NICE Update Bulletin August 2017

(issued Wednesday 23 August 2017)

Hyperlinks to the relevant NICE web page are included.

Details are also available from the NICE website (**http://www.nice.org.uk**)

Type	Guidance title and reference number
Technology Appraisals (TAs)	**Ofatumumab with chemotherapy for treating chronic lymphocytic leukaemia (terminated appraisal) TA470** NICE is unable to make a recommendation about the use in the NHS of ofatumumab with chemotherapy for treating chronic lymphocytic leukaemia because no evidence submission was received from Novartis Pharmaceuticals UK. They will review this decision if the company decides to make a submission. **Idelalisib with ofatumumab for treating chronic lymphocytic leukaemia (terminated appraisal) TA469** NICE is unable to make a recommendation about the use in the NHS of idelalisib with ofatumumab for treating chronic lymphocytic leukaemia because no evidence submission was received from Gilead Sciences. They will review this decision if the company decides to make a submission. **Methylnaltrexone bromide for treating opioid-induced constipation (terminated appraisal) TA468** NICE is unable to make a recommendation about the use in the NHS of methylnaltrexone bromide for treating opioid-induced constipation because no evidence submission was received from Swedish Orphan Biovitrum Ltd. They will review this decision if the company decides to make a submission. **Holoclar for treating limbal stem cell deficiency after eye burns TA467** **Recommendations** 1.1 Holoclar (ex vivo expanded autologous human corneal epithelial cells containing stem cells) is recommended as an option in people with moderate to severe limbal stem cell deficiency after eye burns, only if: • it is only used to treat 1 eye and • people have already had a conjunctival limbal autograft or • there is not enough tissue for a conjunctival limbal autograft or it is contraindicated and • the company provides it with the discount agreed in the patient access scheme. Moderate to severe limbal stem cell deficiency is defined by the presence of superficial corneal neovascularisation in at least 2 corneal quadrants, with central corneal involvement, and severely impaired visual acuity. 1.2 Holoclar is recommended in people with moderate to severe limbal stem cell deficiency after eye burns for treating both eyes only: • in the context of research and • when there is not enough tissue for a conjunctival limbal autograft. Such research should be designed to generate robust evidence of the clinical- and cost-effectiveness of Holoclar in treating 2 eyes in people who do not have

enough tissue for a conjunctival limbal autograft.

1.3 These recommendations are not intended to affect treatment with Holoclar that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Ex vivo expanded autologous human corneal epithelial cells containing stem cells is a treatment used in the eye to replace damaged cells on the corneal surface.

Financial factors

This technology is commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources; it will be less than £5 million per year in England (or £9,100 per 100,000 population). This is because the population size is small (around 75 people are estimated to be eligible in the prevalent population). The ongoing cost will be very small once the prevalent population has been treated and only the incident population is treated each year.

Pemetrexed for the maintenance treatment of non-small-cell lung cancer TA190 (update)

August 2017: Text at the start of the recommendations section stating that people who had had pemetrexed and cisplatin together as a first treatment could not have pemetrexed as maintenance treatment was removed. This was done following the publication of NICE's technology appraisal guidance on pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin.

The technology

Pemetrexed disodium is an antifolate agent that works by disrupting folate-dependent metabolic processes that are essential for cancer cell replication and survival.

Financial factors

This technology is commissioned by NHS England.

NICE has not published any updated resource impact tools in respect of this update.

Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women TA161 (update)

August 2017: This guidance has been partially updated by NICE's technology appraisal guidance on bisphosphonates for treating osteoporosis.

NICE has withdrawn its guidance on the use of etidronate for the secondary prevention of osteoporotic fragility fractures in postmenopausal women because etidronate is no longer marketed in the UK.

This guidance replaces NICE technology appraisal guidance on the clinical effectiveness and cost effectiveness of technologies for the secondary prevention of osteoporotic fractures in postmenopausal women (TA87).

The technologies

The bisphosphonates alendronate, etidronate and risedronate are inhibitors of bone resorption and increase BMD by altering osteoclast activation and function.

Alendronate is an oral bisphosphonate that has a UK marketing authorisation as a once-weekly preparation (70 mg) for the treatment of postmenopausal osteoporosis. It also has a marketing authorisation at a daily dose of 10 mg for the treatment of osteoporosis in postmenopausal women to prevent fractures.

Etidronate is an oral bisphosphonate that has a UK marketing authorisation for the treatment of osteoporosis. The drug is administered in 90-day cycles, with each cycle consisting of etidronate (400 mg/day) for 14 days followed by calcium carbonate (1.25 g/day) for the remaining 76 days.

Risedronate is an oral bisphosphonate that has a UK marketing authorisation at a dosage of 5 mg/day or 35 mg/week for the treatment of postmenopausal osteoporosis, to reduce the risk of vertebral fractures, and for the treatment of established postmenopausal osteoporosis, to reduce the risk of hip fractures..

Financial factors

These technologies are commissioned by CCGs.

NICE has not published any updated resource impact tools in respect of this update.

Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women TA160 (update)

August 2017: This guidance has been partially updated by NICE's technology appraisal guidance on bisphosphonates for treating osteoporosis.

NICE has withdrawn its guidance on the use of etidronate for the primary prevention of osteoporotic fragility fractures in postmenopausal women because etidronate is no longer marketed in the UK.

The technologies

The bisphosphonates alendronate, etidronate and risedronate are inhibitors of bone resorption and increase BMD by altering osteoclast activation and function.

Alendronate is an oral bisphosphonate that has a UK marketing authorisation as a once-weekly preparation (70 mg) for the treatment of postmenopausal osteoporosis. It also has a marketing authorisation at a daily dose of 10 mg for the treatment of osteoporosis in postmenopausal women to prevent fractures.

Etidronate is an oral bisphosphonate that has a UK marketing authorisation for the treatment of osteoporosis. The drug is administered in 90-day cycles, with each cycle consisting of etidronate (400 mg/day) for 14 days followed by calcium carbonate (1.25 g/day) for the remaining 76 days.

Risedronate is an oral bisphosphonate that has a UK marketing authorisation at a dosage of 5 mg/day or 35 mg/week for the treatment of postmenopausal osteoporosis, to reduce the risk of vertebral fractures, and for the treatment of established postmenopausal osteoporosis, to reduce the risk of hip fractures..

Financial factors

These technologies are commissioned by CCGs.

NICE has not published any updated resource impact tools in respect of this update.

Baricitinib for moderate to severe rheumatoid arthritis TA466

Recommendations

1.1 Baricitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with a combination of conventional disease-modifying

antirheumatic drugs (DMARDs), only if:

- disease is severe (a disease activity score [DAS28] of more than 5.1) and
- the company provides baricitinib with the discount agreed in the patient access scheme.

1.2 Baricitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to or who cannot have other DMARDs, including at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- they cannot have rituximab and
- the company provides baricitinib with the discount agreed in the patient access scheme.

1.3 Baricitinib can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in sections 1.1 and 1.2 are met.

1.4 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. After an initial response within 6 months, withdraw treatment if at least a moderate EULAR response is not maintained.

1.5 These recommendations are not intended to affect treatment with baricitinib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Baricitinib has a marketing authorisation in the UK for the 'treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs.' Baricitinib can be given as monotherapy or in combination with methotrexate.

Financial factors

This technology is commissioned by CCGs.

NICE does not expect this guidance to have a significant impact on resources; it will be less than £5 million per year in England (or £9,100 per 100,000 population). This is because the technology is an option alongside current standard treatment options.

Olaratumab in combination with doxorubicin for treating advanced soft tissue sarcoma TA465

Recommendations

1.1 Olaratumab, in combination with doxorubicin, is recommended for use within the Cancer Drugs Fund as an option for advanced soft tissue sarcoma in adults, only if:

- they have not had any previous systemic chemotherapy for advanced soft tissue sarcoma
- they cannot have curative treatment with surgery or their disease does not respond to radiotherapy
- the conditions in the managed access agreement for olaratumab are followed.

1.2 This recommendation is not intended to affect treatment with olaratumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Olaratumab has been granted a conditional marketing authorisation for the 'treatment of adult patients with advanced soft tissue sarcoma who are not amenable to curative treatment with surgery or radiotherapy and who have not been previously treated with doxorubicin'.

Financial factors

This technology is commissioned by NHS England.

Olaratumab will be available to the NHS in line with the managed access agreement with NHS England. As part of this, NHS England and Eli Lilly have a commercial access agreement that makes olaratumab available to the NHS at a reduced cost. The financial terms of the agreement are commercial in confidence.

The resource impact of olaratumab will be covered by the Cancer Drugs Fund budget. The guidance will be reviewed by the date the managed access agreement expires or when the results of the managed access agreement data collection are available, whichever is sooner. The aim of the review is to decide whether or not the drug can be recommended for routine use.

Bisphosphonates for treating osteoporosis TA464

This guidance partially updates NICE technology appraisal guidance on alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women (TA160) and on alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA161).

Recommendations

1.1 Oral bisphosphonates (alendronic acid, ibandronic acid and risedronate sodium) are recommended as options for treating osteoporosis in adults only if:

- the person is eligible for risk assessment as defined in NICE's guideline on osteoporosis (recommendations 1.1 and 1.2) and
- the 10-year probability of osteoporotic fragility fracture is at least 1%.

1.2 Intravenous bisphosphonates (ibandronic acid and zoledronic acid) are recommended as options for treating osteoporosis in adults only if:

- the person is eligible for risk assessment as defined in NICE's guideline on osteoporosis (recommendations 1.1 and 1.2) and
- the 10-year probability of osteoporotic fragility fracture is at least 10% or
- the 10-year probability of osteoporotic fragility fracture is at least 1% and the person has difficulty taking oral bisphosphonates (alendronic acid, ibandronic acid or risedronate sodium) or these drugs are contraindicated or not tolerated.

1.3 Estimate the 10-year probability of osteoporotic fragility fracture using the FRAX or QFracture risk tools, in line with NICE's guideline on osteoporosis.

1.4 The choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient, or their carers, about the advantages and disadvantages of the treatments available. If generic products are available, start treatment with the least expensive formulation, taking into

	account administration costs, the dose needed and the cost per dose. 1.5 These recommendations are not intended to affect treatment with alendronic acid, ibandronic acid, risedronate sodium and zoledronic acid that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. **The technologies** Alendronic acid, ibandronic acid, risedronate sodium and zoledronic acid are bisphosphonates, licensed for treating osteoporosis. Currently clinicians offer bisphosphonates to people with osteoporosis who are eligible for risk assessment and who have a high fracture risk. **Financial factors** These technologies are commissioned by CCGs. NICE does not expect this guidance to have a significant impact on resources; it will be less than £5m per year in England (or £9,100 per 100,000 population). They do not think practice will change substantially as a result of this guidance and the cost of treatment is low. **Cabozantinib for previously treated advanced renal cell carcinoma TA463** **Recommendations** 1.1 Cabozantinib is recommended, within its marketing authorisation, as an option for treating advanced renal cell carcinoma in adults after vascular endothelial growth factor (VEGF)-targeted therapy, only if the company provides cabozantinib with the discount agreed in the patient access scheme. **The technology** Cabozantinib is a small molecule that inhibits multiple receptor tyrosine kinases. **Financial factors** This technology is commissioned by NHS England. NICE has estimated that in England 1,000 people with advanced renal cell carcinoma after VEGF targeted therapy are eligible for treatment with cabozantinib. 260 people will have cabozantinib at second line and 60 at third line from year 2021/22 onwards once uptake has reached 26%.
Highly specialised technology guidance (HSTs)	**Asfotase alfa for treating paediatric-onset hypophosphatasia HST6** **Recommendations** 1.1 Asfotase alfa is recommended as an option for treating paediatric-onset hypophosphatasia only: • for people who meet the criteria for treatment within the managed access arrangement, and • for the duration of this arrangement and in line with the other conditions it specifies, and • when the company provides asfotase alfa with the confidential commercial terms agreed with NHS England. 1.2 These recommendations are not intended to affect treatment with asfotase alfa that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published,

	until they and their NHS clinician consider it appropriate to stop. For children and young people, this decision should be made jointly by the clinician and the child or young person or the child or young person's parents or carers. **The technology** Asfotase alfa is a targeted enzyme replacement therapy designed to restore the regulation of metabolic processes in the bones and teeth, and to reduce complications of dysregulated bone mineral metabolism. Asfotase alfa is administered by subcutaneous injection. **Financial factors** This technology is commissioned by NHS England. The company has proposed that asfotase alfa will be available to the NHS under commercial terms agreed with NHS England. The nature of these terms are commercial in confidence.
NICE Guidelines (NGs)	**Antenatal and postnatal mental health: clinical management and service guidance CG192 (update)** This guideline covers recognising, assessing and treating mental health problems in women who are planning to have a baby, are pregnant, or have had a baby or been pregnant in the past year. It covers depression, anxiety disorders, eating disorders, drug- and alcohol-use disorders and severe mental illness (such as psychosis, bipolar disorder and schizophrenia). It promotes early detection and good management of mental health problems to improve women's quality of life during pregnancy and in the year after giving birth. **August 2017:** NICE added footnotes to recommendations 1.2.3, 1.4.27, 1.4.28 and 1.4.29 with a link to the MHRA toolkit on the risks of valproate medicines in female patients. They also updated a crosslink in recommendation 1.8.23 to link to the NICE guideline on violence and aggression. Footnotes were also added to recommendations 1.4.17 and 1.9.9 advising people that the UK Drugs in Lactation Advisory is available as an additional resource when seeking advice about specific drugs. **Advanced breast cancer: diagnosis and treatment CG81 (update)** This guideline covers care and support for people with advanced (stage 4) breast cancer. It aims to help them and their healthcare professionals make shared decisions about tests and treatments to improve outcomes and quality of life. **August 2017:** NICE reviewed the evidence for assessing oestrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) status on disease recurrence and changed the recommendations in section 1.1. **Developmental follow-up of children and young people born preterm NG72** This guideline covers the developmental follow-up of babies, children and young people under 18 years who were born preterm (before 37+0 weeks of pregnancy). It explains the risk of different developmental problems and disorders, and specifies what extra assessments and support children born preterm might need during their growth and development. The guideline includes recommendations on: • information and support for parents and carers • risk and prevalence of developmental problems and disorders • how to conduct enhanced developmental support and surveillance, who should have it, and who should provide it • neonatal audit.

	Fever in under 5s: assessment and initial management CG160 (update) This guideline covers the assessment and early management of fever with no obvious cause in children aged under 5. It aims to improve clinical assessment and help healthcare professionals diagnose serious illness among young children who present with fever in primary and secondary care. **August 2017:** NICE added recommendation 1.2.1.2. to cross-refer to the NICE guideline on sepsis: recognition, diagnosis and early management. They also added recommendation 1.4.3.3 to highlight that clinicians should not use a response to antipyretic therapy alone as a means to differentiate between serious and non-serious infection. A footnote was also added to recommendation 1.2.2.10 and Table 1 to highlight that some vaccinations have been found to induce fever in children younger than 3 months. **Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition CG32 (update)** This guideline covers identifying and caring for adults who are malnourished or at risk of malnutrition in hospital or in their own home or a care home. It offers advice on how oral, enteral tube feeding and parenteral nutrition support should be started, administered and stopped. It aims to support healthcare professionals identify malnourished people and help them to choose the most appropriate form of support. **August 2017:** NICE updated the links in the footnotes to recommendations 1.3.4 and 1.8.15. Recommendation 1.7.17 was also updated and links added to National Patient Safety Agency documents.
NICE Medicines Practice Guidelines (MPGs)	None published so far this month.
Interventional Procedures Guidance (IPGs)	**Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer IPG590** **Recommendations** 1.1 Current evidence on the safety and efficacy of insertion of a biodegradable spacer to reduce rectal toxicity during radiotherapy for prostate cancer is adequate to support the use of this procedure provided that **standard arrangements** are in place for clinical governance, consent and audit. 1.2 The procedure should only be done by clinicians with training in, and experience of, transperineal interventional procedures. **The procedure** Radiotherapy for prostate cancer can cause rectal damage because of the close proximity of the prostate to the rectum. Symptoms include diarrhoea, incontinence, proctitis and ulceration of the rectal mucosa. Injecting a biodegradable substance or inserting and inflating a biodegradable balloon spacer, in the space between the rectum and prostate is done to temporarily increase the distance between them. The aim is to reduce the amount of radiation delivered to the rectum, and reduce the toxicity to the rectum during prostate radiotherapy. The procedure is usually done with the patient under general anaesthesia. However, it may be done using local or spinal anaesthesia, depending on local protocols. The patient is placed in the dorsal lithotomy position. With gel injection, a needle is used to insert the gel into the space between the prostate and the rectum using a transperineal approach and transrectal ultrasound guidance. The prostate and the rectal wall are separated using hydrodissection with saline. Once the

correct positioning of the needle is confirmed, the biodegradable spacer substance is injected as liquid into the perirectal space. It then polymerises with the saline to form a soft absorbable mass. The spacer degrades slowly over several months. With balloon spacer insertion, a small perineal incision is typically used to insert a dilator and introducer sheath. Using ultrasound guidance, the dilator is advanced towards the prostate base over the needle, which is then removed. A biodegradable balloon is introduced through the introducer sheath and is filled with saline and sealed with a biodegradable plug. The balloon spacer degrades over several months.

Radiofrequency treatment for haemorrhoids IPG589

Recommendations

1.1 Current evidence on the safety and efficacy of radiofrequency treatment for haemorrhoids is inadequate 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 radiofrequency treatment for haemorrhoids should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of all patients having radiofrequency treatment for haemorrhoids.

1.3 NICE encourages further research into radiofrequency treatment for haemorrhoids, preferably randomised controlled trials. It may update the guidance on publication of further evidence. Outcomes should include pain, secondary haemorrhage, recurrence rate, the need for repeat procedures and quality-of-life measures. Details of patient selection should also be reported. Patient selection should only be done by a multidisciplinary team as part of a lymphoedema service.

The procedure

Radiofrequency treatment for haemorrhoids is usually done under local anaesthetic, with or without sedation. A lubricated proctoscope is inserted into the anus to allow good visualisation of the anal canal and to expose the haemorrhoids. Local anaesthetic is injected into tissue surrounding the haemorrhoid. Details of the procedure vary according to the specific device being used. A specially designed probe connected to a radiofrequency generator is inserted into the haemorrhoid, or a ball electrode is rolled over the surface of the haemorrhoid. The tissue within the haemorrhoid heats up and the haemorrhoid shrinks. The haemorrhoids may be treated in several sessions, each taking up to 20 minutes.

Radiofrequency treatment for haemorrhoids is claimed to be faster and less painful than other treatment methods, with a shorter recovery time.

Liposuction for chronic lymphoedema IPG588

This guidance replaces NICE interventional procedures guidance on liposuction for chronic lymphoedema (IPG251).

Recommendations

1.1 Current evidence on the safety and efficacy of liposuction for chronic lymphoedema is adequate to support the use of this procedure provided that **standard arrangements** are in place for clinical governance, consent and audit.

1.2 Patient selection should only be done by a multidisciplinary team as part of a

	lymphoedema service. **<u>The procedure</u>** Liposuction for chronic lymphoedema is usually done under general anaesthesia, but regional nerve blockade is also possible. A few small incisions are made in the limb. Cannulas, connected to a vacuum pump, are inserted into the incisions and oedematous adipose tissue is removed by vacuum aspiration. Liposuction is done around and all the way along the limb. Immediately after liposuction, a compression bandage is applied to the limb to control any bleeding and to prevent postoperative oedema. Antibiotics are typically prescribed after the operation. The limb is elevated during hospital stay for 3 to 7 days after the procedure. From about 2 weeks after the procedure, a custom-made compression garment is worn. This garment is revised 3 or 4 times during the first year until the oedema volume has been reduced as much as possible and a steady state has been reached.
Medical Technologies Guidance	None published so far this month.
Diagnostics Guidance	None published so far this month.
NICE Quality Standards	None published so far this month.

Current NICE consultations with links and end dates for stakeholders to contribute

Title / link	End date of consultation
Alectinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer ID925	29/08/2017
Psychosis and schizophrenia in adults: treatment and management	30/08/2017
Colorectal cancer: diagnosis and management (update)	01/09/2017
Developmental follow-up of children and young people born preterm	01/09/2017
Cystic fibrosis	01/09/2017
Lenvatinib with everolimus for previously treated advanced renal cell carcinoma [ID1029]	04/09/2017
Tivozanib for treating renal cell carcinoma [ID591]	04/09/2017
Oesophago-gastric cancer	07/09/2017
Drug misuse prevention	07/09/2017
Behaviour change: general approaches	11/09/2017
Depression in adults: treatment and management	12/09/2017
Multiple Pregnancy (update)	12/09/2017
Heavy menstrual bleeding (update)	13/09/2017
Cabozantinib and vandetanib for treating unresectable locally advanced or metastatic medullary thyroid cancer [ID56]	14/09/2017
Pancreatic cancer: diagnosis and management in adults	18/09/2017
Diverticular Disease	20/09/2017
Suspected neurological conditions	26/09/2017
Physical activity and the environment (update)	02/10/2017
People's experience in adult social care services: improving the experience of care for people using adult social care services	03/10/2017

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