NICE Update Bulletin January 2016 issued Wednesday 27th January 2016

Hyperlinks to the relevant NICE web page are included, to activate link left click on your mouse. Details are also available from the NICE website (**http://www.nice.org.uk**)

Type	Guidance title and reference number
Technology Appraisals (TAs)	**Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed TA375** **Recommendations** 1.1 Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept, all in combination with methotrexate, **are recommended as options** for treating rheumatoid arthritis, only if: • disease is severe, that is, a disease activity score (DAS28) greater than 5.1 and • disease has not responded to intensive therapy with a combination of conventional disease-modifying antirheumatic drugs (DMARDs) and • the companies provide certolizumab pegol, golimumab, abatacept and tocilizumab as agreed in their patient access schemes. 1.2 Adalimumab, etanercept, certolizumab pegol or tocilizumab can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in section 1.1 are met. 1.3 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. 1.4 After initial response within 6 months, withdraw treatment if a moderate EULAR response is not maintained. 1.5 Start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may need to be varied for some people because of differences in the mode of administration and treatment schedules. 1.6 People whose treatment with adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab or abatacept is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop. **The technology** This technology appraisal includes 7 different biological medicines. In addition, for infliximab, there is an originator biological medicine and 2 biosimilar products available in the NHS. Adalimumab, etanercept, infliximab, certolizumab pegol and golimumab all inhibit the activity of tumour necrosis factor (TNF)-alpha, a pro-inflammatory mediator that is partly responsible for damage to the joints in rheumatoid arthritis. They are referred to as TNF-alpha inhibitors. Tocilizumab inhibits the activity of interleukin-6 (IL-6), a pro-inflammatory cytokine that is also partly responsible for damage to the joints in rheumatoid arthritis. Abatacept is a selective modulator of the T-lymphocyte activation pathway. It binds to molecules on the surface of antigen-presenting cells, preventing full activation of the T-lymphocytes and interrupting the inflammatory process. **Financial factors**

The NICE cost impact report states that organisations should assess costs at a local level. NICE believes that there will be no significant change in resource use in the NHS as a result of the guidance. This is because the recommendations are considered to reflect current clinical practice and existing NICE guidance.

Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases TA376

Recommendations

1.1 Radium-223 dichloride **is recommended as an option** for treating adults with hormone-relapsed prostate cancer, symptomatic bone metastases and no known visceral metastases, only if:

•they have had treatment with docetaxel, and

•the company provides radium-223 dichloride with the discount agreed in the patient access scheme.

1.2 People whose treatment with radium-223 dichloride is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

The technology

Radium-223 dichloride (Xofigo, Bayer) is a radiopharmaceutical agent designed to deliver alpha radiation to bone metastases without affecting normal bone marrow. The marketing authorisation for radium-223 dichloride is 'for the treatment of adults with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastases'. It is administered by intravenous injection at a recommended dose of 50 kBq/kg body weight every 4 weeks for 6 injections.

Financial factors

The company's submission states that radium-223 is available at a radioactivity of 6 MBq in a 6-ml vial at a net price of £4,040 (excluding VAT-giving an average cost of a course of treatment of £24,240, estimated by the company).

The company that holds the marketing authorisation for radium-223 has agreed a patient access scheme with the Department of Health that makes radium-223 available with a discount applied to all invoices. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated TA377

Recommendations

Enzalutamide **is recommended, within its marketing authorisation, as an option** for treating metastatic hormone-relapsed prostate cancer:

•in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated

•and only when the company provides it with the discount agreed in the patient access scheme.

The technology

Enzalutamide (Xtandi, Astellas) is an androgen receptor antagonist that acts on the androgen receptor signalling pathway to decrease the proliferation of cancer cells and induce cancer cell death. It is administered orally. Enzalutamide is indicated for the treatment of 'adult men with metastatic castration-resistant prostate cancer who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated'.

Financial factors

The cost (list price) of enzalutamide is £2,734.67 for a 112-capsule pack of 40 mg enzalutamide. The daily dose of enzalutamide is 160 mg and costs £97.67 per day. The company has agreed a patient access scheme with the Department of Health. This is a simple discount to the list price of enzalutamide. The level of the discount is commercial in confidence, and has been changed from that used in NICE's technology appraisal on enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen.

The same level of discount is applicable to both the indication for enzalutamide in this appraisal and that of the technology appraisal on enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS.

Enzalutamide and abiraterone, taken before chemotherapy is clinically indicated, are currently available from the Cancer Drugs Fund for treating metastatic hormone-relapsed prostate cancer. Enzalutamide will now transfer into routine NHS commissioning.

Populating the NICE resource impact template with undiscounted costs of enzalutamide and abiraterone produces an estimated cost impact of £454K for the area covered by NEW Devon CCG.

Ramucirumab for treating advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy TA378

Recommendations

1.1 Ramucirumab alone or with paclitaxel **is not recommended** within its marketing authorisation for advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy.

1.2 People whose treatment with ramucirumab was started within the NHS before this guidance was published should be able to continue treatment until they and their clinician consider it appropriate to stop.

The technology

Ramucirumab is given as an intravenous infusion over about 60 minutes. Ramucirumab is a human receptor-targeted monoclonal antibody that specifically binds vascular endothelial growth factor (VEGF) receptor-2. This interaction prevents VEGF receptor-2 from binding with activating ligands (VEGF-A, VEGF-C and VEGF-D). Upregulation of VEGF-A, VEGF-C and VEGF-D ligands in gastric cancer is associated with poorer prognosis for people with resected or metastatic disease.

Financial factors

The acquisition cost of ramucirumab is £500 per 10-ml (100 mg) vial and £2,500 per 50-ml (500 mg) vial (excluding VAT; British national formulary [BNF] edition 69). The average costs of a course of ramucirumab combination therapy and monotherapy are £36,000 and £21,000 per person respectively (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts.

Nintedanib for treating idiopathic pulmonary fibrosis TA379

Recommendations

1.1 Nintedanib **is recommended as an option** for treating idiopathic pulmonary fibrosis, only if:

- the person has a forced vital capacity (FVC) between 50% and 80% of predicted
- the company provides nintedanib with the discount agreed in the patient access scheme and treatment is stopped if disease progresses (a confirmed decline in percent predicted FVC of 10% or more) in any 12-month period.

1.2 People whose treatment with nintedanib is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

The technology

Nintedanib (Ofev, Boehringer Ingelheim) targets 3 growth factor receptors involved in pulmonary fibrosis. Nintedanib is thought to block the signalling pathways involved in fibrotic processes, and may reduce disease progression by slowing the decline of lung function. It is administered orally. Nintedanib has a marketing authorisation in the UK 'in adults for the treatment of idiopathic pulmonary fibrosis'.

Panobinostat for treating multiple myeloma after at least 2 previous treatments TA380

Recommendations

1.1 Panobinostat **in combination with bortezomib and dexamethasone is recommended,** within its marketing authorisation, as an option for treating multiple myeloma, that is, for 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent' when the company provides panobinostat with the discount agreed in the patient access scheme.

The technology

Panobinostat (Farydak, Novartis Pharmaceuticals) is an oral potent histone deacetylase inhibitor that disrupts a key mechanism in the transformation of normal cells to cancerous cells and selectively targets tumour cells for cell death. Panobinostat has received a marketing authorisation in combination with bortezomib and dexamethasone, for the treatment of 'adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent'.

Financial factors

Panobinostat costs £776 per 20 mg tablet. The recommended starting dose of panobinostat is 20 mg, taken orally once a day, on days 1, 3, 5, 8, 10 and 12 of a 21-day cycle. Patients should have panobinostat for 8 cycles, after which it is recommended that patients showing clinical benefit continue the treatment for 4 additional cycles of 6 weeks each. The commissioner for this technology is NHS England and providers will be NHS hospital trusts.

Olaparib for maintenance treatment of relapsed, platinum-sensitive, BRCA mutation-positive ovarian, fallopian tube and peritoneal cancer after response to second-line or subsequent platinum-based chemotherapy TA381

Recommendations

1.1 Olaparib **is recommended within its marketing authorisation as an option** for treating adults with relapsed, platinum sensitive ovarian, fallopian tube or peritoneal cancer who have BRCA1 or BRCA2 mutations and whose disease has responded to platinum based chemotherapy only if:

•they have had 3 or more courses of platinum based chemotherapy and

•the drug cost of olaparib for people who remain on treatment after 15 months will be met by the company.

1.2 People whose treatment with olaparib is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

The technology

Olaparib (Lynparza; AstraZeneca) is a poly‑ADP‑ribose polymerase (PARP) enzyme inhibitor that selectively kills tumour cells with an impaired homologous recombination DNA repair pathway while sparing normal cells. Olaparib has a marketing authorisation in the UK as 'monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA‑mutated (germline and/or somatic) high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy'. It is administered orally and the recommended dose is 400 mg twice daily.

Financial factors

The list price of olaparib is £3,550 per pack, with each pack containing 448 capsules of

	50 mg each (equivalent to 28 days' treatment of 16 capsules per day at continuous full dose of treatment, price excludes VAT, 'British national formulary' [BNF] edition 70). The company has agreed a patient access scheme with the Department of Health, and this was updated after the second appraisal committee meeting. This scheme involves the NHS paying for a patient's treatment with olaparib up to a certain time, with the company providing olaparib free of charge beyond that point and for as long as each individual patient continues to have olaparib. This technology is commissioned by NHS England. Providers are secondary care acute trusts. From the resource impact template the cost per person of treatment appears to be approximately £48K (after applying the patient access scheme) for 15 months of treatment. Using the default values in the resource impact template a net increase of expenditure of £253K is predicted for the area covered by NEW Devon CCG **Eltrombopag for treating severe aplastic anaemia refractory to immunosuppressive therapy (terminated appraisal) TA382** **Recommendations** NICE was **unable to make recommendations on eltrombopag** (Revolade) for severe aplastic anaemia refractory to immunosuppressive therapy because no evidence submission was received from Novartis, but will review this decision if the company decides to make a submission
Highly specialized technology guidance (HSTs)	**None published so far this month**

NICE Guidelines (NGs)	**Tuberculosis NG33** **Background** This guideline covers preventing, identifying and managing latent and active tuberculosis (TB) in children, young people and adults. It aims to improve ways of finding people who have TB in the community and recommends that everyone under 65 with latent TB should be treated. It describes how TB services should be organised, including the role of the TB control board. The initial infection clears in over 80% of people but, in a few cases, a defensive barrier is built round the infection and the TB bacteria lie dormant. This is called latent TB; the person is not ill and is not infectious. If the immune system fails to build the defensive barrier, or the barrier fails later, latent TB can spread in the lung (pulmonary TB) or develop in the other parts of the body it has spread to (extrapulmonary TB). Only a small proportion of people with latent TB will develop symptoms ('active TB'). If left untreated, 1 person with active pulmonary TB may infect as many as 10 to 15 people every year. TB incidence in the UK has increased since the early 1990s, but has remained relatively stable since 2005. Despite this, it remains high compared with many other western European countries. Cases tend to cluster in urban areas where populations of at-risk groups are high. These include areas with many people born in countries with a high incidence of TB, areas with a high level of homelessness, poor housing or poverty, and areas with high rates of problem drug use. **Recommendations** 1.1 Preventing TB 1.2 Latent TB 1.3 Active TB 1.4 Drug resistant TB

	1.5 Infection control 1.6 Case finding 1.7 Adherence, treatment completion and follow-up 1.8 Service organisation **Financial factors** The NICE resource impact report states that the net resources impact of implementing the guidance is around £1.8M for the population of England
Interventional Procedures Guidance (IPGs)	**Percutaneous coblation of the intervertebral disc for low back pain and sciatica IPG543** **Recommendations** 1.1 Current evidence on percutaneous coblation of the intervertebral disc for low back pain and sciatica raises no major safety concerns. The evidence on efficacy is adequate and includes large numbers of patients with appropriate follow-up periods. **Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit.** 1.2 As part of the consent process, patients should be informed that there is a range of treatment options available to them and also that further procedures may be needed. **The procedure** Percutaneous coblation of the intervertebral disc is usually done with the patient under sedation and using local anaesthesia. Using fluoroscopic guidance, an introducer needle is inserted into the affected disc. A small radiofrequency probe is then inserted through the needle and into the disc. The probe delivers radiofrequency energy to create a plasma field at its tip, which causes ablation of the tissue at temperatures of 40–70°C. When it has reached a pre-determined depth the probe is removed, coagulating the tissue as it is withdrawn. Around 6 channels are created during the procedure, the number of channels depending on the amount of tissue reduction needed. The aim is to remove tissue from the disc nucleus without damaging surrounding structures. **Percutaneous electrothermal treatment of the intervertebral disc annulus for low back pain and sciatica IPG544** **Recommendations** 1.1 Current evidence on percutaneous electrothermal treatment of the intervertebral disc annulus for low back pain and sciatica raises no major safety concerns. The evidence on efficacy is inconsistent and of poor quality. Therefore, **this procedure should only be used with special arrangements for clinical governance, consent and audit or research.** 1.2 Clinicians wishing to do percutaneous electrothermal treatment of the intervertebral disc annulus for low back pain and sciatica should: •Inform the clinical governance leads in their NHS trusts. •Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In particular, patients should be informed about other treatment options, about the possibility that the procedure may not relieve their symptoms, and about the risk of a flare-up of their pain following treatment. In addition, the use of NICE's information for the public is recommended. •Audit and review clinical outcomes of all patients having percutaneous intradiscal radiofrequency treatment of the intervertebral disc annulus. 1.3 NICE encourages further research into percutaneous electrothermal treatment of the intervertebral disc annulus. Further research should document details of patient selection, including the duration of their symptoms. It should report precise details of the technique used for treatment. Outcome measures should include pain relief and quality of life. Long-term follow-up data should include details of any subsequent

	procedures. **The procedure** Percutaneous electrothermal treatment aims to relieve back pain and sciatica by applying thermal energy to the annulus of a damaged intervertebral disc in order to stiffen the annulus and disrupt nerve endings within it. Thermal treatment of the annulus can be performed using a variety of techniques which use radiofrequency energy. These include Intradiscal Electrothermal Therapy (IDET), biacuplasty, and Percutaneous Intradiscal Radiofrequency Thermocoagulation (PIRFT). PIRFT can be used to treat the intervertebral disc annulus and/or the disc nucleus. This guidance considers only thermal treatment of the annulus **Percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain IPG545** **1 Recommendations** 1.1 Current evidence on percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain raises no major safety concerns. The evidence on its efficacy is limited in quantity and quality. **Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.** 1.2 Clinicians wishing to do percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain should: •Inform the clinical governance leads in their NHS trusts. •Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In particular, patients should be informed about other treatment options, about the possibility that the procedure may not relieve their symptoms, and about the risk of a flare-up of their pain after treatment. In addition, the use of NICE's information for the public is recommended. •Audit and review clinical outcomes of all patients having percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain (see section 7.2). 1.3 NICE encourages further research into percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain. Further research should include details of patient selection, the duration of patients' symptoms, and a precise account of the technique used for treatment. Outcome measures should include pain relief and quality of life. Long-term follow-up data should include details of any subsequent procedures. **The procedure** Percutaneous intradiscal radiofrequency treatment aims to enhance the structural integrity of the intervertebral disc. It aims to reduce low back pain by using radiofrequency heat energy to alter the biomechanics of the intervertebral disc and to destroy the nociceptive pain fibres.
Medical Technologies Guidance	**None published so far this month**
Diagnostics Guidance	**None published so far this month**
NICE Quality Standards	**Preventing unintentional injury in under 15s QS107** This quality standard covers preventing unintentional injury in children and young people under 15. The term ‘unintentional injury’ is used rather than ‘accidents’ to recognise that injuries are the result of events that can be prevented. **Multiple sclerosis QS108** This quality standard covers the diagnosis and management of multiple sclerosis (MS) in

	adults (18 years and over). **Diabetes in pregnancy QS109** This quality standard covers managing diabetes and its complications in women (all females of childbearing potential) who are planning a pregnancy and women who are already pregnant. It also covers areas in which additional or different care should be offered to women with diabetes and their newborn babies. **Pneumonia in adults QS110** This quality standard covers adults (18 years and older) with a suspected or confirmed diagnosis of community-acquired pneumonia. **Obesity in adults: prevention and lifestyle weight management programmes QS111** This quality standard covers ways of preventing adults (aged 18 and over) becoming overweight or obese and the provision of lifestyle weight management programmes for adults who are overweight or obese. Although local definitions vary, these programmes are usually tier 2 interventions covering lifestyle interventions that may include weight management programmes, courses or clubs, and form one part of a comprehensive approach to preventing and treating obesity. This quality standard does not cover specialist management (tier 3 interventions) or bariatric surgery (tier 4 intervention). **Gastro-oesophageal reflux in children and young people QS112** This quality standard covers managing symptoms of gastro-oesophageal reflux (GOR) and recognising, diagnosing and managing gastro-oesophageal reflux disease (GORD) in children and young people under 18. It does not cover dyspepsia and GORD in adults.
Commissioning Guides	**None published so far this month**
Public health briefings for local government	**None published so far this month**

Current NICE consultations with links and start and finish dates for stakeholders to make contribution

Title / link	Start date of consultation	End date of consultation
Children's attachment : Topic engagement	15/01/2016	29/01/2016
Supportive and palliative care in adults (update) : Draft scope consultation	31/12/2016	29/01/2016
ImmunoCAP ISAC 112 and Microtest for multiplex allergen testing : Diagnostics consultation	11/01/2016	01/02/2016
Atopic eczema in under 12s: diagnosis and management : Surveillance consultation	21/01/2016	03/02/2016
Stable angina: management : Surveillance consultation	21/01/2016	03/02/2016
Neonatal jaundice diagnosis (SC update) : Addendum consultation	08/01/2016	04/02/2016
Attention deficit hyperactivity disorder (update) : Draft scope consultation	08/01/2016	05/02/2016
Physical activity: walking and cycling : Surveillance consultation	27/01/2016	09/02/2016
Assessment and Management of Cirrhosis : Draft guidance consultation	18/12/2015	10/02/2016
Liver disease (non-alcoholic fatty [NAFLD]) : Draft guidance consultation	18/12/2015	10/02/2016
Suspected cancer : Quality Standard consultation	13/01/2016	10/02/2016
Chronic heart failure in adults: diagnosis and management : Draft scope consultation	20/01/2016	17/02/2016
Breast cancer QS (update) : Quality Standard consultation	21/01/2016	17/02/2016
Breast cancer QS (update) : Quality Standard consultation	21/01/2016	17/02/2016
Sepsis : Draft guidance consultation	11/01/2016	22/02/2016
Endovenous mechanochemical ablation for varicose veins : Interventional procedure consultation	25/01/2016	22/02/2016
Inserting a biodegradable subacromial spacer for rotator cuff tears : Interventional procedure consultation	25/01/2016	22/02/2016
Transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraine : Interventional procedure consultation	25/01/2016	22/02/2016
Bronchiolitis : Quality Standard consultation	26/01/2016	22/02/2016
Bronchiolitis : Quality Standard consultation	26/01/2016	22/02/2016
Home care : Quality Standard consultation	26/01/2016	22/02/2016
GreenLight XPS 180 W for treating benign prostatic hyperplasia : Draft guidance	26/01/2016	23/02/2016
Psychosis and schizophrenia in children and young people (standing committee update) : Addendum consultation	28/01/2016	25/02/2016

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