NHS
Devon
Clinical Commissioning Group

NICE Update Bulletin: October 2021

Hyperlinks to the relevant NICE web page are included below.

NICE rapid COVID-19 guidelines

COVID-19 rapid guideline: managing COVID-19 NG191 (update)

This guideline covers the management of COVID-19 for children, young people and adults in all care settings. It brings together existing NICE recommendations on managing COVID-19, and new recommendations on therapeutics, so that healthcare staff and those planning and delivering services can find and use them more easily.

27 October 2021: NICE updated existing recommendations on tocilizumab and sarilumab.

4 October 2021: NICE added new recommendations on casirivimab and imdevimab. New data on the use of heparins (from the REMAP-CAP trial results) does not change the current recommendations.

Technology Appraisals (TAs)

Apalutamide with androgen deprivation therapy (ADT) for treating hormone-sensitive metastatic prostate cancer TA741

Recommendations

Apalutamide plus androgen deprivation therapy (ADT) is **recommended** as an option for treating hormone-sensitive metastatic prostate cancer in adults, only if:

- docetaxel is not suitable
- the company provides apalutamide according to the commercial arrangement.

This recommendation is not intended to affect treatment with apalutamide plus ADT 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

Prostate cancer is a condition in which tumours develop in the prostate, a gland in the male reproductive system. The exact cause is unknown but environmental and genetic factors are associated with an increased risk of developing prostate cancer.

The incidence of prostate cancer increases with age and is higher in people of black African-Caribbean family origin and people with a family history of the condition. Metastatic cancer is where the disease has spread to other parts of the body (for example, the bones).

Hormone-sensitive metastatic prostate cancer is usually treated with docetaxel plus ADT, ADT alone or enzalutamide plus ADT.

For newly diagnosed metastatic prostate cancer, NICE CG131 recommends starting docetaxel chemotherapy within 12 weeks of starting ADT. For metastatic prostate cancer, the guideline recommends offering bilateral orchidectomy (removal of the testicles) as an alternative to continuous luteinising hormone-releasing hormone agonist therapy. For people who are willing to accept the adverse impact on overall survival and gynaecomastia (breast swelling) in the hope of retaining sexual function, the guideline recommends offering anti-androgen monotherapy with bicalutamide.

NICE TA404 recommends degarelix, a gonadotrophin-releasing hormone antagonist, for treating advanced hormone-dependent prostate cancer in people with spinal metastases. Metastatic, hormone-sensitive prostate cancer refers to a broader population that includes people with metastatic prostate cancer who are newly diagnosed and hormone naïve or are continuing to respond to ADT.

Apalutamide is an androgen receptor antagonist that acts on different steps in the androgen receptor signalling pathway to decrease proliferation of cancer cells and induce cancer cell death leading to tumour regression. Apalutamide is administered orally.

Financial factors

This technology is commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources because the technology is a further treatment option which is available at a similar price to current treatment options.

The price for apalutamide is £2,735 per pack of 112 tablets, each containing 60 mg of the active ingredient (excluding VAT). The company has a commercial arrangement, this makes apalutamide available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Apalutamide with androgen deprivation therapy (ADT) for treating high-risk hormone-relapsed non-metastatic prostate cancer TA740

Recommendations

Apalutamide plus androgen deprivation therapy (ADT) is **recommended**, within its marketing authorisation, as an option for treating hormone-relapsed non-metastatic prostate cancer that is at high risk of metastasising in adults. High risk is defined as a blood prostate-specific antigen (PSA) level that has doubled in 10 months or less on continuous ADT. It is recommended only if the company provides apalutamide according to the commercial arrangement.

The technology

Prostate cancer is a condition in which tumours develop in the prostate, a gland in the male reproductive system. The exact cause is unknown but environmental and genetic factors are associated with an increased risk of developing prostate cancer.

The incidence of prostate cancer increases with age and is higher in people of black African-Caribbean family origin and people with a family history of the condition.

NICE CG131 classifies localised prostate cancer to be at low, intermediate or high risk of progression based on prostate-specific antigen concentration, Gleason score (based on a biopsy) and clinical stage. People with intermediate or high risk non-metastatic prostate cancer may be offered hormone therapy. Prostate cancer may initially respond to hormone therapy but eventually become resistant to it. This clinical condition is described as 'hormone-relapsed' prostate cancer, but the terms 'castration-resistant prostate cancer', 'hormone-refractory prostate cancer' and 'androgen independent prostate cancer' are also used. Hormone-relapsed prostate cancer is diagnosed by rising prostate-specific antigen levels despite treatment with ADT or orchidectomy.

Hormone-relapsed non-metastatic prostate cancer is usually treated with ADT alone or with darolutamide plus ADT. Although some cancer cells may no longer respond to testosterone withdrawal, stopping hormone therapy completely would increase testosterone levels and decrease the likely time to metastatic disease. For people who have not had previous radiotherapy, they may also be offered this treatment with hormone therapy. Everyone is monitored for evidence of disease metastasis, at which point, other treatments are considered.

Apalutamide is an androgen receptor antagonist that acts on different steps in the androgen receptor signalling pathway to decrease proliferation of cancer cells and induce cancer cell death leading to tumour regression. Apalutamide is administered orally.

Financial factors

This technology is commissioned by NHS England.

The price for apalutamide is £2,735 per pack of 112 tablets, each containing 60 mg of the active ingredient (excluding VAT). The company has a commercial arrangement,

this makes apalutamide available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Clinical trial evidence suggests that, compared with placebo plus ADT, apalutamide plus ADT increases the time until the disease spreads and how long people live. The cost-effectiveness estimates are within what NICE considers to be an acceptable use of NHS resources, this is because the technology is a further treatment option which is available at a similar price to current treatment options and the eligible population is small. Around 700 people in England are expected to be eligible for treatment each year.

Atezolizumab for untreated PD-L1-positive advanced urothelial cancer when cisplatin is unsuitable TA739

This guidance updates and replaces NICE TA492 on atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable, which was available through the Cancer Drugs Fund.

Recommendations

Atezolizumab is **recommended**, within its marketing authorisation, as an option for untreated locally advanced or metastatic urothelial cancer in adults whose tumours express PD-L1 at a level of 5% or more and when cisplatin-containing chemotherapy is unsuitable. This is only if the company provides atezolizumab according to the commercial arrangement.

The technology

Urothelial carcinoma is cancer of the transitional cells which form the inner lining of the bladder, urethra, ureter, or renal pelvis. Transitional cell cancer (TCC) of the renal pelvis and ureter is rare and in the UK accounts for only about 7 out of 100 kidney cancers and is 4 times less common in the ureter. Urothelial carcinoma is most common in the bladder, and accounts for 90% of bladder cancers.

Transitional cell cancers can be split into papillary carcinomas and flat carcinomas. Papillary carcinomas often grow towards the centre of the bladder, without going into deeper layers (non-invasive), but sometimes these can grow deeper into the bladder wall and are more likely to spread (invasive). Flat carcinomas do not grow toward the hollow part of the bladder and remain in the inner layers (non-invasive). Other types of bladder cancers include squamous cell carcinoma (beginning in thin flat cells) and adenocarcinoma (beginning in cells which make and release mucus and other fluids). These types of bladder cancer arise as a result of chronic irritation and inflammation.

Patients with metastatic or advanced urothelial cancer may receive treatment with surgery and/or radiotherapy. Chemotherapy may be given before (neoadjuvant) or after surgery and/or radiotherapy in an attempt to improve cure rates. If the urothelial cancer is too advanced for surgery/radiotherapy, or has recurred after these treatments, chemotherapy can be used to improve quality of life and survival.

Atezolizumab is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

There is separate guidance on atezolizumab for people who have had cisplatin-based chemotherapy (TA525).

Financial factors

This technology is commissioned by NHS England.

The list price for atezolizumab is £3,807.69 per 1,200-mg vial (excluding VAT), which is an annual cost of around £66,000. The company has a commercial arrangement. This makes atezolizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Atezolizumab meets NICE's criteria to be considered a life-extending treatment at the end of life. The cost-effectiveness estimates are likely to be within what NICE considers an acceptable use of NHS resources.

Berotralstat for preventing recurrent attacks of hereditary angioedema TA738

Recommendations

Berotralstat is **recommended** as an option for preventing recurrent attacks of hereditary angioedema in people 12 years and older, only if:

- they have at least 2 attacks per month, and
- it is stopped if the number of attacks per month does not reduce by at least 50% after 3 months.

It is only recommended if the company provides berotralstat according to the commercial arrangement.

This recommendation is not intended to affect treatment with berotralstat 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. For young people, this decision should be made jointly by the clinician and the young person and the young person's parents or carers.

The technology

Hereditary angioedema (HAE) is a rare genetic disorder, associated with the deficiency of the protein C1-esterase inhibitor, which is a regulator of inflammatory pathways. In patients with HAE, at times of physiological or psychological stress, the function of the C1-esterase inhibitor is insufficient, resulting in the accumulation of excessive fluid (oedema) and localised oedematous swellings. The swellings usually

occur in the mouth, the gut (affecting the submucosal tissues) and the airway, causing difficulty with breathing (with potential asphyxia) and severe pain in the stomach. The swellings can also occur in the deep tissues of the skin (affecting the dermis and subcutaneous tissues) causing significant impact, for example if the hands, feet or genitals are affected.

Most angioedema attacks are associated with trauma, medical procedures, emotional stress, menstruation, oral contraceptive use, infections, or the use of medications such as Angiotensin-converting enzyme (ACE) inhibitors. Attacks are unpredictable; severity and frequency of previous attacks do not predict severity and frequency of future attacks. Attacks usually last approximately 2 to 5 days before resolving spontaneously.

It is estimated that HAE affects between 1 per 50,000 to 1 per 100,000 of the population. Most cases develop in childhood and some cases develop in early adulthood. HAE usually occurs during the first 10 to 20 years of life.

There are 3 approaches to managing HAE: avoidance of factors that trigger HAE (e.g. minor trauma, hormone replacement therapy), acute treatments and preventive (prophylactic) treatments of acute attacks. Short-term preventive treatments aim to prevent an attack before known triggers for example, dental work or surgery. Long-term preventative treatments are used routinely to reduce the need for treatment of acute attacks.

NICE TA606 recommends lanadelumab for preventing recurrent attacks of hereditary angioedema in people aged 12 and older, only if they are eligible for preventative C1-INH in line with NHS England's commissioning policy and the lowest dosing frequency of lanadelumab is used when the condition is in a stable, attack-free phase.

Berotralstat is a potent oral synthetic inhibitor of protein kallikrein. It is administered orally. Berotralstat is indicated for 'routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older'.

There are not many effective treatments available for preventing recurrent attacks of hereditary angioedema. Clinical trial evidence suggests that berotralstat is effective at reducing the number of attacks per month compared with placebo.

Financial factors

This technology is commissioned by NHS England.

The list price of berotralstat is £10,205 for a 28-pack of 150 mg capsules (company submission), which equates to an annual cost of £133,120.60.

NICE does not expect this guidance to have a significant impact on resources, this is because the population size is small (the number of people eligible for treatment with berotralstat each year in England is less than 300). The cost of treatment with berolralstat is expected to be mitigated by the reduction in recurrent attacks of hereditary angioedema and its associated cost of treatment.

Pembrolizumab with platinum and fluoropyrimidine-based chemotherapy for untreated advanced oesophageal and gastro-oesophageal junction cancer TA737

Recommendations

Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is **recommended**, within its marketing authorisation, as an option for untreated locally advanced unresectable or metastatic carcinoma of the oesophagus or HER2-negative gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more. Pembrolizumab is only recommended if the company provides it according to the commercial arrangement.

The technology

Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus (gullet), which is the muscular tube through which food passes from the throat to the stomach. Gastroesophageal junction cancer can develop directly at the gastroesophageal junction (where the stomach joins the oesophagus). It can also spread from the oesophagus across the gastroesophageal junction or from the stomach across the gastroesophageal junction.

The two main types of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. In the upper and middle part of the oesophagus, cancers tend to be squamous cell carcinomas, which develop from cells that make up the inner lining of the oesophagus. Cancers in the lower part (including gastroesophageal junction cancer) tend to adenocarcinomas, which usually develop in gland cells. The most common symptoms are difficulty swallowing, food regurgitation, nausea or vomiting, unexplained weight loss and persistent indigestion or cough.

Oesophageal cancer is more common in men than women. The risk of developing oesophageal cancer increases with age. Because of the nature of symptoms, oesophageal cancer is often diagnosed at an advanced stage.

The aim of treatment in advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma is primarily palliative. NICE NG83 recommends chemotherapy combination regimens for people who have a performance status 0 to 2 and no significant comorbidities. Chemotherapy regimens include doublet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin or triplet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin plus epirubicin.

Pembrolizumab is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as PD-1. The PD-1 receptor is part of the immune checkpoint pathway and blocking its activity may promote an anti-tumour immune response. It is administered intravenously.

Financial factors

This technology is commissioned by NHS England.

NICE estimates that 990 people in England with untreated locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastro-oesophageal junction adenocarcinoma are eligible for treatment with pembrolizumab with platinum and flouropyrimidine-based chemotherapy each year.

The list price for pembrolizumab is £2,630 for a 100-mg vial (excluding VAT). Pembrolizumab meets NICE's criteria to be considered a life-extending treatment at the end of life. The cost-effectiveness estimates are likely to be within what NICE considers an acceptable use of NHS resources.

Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy TA736

This guidance replaces NICE TA490 on the use of nivolumab for treating squamous cell carcinoma of the head and neck after platinum-based chemotherapy.

Recommendations

Nivolumab is **recommended** as an option for treating recurrent or metastatic squamous cell carcinoma of the head and neck in adults whose disease has progressed on platinum-based chemotherapy, only if:

- the disease has progressed within 6 months of having chemotherapy and
- the company provides it according to the commercial arrangement.

The technology

Head and neck cancer is a heterogeneous group of malignant tumours that arise in the head and neck at the following sites: skin and lip, oral cavity, oropharynx, larynx, hypopharynx, nasopharynx, salivary glands, nasal cavity and paranasal sinuses, and external auditory meatus and middle ear. The most common histological type of head and neck cancer is squamous cell carcinoma, particularly that affecting the oral cavity, oropharynx and larynx. Although local metastases of head and neck cancer occur frequently (usually spreading through the lymphatic system in the neck), distant metastases are less common.

The annual incidence of head and neck cancer is estimated to be approximately 8,000 cases in England. Treatment options for squamous head and neck cancer vary according to the specific sites involved. In some people with recurrent disease, the tumour may be amenable to surgery or radiotherapy with curative intent. In people with metastatic disease or who have previously received radiotherapy, palliative chemotherapy is normally given to control the disease and improve quality of life. Platinum-based chemotherapy is commonly used for recurrent or metastatic head and neck cancer. There is no established pathway of care when platinum-based therapy is not clinically appropriate.

Nivolumab is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune

checkpoint pathway and blocking its activity may promote an anti-tumour immune response. Nivolumab is administered by IV infusion.

New evidence shows that people who have nivolumab are likely to live up to 9 months longer than those who have other treatments. But it is unclear how well nivolumab works compared with docetaxel, which is the most relevant comparator.

Financial factors

This technology is commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources because the population size is small, with around 500 people in England expected to be eligible for treatment each year, and the overall incremental cost of treatment is low.

The list price of nivolumab is £439 per 40-mg vial, £1,097 per 100-mg vial and £2,633 per 240-mg vial (excluding VAT). The company has a commercial access agreement. This makes nivolumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Nivolumab meets NICE's criteria to be considered a life-extending treatment at the end of life. Despite the uncertainty in the clinical evidence, the cost-effectiveness estimates are likely to be within the range NICE considers an acceptable use of NHS resources.

Tofacitinib for treating juvenile idiopathic arthritis TA735

Recommendations

Tofacitinib is **recommended** as an option for treating active polyarticular juvenile idiopathic arthritis (JIA; rheumatoid factor positive or negative polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis in people 2 years and older. This is if their condition has responded inadequately to previous treatment with disease-modifying antirheumatic drugs (DMARDs), and only if:

- a tumour necrosis factor (TNF)-alpha inhibitor is not suitable or does not control the condition well enough, and
- the company provides tofacitinib according to the commercial arrangement.

Tofacitinib can be used with methotrexate, or as monotherapy when methotrexate is not tolerated or if continued treatment with methotrexate is inappropriate.

If tofacitinib is one of a range of treatments considered suitable by patients, or their parents or carers, and their clinicians, choose the least expensive (taking into account administration costs and commercial arrangements).

This recommendation is not intended to affect treatment with tofacitinib that was started in the NHS before this guidance was published. Children and young 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. This decision should be made jointly by the clinician, the child or young person, and their parents or carers.

The technology

Juvenile idiopathic arthritis (JIA) describes a group of conditions that involve joint inflammation which lasts for more than 6 weeks in people under 16 years of age. JIA causes pain, swelling and limitation of movement, which can change from day to day. When the condition becomes more active and the symptoms worsen, this is known as a 'flare'. In more severe cases, JIA can cause growth retardation, joint contractures, joint disease requiring joint replacements, eye problems and other extra-articular manifestations (such as inflammatory bowel disease and psoriasis), and permanent disability.

JIA can impair personal and social functioning and development. Children often miss out on schooling and other childhood activities, and as adults they may be limited in their ability to work. About 50% of children with JIA will not achieve remission from the condition, despite treatment, and will need further rheumatological care as adults. The prevalence of JIA is approximately 1 per 1,000 children.

Current treatment aims to control joint pain and inflammation; reduce joint damage, disability and loss of function; and maintain or improve quality of life. Standard treatment for JIA includes the use of the disease-modifying anti-rheumatic drugs (DMARDs), usually methotrexate, alongside intra-articular and systemic corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDS).

NICE TA373 recommends abatacept, adalimumab, etanercept and tocilizumab, within their marketing authorisations, as options for treating polyarticular JIA, including polyarticular-onset, polyarticular-course and extended oligoarticular JIA.

Tofacitinib is a janus kinase (JAK) inhibitor and is a targeted synthetic small molecule. Janus kinases are intracellular enzymes that transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of creating new blood cells in the body (hematopoiesis) and immune cell function. Tofacitinib is administered orally.

Tofacitinib can be used with methotrexate, or as monotherapy when methotrexate is not tolerated or if continued treatment with methotrexate is inappropriate.

Financial factors

This technology is commissioned by NHS England.

The list price of a 56-tablet pack of 5 mg tofacitinib is £690.03 (excluding VAT). Tofacitinib is also available as an oral 1 mg/ml solution in 240 ml bottles.

NICE do not expect this guidance to have a significant impact on resources this is because the technology is a further treatment option which is available at a similar price to current treatment options and the eligible population is small. Around 1,100

children and young people in England are expected to be eligible for treatment. Tofacitinib may be preferred by some patients because it is administered orally whereas current treatment options are administered subcutaneously or by intravenous infusion.

Secukinumab for treating moderate to severe plaque psoriasis in children and young people TA734

Recommendations

Secukinumab is **recommended** as an option for treating plaque psoriasis in children and young people aged 6 to 17 years, only if:

- the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and
- the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and
- the company provides the drug according to the commercial arrangement.

Stop secukinumab treatment at 12 weeks if the psoriasis has not responded adequately. An adequate response is defined as a 75% reduction in the PASI score (PASI 75) from when treatment started.

Choose the least expensive treatment if patients (or their parents or carers) and their clinicians consider secukinumab to be one of a range of suitable treatments. Take into account availability of biosimilar products, administration costs, dosage, price per dose and commercial arrangements.

Take into account how skin colour could affect the PASI score and make any appropriate clinical adjustments.

These recommendations are not intended to affect treatment with secukinumab 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. This decision should be made jointly by the clinician, the child or young person and their parents or carers.

The technology

Plaque psoriasis is an inflammatory skin condition characterised by an accelerated rate of turnover of the upper layer of the skin (epidermis). This leads to an accumulation of skin cells forming raised plaques on the skin. These plaques can be flaky, scaly, itchy and red or a darker colour to the surrounding skin. Plaque psoriasis may affect the scalp, elbows, knees and lower back and sometimes the face, groin, nails, armpits or behind the knees. Although it is a chronic, persistent, severe condition, its course may be unpredictable, with flare-ups and remissions.

Psoriasis is generally graded as mild, moderate or severe and takes into account the location, surface area of skin affected and the impact of the psoriasis on the person. The Children's Dermatology Life Quality Index (CDLQI) is a validated tool that can be used to assess the impact of psoriasis on physical, psychological and social wellbeing in children and young people.

There is no cure for psoriasis but there is a wide range of topical and systemic treatments that can manage the condition. Most treatments reduce the severity of psoriasis flares rather than prevent episodes. Psoriasis has to be treated continually and on a long-term basis.

Secukinumab is a possible alternative to other biological treatments (adalimumab, etanercept and ustekinumab) already recommended by NICE for treating severe plaque psoriasis in children and young people. Secukinumab is a high-affinity fully human monoclonal antihuman interleukin-17A (IL-17A) antibody of the IgG1/kappa isotype. It is administered by subcutaneous injection.

Evidence from clinical trials shows that secukinumab is more effective than etanercept. Evidence from an indirect comparison suggests that it is similarly effective to ustekinumab. How its effectiveness compares with that of adalimumab is uncertain because of a lack of evidence, but adalimumab is thought to be similarly effective to ustekinumab.

Financial factors

This technology is commissioned by NHS England.

NICE do not expect this guidance to have a significant impact on resources for implementing the recommendations in England. This is because the technology is a further treatment option which is available at a similar or lower price to current treatment options (adalimumab, etanercept and ustekinumab) and the eligible population is small. Around 180 children and young people in England are expected to be eligible for treatment.

The list price of secukinumab is £609.39 for a 150 mg/ml prefilled syringe. The company has a commercial arrangement. This makes secukinumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia TA733

Recommendations

Inclisiran is **recommended** as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended only if:

- there is a history of any of the following cardiovascular events:

  - acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation)
  - coronary or other arterial revascularisation procedures
  - coronary heart disease
  - ischaemic stroke or
  - peripheral arterial disease, and

- low-density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/l or more, despite maximum tolerated lipid-lowering therapy, that is:

  - maximum tolerated statins with or without other lipid-lowering therapies or,
  - other lipid-lowering therapies when statins are not tolerated or are contraindicated, and

- the company provides inclisiran according to the commercial arrangement.

Inclisiran is recommended only in research for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia in adults who have no history of cardiovascular events. This research is in the form of a clinical trial currently in development.

These recommendations are not intended to affect treatment with inclisiran 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

Dyslipidaemia is a broad term describing a number of conditions, including hypercholesterolaemia, hyperlipidaemia and mixed dyslipidaemia, in which disturbances in fat metabolism lead to changes in the concentrations of lipids in the blood. Mixed dyslipidaemia is defined as elevations in low-density lipoprotein (LDL) cholesterol and triglyceride levels that are often accompanied by low levels of highdensity lipoprotein (HDL) cholesterol.

Hypercholesterolaemia is the presence of high concentrations of cholesterol in the blood, typically including elevated LDL cholesterol. Primary hypercholesterolaemia is associated with an underlying genetic cause, which may be caused by a single genetic defect (familial), or more commonly, by the interaction of several genes with dietary and other factors (non-familial).

Most people with hypercholesterolaemia have cholesterol concentrations that are only mildly or moderately elevated and show no clinical symptoms. Severe hypercholesterolaemia, however, can cause xanthomas (lesions on the skin containing cholesterol and fats) and arcus corneae (cholesterol deposits in the eyes).

People with hypercholesterolaemia are at increased risk of cardiovascular disease (CVD) because long-term elevations of cholesterol accelerate the build-up of fatty deposits in the arteries (atherosclerosis). The narrowed arteries can cause diseases

such as angina, myocardial infarction and stroke, particularly in familial hypercholesterolaemia.

Managing primary hypercholesterolaemia and mixed dyslipidaemia involves dietary and lifestyle changes such as smoking cessation, weight loss and increased physical activity. CG181 and CG71 recommend initial treatment with statins. TA385 recommends ezetimibe as an option for treating primary hypercholesterolaemia, as a monotherapy when statins are contraindicated or not tolerated, and in combination with statins when initial statin therapy does not provide appropriate control of LDL-cholesterol. TA393 and TA394 recommend alirocumab and evolocumab, respectively, as options for treating primary hypercholesterolaemia and mixed dyslipidaemia, depending on LDL concentrations.

Inclisiran is a small interfering RNA molecule that inhibits production of PCSK9 in the liver. It is administered as a subcutaneous injection.

Clinical trial evidence shows that inclisiran can lower LDL-C levels when statins or other lipid-lowering therapies have not reduced them enough. Early results from the trials suggest that inclisiran could help prevent heart attacks and strokes. However, the effect on cardiovascular event risk is uncertain as there is a lack of long-term evidence.

Financial factors

This technology is commissioned by CCGs.

Inclisiran costs £1,987.36 per 284-mg dose pack (company submission). The company has a commercial arrangement. This makes inclisiran available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Despite uncertainties, inclisiran is still considered cost effective in people who have previously had a cardiovascular event and have persistently high LDL-C levels (2.6 mmol/l or more) despite maximum lipid-lowering therapy. Therefore, inclisiran is recommended as an option in this population.

In people who have never had a cardiovascular event, the cost-effectiveness estimates were very uncertain and likely to be above what NICE considers an acceptable use of NHS resources.

The Accelerated Access Collaborative and NHS England and NHS Improvement plan to support the implementation of inclisiran. Further information about funding arrangements will be provided by NHS England and NHS Improvement.

Baloxavir marboxil for treating acute uncomplicated influenza *(terminated appraisal)* TA732

NICE is **unable to make a recommendation** on baloxavir marboxil for treating acute uncomplicated influenza in people aged 12 and over. This is because Roche did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Highly specialised technology guidance (HSTs)

None published this month.

NICE Guidelines (NGs)

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management NG206

This guideline updates and replaces NICE guideline CG53

This guideline covers diagnosing and managing myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome (ME/CFS) in children, young people and adults. It aims to improve awareness and understanding about ME/CFS and when to suspect it, so that people are diagnosed earlier. It includes recommendations on diagnosis, assessment and care planning, safeguarding, access to care and managing ME/CFS and its symptoms.

This guideline includes recommendations on:

- suspecting ME/CFS and diagnosis
- information and support, including advice when ME/CFS is suspected
- assessment and care and support planning
- safeguarding
- access to care and support
- managing ME/CFS
- symptom management
- flare-ups and relapse
- care for people with severe or very severe ME/CFS

Public Health Guidelines

None published this month.

Antimicrobial prescribing guidelines

None published this month.

Social Care guidelines

Looked-after children and young people NG205

This guideline updates and replaces NICE guideline PH28

This guideline covers how organisations, practitioners and carers should work together to deliver high-quality care, stable placements and nurturing relationships for looked-after children and young people. It aims to help these children and young people reach their full potential and have the same opportunities as their peers.

This guideline includes recommendations on:

- supporting positive relationships
- valuing carers
- safeguarding
- health and wellbeing
- learning and education
- transition between care placements and to permanent placements, and out of care to independence

Interventional Procedures Guidance (IPGs)

Percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis access IPG710

Recommendations

Evidence on the safety of percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis access raises no major safety concerns. However, 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.

Clinicians wanting to do percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis should:

- Inform the clinical governance leads in their healthcare organisation.
- Give patients (and their families and carers as appropriate) clear written information to support shared decision making, including NICE's information for the public.

- Ensure that patients (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.

- Audit and review clinical outcomes of all patients having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).

- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

Healthcare organisations should:

- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for every patient having this procedure.

- Regularly review data on outcomes and safety for this procedure.

Patient selection should be done by a multidisciplinary team including a vascular access surgeon, nephrologist and interventional radiologist.

Report any problems with a medical device using the Medicines and Healthcare products Regulatory Agency's Yellow Card Scheme.

NICE encourages further research, preferably randomised controlled trials, into percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis access. This should report details of patient selection, particularly about vascular anatomy, technique used, need for training, patency of the fistula and its subsequent ease of use, and quality of life.

The condition

Chronic (long-term) haemodialysis is used to treat advanced chronic kidney disease in many people who have renal replacement therapy.

An arteriovenous fistula is considered the best type of vascular access for haemodialysis. The preferred way of creating such access is to surgically join an artery and vein together in the distal forearm (radiocephalic fistula). However, other anatomical sites may be used. Alternative surgical approaches for vascular access include arteriovenous grafts and placing tunnelled catheters into a large vein. A minimally invasive, percutaneous, endovascular procedure is another way of creating an arteriovenous fistula.

The procedure

This procedure can be done using different systems and is usually done in a day-case facility under local anaesthesia, with or without conscious sedation. Using ultrasound or fluoroscopic guidance, 2 small needles are inserted into an artery and a vein in the proximal forearm, that is, the radial, ulnar or brachial artery and adjacent vein. Thin,

flexible, specially designed catheters are then advanced and positioned by guidewires in the chosen vessels.

The catheters are aligned close to each other (using inbuilt magnets or mechanically, depending on the system). The arterial and venous walls are then fused side to side using heat and pressure, or a small burst of radiofrequency energy released from the catheters. This creates an arteriovenous fistula between the target vessels.

The catheters are then removed. High-flow arterial blood passes through the vein and, with time, it arterialises. This allows needles to be inserted into the vein to provide vascular access during haemodialysis.

The exact technique may vary slightly depending on the device used.

Laparoscopic renal denervation for loin pain haematuria syndrome IPG709

Recommendations

Evidence on the safety and efficacy of laparoscopic renal denervation for loin pain haematuria syndrome is inadequate in quality and quantity. Therefore, this procedure should only be used in the **context of research**.

Further research should report details of patient selection, technique used and long-term follow-up outcomes.

The condition

Loin pain haematuria syndrome (LPHS) causes pain near the kidney on one or both sides of the body (loin pain) and blood in the urine (haematuria; either macroscopic or microscopic). The cause of LPHS is unknown and diagnosis is only made after excluding all other possible renal causes of flank pain and haematuria.

Initial treatment of LPHS involves prescription of analgesics, up to and including opioids. Other treatments include transcutaneous electrical nerve stimulation, regional nerve blocks and radiofrequency ablation. If these are unsuccessful, surgical intervention can be tried, including open surgical renal denervation, capsulotomy (often done in conjunction with open surgical renal denervation), nephrectomy, and renal auto transplantation.

The procedure

Laparoscopic renal denervation is a minimally invasive procedure to interrupt the sensorial and sympathetic innervation of the kidney to control pain. The procedure is done under general anaesthesia, using a retroperitoneal approach. Lymphatic and nervous tissue is stripped off the renal artery and vein with subsequent division of all perihilar nervous tissue, with or without mobilisation of the kidney. The aim is to relieve pain. Laparoscopic renal denervation does not include capsulotomy, which may be included in open surgical renal denervation.

The laparoscopic technique aims to reduce the anaesthetic time and produce a quicker recovery time than open surgery.

Genicular artery embolisation for pain from knee osteoarthritis IPG708

Recommendations

Evidence on the safety of genicular artery embolisation for pain from knee osteoarthritis shows no major safety concerns in the short term. Evidence on its efficacy and long-term safety is inadequate in quality and quantity. Therefore, this procedure should only be used in the **context of research.**

Research should preferably be randomised controlled trials against sham and current best practice. It should report details of patient selection and identify those who would most benefit from this procedure. It should also report details of the technique used, long-term safety, and patient-reported outcomes.

The procedure should only be done by interventional radiologists with specific training in this technique.

The condition

Osteoarthritis is characterised by localised loss of cartilage, remodelling of adjacent bone, and associated inflammation. Knees are one of the most affected joints, with pain being a significant symptom. In knee osteoarthritis, new blood vessels can grow (angiogenesis) from the blood vessel that supplies blood to the knee (the genicular artery).

Angiogenesis may contribute to inflammation, structural damage and pain. This is because the increased vascular network carries inflammatory cells to the synovium and other joint tissues and promotes additional hyperplasia and inflammation in other vessels, leading to bone and cartilage destruction. Angiogenesis also enables the growth of new unmyelinated sensory nerves, which contributes to pain.

For pain secondary to knee osteoarthritis, various treatments are available including non-pharmacological (such as physiotherapy), pharmacological (such as analgesics and intra-articular steroids) and surgical approaches (such as knee arthroplasty).

Treatment most commonly involves a combination of pharmacological and non-pharmacological interventions. When non-pharmacological and pharmacological interventions do not work or symptoms are severe, surgery may be needed.

The procedure

This procedure aims to relieve pain by blocking (embolising) the pathological new vessels while maintaining the larger vascular supply to the bone.

Before the procedure, contrast-enhanced MRI of the knee is done to allow non-invasive assessment of synovial hypervascularity. The procedure is usually done using local anaesthesia with or without sedation. A catheter is passed through an introducer sheath in the femoral artery and then navigated into the genicular arteries supplying the knee to perform lower extremity angiography on the targeted side. Once

the abnormal new vessels arising from these arteries are identified, a microcatheter is navigated into them and, under fluoroscopic guidance, tiny embolisation particles are then delivered until the blood flow is stopped.

After the introducer sheath and catheter are removed, haemostasis is achieved with manual compression or a vascular closure device. The patient often goes home the same day. This procedure takes approximately 1 to 2 hours to complete.

Medical Technologies Guidance (MTGs)

DyeVert Systems for reducing the risk of acute kidney injury in coronary and peripheral angiography MTG60

Recommendations

DyeVert Systems show promise for reducing the risk of acute kidney injury (AKI) in coronary and peripheral angiography after using contrast media. However, **there is not enough evidence to support the case for routine adoption**. This is because there is not enough good-quality evidence that using the system reduces AKI incidence after having contrast media.

A randomised controlled trial is recommended to compare DyeVert Systems with standard care. The aim of this research would be to address uncertainties about whether using DyeVert Systems reduces AKI incidence and rate of renal replacement therapy after using contrast media. This must include people with stage 4 chronic kidney disease (with an estimated glomerular filtration rate [eGFR] under 30 ml/min/1.73 m^2), who are at risk of AKI and need elective coronary or peripheral angiography.

The technology

DyeVert Systems are designed to reduce the amount of contrast media given during coronary and peripheral angiography in a cardiac catheterisation or vascular radiology suite. The system uses a pressure-responsive valve to divert excess contrast medium while maintaining image quality, to reduce the risk of contrast-induced AKI.

There are 2 models of the DyeVert System. DyeVert Plus EZ Contrast Reduction System is compatible with manual contrast injectors. A smart syringe connects to a standard manifold and is manually operated by the clinician to inject the dye into the module that contains the diversion valve. A monitor displays both the total administered and total diverted contrast volume using Bluetooth communication with the smart syringe. DyeVert Power XT Contrast Reduction System is compatible with power injectors. There is no reusable monitor, but the contrast collection bag has a digital display showing the diverted dye volume.

Diagnostics Guidance (DGs)

None published this month.

NICE Quality Standards

None published this month.

Current NICE consultations

Title / link	End date of consultation
Intramedullary distraction for upper limb lengthening	02/11/2021
Percutaneous insertion of a cystic duct stent after cholecystostomy for acute calculous cholecystitis	02/11/2021
Liposuction for chronic lipoedema	02/11/2021
Integrated health and social care for people experiencing homelessness	03/11/2021
EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules	03/11/2021
Prostate cancer (update)	04/11/2021
GID-MT551 Prontosan for acute and chronic wounds	08/11/2021
Nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma [ID1465]	11/11/2021
Tucatinib with trastuzumab and capecitabine for treating HER2-positive unresectable locally advanced or metastatic breast cancer after 2 or more anti-HER2 therapies [ID3828]	16/11/2021
Intramedullary distraction for lower limb lengthening	18/11/2021
Endoscopic balloon dilation for subglottic or tracheal stenosis	18/11/2021
Endoscopic full thickness removal of gastrointestinal stromal tumours of the stomach	18/11/2021
DHT001 (DHT pilot) myCOPD for self-management of chronic obstructive pulmonary disease (COPD)	24/11/2021
Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults	02/12/2021

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