit suggest that more than a third of patients (37%) with diabetes experienced a medication error, down from 39.9% in 2011. Patients who had experienced a medication error were more than twice as likely to suffer a severe hypoglycaemic episode (15.3%) compared to those with no error in their medication (6.8%).

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**Disease or Indication:** National targets and guidance

**Epidemiology, potential financial implications for a population of 100,000 and other comments**
Canagliflozin (Invokana®) is the second sodium-glucose co-transporter-2 (SGLT2) inhibitor to be licensed in the UK for the treatment of type 2 diabetes. NICE recommends the use of canagliflozin in:

i. a dual therapy regimen in combination with metformin as an option for treating type 2 diabetes, only if:
   - a sulfonylurea is contraindicated or not tolerated or
   - the person is at significant risk of hypoglycaemia or its consequences.

ii. a triple therapy regimen as an option for treating type 2 diabetes in combination with:
   - metformin and a sulfonylurea or
   - metformin and a thiazolidinedione.

iii. combination with insulin with or without other antidiabetic drugs as an option for treating type 2 diabetes

The recommendations for canagliflozin are wider than those issued by NICE for dapagliflozin in June 2013, which did not support use of dapagliflozin in a triple therapy regimen.

The costing information for canagliflozin estimates that the annual cost associated with implementing the recommendations is £26,400 per 100,000 population. The additional cost is predominantly driven by increased drug spending, where canagliflozin is used as an alternative to other oral antidiabetics in dual and triple therapy.

Empagliflozin (Jardiance®) is the most recently licensed SGLT2 inhibitor to be launched in the UK (June 2014). It is indicated as monotherapy (if metformin is not tolerated) and in combination with other glucose-lowering drugs in adults with type 2 diabetes mellitus if glycaemic control is inadequate despite other measures. The final scope for this guidance indicates that NICE will consider the use of empagliflozin in dual and triple therapy regimens and in combination with insulin. As empagliflozin will compete with dapagliflozin and canagliflozin, the cost impact is likely to be a substitution.

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

These three guidelines will review and update previous versions and are unlikely to result in further additional significant resource impact on medicines use.

This review is at an early stage of development but the final scope indicates that the review will include the pharmacological management of blood glucose levels, target values for blood glucose control, self-monitoring of blood glucose levels for blood glucose control, antithrombotic therapy and drug therapy for erectile dysfunction.
<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>Diabetes cont’d</strong></td>
<td>The updated NICE clinical guideline on lipid modification includes revised recommendations for lipid management in type 1 and type 2 diabetes.</td>
</tr>
<tr>
<td>▪ Updated NICE clinical guideline on lipid modification, issued Jul 2014</td>
<td><strong>Type 1 diabetes:</strong></td>
</tr>
<tr>
<td></td>
<td>▪ Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes</td>
</tr>
<tr>
<td></td>
<td>▪ Consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes</td>
</tr>
<tr>
<td></td>
<td>Offer statin treatment for the primary prevention of CVD to adults with type 1 diabetes who:</td>
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<td>- are older than 40 years or</td>
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<td>- have had diabetes for more than 10 years or</td>
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<td></td>
<td>- have established nephropathy or</td>
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<td>- have other CVD risk factors.</td>
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<td></td>
<td>▪ Start treatment for adults with type 1 diabetes with atorvastatin 20mg</td>
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<tr>
<td></td>
<td><strong>Type 2 diabetes:</strong></td>
</tr>
<tr>
<td></td>
<td>▪ Use the QRISK2 risk assessment tool to assess CVD risk in people with type 2 diabetes</td>
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<tr>
<td></td>
<td>▪ Offer atorvastatin 20mg for the primary prevention of CVD to people with type 2 diabetes who have a 10% or greater 10-year risk of developing CVD.</td>
</tr>
<tr>
<td></td>
<td>In terms of monitoring, the guideline also notes that statins should not be stopped because of an increase in blood glucose level or HbA1c.</td>
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<td></td>
<td>The costing information for this guideline does not separate out the cost of implementing the diabetes related recommendations (see chapter 2 of this document for overall cost impact information).</td>
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<tr>
<td></td>
<td>This guideline will update and replace all of NICE clinical guidelines 10 (footcare in type 2 diabetes) and 119 (inpatient management of footcare problems) and will replace the recommendations on foot care in NICE clinical guideline 15 (type 1 diabetes). This update is being undertaken to bring together all NICE diabetic foot guidance into one guideline. The guideline will consider the use of wound dressings, antibiotic and antimicrobial regimens and other adjunctive treatments (such as dermal or skin substitutes). The guideline unlikely to result in further additional impact on medicines resource use for the NHS.</td>
</tr>
<tr>
<td>▪ NICE guideline on prevention and management of foot problems in people with diabetes, expected Jun 2015</td>
<td><strong>Actions/ issues which may be considered by commissioners and providers</strong></td>
</tr>
<tr>
<td></td>
<td>▪ The redesign of diabetes services is underway 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.</td>
</tr>
<tr>
<td></td>
<td>▪ 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).</td>
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<td>▪ Develop local guidance on self-monitoring of blood glucose by patients with type 2 diabetes. A UKMi Medicines Q&amp;A document summarises the current available data in this area.</td>
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<td>▪ Consider developing a locally approved list of 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.</td>
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### Disease or Indication: National targets and guidance

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

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<th>Actions/ issues which may be considered by commissioners and providers cont’d</th>
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| • 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.  
  • Commissioners may wish to refer to the following commissioning guides produced by NICE in relation to diabetes: [insulin pump services](https://www.nice.org.uk/), [patient education programmes](https://www.nice.org.uk/) for type 2 diabetes, and [foot care services](https://www.nice.org.uk/).  
  • Insulin pumps and consumables are listed as an exclusion in the National Tariff for 14/15. A decision on funding will need to be agreed locally for these for indications outside NICE recommendations. [Drug exclusions under Payment by Results 14/15](https://www.nice.org.uk/). 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](https://www.nice.org.uk/) produced by the LNDG helpful. The document aims to inform commissioners about insulin pumps available in the UK, their features, and the cost of the pump and associated sundries. A “[How to Why to](https://www.nice.org.uk/)” 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](https://www.nice.org.uk/) under development, expected Feb 2015  
  NICE pathway available
- NICE guideline on the [assessment and management of complex fractures](https://www.nice.org.uk/), expected Apr 2016. NICE guideline on the [diagnosis, management and follow up of fractures](https://www.nice.org.uk/) (non-complex), expected Apr 2016
- NICE guidance on [bisphosphonates for preventing osteoporotic fragility fractures](https://www.nice.org.uk/) (including a partial update of NICE technology appraisal guidance 160 and 161), expected Nov 2015

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

This Quality Standard topic has been referred to NICE and is at an early stage of development.

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.

The [draft scope](https://www.nice.org.uk/) 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.
Disease or Indication: National targets and guidance

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

**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.

**Fertility**

- NICE Quality Standard on fertility problems, expected Oct 2014
- NICE pathway available
- NICE guideline on fertility (review), issued Feb 2013

This is an area of moderate financial risk

This quality standard will cover 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.

This guideline updates and replaces previous NICE guideline issued in February 2004. New and updated recommendations have been included in areas of diagnosis and treatment for fertility problems. The revised guideline increases uptake of IVF as it raises the age limit to 42 years for one cycle of IVF and supports provision of 3 full cycles of IVF to women under 40 years, with caveats.

The previous guideline had recommended that couples in which the woman is aged 23-39 years at the time of treatment and who have an identified cause for their fertility problems or who have infertility of at least three years' duration should be offered up to three stimulated cycles of IVF treatment.

The costing template and report for this guideline focus on recommendations likely to have the most significant resource impact. This includes the revised criteria for referral for IVF: “In women aged under 40 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where 6 or more are by intrauterine insemination) offer 3 full cycles of IVF, with or without intracytoplasmic sperm injection (ICSI).”

The costing report states that if commissioners move to being consistent with access to IVF services across the NHS, in line with the previous NICE guideline, there is likely to be an increase in the annual recurrent cost of around £129,000 for IVF treatment per 100,000 population once a steady state is reached. It is anticipated that implementation may occur over 3 years and that it would take this time to reach a steady state. The total cost of offering IVF treatment to women aged 40–42 years in line with the recommendations is not included in the costing model. Based on expert opinion, women aged 40–42 years do not currently receive NHS-funded IVF treatment and it is anticipated that only a small number of women will become eligible to receive such treatment.

Although not included in the costing documentation, the guideline also contains some new recommendations regarding the use of gonadotrophins in women with:
**Fertility cont’d**

- NICE guideline on fertility (review), cont’d
- Legal ruling relating to fertility guideline, May 2014

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

- WHO Group I ovulation disorders (hypothalamic pituitary failure (hypothalamic amenorrhoea or hypogonadotrophic hypogonadism)
- WHO Group II ovulation disorders (hypothalamic-pituitary-ovarian dysfunction - predominately polycystic ovary syndrome) who are known to be resistant to clomifene citrate

The impact of these recommendations should be assessed locally (drug and service delivery).

A recent 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 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 guidance 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**

- Use the costing template for the fertility guidance to assess whether there is a cost implication locally of providing IVF to women in the higher age bracket (aged 40-42 years).
- Assess the impact of recommendations not highlighted within the costing template locally – including new recommendations on the use of gonadotrophins for stimulating ovulation. Although the drugs are not excluded from tariff, there may be a cost impact involved - commissioners and providers should agree how these new recommendations will be managed along with “do not do” recommendations.
- 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 Q2 2015. This is likely to result in some cost savings in this area (up to 30%)

**Autosomal dominant polycystic kidney disease**

NICE guidance on the use of tolvaptan for treating autosomal dominant polycystic kidney disease, expected Aug 2015

- Tolvaptan is not currently licensed in this indication, it has been filed in the EU and launch is expected in Q1 2015. 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. A published cost effectiveness analysis concludes that, assuming the benefits of tolvaptan persist in the longer term, the drug may slow progression to end stage renal disease and reduce mortality rates.

However, without an approximately 95% reduction in price, cost-effectiveness does not compare favorably with other commonly accepted options. The number of patients eligible for therapy and uptake is difficult to estimate. The NHSC estimates that in 2008, the incidence rate of polycystic kidney disease as the primary cause of renal disease in patients starting renal replacement therapy was 7.3 per million population in England (approximately 395 people in total or 0.7 cases per 100,000 population). Dosing in the trials varied, it is administered orally at 60-120mg daily. Using the current list price for tolvaptan (£746.80 for 10 x30mg tablets) and assuming a dose of 60mg daily, would result in a drug cost of £4,480 per patient per month.

Assuming 0.5 patients per 100,000 population are treated, this would result in a cost of ~£27,000 per 100,000 population.

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

- Tolvaptan is listed as an exclusion in the National Tariff for 14/15 - Drug exclusions under Payment by Results 14/15. NHS England is the responsible commissioner for this drug.
### 7. Obstetrics, gynaecology and urinary tract disorders

#### Patent expiries

According to *Prescribing Outlook New Medicines 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: ulipristal acetate (Jun 2014); darifenacin (Mar 2015); estradiol + drospirenone (May 2015).

#### Incontinence

- **NICE Quality Standard on [urinary incontinence in women](http://www.nice.org.uk), expected Jan 2015**
- **NICE Quality Standard on [nocturnal enuresis (bedwetting)](http://www.nice.org.uk) in children and young people, issued Sep 2014**

This Quality Standard will cover the management of urinary incontinence in women aged 18 years and over. This Quality Standard covers the assessment and management of nocturnal enuresis (bedwetting) in children and young people aged 18 years or younger. A [commissioning support tool](http://www.nice.org.uk) is available to assist commissioners in its implementation.

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

- Commissioners and providers should agree a local policy on choice of PDE5i agents for the treatment of erectile dysfunction. Generic sildenafil (available since 2013) has been removed from the SLS list (Drug Tariff Part XVIIIB), which means that generically written prescriptions will no longer require annotation with “SLS” to be valid. Viagra® and avanafil have been added to this list as of 1st August 2014, so prescriptions for these will require annotation.
- The Paediatric Continence Forum issued a [Paediatric Continence Commissioning Guide](http://www.nice.org.uk) in Sep 2014 – this tool aims to support the commissioning of integrated, community-based, paediatric continence services.

#### Benign prostatic hyperplasia

- **NICE guidance on [tadalafil for benign prostatic hyperplasia](http://www.nice.org.uk), terminated Jan 2013**
- **NICE New Medicines Evidence Summary (May 2013)**

NICE is unable to recommend the use of tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia because no evidence submission was received from the manufacturer.

#### Contraception

- **Health & Social Care Information Centre annual report on [contraceptive services](http://www.nice.org.uk), Oct 2014**
- **NICE guideline on [long-acting reversible contraception (standing committee update)](http://www.nice.org.uk), issued Sep 2014**

This annual report on NHS community contraceptive clinics primarily presents information on family planning clinics and clinics run by voluntary organizations, and covers Apr 2013 to Mar 2014. There were 2.21 million attendances made by 1.34 million individuals (decrease of 2.2% and 0.9%, respectively, compared to the previous year), and oral contraception remains the most commonly used primary method (47% of women attending). Use of LARC continues to increase, now accounting for 31% of primary methods. The number of prescriptions dispensed for emergency contraceptives has been falling since 2000-2001, possibly due to its reclassification in 2001 which made it available for women aged 16 and over to buy EHC at pharmacies without a prescription.

This update to NICE clinical guideline 30 includes revised recommendations on progesterogen-only subdermal implants (section 1.5), following the replacement of Implanon® by Nexplanon®, which contains the same drug (etonogestrel) but contains barium to make it radio-opaque, and has a different insertion device. None of the other sections of the guideline have been updated.

Nexplanon®, the only currently available subdermal contraceptive implant in the UK, is bioequivalent to Implanon®, and has a similar cost; the Appraisal Committee therefore agreed that it was reasonable to assume that etonogestrel implants are very likely to remain a cost effective option. This guideline addendum is unlikely to have any impact on current medicines spend.
### Contraception cont’d

- NICE public health guideline on contraceptive services with a focus on young people up to the age of 25, issued Mar 2014

- NICE local government briefing on contraceptive services, issued Mar 2014

This guideline makes 12 recommendations covering the commissioning and provision of contraceptive services. The aim is to improve access to high quality contraceptive services, especially for young people up to the age of 25 years. There may be costs associated with commissioning and providing contraceptive services in addition to existing services. Implementation of the recommendations is however expected to reduce the number of abortions and unintended pregnancies, leading to cost savings for the NHS and wider society as a whole. A local costing template is available to help estimate the local cost impact of implementing the guidance.

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.

### Antenatal, intrapartum and postnatal care

- NICE guideline on intrapartum care, expected Dec 2014

- NICE guideline on post-natal care (update), expected Dec 2014

- NICE guideline on pre-term labour and birth, expected Nov 2015

This guideline will focus on the care of healthy women and their babies during childbirth. It is a partial update of NICE clinical guideline 55 (issued 2007). Although the draft guideline covers some pharmacological interventions (such as pain control and the use of oxytocin), the updated guideline is unlikely to have a significant financial impact on medicines spend.

This addendum to clinical guideline 37 will update recommendations on reducing the risk of sudden infant death syndrome (SIDS), following the publication of new information on the association between co-sleeping and SIDS in 2013. The core of the recommendations will be 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 is at an early stage of development. The final scope states that the following pharmacological strategies will be included:

- Antenatal antibiotic prophylaxis for women diagnosed with preterm pre-labour rupture of membranes
- Use of progesterone/progestogens for women with suspected or diagnosed preterm labour to improve the outcomes of preterm labour
- Use of tocolytic agents (e.g. beta-sympathomimetics, oxytocin receptor antagonists, calcium channel blockers, cyclooxygenase enzyme inhibitors, NSAIDs, nitroglycerin, magnesium sulphate) for women with suspected or diagnosed preterm labour to improve the outcomes of preterm labour
- Interventions to improve neonatal outcomes including maternal corticosteroids for foetal lung maturation and magnesium sulphate for preterm neonatal neuroprotection

This guideline is unlikely to result in a significant financial impact on medicines spend.

### 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.

- 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).
### 8. Immunosuppression

#### Patent expiries

According to *Prescribing Outlook – New Medicines 2014*, the following patent expiries may have a significant impact on prescribing costs: rituximab (Nov 2013), alemtuzumab (Feb 2014), trastuzumab (Jul 2014), cetuximab (Sep 2014), bevacizumab (Dec 2014), tegafur/uracil (Mar 2015), sirolimus (Sept 2015), pemetrexed (Dec 2015). The first five of these agents are monoclonal antibodies and savings will require the launch and uptake of biosimilars – at present it is not clear if these are currently at a stage of clinical development suitable for launch within the next few years.

#### 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 Guidance on alemtuzumab for treating relapsing-remitting MS, issued May 2014**
- **NICE Guidance on dimethyl fumarate for treating relapsing remitting MS, issued Aug 2014**

This is an area of high financial risk – due to NICE-approved new oral treatments and an annually administered injectable treatment.

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, teriflunomide 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.

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)

Alemtuzumab is recommended as an option, within its marketing authorisation, for treating adults with active relapsing–remitting multiple sclerosis.

**NICE** estimate that this will increase MS treatment costs by £20,400 per 100,000 population in Year 1 rising to £58,400 by Year 3 and reaching steady state of around £37,000 by year 5. This assumes that there are currently 23 eligible patients per 100,000 currently receiving treatment for MS (and 3 electing not to) and that 10 of these are currently receiving teriflunomide, 3 natalizumab and 2 fingolimod and that in future 6 of these patients would be treated with alemtuzumab (3 would be switched from an interferon-beta and 3 from another treatment). This estimate is therefore very sensitive to current prescribing patterns and if local practice is to use more interferon beta/ glatiramer the cost implications could be considerably higher.

Dimethyl fumarate is recommended as an option for treating adults with active relapsing-remitting multiple only if:

- they do not have highly active or rapidly evolving severe relapsing-remitting multiple sclerosis and
- the manufacturer provides dimethyl fumarate with the discount agreed in the patient access scheme.

**NICE** estimate that the overall cost impact will be £8800 per 100,000 population in Year 1 rising to £43,900 by Year 5. This is based on very similar assumptions to those outlined above in terms of baseline prescribing patterns. The predicted cost increase is as a result of a 5 year transition from teriflunomide to dimethyl fumarate, so that instead of 11 eligible patients per 100,000 population taking teriflumide and 2 opting for no treatment, 6 will take teriflunomide, 6 will take dimethyl fumarate and one will opt for no treatment. Dimethyl fumarate is estimated to be approximately £4400 per year more expensive than teriflunomide. Again this assumption is very sensitive to the NICE estimate on teriflumide uptake and the cost implications will be much higher if patients switch directly from a beta-interferon to dimethyl fumarate.
### MS cont’d

- **NICE Guidance on** [teriflunomide for treating relapsing–remitting multiple sclerosis](https://www.nice.org.uk/guidance/td31), **issued Jan 2014**

- **NICE Guideline on** [multiple sclerosis](https://www.nice.org.uk/guidance/cg162) published October 2014

  **NICE pathway** available

Teriflunomide is recommended as an option for treating adults with active relapsing–remitting multiple sclerosis only if they do not have highly active or rapidly evolving severe relapsing–remitting multiple sclerosis and the manufacturer provides teriflunomide with the discount agreed in the patient access scheme.

**NICE** estimate that the overall cost impact of this guidance will be £99,284 per 100,000 population. This is based on an assumption that 11 of the estimated 22 patients previously receiving either beta-interferon or glatiramer will switch to teriflunomide which is £4-5,000 per patient more expensive.

Overall these 3 pieces of Guidance will take estimated spend on disease-modifying drugs in MS from a baseline of £132,300 per 100,000 population to £305,584 within 5 years. However as outlined above there is potential for that increase to be even higher if they are initiated or switched to the more expensive agents such as dimethyl fumarate or alemtuzumab.

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 methylprednisolone 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).

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

- Drugs for multiple sclerosis are listed as exclusions in the National Tariff for 14/15. In England, NHS England is the responsible commissioner for these drugs. **Drug exclusions under Payment by Results 14/15**
Organ transplantation

- NICE guidance on immunosuppressive therapy for renal transplantation in children and adolescents (review of existing guidance 99), expected Oct 2015
- NICE guidance on kidney transplantation (adults) - immunosuppressive therapy (Review of TA 85), expected Oct 2015
- NICE guidance on belatacept in treatment of kidney transplantation rejection, expected date TBC
- NICE guidance on everolimus in prevention of kidney transplantation rejection, expected date TBC
- NICE guidance on everolimus in cardiac transplantation rejection, expected date TBC
- NICE guidance on everolimus for the prevention of organ rejection in allogeneic liver transplantation, expected Jun 2015

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.
### 9. Nutrition and blood

#### Patent expiries
According to *Prescribing Outlook New Medicines 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: sevelamer (Jan 2015); darbepoetin alfa (Jun 2016); agalsidase beta (Aug 2016); pegfilgrastim (Aug 2017).

#### Anaemia
- **NICE clinical guideline on anaemia management in CKD (update), expected May 2015**
- **NICE guidance on erythropoiesis-stimulating agents (epoetin and darbepoetin) for cancer-treatment induced anaemia (including review of TA142), expected Nov 2014**

This is an area of low financial risk

This will update and replace NICE clinical guideline 114 (2011). According to the final scope, the following issues will be reviewed and updated:
- The use of diagnostic tests to predict response to iron therapy in patients with CKD.
- The treatment of iron deficiency, including assessment of comparative efficacy of agents (both prior to and during ESA treatment).

In addition the following new areas will be addressed:
- The optimal management of anaemia of CKD in hospital inpatients who have a concurrent acute infectious illness.
- The effectiveness of high dose ESA compared with blood transfusions in the management of chronic ESA-resistant anaemia of CKD.

The update is in early stages of development and no information on cost impact is available. It is however unlikely that this review will result in a significant change in resource use in the NHS.

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 will review and update TA 142 (issued 2008). The final appraisal determination 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. This FAD recommends use of ESAs in a wider patient group than the current guidance, which restricts use to women receiving platinum-based chemotherapy for ovarian cancer who have Hb ≤8g/100mL, and to those who have very severe anaemia and cannot receive blood transfusions.

Data from the HSCIC show total spend on ESAs across primary and secondary care was approximately £80,500,000 in 2012. If it is assumed that a third of this was in the oncology setting and that spend increases by 50%, the guidance may be associated with additional costs of around £25,000 per 100,000.

#### Nutrition
- **NICE guideline on intravenous fluid therapy in adults in hospital, issued Dec 2013**
- **NICE Pathway available.**

This guideline is unlikely to have a significant impact on medicines spend. It will, however, aim to improve safety by advising on how prescribing errors could be reduced in this area.

This guideline provides recommendations about general principles for managing IV fluids, and applies to a range of conditions and different settings. It does not include recommendations relating to specific conditions. The aim of the guideline is to help prescribers understand the:
### Nutrition cont’d

- **NICE guideline on intravenous fluid therapy in adults in hospital**, cont’d
- **NICE Quality Standard on intravenous fluid therapy in adults in hospital**, issued Aug 2014
- **MHRA – suspension of licences for hydroxyethyl starch (HES) intravenous infusion**, Jun 2013
- **NICE guideline on intravenous fluids therapy in children**, expected Oct 2015

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

- physiological principles that underpin fluid prescribing
- pathophysiological changes that affect fluid balance in disease states indications for IV fluid therapy
- reasons for the choice of the various fluids available and
- principles of assessing fluid balance

It is hoped that the guideline will lead to better fluid prescribing in hospitalised patients, reduce morbidity and mortality, and lead to better patient outcomes.

A **costing statement** has been produced for this guideline because of variation in clinical practice across the country and also in the different hospital settings that this guidance encompasses. Organisations are encouraged to evaluate their own practices against the recommendations and assess costs locally. Although there are potential areas for additional costs (e.g. additional specialist hours), implementation of this guidance is expected to produce significant overall cost savings across the NHS by reducing the number of prescribing errors as well as subsequent adverse effects on morbidity and mortality, while improving patient safety. Local savings may be generated due to a reduction in the number of hospital bed-days, due to a reduction in complications created by IV fluid mismanagement.

This Quality Standard covers the assessment and management of adults’ IV fluid needs in hospital. A **commissioning support tool** is available to assist commissioners in its implementation. A **learning tool** to support all prescribers to safely and effectively assess, prescribe for and review adult patients requiring IV fluids is also available.

Results from large randomised clinical trials have reported an increased risk of renal dysfunction and mortality in critically ill or septic patients who received HES compared with crystalloids. The MHRA concluded that the risks of HES products for plasma volume expansion outweigh the benefits in all patient groups and clinical settings. The licences for all HES products have therefore been suspended, however, there is a possibility of one product being reintroduced (no further details are available on this at time of writing).

The scope of this guideline is similar to the adult guideline. It will include 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. According to the **final scope**, this guidance represents a major opportunity to improve patient safety for children receiving intravenous fluid therapy in hospital.

**Key issues that will be 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

As with the adult guideline, this guidance would be expected to result in cost savings across the NHS by improving patient safety and reducing errors and complications due to IV fluid mismanagement.
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### Nutrition cont’d
- NICE guideline on [assessment for and management of blood transfusion](#), expected May 2015

According to the [final scope](#), this guideline will focus on the general principles of transfusion and the appropriate use of blood. The detailed management of specific clinical conditions will not be considered. The key clinical issues to be addressed are outlined in the scope and in terms of medicines include:

- Alternative treatments to blood transfusion in surgical patients (oral and IV iron, recombinant EPO, tranexamic acid as an adjunct to minimise transfusion, cell salvage therapy)
- Patient safety

The guideline is at an early stage of development and no information on its likely cost impact is available.

### Renal
- NICE guideline on [early identification and management of chronic kidney disease in adults in primary and secondary care](#), issued Jul 2014
- NICE guideline on [early identification and management of chronic kidney disease in adults in primary and secondary care](#), cont’d

This guideline on the care and treatment of adults with chronic kidney disease updates and replaces clinical guideline 73 (issued 2008). Although diagnosis of kidney disease has improved since the introduction of national estimated GFR reporting and CKD indicators in the QoF, late presentation was still reported as 19% in the Renal Association’s 2013 [UK Renal Registry report](#). Late presentation of people with kidney failure increases morbidity, mortality and associated healthcare costs. This guideline seeks to address these issues.

The updated guideline includes new recommendations on the use of albumin: creatinine ratio (ACR) alongside eGFR for classification, and use of cystatin C testing to help to more accurately classify CKD in people who have a creatinine-based eGFR of 45–59 ml/min/1.73 m² and no signs of proteinuria.

According to the [costing statement](#), these new recommendations are expected to increase costs at a local level. Improved classification of people with CKD is however likely to reduce the number of people receiving pharmacological treatment and monitoring, which will lead to savings. The number of people currently receiving pharmacological treatment (stages G3a–G5) who would not fall into this category under the diagnostic methodology being recommended is unknown; expert opinion has however suggested that it may be up to 20% of the CKD population. Due to the uncertainty, likely overall cost savings cannot be estimated.

A number of recommendations regarding pharmacological therapy have been added/ revised (including choice of antihypertensive; oral antiplatelets and anticoagulants; vitamin D supplements in the management of CKD–mineral and bone disorders); none of these are however expected to have a significant impact on medicines spend.

NICE also published a clinical guideline on [acute kidney injury](#) in August 2013.

This Quality Standard will cover 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.

This quality standard will cover renal replacement therapy services for kidney failure in adults, young people and children. It is a partial update of the [chronic kidney disease](#) quality standard, and consideration will be given to the development of a single amalgamated quality standard.
### 10. Musculoskeletal and joint diseases

<table>
<thead>
<tr>
<th>Patent expiries</th>
<th>According to the CMJ, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: infliximab (Aug 2014; expected launch Q1 2015 for biosimilar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</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></td>
<td>The therapeutic area on NSAIDs offers the following options for implementation:</td>
</tr>
<tr>
<td></td>
<td>(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)</td>
</tr>
<tr>
<td></td>
<td>(ii) If an NSAID is needed, use ibuprofen (1200 mg per day or less) or naproxen (1000 mg per day or less).</td>
</tr>
<tr>
<td></td>
<td>(iii) Review and, if appropriate, revise prescribing of etoricoxib to ensure it is in line with MHRA advice and the NICE clinical guideline on osteoarthritis.</td>
</tr>
<tr>
<td></td>
<td>(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.</td>
</tr>
<tr>
<td>RA</td>
<td>The following comparators are available for this QIPP area:</td>
</tr>
<tr>
<td></td>
<td>• 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).</td>
</tr>
<tr>
<td></td>
<td>• Ibuprofen &amp; naproxen % items: the total number of ibuprofen and naproxen items prescribed as a percentage of the total number of all NSAID prescription items.</td>
</tr>
<tr>
<td></td>
<td>The EMA’s Pharmacovigilance Risk Assessment Committee (PRAC) has begun a review to evaluate the cardiovascular risks with systemic ibuprofen. The cardiovascular risks being evaluated concern the use of high-dose ibuprofen (2,400 mg per day) taken regularly for long periods. The PRAC will also evaluate evidence on the interaction of ibuprofen with low-dose aspirin.</td>
</tr>
</tbody>
</table>

### Rheumatology

**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
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). 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.
### Rheumatology

**RA cont’d**

- NICE guidance on the use of adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab for the treatment of rheumatoid arthritis (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247), expected date TBC.

- NICE guidance on the use of tofacitinib in RA after the failure of DMARDs, suspended indefinitely.

### Juvenile Idiopathic Arthritis (JIA)

- NICE guidance on the use of abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (including review of TA35), expected Feb 2016.

### Ankylosing spondylitis (AS)

- NICE Quality Standard on seronegative arthropathies, expected date TBC.

- NICE guidance on adalimumab, etanercept, infliximab and golimumab for treating AS and non-radiographic axial spondyloarthritis (including review of previous guidance - TA143 and TA233), expected Jan 2015.

- NICE clinical guideline on the diagnosis and management of spondyloarthritis, expected date TBC.

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This guidance will review previous sets of guidance in this area. According to the final scope, the guidance will consider the use of all agents for moderate to severe and severe active RA that has been previously treated with conventional DMARDs only. It will also consider the use of adalimumab, etanercept, infliximab or golimumab for severe active RA not previously treated with methotrexate, or other DMARDs. If the guidance enables treatment of RA at an earlier stage, this could have significant cost implications. If the guidance increases current spend on biologics by 20%, this could result in an increased spend of around £240,000 per 100,000 population. Some of this spend may already be occurring.

Tofacitinib (Xeljanz®) is an orally administered selective inhibitor of the Janus kinase (JAK) family of kinases, including JAK1 and JAK3 and acts as a targeted immunomodulating agent. This guidance is indefinitely suspended following a negative opinion and refusal of a marketing authorisation for the drug from the CHMP. Tofacitinib is unlikely to have a financial impact over the next year.

This is an area of low financial risk.

The draft scope indicates that this guidance will cover people with JIA but will exclude systemic JIA. Where the evidence allows, subgroups by type of JIA will be considered: oligoarthritis, polyarthritis (rheumatoid factor positive, rheumatoid factor negative, and extended oligoarthritis), enthesitis-related arthritis and psoriatic arthritis.

As this is a review of previous guidance (which covered etanercept) 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.

This Quality Standard has been referred to NICE and is at an early stage of development.

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

This guideline is at an early stage of development and is unlikely to impact over the next year. No drafts are currently available. The guideline will discuss 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.
<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>Rheumatology Psoriatic Arthritis (PsA)</td>
<td>Final NICE guidance does not support the use of ustekinumab for PsA (alone or in combination with methotrexate) in adults when the response to previous non-biological DMARD therapy has been inadequate. As a result the costing statement notes that no significant costs are anticipated. NICE guidance supporting the use of adalimumab, etanercept, infliximab (TA199) and golimumab (TA220) in PsA (provided certain criteria are met) is available. Apremilast is an orally active agent that inhibits multiple pro-inflammatory mediators including, TNF-alpha, interleukins 6, 17 &amp; 23, and interferon-gamma. Apremilast does not currently have a UK marketing authorisation for this indication but has been filed for approval in the EU, with an expected UK launch date of Q1 2015. It has already been launched in the US for this indication. Apremilast is likely to be used after conventional systemic therapies, but as an oral preparation, it may be used before parenteral biological therapies. According to Prescribing Outlook – New Medicines, estimates of UK prevalence of severe PsA vary widely. NIHR HSC suggests about 60,000 people in England are affected, other estimates suggest up to 1% of the population may be affected. It also notes that the production costs for apremilast and therefore price are likely to be lower than for biologicals (£8,000-£11,000/year, PAS for golimumab). The US price is about 75% of most biologicals. Administration costs will be lower with apremilast. 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 will cost £7,500 per patient per year and - 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 around £4,000 to £11,000 per 100,000 population.</td>
</tr>
<tr>
<td>• NICE guidance on the use of ustekinumab for the treatment of active and progressive PsA, issued May 2014</td>
<td></td>
</tr>
<tr>
<td>• NICE guidance on the use of apremilast for treating active PsA in people for whom DMARDs have been inadequately effective, not tolerated or contraindicated, expected Aug 2015</td>
<td></td>
</tr>
</tbody>
</table>
**Disease or Indication:** National targets and guidance

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

<table>
<thead>
<tr>
<th>Actions/ issues which may be considered by commissioners and providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Cytokine modulators, such as TNF-inhibitors are listed as exclusions in the National Tariff for 14/15. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. NHS England is the responsible commissioner when cytokine modulators are used in children (aged 18 years or younger). CCGs are the responsible commissioners for use of these agents in adults.</td>
</tr>
<tr>
<td>▪ 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, AS and PsA including use of biologic agents.</td>
</tr>
<tr>
<td>▪ 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.</td>
</tr>
<tr>
<td>▪ 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.</td>
</tr>
<tr>
<td>▪ Trusts should audit this area of prescribing to ensure that any variations to the drug regimens recommended in the NICE guidance are appropriate.</td>
</tr>
</tbody>
</table>

**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 set criteria – interim 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:

(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 SELENA-SLEDAI 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.
SLE cont’d

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

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.

A 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 £6,156 (drug only). Using belimumab in the population estimated by the company for 6 months would result in a total cost of £46,170 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 14/15. As of April 2013, NHS England is the responsible commissioner for this drug, Drug exclusions under Payment by Results 14/15.
- NHS England has set out criteria for use of rituximab in SLE in an interim policy.

Osteoarthritis (OA)

- NICE guidance on the use of diacerein for the treatment of OA, expected date TBC

This guidance is unlikely to impact over the next year

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 have 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 an impact on NHS resources.
**OA cont’d**

- NICE clinical guideline on the management of OA (update), issued Feb 2014
- NICE Quality Standard on OA, expected date TBC
- NICE pathway available

**Spasticity**

- NICE clinical guideline on the management of multiple sclerosis in primary and secondary care (update), issued Oct 2014 – use of Sativex in MS associated spasticity
- NICE guidance on the use of collagenase clostridium histolyticum for treating Dupuytren’s contracture, expected Apr 2015

**This guideline is unlikely to have a significant financial impact on medicines spend**

This guideline presents an update to the previous guideline. The guideline update was originally intended to include recommendations based on a review of new evidence about the use of paracetamol, etoricoxib and fixed-dose combinations of NSAIDs plus gastroprotective agents in the management of OA. The draft version of the guideline recommended that paracetamol should not be routinely offered for the management of OA (identified as a key priority). However in view of feedback received during the consultation phase (particularly in relation to paracetamol) and an ongoing review by the MHRA of the safety of OTC analgesics, NICE now intends to commission a full review of evidence on the pharmacological management of OA. Until that update is published, the original recommendations (from 2008) on the pharmacological management of osteoarthritis remain current advice.

The Guideline Development Group (GDG) would like to draw attention to the findings of the evidence review on the effectiveness of paracetamol that was presented in the consultation version of the guideline. That review identified reduced effectiveness of paracetamol in the management of OA compared with what was previously thought. The GDG believes that this information should be taken into account in routine prescribing practice until the planned full review of evidence on the pharmacological management of osteoarthritis is published.

The guideline states that glucosamine/chondroitin products and acupuncture should not be offered for the management of OA.

This Quality Standard topic has been referred to NICE and is at an early stage of development.

**This area could have a moderate financial impact**

This updated NICE Guideline covers the management of multiple sclerosis (MS) in primary and secondary care and includes the pharmacological management of spasticity using baclofen, tizanidine, gabapentin, dantrolene, benzodiazepines and the cannabinoid spray Sativex. Baclofen or gabapentin are recommended as a first-line drug for treating spasticity in MS depending on contraindications and the person’s co-morbidities and preferences.

Sativex is licensed as add on therapy for symptom improvement in patients with moderate to severe spasticity due to MS who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy.

The updated NICE guideline recommends that Sativex should not be offered to treat spasticity in people with MS because it is not a cost effective treatment. The guideline notes that this recommendation doesn’t apply to people already on Sativex in the NHS who should be able to continue treatment until they and their NHS clinician think it appropriate to stop. As NICE does not recommend the use of Sativex, it is anticipated that it will not result in additional spend in this area.

**This area could have a moderate financial impact**

Collagenase clostridium histolyticum (Xiapex®) is licensed for the treatment of Dupuytren’s contracture in adult patients with a palpable cord. 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.
<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>Spasticity cont’d</strong></td>
<td>Treatment 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 final scope for this 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.</td>
</tr>
<tr>
<td>‧ NICE guidance on the use of collagenase clostridium histolyticum for treating Dupuytren’s contracture, cont’d</td>
<td></td>
</tr>
<tr>
<td>Actions/ issues which may be considered by commissioners and providers</td>
<td>Collagenase (when used in outpatients) is listed as exclusion in the National Tariff for 14/15. As CCGs are the responsible commissioners for this agent, a decision on funding will need to be agreed locally. Drug exclusions under Payment by Results 14/15</td>
</tr>
<tr>
<td>‧ In view of the recommendation for Sativex within the updated NICE MS guideline, commissioners and providers should agree how existing patients will be reviewed to ensure that they are still gaining benefit from treatment.</td>
<td></td>
</tr>
</tbody>
</table>
### 11. Eye

**Patent expiries**

According to *Prescribing Outlook New Medicines 2014*, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: verteporfin (Jul 2014); brinzolamide (Dec 2014); travoprost (Nov 2016); bimatoprost (Mar 2017); olopatadine (May 2017).

<table>
<thead>
<tr>
<th>Macular oedema</th>
<th>This is an area of major financial risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE guidance on the use of aflibercept treatment of macular oedema caused by central retinal vein occlusion, issued Feb 2014</td>
<td>Aflibercept is recommended as an option for treating visual impairment caused by macular oedema secondary to CRVO, as long as it is provided with the discount agreed in the patient access scheme. It will compete with anti-VEGF drugs (especially ranibizumab) and dexamethasone in this indication. The costing report estimates that implementation of this guidance will be associated with an additional annual cost of £3,849 per 100,000. This is based on the following assumptions:</td>
</tr>
<tr>
<td>• NICE guidance on the use of fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy (rapid review of technology appraisal guidance 271), issued Nov 2013</td>
<td>▪ An eligible population of 11 per 100,000</td>
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<td></td>
<td>▪ An equal share of uptake of ranibizumab and aflibercept (with no change in the uptake for dexamethasone)</td>
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<td></td>
<td>▪ A treatment period of up to three years</td>
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<td></td>
<td>▪ No increased cost of adverse events (aflibercept and ranibizumab have a similar safety profile)</td>
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<tr>
<td></td>
<td>The difference in cost is because of the drug cost and increased number of injections that may be needed in future years with aflibercept. For example the model assumes that more patients receiving aflibercept require three years of treatment than ranibizumab (20% vs. 10%, respectively).</td>
</tr>
<tr>
<td></td>
<td>In January 2013 NICE did not recommend the use of fluocinolone acetonide intravitreal implant for the treatment of chronic diabetic macular oedema considered insufficiently responsive to available therapies (TA271). However, after publication, the manufacturer agreed a patient access scheme with the Department of Health and submitted revised analyses to be considered in a rapid review of the original guidance. The updated guidance now recommends fluocinolone acetonide intravitreal implant as an option for treating chronic diabetic macular oedema that is insufficiently responsive to available therapies only if:</td>
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<tr>
<td></td>
<td>▪ the implant is to be used in an eye with an intraocular (pseudophakic) lens and</td>
</tr>
<tr>
<td></td>
<td>▪ the manufacturer provides fluocinolone acetonide with the discount agreed in the patient access scheme</td>
</tr>
<tr>
<td></td>
<td>The costing template for this guidance estimates a net cost impact in England of £8.6 million in year 1 (or ~£16,000 per 100,000 population), £1.2 million in year 2 (or ~£2,300 per 100,000 population) and £1.3 million in year 3 (or ~£2,500 per 100,000 population). These costs are based on the list price of the drug (not the revised price from the patient access scheme, which is commercial in confidence). The unit cost of the implant is taken as £5,500 within the template.</td>
</tr>
<tr>
<td></td>
<td>The Year 1 costs consist of:</td>
</tr>
<tr>
<td></td>
<td>- Increased cost of fluocinolone acetonide intravitreal implant £7.85m</td>
</tr>
<tr>
<td></td>
<td>- Increased cost of vitreous retinal procedures £544K</td>
</tr>
<tr>
<td></td>
<td>- Increased cost of outpatient follow up appointments £244K</td>
</tr>
<tr>
<td></td>
<td>The template assumes that:</td>
</tr>
<tr>
<td></td>
<td>- 10% of people have chronic diabetic macular oedema insufficiently responsive to other therapies (n=6,216)</td>
</tr>
<tr>
<td></td>
<td>- Of these, ~61% have chronic diabetic macular oedema (n= 3,767)</td>
</tr>
<tr>
<td></td>
<td>- Of these, 43% have had an intraocular (pseudophakic) lens (n= 1,586)</td>
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<tr>
<td></td>
<td>In year 1, 90% of this population (n = 1,427) will receive the fluocinolone acetonide. There will be ongoing costs of outpatient follow up attendances which continue for 3 years after the procedure.</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>Macular oedema cont’d</strong></td>
<td>According to the final scope, this appraisal will consider the clinical and cost effectiveness of dexamethasone intravitreal implant (Ozurdex®), alone or in combination with laser photoagulation, for the treatment of diabetic macular oedema. For this indication (launched in the UK in 2014), it is specifically licensed for use in patients who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy. This is likely to compete with fluocinolone and therefore is unlikely to be associated with any significant additional costs.</td>
</tr>
<tr>
<td>- NICE guidance on dexamethasone intravitreal implant for diabetic macular oedema expected Apr 2015</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 content or impact is currently available.</td>
</tr>
<tr>
<td>- NICE guideline on the diagnosis and management of macular degeneration, date expected TBC</td>
<td></td>
</tr>
<tr>
<td><strong>Choroidal neovascularisation (CNV)</strong></td>
<td>NICE recommends ranibizumab as an option for treating visual impairment due to CNV secondary to pathological myopia when the manufacturer provides ranibizumab with the discount agreed in the patient access scheme. The costing statement states that the guidance is unlikely to result in a significant change in resource use in the NHS as the estimated eligible population per year is small. Ranibizumab is an alternative treatment option to verteporfin photodynamic therapy (vPDT) and bevacizumab. The statement notes that any people newly diagnosed with CNV associated with pathological myopia who are eligible for treatment can be treated with ranibizumab, vPDT or bevacizumab. Commissioners and healthcare providers are reminded that the manufacturer of ranibizumab has agreed a patient access scheme with the Department of Health, in which a confidential discount is applied to all invoices. This is an area of low financial risk</td>
</tr>
<tr>
<td>- NICE guidance on the use of ranibizumab for treating CNV associated with pathological myopia, issued Nov 2013</td>
<td></td>
</tr>
<tr>
<td><strong>Vitreomacular traction (VMT)</strong></td>
<td>Ocriplasmin is a non-surgical treatment for VMT, (intravitreal injection). NICE recommends ocriplasmin as an option for treating VMT in adults, only if: an epiretinal membrane is not present and they have a stage II full-thickness macular hole with a diameter of 400 micrometres or less and/or they have severe symptoms. The annual cost associated with implementing the guidance is estimated at £2million for England, based on assumptions in the costing template (or ~£3,800 per 100,000 population). For patients with macular hole, the costing template estimates: - that 100% of eligible patients (listed for surgery) will receive ocriplasmin before surgery. - Of these, 40% will achieve macular hole closure by day 28 of ocriplasmin treatment. - The condition will not be resolved in ~60% of patients (and these would therefore presumably be considered for surgery).</td>
</tr>
<tr>
<td>- NICE guidance on the use of ocriplasmin in VMT, issued Oct 2013</td>
<td></td>
</tr>
</tbody>
</table>
### Disease or Indication: National targets and guidance

#### VMT cont’d
- NICE guidance on the use of [ocriplasmin in VMT](#), cont’d

For patients with VMT without macular hole, it is assumed:
- 45% will be managed through “watch and wait”
- 45% will be listed for surgery and will receive ocriplasmin before surgery. Of these, ~30% will experience a resolution of their VMT and 70% will not (and would therefore presumably go onto have surgery).
- 10% will have severe symptoms but are not listed for surgery and will receive ocriplasmin. Of these 70% will not experience resolution of their symptoms.

Although the costing template notes that there may be savings through reduced surgical procedures, ocriplasmin does represent an additional step and therefore cost where it is used but fails to resolve the VMT. These patients are still likely to go onto surgery.

The recommended dose is 0.125 mg (0.1 ml of the diluted solution) to the affected eye once as a single dose. Repeated administration in the same eye is not recommended. The cost of one injection is £3000 (inc. VAT). The administration cost for ocriplasmin is give as £177 in the costing template. As repeat injections are not recommended, this is the cost for a full treatment course.

#### Dry eye disease
- NICE guidance on [ciclosporin for dry eye disease](#) expected Aug 2015

This appraisal will consider the clinical and cost-effectiveness of ciclosporin for the treatment of dry eye syndrome (keratoconjunctivitis sicca), an inflammation of the eyes caused by reduced tear production or excessive tear evaporation.

According to [Prescribing Outlook New Medicines 2014](#), ciclosporin (0.1% w/w ophthalmic emulsion; not yet licensed in the UK) is an immunomodulator that reduces ocular inflammation by increasing secretions from the lacrimal gland. It represents an additional treatment option, and is likely to be more expensive than topical tear replacement therapies. Currently ophthalmic ciclosporin preparations are unlicensed in the UK (such products have however been available for many years). This treatment is likely to be CCG commissioned.

The final scope for the NICE guidance notes that the prevalence of dry eye disease is difficult to estimate as there is no defined diagnostic test. Although it can affect people of any age, it is more prevalent in women and in older people. It is reported that 15 to 33% of people aged 65 years or over have dry eye disease. This is likely to be an underestimate of the true prevalence as people with mild symptoms may not report the condition to their doctor. Approximately 20% of people with dry eye disease have severe disease. Data from the [ONS](#) suggest that the population of the UK aged 65 and over was 11.1 million mid-2013. If it is assumed that:
- 25% (2.8 million) of these people have dry eye disease (or 4,329 people per 100,000 population)
- 20% have severe disease (or 865 people per 100,000 population)
- Ciclosporin is used in 10% of these people (or 87 people per 100,000 population)
- 20% of people use the treatment for 3 months then stop (e.g. due no response, n=17 people per 100,000 population) and 80% of people persist with treatment long-term (or 70 people per 100,000 population) and
- Treatment with the eye drops costs £45 per month

the overall cost implication could be ~ £40,000 per 100,000 population.
This excludes the cost impact arising from use in people aged less than 65 years and would need to be modelled locally.
Disease or Indication: National targets and guidance

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

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

- Locally agree 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).
- 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 14/15. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. *Drug exclusions under Payment by Results 14/15* 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.
- Some centres are assessing the role of bevacizumab for AMD and other eye conditions such as CNV in view of the lower cost associated with its use. However, there have been some safety concerns about its use in this way. Although bevacizumab costs much less than other agents such as ranibizumab, it is unlicensed for any indication in the eye. Determine whether it is appropriate to support centres that are using intravitreal bevacizumab instead of the licensed products available to treat AMD and other eye related conditions and agree a commissioning decision in this area.
- Two recent Cochrane reviews supported the *systemic safety* of intravitreal ranibizumab and bevacizumab and the *effectiveness* in AMD. Based on this and other evidence, the Royal College of Ophthalmologists has recently called for UK regulatory bodies to review and appraise use of bevacizumab for use in AMD treatment in a *BMJ Editorial*. The editorial refers to the IVAN study, which estimated that using bevacizumab instead of ranibizumab to treat neovascular AMD would save the NHS in England £102m (or £192,000 per 100,000 population) a year. The editorial notes that commissioners are expected to enact NICE guidance, and NICE has not considered bevacizumab. This makes it difficult to commission the use of bevacizumab. The editorial therefore calls for NICE to appraise bevacizumab along with licensed drugs for the treatment of neovascular AMD.
### Patent expiries

<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>Psoriasis</strong></td>
<td><strong>13. Skin</strong></td>
</tr>
<tr>
<td>§ NICE guidance on apremilast for moderate to severe plaque psoriasis, expected Aug 2015</td>
<td>According to <a href="#">Prescribing Outlook New Medicines 2014</a>, the following patent expiries (which may have a significant impact on prescribing costs) are due within the next couple of years: infliximab (Feb 2015); etanercept (Jul 2015); alitretinoin (Oct 2015); pimecrolimus (Nov 2015)</td>
</tr>
</tbody>
</table>
| § NICE guidance on secukinumab for moderate to severe plaque psoriasis, expected 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. It is not currently licensed in the UK (launch anticipated in Q1 2015). The draft scope notes that it will be compared to systemic therapies (e.g. acitretin; ciclosporin; methotrexate) and also to biologics in people with severe disease who are unsuitable for biological therapy, or in whom such therapy has been ineffective. According to [Prescribing Outlook New Medicines](#), it is likely to be used as an additional option after current first line systemic treatments have failed or are contraindicated, and before moving onto biological therapy. As an oral formulation, drug and administration costs are likely to be lower than biologic therapies. 

According to [Prescribing Outlook New Medicines](#), it is likely to be used as a substitution of one agent for the other. 

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. It is not currently licensed in the UK (launch anticipated in Q1 2015). The draft scope notes that it will be compared to systemic therapies (e.g. acitretin; ciclosporin; methotrexate) and also to biologics in people with severe disease who are unsuitable for biological therapy, or in whom such therapy has been ineffective. According to [Prescribing Outlook New Medicines](#), it is likely to be used as an additional option after current first line systemic treatments have failed or are contraindicated, and before moving onto biological therapy. As an oral formulation, drug and administration costs are likely to be lower than biologic therapies. 

According to the costing template for TA146, the prevalence of psoriasis is 1.63% (1,275 per 100,000), and an estimated 1% of patients (14 per 100,000) have severe disease and are eligible for biological therapy. 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, and depending on the license may also be an option for patients failing anti-TNF treatment. 

According to the costing template for TA146, the prevalence of psoriasis is 1.63% (1,275 per 100,000), and an estimated 1% of these patients (14 per 100,000) have severe disease and are eligible for biological therapy. If it is assumed that secukinumab will be used in a similar population to efalizumab, then the following assumptions can be made: 

- 50% of patients do not respond to the first anti-TNF (7 per 100,000) 
- 100% of these (7 per 100,000 population) receive a second anti-TNF and 
- 50% fail 2nd line treatment and therefore receive secukinumab (3.5 people per 100,000 population) 

If secukinumab is to be used after efalizumab (£8,800), and if a cost of around £10,000 per year is assumed, then this could result in an additional cost implication of around £35,000 per 100,000 population. 

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### Psoriasis

- NICE guidance on apremilast for moderate to severe plaque psoriasis, expected Aug 2015
- NICE guidance on secukinumab for moderate to severe plaque psoriasis, expected Jul 2015
Urticaria  
- NICE guidance on omalizumab for previously treated chronic spontaneous urticaria, expected Apr 2015

According to the final scope, this appraisal will consider the clinical and cost effectiveness of omalizumab within its licensed indication as an add-on treatment for people aged 12 years and older with chronic spontaneous urticaria refractory to H1 antihistamine treatment. It will be compared to current established treatment, including leukotriene receptor antagonists, H2 antagonists and immunosuppressants (e.g. ciclosporin; mycophenolate mofetil; methotrexate). In draft guidance (ACD) NICE is minded not to recommend omalizumab in this setting and has requested further analyses from the manufacturer. However, if following further analyses, NICE approve use:

A NHSC review (2012) notes that the point prevalence of chronic urticaria in the UK is 1-5 per 1000 (100-500 per 100,000). The recommended dose of omalizumab for chronic urticaria is 300mg by subcutaneous injection every four weeks; the need for continued therapy should be reassessed periodically (clinical trial experience of use beyond six months in this indication is limited).

If it is assumed:
- 50% of these (150 per 100,000) require drug treatment
- 25% (37 per 100,000) do not respond completely to 2+ antihistamines (licensed or high-dose therapy)
- 50% of these (18 per 100,000) do not respond to other second-line therapies
- 10% (2 per 100,000) do not respond to immunosuppressants
- 50% of these (1 per 100,000) are eligible for and go on to receive omalizumab

Omalizumab is used for an average of 6 months per year (at a cost of £3074 per person, based on 2 x 150mg syringes every 4 weeks for 6 months)

This could result in an additional cost of around £3,000 per 100,000 population (drug cost only; this excludes any additional costs related to service delivery). If it is used as an earlier line of treatment then costs will be much higher.

Wound care  
- QIPP area - wound care
- Public Health England guidance on wound care
- NICE guideline on the prevention and management of pressure ulcers, issued Apr 2014
- NICE Quality Standard on Pressure Ulcers, expected May 2015

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 wound care related comparators have been developed:

Cost (NIC) per item for wound care products.

PHE is due to issue guidance on wound care (no information currently available)

This guideline covers the prevention, assessment and management of pressure ulcers in all age groups and all settings. It updates and replaces two previous clinical guidelines: ‘Pressure ulcers’ (clinical guideline 29; 2005) and ‘The use of pressure relieving devices’ (clinical guideline 7; 2003). It includes recommendations on debridement (including larval therapy), pressure-reducing devices, nutritional interventions, antiseptics, antimicrobials and antibiotics, wound dressings, management of heel pressure ulcers and other therapies. The costing statement notes that it is unlikely to have a significant national impact on NHS resources, as many of the recommendations are believed to be highlighting current standard practice. Organisations are however advised to assess the resource implications locally.

This Quality Standard will cover the prevention, assessment and management of pressure ulcers in people of all ages.
### Extemporaneous Specials

<table>
<thead>
<tr>
<th>British Association of Dermatologists (BAD) specials list</th>
</tr>
</thead>
</table>

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.

### 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.
- 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.
- Cytokine inhibitors are listed as exclusions in the National Tariff for 14/15. A decision on funding will need to be agreed locally for these agents for indications outside NICE guidance. [Drug exclusions under Payment by Results 14/15](#).
  - As of April 2013, NHS England is the responsible commissioner when these agents are used in children (aged 18 years or younger). CCGs are the responsible commissioners for use of these agents in adults.
- Alitretinoin is listed as an exclusion in the National Tariff for 14/15. [Drug exclusions under Payment by Results 14/15](#).
  - A decision on funding will need to be agreed locally for this agent for indications outside NICE guidance.
- Users may wish to refer to the NICE commissioning guide on biologic drugs for the treatment of inflammatory disease in rheumatology, dermatology and gastroenterology (2012).
- 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 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 detailed only cover the basic, manufacturing patent. Additional patents on formulations and uses can influence when a generic or biosimilar becomes available commercially.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patent expiry date (includes paediatric extension ♦)</th>
<th>Generic or biosimilar available/ in development</th>
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