NICE Update Bulletin: March 2019

Hyperlinks to the relevant NICE web page are included below.

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

Type	Guidance title and reference number
Technology Appraisals (TAs)	**Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes TA572** **Recommendations** 1.1 Ertugliflozin as monotherapy is recommended as an option for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if: • a dipeptidyl peptidase 4 (DPP-4) inhibitor would otherwise be prescribed and • a sulfonylurea or pioglitazone is not appropriate. 1.2 Ertugliflozin in a dual-therapy regimen in combination with metformin is recommended as an option for treating type 2 diabetes, only if: • a sulfonylurea is contraindicated or not tolerated or • the person is at significant risk of hypoglycaemia or its consequences. 1.3 If patients and their clinicians consider ertugliflozin to be 1 of a range of suitable treatments including canagliflozin, dapagliflozin and empagliflozin, the least expensive should be chosen. 1.4 These recommendations are not intended to affect treatment with ertugliflozin 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** Ertugliflozin is indicated in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control: • as monotherapy in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications • in addition to other medicinal products for the treatment of diabetes. The recommended starting dose of ertugliflozin is 5 mg once daily. In patients tolerating ertugliflozin 5 mg once daily, the dose can be increased to 15 mg once daily if additional glycaemic control is needed. **Financial factors** This technology is commissioned by CCGs.

NHS organisations involved:
Northern, Eastern and Western Devon Clinical Commissioning Group
South Devon and Torbay Clinical Commissioning Group

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

Brigatinib for treating ALK-positive advanced non-small-cell lung cancer after crizotinib TA571

Recommendations

1.1 Brigatinib is recommended, within its marketing authorisation, for treating anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer (NSCLC) in adults who have already had crizotinib. It is recommended only if the company provides it according to the commercial arrangement.

The technology

Brigatinib has a marketing authorisation for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer previously treated with crizotinib.

The recommended starting dosage of brigatinib is 90 mg once daily for the first 7 days, then 180 mg once daily. Treatment should continue as long as there is clinical benefit.

If brigatinib treatment is interrupted for 14 days or longer for reasons other than adverse reactions, treatment should be resumed at 90 mg once daily for 7 days before increasing to the previously tolerated dose.

If a dose is missed or vomiting occurs after taking a dose, an additional dose should not be administered, and the next dose should be taken at the scheduled time.

Financial factors

This technology is commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources; that is, it will be less than £5 million per year in England (or £9,100 per 100,000 population).

This is because the population eligible for brigatinib is small (up to 150 people). The guidance states “clinical experts explained that fewer people are starting treatment on crizotinib because of the availability of ceritinib and alectinib. Therefore, the population eligible for brigatinib after crizotinib is small and will decrease as fewer people start treatment with crizotinib.”

The company has a commercial arrangement which makes brigatinib available to the NHS with a discount, the size of which is commercial in confidence.

Pembrolizumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy TA570 (terminated appraisal)

NICE is unable to make a recommendation about the use in the NHS of pembrolizumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy because no evidence submission was received from Merck Sharp & Dohme. NICE will review this decision if the company decides to make a submission.

Pertuzumab for adjuvant treatment of HER2-positive early stage breast cancer TA569

Recommendations

1.1 Pertuzumab, with intravenous trastuzumab and chemotherapy, is recommended for the adjuvant treatment of human epidermal growth factor receptor 2 (HER2)-positive early stage breast cancer in adults, only if:

- they have lymph node-positive disease
- the company provides it according to the commercial arrangement.

1.2 This guidance is not intended to affect adjuvant treatment with pertuzumab 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

Pertuzumab is indicated as adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early stage breast cancer at high risk of recurrence.

The dosage in the marketing authorisation is Intravenous 840 mg loading dose, then 420 mg every 3 weeks. Pertuzumab should be given with trastuzumab and chemotherapy for 1 year (maximum 18 cycles) for patients with high-risk disease, regardless of the timing of surgery.

Financial factors

This technology is commissioned by NHS England.

NICE estimates that 1,400 people with HER2-positive breast cancer with lymph node involvement are eligible for treatment with pertuzumab, and 1,300 people will have pertuzumab from year 2 onwards once uptake has reached 90%.

Abatacept for treating psoriatic arthritis after DMARDs TA568 (terminated appraisal)

NICE is unable to make a recommendation about the use in the NHS of abatacept for treating psoriatic arthritis after DMARDs in adults because no evidence submission was received from Bristol–Myers Squibb. NICE will review this decision if the company decides to make a submission.

Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies TA567

Recommendations

1.1 Tisagenlecleucel therapy is recommended for use within the Cancer Drugs Fund as an option for treating relapsed or refractory diffuse large B-cell lymphoma in adults after 2 or more systemic therapies, only if the conditions in the managed access agreement are followed.

1.2 This recommendation is not intended to affect both treatment in preparation for and treatment with tisagenlecleucel 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

Tisagenlecleucel is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma after 2 or more lines of systemic therapy.

Tisagenlecleucel is an immunocellular CAR T-cell therapy. It contains the patient's own T cells (a type of white blood cell) that have been modified genetically in the laboratory so that they make a protein called chimeric antigen receptor (CAR). CAR can attach to another protein on the surface of cancer cells called CD-19. When tisagenlecleucel is given to the patient, the modified T cells attach to and kill cancer cells, thereby helping to clear the cancer from the body.

Treatment with tisagenlecleucel comprises a single-dose intravenous infusion of tisagenlecleucel. It is intended for autologous use only and the dosage for adults with diffuse large B-cell lymphoma is 0.6 to 6.0x108 CAR-positive viable T cells.

Financial factors

This technology is commissioned by NHS England.

NICE estimates that around 200 people per year in England with diffuse large B-cell lymphoma are eligible for treatment with tisagenlecleucel. Tisagenlecleucel will be available to the NHS in line with the managed access agreement with NHS England. As part of this, NHS England and Novartis have a commercial access agreement that makes tisagenlecleucel available to the NHS at a reduced cost, which is commercial in confidence.

The resource impact of tisagenlecleucel will be covered by the Cancer Drugs Fund budget. The guidance will be reviewed by the date the managed access agreement expires in February 2023 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.

Cochlear implants for children and adults with severe to profound deafness TA566

Recommendations

1.1 Unilateral cochlear implantation is recommended as an option for people with severe to profound deafness who do not receive adequate benefit from acoustic hearing aids, as defined in 1.5.

If different cochlear implant systems are considered to be equally appropriate, the least costly should be used. Assessment of cost should take into account acquisition costs, long-term reliability and the support package offered.

1.2 Simultaneous bilateral cochlear implantation is recommended as an option for the following groups of people with severe to profound deafness who do not receive adequate benefit from acoustic hearing aids, as defined in 1.5:

- children
- adults who are blind or who have other disabilities that increase their reliance on auditory stimuli as a primary sensory mechanism for spatial awareness.

Acquisition of cochlear implant systems for bilateral implantation should be at the lowest cost and include currently available discounts on list prices equivalent to 40% or more for the second implant.

1.3 Sequential bilateral cochlear implantation is not recommended as an option for people with severe to profound deafness.

1.4 People who had a unilateral implant before publication of this guidance, and who fall into one of the categories described in 1.2, should have the option of an additional contralateral implant only if this is considered to provide sufficient benefit by the responsible clinician after an informed discussion with the individual person and their carers.

1.5 For the purposes of this guidance, severe to profound deafness is defined as hearing only sounds that are louder than 80 dB HL (pure-tone audiometric threshold equal to or greater than 80 dB HL) at 2 or more frequencies (500 Hz, 1,000 Hz, 2,000 Hz, 3,000 Hz and 4,000 Hz) bilaterally without acoustic hearing aids. Adequate benefit from acoustic hearing aids is defined for this guidance as:

- for adults, a phoneme score of 50% or greater on the Arthur Boothroyd word test presented at 70 dBA
- for children, speech, language and listening skills appropriate to age, developmental stage and cognitive ability.

1.6 Cochlear implantation should be considered for children and adults only after an assessment by a multidisciplinary team. As part of the assessment children and adults should also have had a valid trial of an acoustic hearing aid for at least 3 months (unless contraindicated or inappropriate).

1.7 When considering the assessment of adequacy of acoustic hearing aids, the multidisciplinary team should be mindful of the need to ensure equality of access. Tests should take into account a person's disabilities (such as physical and cognitive impairments), or linguistic or other communication difficulties, and may need to be adapted. If it is not possible to administer tests in a language in which a person is sufficiently fluent for the tests to be appropriate, other methods of assessment should be considered.

The technology

Cochlear implant systems consist of internal and external components. A microphone and sound processor are worn externally behind the ear. The sound processor is connected to a transmitter coil, which is worn on the side of the head. Data from the transmitter coil are passed to a receiver–stimulator package that is implanted into a surgically fashioned depression in the mastoid bone. The receiver–stimulator translates the data into electrical pulses that are delivered to an array of electrodes. These are placed surgically within the cochlea. The electrodes stimulate spiral ganglion cells that innervate fibres of the auditory nerve. The activation of electrodes provides a sensation of hearing, but does not restore hearing.

Financial factors

This technology is commissioned by NHS England.

NICE estimates that currently around 1,260 people per annum in England have cochlear implants. The total number of people treated is estimated to increase to 2,790 by 2023/24. This includes people who are eligible under the current recommendations (1,260 people per year) plus people who are eligible under the updated recommendations (890 people per year, not all of these people are treated in year before 2024/25). Thereafter, all the newly eligible 890 people per year are expected to be treated in year. This gives a total of 2,150 people treated per year from 2024/25.

Benralizumab for treating severe eosinophilic asthma TA565

Recommendations

1.1 Benralizumab, as an add-on therapy, is recommended as an option for treating severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids and long-acting beta-agonists, only if:

- the person has agreed to and followed the optimised standard treatment plan and
- the blood eosinophil count has been recorded as 300 cells per microlitre or more and the person has had 4 or more exacerbations needing systemic corticosteroids in the previous 12 months, or has had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months (that is, the person is eligible for mepolizumab) or
- the blood eosinophil count has been recorded as 400 cells per microlitre or more with 3 or more exacerbations needing systemic corticosteroids in the past 12 months (that is, the person is eligible for reslizumab).

Benralizumab is recommended only if the company provides it according to the commercial arrangement.

1.2 If benralizumab, mepolizumab or reslizumab are equally suitable, start treatment with the least expensive option (taking into account drug and administration costs).

1.3 At 12 months:

- stop benralizumab if the asthma has not responded adequately or
- continue benralizumab if the asthma has responded adequately and assess response each year.

An adequate response is defined as:

  - a clinically meaningful reduction in the number of severe exacerbations needing systemic corticosteroids or
  - a clinically significant reduction in continuous oral-corticosteroid use while maintaining or improving asthma control.

1.4 Benralizumab is not recommended if neither mepolizumab nor reslizumab are recommended (see NICE's technology appraisal guidance 431 and technology appraisal guidance 479).

1.5 These recommendations are not intended to affect treatment with benralizumab 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

Benralizumab is indicated as add-on maintenance treatment in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus long-acting beta-agonists.

The recommended dosage is 30 mg every 4 weeks for the first 3 doses then every 8 weeks, given by subcutaneous injection using a pre-filled syringe.

	Financial factors This technology is commissioned by NHS England. NICE estimates that 56,300 people in England with severe eosinophilic asthma are eligible for treatment with benralizumab and 2,300 people will have benralizumab from year 5 onwards once uptake has reached 4%.
Highly specialised technology guidance (HSTs)	None published so far this month.
NICE Guidelines (NGs)	**Delirium: prevention, diagnosis and management CG103 (update)** This guideline covers diagnosing and treating delirium in people aged 18 and over in hospital and in long-term residential care or a nursing home. It also covers identifying people at risk of developing delirium in these settings and preventing onset. It aims to improve diagnosis of delirium and reduce hospital stays and complications. **March 2019:** NICE removed the use of olanzapine for the treatment of delirium in people who are distressed or considered a risk to themselves or others. **Lung cancer: diagnosis and management NG122** This guideline covers diagnosing and managing non-small-cell and small-cell lung cancer. It aims to improve outcomes for patients by ensuring that the most effective tests and treatments are used, and that people have access to suitable palliative care and follow-up. **March 2019:** NICE reviewed the evidence and made new recommendations on: • intrathoracic lymph node assessment • brain imaging for people with non-small-cell lung cancer • radical radiotherapy (including stereotactic ablative radiotherapy [SABR]) for people with non-small-cell lung cancer • chemoradiotherapy and surgery for people with stage IIIA-N2 non-small-cell lung cancer • thoracic radiotherapy and prophylactic cranial irradiation for people with small-cell lung cancer **Intrapartum care for women with existing medical conditions or obstetric complications and their babies NG121** This guideline covers care during labour and birth for women who need extra support because they have a medical condition or complications in their current or previous pregnancy. The guideline also covers women who have had no antenatal care. It aims to improve experiences and outcomes for women and their babies. This guideline includes recommendations on: • heart disease, bleeding disorders and subarachnoid haemorrhage • asthma, long-term systemic steroids and obesity • acute kidney injury and chronic kidney disease • sepsis and intrapartum haemorrhage • previous caesarean section and labour after 42 weeks • small-for-gestational-age baby and large-for-gestational-age baby

	• no antenatal care
Public Health Guidelines	None published so far this month.
Antimicrobial prescribing guidelines	None published so far this month.
Social Care Guidelines	None published so far this month.
Interventional Procedures Guidance (IPGs)	**Radially emitting laser fibre treatment of an anal fistula IPG644** **Recommendations** 1.1 Current evidence on the safety and efficacy of radially emitting laser fibre treatment of an anal fistula is limited in quantity and quality. Therefore, although there are no major safety concerns, this procedure should only be used with **special arrangements** for clinical governance, consent, and audit or research. 1.2 Clinicians wishing to do radially emitting laser fibre treatment of an anal fistula should: • Inform the clinical governance leads in their NHS trusts. • Ensure that patients understand the procedure's safety and efficacy, as well as any uncertainties about these. Provide them with clear written information to support shared decision making. In addition, the use of NICE's information for the public is recommended. • Audit and review clinical outcomes of all patients having radially emitting laser fibre treatment of an anal fistula. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion). 1.3 The procedure should only be done by clinicians experienced in cannulating fistulas, and who are trained in the use of lasers. 1.4 Further research should report details of patient selection, including fistula size, recurrence rates in the medium and long term, and quality-of-life outcomes. **The condition** An anal fistula is an abnormal tract between the anal canal and the skin around the anus. It may cause symptoms such as pain or discomfort in the anal area, and leakage of blood or pus. It usually results from previous anal abscesses (cryptoglandular), and can be associated with other conditions such as inflammatory bowel disease and cancer. Anal fistulas can be classified according to their relationship with the external sphincter. Intersphincteric fistulas are the most common type and cross only the internal sphincter. Trans-sphincteric fistulas pass through the internal and external sphincter. Treatment of anal fistulas commonly involves surgery. The type of surgery depends on the location and complexity of the fistula. For intersphincteric and low trans-sphincteric anal fistulas, the most common treatment is a fistulotomy or laying open of the fistula track. For deeper fistulas that involve more muscle, and for recurrent fistulas, a seton (a piece of suture material or rubber sling) may be used, either alone or with fistulotomy. Fistulas that cross the external sphincter at a high level are sometimes treated with a mucosal advancement

	flap or other procedures to close the internal opening. Another less commonly used option for treating anal fistulas is to fill the track with either a plug or paste. **The procedure** Radially emitting laser fibre treatment of an anal fistula can be done with the patient under regional or general anaesthesia. With the patient in lithotomy position, the external and internal openings of the fistula tract are identified. The fistula is then catheterised using a probe and cleaned by irrigation. Under ultrasound guidance, a radially emitting laser fibre is advanced from the external to internal orifice, activated and gradually withdrawn at about 1 mm/second. The aim is to cause destruction and sealing of the fistula tract, allowing primary closure. The procedure may be used with techniques that close the internal orifice of the tract such as an advancement flap.
Medical Technologies Guidance	**The Debrisoft monofilament debridement pad for use in acute or chronic wounds MTG17 (update)** **March 2019:** This guidance has been updated to include a review of the cost model using more recent values. **Recommendations** 1.1 The case for adopting the Debrisoft monofilament debridement pad as part of the management of acute or chronic wounds in the community is supported by the evidence. The available evidence is limited, but the likely benefits of using the Debrisoft pad on appropriate wounds are that they will be fully debrided more quickly, with fewer nurse visits needed, compared with other debridement methods. In addition, the Debrisoft pad is convenient and easy to use, and is well tolerated by patients. Debridement is an important component of standard woundcare management as described in the NICE guidelines on pressure ulcers and diabetic foot problems. 1.2 The Debrisoft pad is indicated for adults and children with acute or chronic wounds. The available evidence is mainly in adults with chronic wounds needing debridement in the community. The data show that the device is particularly effective for chronic sloughy wounds and hyperkeratotic skin around acute or chronic wounds. 1.3 The Debrisoft pad is estimated to be cost saving for complete debridement compared with other debridement methods. When compared with hydrogel, gauze and bagged larvae, cost savings per patient (per complete debridement) are estimated to be £99, £154 and £373 respectively in a community clinic, and £213, £292 and £277 respectively in the home. **The condition** Debridement is the removal of dead, damaged tissue or haematoma from a wound. Several techniques are used for debridement, depending on the nature of the wound. In the community these are likely to include mechanical, autolytic and biosurgical techniques. Debridement can be carried out with or without analgesia depending on the degree of wound pain, the site, size and severity of the wound as well as the patient's preference. **The procedure** The Debrisoft range are sterile and single-use monofilament debridement devices intended for nurses and other healthcare professionals to use on adults and children to remove devitalised tissue, debris, and hyperkeratotic skin

	around acute or chronic wounds. They are made of monofilament polyester fibres with a reverse side of polyacrylate. The monofilament fibres are cut with angled tips designed to penetrate irregularly shaped areas and remove devitalised skin and wound debris. The Debrisoft pad is moistened with tap water, sterile water or saline, folded and then, using the soft fleecy side, wiped across the wound with gentle pressure. Cellular debris, slough tissue, exudate and hyperkeratotic tissues become integrated into the monofilaments and are removed from the wound site. The Debrisoft pad is intended for use without analgesia, and the process takes, on average, 2 to 4 minutes. A new pad is normally needed for each separate wound being treated. For large areas, more than 1 pad may be needed.
Diagnostics Guidance	None published so far this month.
NICE Quality Standards	**Lung cancer in adults QS17 (update)** This quality standard covers diagnosing and managing lung cancer in adults (aged 18 and over). It describes high-quality care in priority areas for improvement. **March 2019:** this quality standard was updated to reflect changes to the updated NICE guideline on lung cancer. Statements 3 and 8 were removed and statements 10, 11 and 12 were amended.

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

Title / link	End date of consultation
Therapeutic monitoring of TNF-alpha inhibitors in rheumatoid arthritis	04/04/2019
Cerebral palsy in adults	04/04/2019
Coexisting severe mental illness and substance misuse	10/04/2019
Ultrasound-guided high-intensity transcutaneous focused ultrasound for the treatment of symptomatic uterine fibroids	18/04/2019
Transurethral laser ablation for recurrent non-muscle-invasive bladder cancer	18/04/2019
Hypertension in adults: diagnosis and management	23/04/2019
Fluocinolone acetonide ocular implant for treating recurrent non-infectious uveitis ID1039	24/04/2019
Intrapartum care: women with existing medical conditions or obstetric complications and their babies	02/05/2019
Twin and triplet pregnancy (update)	09/05/2019

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