Prescribing Outlook

Cancer Medicines being evaluated by NICE

2014

A resource for the NHS to help with budget setting, prescribing planning and medicines management
## Malignant disease

The Cancer Drugs Fund (or Interim predecessor) has now been in place for over 4 years in England. Originally a figure of £200m per year was made available to fund cancer medicines which were not routinely available on the NHS – this equates to a sum of around £400,000 per 100,000 population (actually £320,000 per 100,000 population once the VAT has been excluded). Recently it has been announced that this figure will increase to £280m for the next two years and that the fund will continue to administered centrally by NHS England. However it is also likely that there will be a revision of evidence to support the drugs currently funded to ensure that ongoing funding is justified and that NHS England will work more closely with NICE to align their assessment processes.

## Breast cancer

NICE issued a quality standard for breast cancer in 2011.

Update to NICE guideline on advanced breast cancer issued Jul 2014

Update to NICE guideline on early and locally advanced breast cancer: Diagnosis and treatment – decision on whether update necessary in Jun 2015

NICE guidance on pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer, which has not been previously treated, or has relapsed after adjuvant therapy - expected date TBC.

This is an area of high financial risk as there is likely to be considerable ongoing interest in several new developments.

This update related to advice about lymphoedema and exercise, no changes were made to drug-treatment recommendations issued in 2009.

Unlike likely to impact in next financial year

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

NICE estimate that the annual incidence of women presenting with advanced breast cancer in England is 11,384 (2013 presenting at that stage and 9371 presenting following disease progression) – this equates to an incidence of 21 cases per 100,000 population. If we assume that 70% are eligible for chemotherapy and that 25% are HER2 positive and would receive a trastuzumab-based regimen this would equate to about 4 patients per 100,000 population per year. If 50% of these received pertuzumab then potentially an uptake of 2 patients per 100,000 is feasible. If we assume that the treatment costs £2400 per cycle, and that patients get treated for 18 months, then this
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<th><strong>Breast cancer cont’d</strong></th>
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<tr>
<td>NICE guidance on trastuzumab emtansine for treating unresectable metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane – expected date TBC</td>
<td>Draft Guidance from NICE outlined in a FAD indicates that they do not recommend the use of trastuzumab emtansine within its marketing authorisation. In the meantime trastuzumab emtansine is available via the CDF for the treatment of HER2-positive locally advanced/ unresectable or metastatic (Stage IV) breast cancer provided certain additional criteria are met. This decision was based on evidence showing a 3.2 month increase in PFS, a 5.8 month increase in OS and some evidence of improvement in QoL. Based on the assumptions outlined above – if we assume that 3 patients per 100,000 population receive trastuzumab for metastatic or recurrent breast cancer and that 1.5 progress and are eligible for consideration for trastuzumab emtansine at a cost of £90,000 per treatment course, this would equate to an additional expenditure of £135,000 per 100,000 population.</td>
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<tr>
<td>NHS England support use of subcutaneous trastuzumab – issued Sept 2013</td>
<td>NHS England supports the use of subcutaneous trastuzumab as a means of improving patient experience and reducing waste and overall drug costs. The SMC accepted the findings of a manufacturer-authored cost minimisation analysis which estimated that for the overall analysis (medicine and non-medicine costs) there were cost savings per early breast cancer patient of £3,454 over a full 1-year treatment, and for metastatic breast cancer patients of £3,162 over a full 1-year treatment. If restrict analysis to medicine costs only, the cost savings per patient per year are £1,441 and £1,239 for EBC and MBC respectively. These results may no longer be valid once we have access to biosimilar versions of trastuzumab – when decreases of over 25% of list price of branded product are anticipated.</td>
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Gastrointestinal (GI) cancer

Colorectal/anal cancer

- NICE colorectal cancer quality standard – published Aug 2012

- NICE support for commissioners and others implementing the quality standard – published Aug 2012

- NICE guidance on aflibercept in combination with irinotecan and fluorouracil based therapy for the treatment of metastatic colorectal cancer which has progressed following prior oxaliplatin-based chemotherapy, - published Mar 2014.

- NICE guidance on cetuximab (review of TA176) and panitumumab (partial review of TA246) for the first line treatment of metastatic colorectal cancer – expected Apr 2016

This is an area of low financial risk

NICE do not support the use of aflibercept for this indication. It is however available via the CDF for this indication. The cost implications of approval are difficult to determine as NICE do not currently support the use of any biologic therapy as part of a second or subsequent line regimen although both bevacizumab and cetuximab are funded through the CDF.

NICE currently support the use of cetuximab in combination with FOLFIRI or FOLFOX as a first-line treatment in patients whose primary tumour has been resected or is potentially operable and whose metastatic disease is confined to the liver and is currently unresectable but the patient is fit enough to undergo surgery should the tumour become resectable. NICE were unable to recommend panitumimab for this indication previously as the manufacturer did not provide an evidence submission.

Cetuximab is currently available via the CDF for patients who do not meet NICE criteria for 1st line therapy provided they have wild-type KRAS and it is given in combination with irinotecan. This guidance is therefore not expected to impact significantly in the next financial year.
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<tr>
<th><strong>Colorectal/ anal cancer</strong></th>
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<tr>
<td>- NICE guidance on <a href="#">regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease</a> - currently suspended</td>
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<tr>
<td>- Update on NICE Clinical guideline on <a href="#">colorectal cancer</a> – published Dec 2014.</td>
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<tr>
<td>- NICE guidance on <a href="#">fluorouracil plasma monitoring; the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion</a> – expected Jan 2015</td>
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### Pancreatic cancer

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<tr>
<td>- NICE guidance on <a href="#">paclitaxel as albumin-bound nanoparticles in combination with gemcitabine for previously untreated metastatic pancreatic cancer</a> - expected Jan 2015</td>
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<tr>
<td>- NICE guidance on <a href="#">nimotuzumab for the first line treatment of metastatic pancreatic cancer</a> - expected date TBC</td>
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This drug was launched in the UK in 2013 but NICE has suspended appraisal as the manufacturer is unable to provide an evidence base which compares regorafenib with existing clinical practice in the UK. The drug is not currently available via the CDF for this indication. It is unlikely therefore to have a significant impact in the next financial year.

This update was restricted to a review of the evidence to support stents to reduce GI obstruction and the management of early rectal cancer and is not therefore expected to impact significantly on drugs budgets.

This would not be expected to significantly impact on drug costs per se but may have service implications when used as part of treatment regimens for colorectal cancer and various other cancers.

Draft guidance from NICE outlined in the ACD indicates that they do not support the use of paclitaxel as albumin-bound particles in combination with gemcitabine for this indication. This recommendation seems to be based on findings that this formulation of paclitaxel plus gemcitabine was less effective than FOLFIRINOX and similarly effective to capecitabine plus gemcitabine but potentially less well tolerated. The calculated ICER over gemcitabine alone was £78,500. Given these findings it seems unlikely that this agent will be approved and thus there are unlikely to be significant cost implications in the next financial year.

In the meantime albumin-bound paclitaxel is available via the CDF for the first-line treatment of pancreatic cancer provided certain additional criteria are met.

This drug has not yet been submitted for license despite the key Phase III trial being completed over one year ago and showing a 12% difference in overall rate at 12 months when given in combination with gemcitabine versus gemcitabine alone (but not a significant difference in median overall survival). Unlikely to impact in the next financial year.
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<td>- NICE guidance on masitinib for the treatment of locally advanced or metastatic pancreatic cancer - suspended</td>
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<th>Gastrointestinal stromal tumours (GIST)</th>
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<td>- NICE guidance on imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196) – published Nov 2014</td>
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<tr>
<td>- NICE guidance on masitinib for treating unresectable or metastatic gastrointestinal stromal tumours after treatment with imatinib - suspended</td>
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The CHMP has recommended that marketing authorisation is refused and therefore NICE has suspended work on this technology appraisal. Unlikely to impact in the next financial year.

NICE support use in as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria. This is broadly similar to the criteria defined by NHS England in order to qualify for access via the CDF. The SMC accepted an estimate that around 15 patients per year would be eligible for adjuvant treatment with imatinib – this equates to an incidence of about 0.3 cases per 100,000 population. If we assume that each patient takes the drug for 3 years then this would increase drug costs by around £20,000 per 100,000 population. NICE estimate that the number of new people eligible for treatment with imatinib is around 170 per year for the population of England. The cumulative cost impact is therefore £2.8 million in year 1, £4.3 million in year 2 and £5.1 million from year 3 onwards – which equates to between £5400 and £9800 per 100,000 population.

NICE has suspended this appraisal because the Committee for Medicinal Products for Human Use (CHMP) has decided not to approve masitinib for treating unresectable or metastatic gastrointestinal stromal tumours after treatment with imatinib.
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<td>- NICE guidance on <a href="#">bosutinib for the treatment of chronic myeloid leukaemia</a> – issued Nov 2013</td>
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<td>- NICE guidance on <a href="#">obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia</a> – expected Feb 2015</td>
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<td>- NICE guidance on <a href="#">ofatumumab for treating previously untreated chronic lymphocytic leukaemia</a> – expected Apr 2015</td>
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<td>- NICE guidance on <a href="#">ofatumumab for maintenance treatment of relapsed chronic lymphocytic leukaemia</a> – expected Apr 2016</td>
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This is an area of moderate to high financial risk

NICE do not support the use of bosutinib for treating Philadelphia-chromosome-positive chronic myeloid leukaemia (CML) and as such there are no financial implications for this guidance. However the drug is available via the CDF for patients refractory to nilotinib or dasatinib.

Draft guidance from NICE outlined in the ACD indicates that NICE do not currently support the use of obinutuzumab in combination with chlorambucil for adults with untreated chronic lymphocytic leukaemia who have comorbidities that make full-dose fludarabine-based therapy unsuitable for them. NICE currently have concerns over the relevance of the evidence to support both clinical and cost effectiveness.

If we assume that this would be offered as an alternative to bendamustine in this population and it costs around £19,000 more per patient treated. Then according to NICE estimates of likely uptake of bendamustine as a first-line treatment then there are 676 patients likely to be treated each year. If half of these opt for obinutuzumab instead of bendamustine then this would increase costs by around £12,000 per 100,000 population.

This was licensed for use in combination with chlorambucil or bendamustine in patients unable to tolerate fludarabine in July 2014. As such it will compete with obinutuzumab as outlined above and is unlikely to carry additional cost implications to those described in that entry.

Ofatumumab may get licensed for this indication in the latter part of 2015, Interim results of a phase III study indicate that when given as an 8 weekly treatment to patients that responded to treatment after relapse it prolonged progression free survival. NICE estimate that there are around 1140 patients with CLL that relapse and receive treatment each year. If we assume that 30% of these were to receive 10 cycles of ofatumumab costing £38,000 that would increase costs by around £13m which equates to £25,000 per 100,000 population.
Haematological cancers cont’d

Chronic lymphocytic leukaemia

- NICE guidance on idelalisib for treating chronic lymphocytic leukaemia – expected Oct 2015

Multiple myeloma

- NICE guideline on diagnosis and management of myeloma – expected Jan 2016

- NICE guidance on bortezomib for induction therapy prior to high dose chemotherapy and autologous stem cell transplantation for the treatment of multiple myeloma – published Apr 2014

- NICE guidance on lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib (part-review of TA171) - expected Dec 2014

Idelalisib is licensed for use in adults with chronic lymphocytic leukaemia who have received at least one therapy and in adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable. It is currently available via the CDF for the first of these indications provided certain criteria are met. Idelalisib is given orally and is used in combination with rituximab. NICE estimate that around 720 patients/year of the 1140 currently eligible for rituximab receive either FCR or CHOP as a second-line treatment for CLL. If we assume that 20% of these were switched to idelalisib plus rituximab and it costs £50,000 more per patient treated, this would increase treatment costs by £14,000 per 100,000 population.

This guideline will not revisit existing NICE guidance on specific treatments for myeloma but according to the scope will cover post-third line systemic therapy regimens for patients with relapsed or refractory myeloma. It is currently unclear whether there will be significant cost implications for drugs budgets although it seems unlikely from the scoping document.

NICE supports the use of bortezomib as an option, in combination with dexamethasone, or with dexamethasone and thalidomide, for the induction treatment of adults with previously untreated multiple myeloma, who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. NICE estimate that ultimately this guidance will cost an additional £6.3m across England when fully implemented – this equates to about £12,000 per 100,000 population. They do not provide any detail on how this figure has been derived but it is similar to an SMC estimates based on an eligibility of 1.2 patients per 100,000 population and an uptake rate of between 4% and 27% over 5 years. The SMC also points out that the financial effects of displacement of thalidomide and dexamethasone are likely to be relatively marginal.

In current guidance described in TA171 NICE support the use of lenalidomide as an option in patients who have received two or more prior therapies. In this ACD the preliminary advice from NICE is that this should not be extended to patients who have received one prior treatment with bortezomib and for whom thalidomide is not appropriate. This indication for lenalidomide is currently funded via the CDF.
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- NICE guidance on [panobinostat for treating multiple myeloma in people who have received at least one prior therapy](#) - expected Jan 2016

  This drug is expected to be licensed in the latter part of 2015. In trials it has been tested in combination with bortezomib and dexamethasone in patients with relapsed or refractory MM. In the PANARMA study it is reported that median progression-free survival was significantly longer in the panobinostat group than in the placebo group (11.9 months vs 8.08 months). Overall survival data are not yet mature. NICE estimate that around 2794 patients would qualify for bortezomib for this indication each year – which equates to around 5 patients per 100,000 population per year. If we assume that 60% of these patients receive panobinostat in addition to bortezomib and it is launched at £30,000 per treatment course this would increase costs by around £90,000 per 100,000 population.

- NICE guidance on [vorinostat in combination with bortezomib for the treatment of multiple myeloma in people who have received at least one prior therapy](#) - currently suspended

  This guidance is currently suspended – but even if re-initiated it is competing with panobinostat for this indication and is unlikely to represent additional financial implications.


  In this TA, NICE will assess the use of lenalidomide instead of a thalidomide or bortezomib-based regimen in the first-line treatment setting. The cost implications in this setting are probably insignificant as it involves relatively small numbers of patients (maybe 1 per 100,000 population) treated for short periods of time and if used lenalidomide would be displacing similarly costly medicines.

- NICE Guidance on [pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib](#) – expected Feb 2015

  Pomalidomide was launched in the UK in 2013 and is available through the CDF. Results from results from the MM-003 study comparing pomalidomide plus dexamethasone with dexamethasone indicate that in trms of PFS and OS there is advantage in favour of pomalidomide + dexamethasone - median PFS 4 vs. 1.9 months and OS 12.7 vs. 8.1 months (p=0.028). NICE estimate that there are around 800 patients in England that meet criteria to receive lenalidomide as a second line treatment. If we assume that 50% of these would on to receive pomalidomide as a 3rd or subsequent line treatment and that they receive an average 4 cycles costing £8900 per cycle – this would increase costs by £7000 per 100,000 population.
Multiple myeloma (contd)

- NICE Guidance on bortezomib for consolidation therapy after autologous stem cell transplantation for the treatment of multiple myeloma – currently suspended
- NICE Guidance on lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation – currently suspended

Myelodysplastic syndrome

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

Both these technology appraisals are currently suspended. In the case of lenalidomide this is because the manufacturer has withdrawn the license application until more mature data are available, in the case of bortezomib the manufacturer has informed NICE that they will not be pursuing a license for this indication.

There are RCT data to indicate that lenalidomide maintenance therapy is associated with a significant prolongation of PFS in this population – in the Phase III (NCT00114101) trial comparing efficacy of lenalidomide vs placebo as maintenance therapy after ASCT median PFS was 39 months (36 to NA) in the lenalidomide gp vs. 21 months (18 to 28) in the placebo group.

According to the original scope for bortezomib for induction therapy there are about 800 patients that receive stem cell transplant for multiple myeloma each year in England and Wales that might be considered eligible for maintenance treatment each year. If we assume that 50% of these patients go on to receive lenalidomide maintenance costing £50,000 per year then costs are likely to be up to £37,500 per 100,000 population but increase incrementally, so that if we assume the average patient remains on treatment for about 3 years then costs are likely to plateau at about £100,000 per 100,000 population. Should the manufacturer of bortezomib change their mind bortezomib would be competing directly with lenalidomide for the same market. Therefore clinicians are likely to choose between bortezomib and lenalidomide and this choice is likely to be influenced by evidence, NICE approval status, patient choice and cost. It is unlikely that this intervention will increase costs by a greater amount than described for lenalidomide.

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

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

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

- NICE guideline on diagnosis and management of non-Hodgkin’s lymphoma – expected August 2016
  
  This guideline will cover a wide-range of issues including the following – but is unlikely to impact significantly in terms of costs in the next financial year.
  
  - The most effective first-line treatment for early-stage follicular lymphoma.
  - The role of autologous and allogeneic transplantation in people with follicular lymphoma.
  - The role of immediate compared with deferred chemotherapy (watch and wait) in treating advanced asymptomatic follicular lymphoma.
  - The most effective first-line treatment for people with MALT lymphoma, including the role of antibiotic therapy, radiotherapy and chemo-immunotherapy.
  - The most effective first-line treatment for people with mantle cell lymphoma, including the choice of first-line treatment, the role of consolidation of high-dose therapy with stem cell support and the role of maintenance treatment.
  - The most effective first-line treatment for peripheral T-cell lymphoma.
  - The most effective first-line treatment for Burkitt's lymphoma.
  - The initial treatment of composite/discardant and transformed follicular lymphoma.
  - The most appropriate salvage strategies, including indication for autologous and allogeneic transplantation, for people with diffuse large B-cell lymphoma.
  - Indications and methods for central nervous system prophylaxis for people with diffuse large B-cell lymphoma.

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

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


- NICE guidance on pralatrexate for the treatment of relapsed or refractory peripheral T-cell lymphoma – suspended

- NICE guidance on bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma – issue date TBC


NICE support the use of pixantrone for this indication provided the person has previously been treated with rituximab and is receiving 3rd or 4th line treatment. NICE estimate that this guidance will increase costs by £4.2m which equates to about £8000 per 100,000 population. NICE do not provide any detail as to how these estimates were derived. In 2003 NICE estimated that around 2100 patients might go on to receive rituximab-based chemotherapy for aggressive NHL – if we assume that 30% of these might be considered suitable for a 3rd-line treatment and that that treatment was launched at a cost of £20,000 per treatment course (3 vials per dose given for 4 cycles) then this would increase drug costs by around £32,000 per 100,000 population.

This was given a negative opinion by the CPMP and the NICE appraisal has been suspended. Now thought that it is unlikely to be licensed before 2016 and therefore unlikely to have cost implications in the next financial year.

It is expected that bendamustine will be licensed for this indication in the near future. In the scope NICE estimate that there are around 670 new cases of mantle cell lymphoma diagnosed each year in England and Wales. In a Phase 3 comparative study this combination was shown to be associated with a 38 month improvement in median PFS compared with the current standard of treatment R-CHOP (69.5 versus 31.2 months). If we assume that 90% of these patients receive chemotherapy and that 90% receive this regimen and it costs £5000 more than R-CHOP – then this regimen could increase costs by £4800 per 100,000 population.

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

- NICE guidance on **romidepsin for the treatment of relapsed or refractory peripheral T-cell lymphoma** – currently suspended

- NICE guidance on **bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin’s lymphoma** – currently suspended

- NICE guidance on **idelalisib for treating refractory indolent non-Hodgkin’s lymphoma** – currently suspended

This appraisal is currently suspended following a negative CHMP opinion in 2012. Therefore unlikely to impact in the next financial year.

This guidance is currently suspended pending clarification of licensing schedule. At present it has not been submitted for license and therefore unlikely to impact in the next financial year.

This guidance is currently suspended as NICE has not received a submission from the manufacturer. This drug is currently funded via the CDF as a ≥3rd line treatment of indolent non-Hodgkin’s lymphoma and also for patients not responding to a 1st line combination of an alkylating agent plus rituximab and in whom a conventional rituximab-based treatment plus an anthracycline- or fludarabine-based combination is not suitable.
**Lung cancer**

*Non-small cell lung cancer (NSCLC)*

- NICE [pathway for lung cancer](#)

- NICE [guidance on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175)](#) – expected Dec 2014

- NICE [guidance on cetuximab for the treatment of advanced non-small cell lung cancer](#) - currently suspended

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

This standard and pathway reflects previously published NICE Guidance on treatment and as such should have minimal impact on associated drug budgets.

A review of the existing guidance is underway. NICE currently support the use of erlotinib as an alternative to docetaxel in the second line treatment of NSCLC provided the overall treatment cost is the same. It is not recommended for use in patients in whom docetaxel is considered unsuitable or as a third-line treatment option. Conversely NICE were unable to support the use of gefitinib as the manufacturer did not provide an evidence submission. Within the ACD, draft guidance from NICE indicates that this is unlikely to change significantly in that EGFR status is now assessed routinely and if mutation positive a targeted treatment (erlotinib or gefitinib) is given first line. In the revised guidance erlotinib is provisionally recommended as an option for patients that have progressed after non-targetted chemotherapy provided it is now known to be EGFR-TK mutation positive or there is reason to suspect it is. Gefitinib remains unapproved for the treatment of EGFR-TK positive NSCLC. This revised guidance is likely to have minimal cost implications.

The manufacturer has informed NICE that they have withdrawn their license application from the EMA. It is currently unclear when or if they will resubmit but it is now unlikely that this intervention will be licensed in the next financial year.
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<tr>
<td>- NICE guidance on afatinib for the treatment of locally advanced or metastatic non-small cell lung cancer after previous platinum containing chemotherapy and gefitinib or erlotinib – currently suspended.</td>
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NICE do not support the use of pemetrexed for maintenance treatment following induction therapy with pemetrexed and cisplatin. As such it has no cost implications. Pemetrexed is however available via the CDF for maintenance treatment of patients following carboplatin and pemetrexed.

In their costing report for approval of pemetrexed as a first-line treatment, NICE estimate that ultimately 75% of suitable patients (estimated at 1839 for England) will receive pemetrexed as a first-line treatment. If we assume that currently 50% of patients receive pemetrexed as a first-line treatment and that 30% of those go on to receive it as a maintenance treatment costing £11,500 per year, then the potential cost implication is about £6000 per 100,000 population.

NICE support the use of afatinib provided the tumour tests positive for EGFR-TK mutation and the person has not previously had an EGFR-TK inhibitor and the manufacturer provides afatinib with the discount agreed in the patient access scheme. NICE expect around 450 patients per year to qualify for this type of treatment (or around 9 per 100,000 population). It will compete with erlotinib and gefitinib and with the PAS in place NICE do not expect there to be a significant cost implication.

This guidance is currently suspended as the manufacturer has informed NICE that it does not expect to get marketing authorisation for this specific indication.
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<tr>
<td><strong>NICE guidance on nintedanib for treating previously treated metastatic non-small cell lung cancer</strong> – expected May 2015</td>
</tr>
<tr>
<td>Nintedanib has received EMA marketing approval for use in combination with docetaxel for the treatment of patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy. In a Phase III trial this oral treatment was shown to be associated with a 2.3-month increase in OS (12.6 months vs 10.3 months) in this subgroup of patients when given in combination with docetaxel compared to treating with docetaxel alone. NICE has previously estimated that there are around 10 patients per 100,000 population that would qualify to receive second line chemotherapy but in reality only about 4 actually do receive it. Adenocarcinoma probably constitutes about 65% of cases of NSCLC. If we assume that treatment uptake has improved since NICE made those estimates so that 6 patients per 100,000 now receive 2nd line treatment, of whom 65% are eligible for this combination and it is used in half of those, then we might expect 2 patients per 100,000 to receive this combination. If it costs around £30,000 per treatment course then it would increase expenditure by around £60,000 per 100,000 population.</td>
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<tr>
<td><strong>NICE guidance on ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer</strong> - expected Jan 2016</td>
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<tr>
<td>Ceritinib has been approved in the US in patients with metastatic ALK-positive NSCLC previously treated with crizotinib. Clinical trial data suggest that ceritinib is associated with a median PFS of 6.9 months in patients previously treated with crizotinib. If approved for the same indication in the EU it is expected to be launched in Q2 2015. At present NICE do not recommend crizotinib for people with a type of advanced non-small-cell lung cancer that is ‘ALK-positive’ and has been treated before but it is available via the CDF. It has previously been estimated by LCNDG that around 0.5 cases per 100,000 population might be eligible for crizotinib. If we assume that these patients are accessing that medicine via the CDF and that 60% would be eligible for a 3rd line treatment and that it costs £50,000 per treatment course then this drug could increase costs by around £30,000 per 100,000 population.</td>
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This is an area of moderate to high financial risk

This includes links to NICE advice to health care professionals to support the primary prevention of skin cancer.

NICE are developing a clinical guideline on the assessment and management of malignant melanoma. Amongst the medicine-related issues are the following:

- The most effective treatment for in-transit melanoma metastases.
- The role of systemic anti-cancer therapy in the treatment of metastatic melanoma (for example, dacarbazine and temozolomide).
- The role of measuring vitamin D levels and of supplementation in people who have been diagnosed with melanoma.
- The role of imiquimod in the treatment of melanoma.
- Management of other intercurrent conditions with drug therapies which may increase the risk of death from melanoma (for example, immunosuppressants, levodopa, metformin)

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

NICE support the use of ipilimumab for this indication provided the manufacturer provides the drug at the price agreed in the patient access scheme. NICE estimate that this will cost £2.5m rising to £3.9m over 5 years. This equates to between £4700 and £6800 per 100,000 population. NICE do not provide any details of the assumptions behind those estimates and the details of the PAS remain confidential. Based on that fact that around 1500 patients per year die from this form of cancer, equating to around 3 cases per 100,000 population and that it costs around £75,000 to treat a patient with this drug – it would seem reasonable to assume that NICE predict a very low level of uptake in first-line setting and perhaps that first-line approval will ultimately reduce use in patients with recurrent disease. In the costing statement issued to support use in relapsed patients NICE estimated at there are 700 patients per year that present with metastatic or unresectable melanoma in whom chemotherapy/active treatment is suitable. NICE estimated that perhaps 20% of these might be considered for ipilimumab in the relapsed disease setting – if we assume that therefore 40% could be considered suitable in the first-line setting then that would equate to 280 patients (or 0.5 cases per 100,000 population) which at £75,000 per 100,000 population would equate to an expenditure of about £38,000 per 100,000 population (not taking account of any PAS scheme)
Skin and connective tissue cancers cont’d

- NICE guidance on dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma – published Oct 2014
- NICE guidance on dabrafenib and trametinib for treating advanced unresectable or metastatic BRAFV600 mutation-positive melanoma – currently suspended
- NICE guidance on paclitaxel (as albumin-bound nanoparticles) for the first-line treatment of metastatic melanoma – currently suspended
- NICE guidance on ipilimumab for the adjuvant treatment of completely resected high risk stage III or IV melanoma – issue date TBC

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

NICE has announced that the manufacturer has withdrawn its application to the EMA for the use of trametinib in combination with dabrafenib. Therefore the appraisal process has been suspended until more information becomes available.

NICE has announced that the manufacturer will no longer be pursuing a license for this indication and therefore this appraisal has been suspended.

Data have been presented at conference showing that ipilimumab [10 mg/kg (n=475)] significantly improved recurrence-free survival vs. placebo (n=476) for patients with stage 3 melanoma who are at high risk of recurrence following complete surgical resection. At three years, an estimated 46.5% of patients treated with Yervoy were free of disease recurrence compared to an estimated 34.8% of patients on placebo. The median RFS was 26.1 months for Yervoy vs. 17.1 months for placebo, with a median follow-up of 2.7 years. The manufacturer has not yet applied for license so this is unlikely to impact in the next financial year. NICE will confirm appraisal dates once regulatory timelines are known.
Urogenital and renal cancers

- NICE guidance on axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment – issue date TBC

- NICE Guideline on the diagnosis and management of bladder cancer – expected Feb 2015

This is an area of low financial risk

This drug was launched for use in the UK in September 2012. Provisional advice from NICE in the revised ACD indicates that they support the use of axitinib after failure of prior treatment with sunitinib or a cytokine in patients with advanced renal cell carcinoma if the manufacturer provides the drug at the discount agreed in the patient access scheme. However NICE also note that the appraisal is currently delayed in order to reconcile the axitinib marketing authorisation and English clinical practice for people who have received prior treatment. This drug is currently funded via the CDF as a second-line treatment (after a cytokine or a tyrosine kinase inhibitor)

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

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

These recommendations if finally approved are unlikely to have significant financial implications for current management pathways but may impact on recommended follow up patterns.
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<tr>
<th><strong>Ovarian cancer</strong></th>
<th><strong>This is an area of moderate financial risk</strong></th>
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<tbody>
<tr>
<td>• NICE ovarian cancer quality standard—published May 2012</td>
<td>This is not expected to have any significant impact on drug expenditure in this area</td>
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<tr>
<td>• NICE guidance on topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for advanced ovarian cancer (for recurrent disease only) (Review of TA 91 &amp; TA 222) – issue date TBC</td>
<td>This is a review of two TAs – NICE currently support the use of topotecan, pegylated liposomal doxorubicin hydrochloride (PDLH) and paclitaxel, but not the use of trabectedin for the treatment of recurrent advanced disease. They have not considered the merits of the case for use of gemcitabine before. In the ACD which was published Sept 2013 NICE continue to support the use of paclitaxel and pegylated doxorubicin but are no longer supportive of topotecan. Similarly they are not supportive of the use of trabectedin (used with PDL) or gemcitabine. It is unclear from the NICE website why there has been no progress towards publication in the last 12 months but as it stands it seems unlikely that this guidance will have significant cost implications.</td>
</tr>
<tr>
<td>• NICE guidance on vintafolide in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate receptor positive, platinum resistant ovarian cancer – currently suspended</td>
<td>NICE has been informed by the manufacturer that it has withdrawn its application for a conditional marketing authorisation for vintafolide in this indication. Therefore NICE has decided to suspend this appraisal on its current work programme and it is unlikely to impact significantly in the next financial year.</td>
</tr>
<tr>
<td>• NICE guidance on pazopanib for the maintenance treatment of epithelial ovarian, fallopian and peritoneal cancer in patients whose disease has not progressed after first line therapy – currently suspended</td>
<td>NICE has been informed by the manufacturer that it has withdrawn its application for a marketing authorisation for pazopanib in this indication. Therefore NICE has decided to suspend this appraisal on its current work programme.</td>
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Olaparib is an orally administered treatment and has received an EU positive opinion and is expected to be launched in early 2015. A study published in The Lancet Oncology (n=162) showed that PFS was significantly longer in the olaparib plus chemotherapy group (median 12.2 months than in the chemotherapy alone especially in patients with BRCA mutations (HR 0.21 p=0.0015). If we assume there are around 300 women per year that are eligible for this treatment (around 15% carry the BRCA mutation and around 4000 women die each year from this form of cancer), that the manufacturer launches it at a price of £50,000 per year and that the average patient takes it for 12 months, then this would increase costs by around £29,000 per 100,000 population.
<table>
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<tr>
<th>Bone cancers and metastases</th>
<th>This is an area of low financial risk</th>
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<tbody>
<tr>
<td>• NICE guidance on the use of ridaforolimus for the maintenance treatment of metastatic soft tissue or bone sarcoma, currently suspended</td>
<td>The manufacturers have notified NICE that they will not be providing an evidence submission for this product. NICE has therefore suspended work and it is unlikely to impact over the next financial year.</td>
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<tr>
<th>Prostate cancer</th>
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<tr>
<td>• Review of NICE Guidance on prostate cancer, diagnosis and management – published Jan 2014</td>
</tr>
<tr>
<td>• NICE prostate cancer quality standard – date expected Jun 2015</td>
</tr>
<tr>
<td>• NICE guidance on enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen – published July 2014.</td>
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<td></td>
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<tr>
<td>This is an area of high financial risk</td>
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<tr>
<td>Overall this guideline is unlikely to have major cost implications in terms of the drug therapies used: key new medicine-related recommendations include the following:</td>
</tr>
<tr>
<td>• Offer men with intermediate- and high-risk localised prostate cancer a combination of radical radiotherapy and androgen deprivation therapy, rather than radical radiotherapy or androgen deprivation therapy alone. Specifically offer men with intermediate- and high-risk localised prostate cancer 6 months of androgen deprivation therapy before, during or after radical external beam radiotherapy.</td>
</tr>
<tr>
<td>• Consider continuing androgen deprivation therapy for up to 3 years for men with high-risk localised prostate cancer and discuss the benefits and risks of this option with them</td>
</tr>
<tr>
<td>• Ensure that men have early and ongoing access to specialist erectile dysfunction services.</td>
</tr>
<tr>
<td>• Consider intermittent therapy for men having long-term androgen deprivation therapy (not in the adjuvant setting),</td>
</tr>
<tr>
<td>NICE support the use of as an option for treating metastatic hormone-relapsed prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy, only if the manufacturer provides enzalutamide with the discount agreed in the patient access scheme. NICE do not expect this guidance to have significant cost implications as enzalutamide would be competing with abiraterone which has a similar cost. However they note that this estimate does not factor in the cost implications of using enzalutamide after abiraterone. If we assume that 3.75 patients per 100,000 population are currently receiving abiraterone (NICE estimate) and that 30% of those go on to receive enzalutamide as a follow on agent then this would increase costs by about £30,000 per 100,000 population. Prior to NICE approval enzalutamide was available via the CDF for this indication</td>
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Prostate cancer (contd)

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

- NICE guidance on denosumab for preventing bone metastases in castrate resistant prostate cancer – currently suspended

- NICE guidance on Degarelix depot for treating advanced hormone dependent prostate cancer – expected Jun 2015

This appraisal is suspended whilst NICE await a revised submission from the manufacturer which will include an amended patient access scheme. In the FAD NICE do no support the use of abiraterone for this indication primarily on grounds of cost-effectiveness.

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

In their costing model for 2nd-line use of abiraterone NICE estimate that there are around 13 patients per 100,000 population that might be considered for first line treatment and of these 7 currently get treated with docetaxel. If we assume that approval of abiraterone would lead to 5 patients per 100,000 receiving it instead of docetaxel at an average cost per patient of £30,000 (ie 60% of list price to reflect potential PAS and cost of docetaxel offset), then this could increase costs by around £150,000 per 100,000 population. In the longer term it is likely that abiraterone will be used in either first-line or second-line setting but in the short-term there will be patients in each group that may receive this form of treatment.

NICE has suspended this appraisal following notification from the manufacturer that they will not be pursuing a license for this indication.

In the FAD, NICE restrict approval to being considered as a potential option for treating advanced hormone-dependent prostate cancer, only in adults with spinal metastases who present with signs or symptoms of spinal cord compression. However an appeal against this preliminary guidance has been upheld on the basis that NICE should have issued a 2nd ACD following a significant change in advice between the ACD and the FAD and that there should be more clarity on restricting to patients with signs of spinal compression as opposed to being “at risk” of spinal compression.

Depending on the outcome of the re-evaluation it is likely that between 500 and 3500 patients will be eligible for Degarelix depot per year. If we assume that the average patient stays on treatment for 6 years and that Degarelix costs £600 more per year than existing treatments then this will increase costs by between £600 and £4200 per 100,000 population in Year 1 rising to between £3,600 and £25,000 per 100,000 at steady state.
Prostate cancer (contd)

- NICE guidance on **radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases** – expected Feb 2015

  In the ACD provisional advice from NICE is that they do not currently support the use of radium-223 for this indication. This provisional decision was based on fact that the clinical and cost-effectiveness data presented for radium-223 was based on comparisons with BSC whereas the standard of care is docetaxel or abiraterone and therefore NICE felt unable to determine whether radium-223 represents a cost-effective use of NHS resources. NICE state that it costs around £24,000 to treat a patient with a 6-month course of radium-223. NICE estimate that there are around 4 patients per 100,000 population that might be considered eligible for abiraterone in the 2nd-line treatment setting and it would expect an uptake of 3 patients per 100,000 population. If this drug is used instead of abiraterone then it is cost neutral, if however it is used in addition to abiraterone in 50% of eligible patients then it would increase costs by £36,000 per 100,000 population.

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

  As outlined in the ACD, provisional advice from NICE is that they do not currently support the use of Sipuleucel-T for this indication. Sipuleucel-T is an autologous cellular immunotherapy that stimulates the patient’s own immune cells to identify and attack prostate cancer cells. The treatment involves collecting white blood cells from the patient, combining the cells with a protein to make sipuleucel-T, and then infusing the cells back into the patient. Sipuleucel-T has a marketing authorisation in the UK “for the treatment of asymptomatic or minimally symptomatic metastatic (non-visceral) castrate resistant prostate cancer in male adults in whom chemotherapy is not yet clinically indicated”, but it has not been launched yet. NICE state that the cost of a treatment course will be over £47,000 per patients based on a mean of 2.92 doses per patient. NICE noted that there was evidence that ipuleucel-T extended life but had no impact on disease progression. They also felt that it was reasonable to assume that it was similarly effective in terms of prolonging survival to abiraterone, but that the incremental cost-effectiveness ratio was well above the normal threshold of acceptance. NICE estimate that there are around 13 patients per 100,000 population per year that present with castration-resistant metastatic prostate cancer. If we assume that 2 of these were offered Sipuleucel-T instead of alternative treatments and that this treatment was £40,000 more expensive than treatment alternatives this would increase costs by £80,000 per 100,000 population. However at present the ICER (over abiraterone) is estimated to be in excess of £950,000 per QALY gained so it is unlikely that NICE will approve this treatment.

- NICE guidance on **enzalutamide for treating metastatic hormone-relapsed prostate cancer not previously treated with chemotherapy** – expected Sep 2015

  Enzalutamide will be competing with abiraterone for this indication (which is already NICE-approved) and as the two drugs are similarly priced this guidance is unlikely to have significant cost implications. similarly