NHS Devon

NICE Update Bulletin: June 2024

This bulletin includes details of the following new and updated NICE guidance – click on the titles below for further details:

1. **Tafamidis for treating transthyretin amyloidosis with cardiomyopathy TA984**
2. **Pembrolizumab with trastuzumab and chemotherapy for untreated locally advanced unresectable or metastatic HER2- positive gastric or gastro-oesophageal junction adenocarcinoma TA983**
3. **Baricitinib for treating juvenile idiopathic arthritis in people 2 years and over (*terminated appraisal*) TA982**
4. **Voxelotor for treating haemolytic anaemia caused by sickle cell diseaseTA981**
5. **Nivolumab for adjuvant treatment of completely resected melanoma at high risk of recurrence in people 12 years and over (*terminated appraisal*) TA980**
6. **Ivosidenib with azacytidine for untreated acute myeloid leukaemia with an IDH1 R132 TA979**
7. **Minimally invasive percutaneous surgical techniques with internal fixation for correcting hallux valgus IPG789**
8. **Current NICE Consultations**

Technology Appraisals (TAs)

Tafamidis for treating transthyretin amyloidosis with cardiomyopathy TA984

This guidance updates and replaces TA696 (published May 2021)

Recommendations

Tafamidis is **recommended**, within its marketing authorisation, as an option for treating wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM) in adults. Tafamidis is only recommended if the company provides it according to the commercial arrangement.

The Technology

Transthyretin amyloidosis (ATTR) is caused by abnormal transthyretin (TTR) proteins being produced by the liver and accumulating as deposits in the tissues of the body (amyloidosis). Transthyretin amyloid cardiomyopathy (ATTR-CM) is a type of transthyretin amyloidosis in which most deposits accumulate in the heart, causing the heart tissue to thicken and stiffen. There are two causes of ATTR-CM:

1. Wildtype ATTR-CM mostly affects older individuals and more men than women.
2. Hereditary ATTR-CM affects people born with inherited mutations in the TTR gene. These variants are thought to be less stable than the wildtype and so are more likely to form amyloid fibrils.

Symptoms of ATTR-CM can include shortness of breath, palpitations and abnormal heart rhythms, most frequently atrial fibrillation or atrial flutter, ankle swelling, fatigue, fainting and chest pain. ATTR-CM is a progressive disease with symptoms usually starting after the age of 70 years in people with wildtype ATTR-CM or after the age of 60 years in people with Val112Ile and T60A variants of hereditary ATTR-CM. As the disease progresses, people with ATTR-CM rely more on carers to perform daily activities. Death in most people with ATTR-CM is from sudden death and progressive heart failure.

Current treatment options for ATTR-CM, such as diuretics, focus on symptom management and supportive care. A small proportion of people with cardiomyopathy as a result of transthyretin amyloidosis also have polyneuropathy.

Inotersen (HST9), patisiran (HST10) and vutrisiran (TA868) are recommended as options for treating stage 1 and 2 polyneuropathy in adults with hereditary transthyretin amyloidosis. Liver or heart transplantation are options for some people with ATTR-CM and aspecific genetic mutation. However, transplantation can only take place early in the course of the disease, so it is rarely used in England.

Tafamidis binds to transthyretin (TTR) in the blood. This binding stabilises the shape of TTR and prevents the formation of abnormal proteins. In turn, this then stops the formation of amyloids. Tafamidis is taken orally.

Financial Factors

This technology is commissioned by NHS England.

ATTR-CM is a progressive condition that can lead to heart failure, but treatment options are limited to managing symptoms and best supportive care. Tafamidis is the first treatment for ATTR-CM that aims to treat the condition.

Evidence from the main clinical trial shows that tafamidis reduces deaths and hospitalisations from conditions affecting the heart and blood vessels compared with placebo. But it is uncertain how long people live when having tafamidis and how long they take it for. Longer-term evidence from a different study reduces this uncertainty.

The most likely cost-effectiveness estimate for tafamidis is within the range that NICE considers an acceptable use of NHS resources, therefore, tafamidis is recommended.

The company has a commercial arrangement. This makes tafamidis available to the NHS with a discount.

Pembrolizumab with trastuzumab and chemotherapy for untreated locally advanced unresectable or metastatic HER2- positive gastric or gastro-oesophageal junction adenocarcinoma TA983

Recommendations

Pembrolizumab with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy is **not recommended**, within its marketing authorisation, for untreated locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction (GOJ) adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 1 or more.

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

The Technology

Gastric cancer is a malignant tumour arising from cells in the stomach. The most common type of stomach cancer is gastric or gastro-oesophageal junction.

Gastro-oesophageal junction cancer describes cancers where the centre of the tumour is less than 5 cm above or below where the oesophagus meets the stomach.

Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus. The most common histological subtype of gastric, gastro-oesophageal junction and oesophageal cancer is adenocarcinoma.

Initial symptoms of gastric or oesophageal cancer are vague and are similar to other stomach conditions, but symptoms of advanced stages may include a lack of appetite and subsequent weight loss; fluid in the abdomen, vomiting blood, blood in the stool or black stool. Because of the nature of symptoms, gastric and oesophageal cancer are often diagnosed at an advanced stage.

The aim of treatment in advanced or metastatic gastric, gastro-oesophageal junction cancer or oesophageal adenocarcinoma is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects.

NICE have published the following related technology appraisals; **TA191** and **TA208** and the following clinical guideline **NG83** (Oesophago-gastric: assessment and management in adults).

Financial Factors

This technology is commissioned by ICBs.

Clinical trial evidence suggests that pembrolizumab plus trastuzumab and chemotherapy increases how long people have before their cancer gets worse compared with trastuzumab plus chemotherapy. The evidence suggests it is also increases how long they live, but the long-term effect is very uncertain.

When taking into account the committee's preferred assumptions, the cost-effectiveness estimate is not within the range that NICE usually considers an acceptable use of NHS resources. Therefore, pembrolizumab plus trastuzumab and chemotherapy is not recommended.

Baricitinib for treating juvenile idiopathic arthritis in people 2 years and over (*terminated appraisal*) TA982

NICE is **unable to make a recommendation** about the use in the NHS of baricitinib for treating juvenile idiopathic arthritis in people 2 years and over. This is because the company did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Voxelotor for treating haemolytic anaemia caused by sickle cell disease TA981

Recommendations

Voxelotor, with or without hydroxycarbamide, is **recommended** as an option for treating haemolytic anaemia caused by sickle cell disease in people 12 years and over. It is recommended only if:

- people are ineligible for, or intolerant of hydroxycarbamide, or
- hydroxycarbamide alone is insufficiently effective.

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

This recommendation is not intended to affect treatment with voxelotor 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 healthcare professional consider it appropriate to stop. For children or young people, this decision should be made jointly by the healthcare professional, the child or young person and their parents or carers.

The Technology

Sickle cell disease is the name given to a group of lifelong inherited conditions that affect haemoglobin. The most common and often severe type of sickle cell disease occurs when people inherit a copy of the beta globin gene with the sickle mutation from both parents (homozygous). Heterozygous sickle cell anaemia occurs when people inherit one copy of the beta globin gene with the sickle mutation from one parent and a different variant of the beta globin gene from the other parent. In all cases, the abnormal haemoglobin, known as haemoglobin S, tends to form polymers with other haemoglobin S molecules. These polymers cause red blood cells to become rigid and misshapen, resembling a crescent (or sickle).

Sickle-shaped red blood cells do not last as long in the body as a regular shaped round blood cells and get broken down more readily in a process known as haemolysis. People with sickle cell disease often have anaemia because too much haemolysis occurs and there are not enough red blood cells to carry oxygen throughout the body. Sickle-shaped red blood cells also do not flow easily through blood vessels and bond abnormally with other blood cells and blood vessels wall walls which can cause blockages. This may lead to insufficient oxygen being delivered to tissues, causing ischaemic injuries and excruciating pain (known as acute sickle cell crisis). Chronic complication caused by anaemia and sickle cell crises include progressive organ damage, fatigue and shortness of breath. Acute complications may also include acute chest syndrome and stroke.

The prevalence of sickle cell disease varies considerably across different ethnic communities, mainly affecting people of African or African-Caribbean family background, although the sickle gene is found in all ethnic groups. The prevalence of the disease is increasing because of immigration into the UK, new births and increased survival.

Sickle cell disease causes significant morbidity and mortality and usually requires lifelong treatment. Management in England focuses on reducing the changes of experiencing a sickle cell crisis by avoiding dehydration, sudden changes in temperature and infection. Sickle cell crises may be extremely painful and will often require emergency admission to hospital and pain management with paracetamol, non-steroidal anti-inflammatory drugs and opiates. Hydroxycarbamide can also be used to increase the production of foetal haemoglobin, which improves blood cell hydration and reduces red blood cell adhesion. This can reduce both acute painful crises and acute chest syndrome. Blood transfusions including exchange transfusions and simple top-up transfusions can help to maintain a healthy proportion of normal red blood cells to sickle red blood cells. Allogenic stem cell transplants may be considered but are not done often because of the significant risks involved.

Voxelotor is a haemoglobin S allosteric modulator. Voxelotor increases haemoglobin's ability to hold on to more oxygen, which prevents polymerisation and keeps red blood cells in their normal shape, helping to prevent haemolysis and associated anaemia. It is administered orally.

Financial Factors

This technology is commissioned by NHS England.

Based on clinical experts' experience of using voxelotor in the early access to medicines scheme there was a clinical effect of an improvement in haemoglobin which occurred within 1 to 2 weeks. The treatment raises baseline haemoglobin so people are better able to tolerate any exacerbations of disease.

Voxelotor has been available in the early access to medicines scheme, therefore the cost of the drug has so far met by the company. The overall incremental cost of voxelotor to the NHS when transitioning to routine commissioning is likely to be offset by savings from reduced use of regular blood transfusions and fewer adverse events that occur in sickle cell disease which require a stay in hospital. These include the need for acute top up transfusions and vaso-occlusive crises.

NICE estimate that 114 people will be eligible for treatment in Devon.

The company has a commercial arrangement. This makes voxelotor available to the NHS with a discount.

Nivolumab for adjuvant treatment of completely resected melanoma at high risk of recurrence in people 12 years and over (*terminated appraisal*) TA980

NICE is **unable to make a recommendation** on nivolumab for adjuvant treatment of completely resected melanoma at high risk of recurrence in people 12 years and over. This is because the company did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Ivosidenib with azacytidine for untreated acute myeloid leukaemia with an IDH1 R132 TA979

Recommendations

Ivosidenib plus azacytidine is **recommended**, within its marketing authorisation, as an option for untreated acute myeloid leukaemia (AML) with an IDH1 R132 mutation in adults who cannot have standard intensive induction chemotherapy. It is only recommended if the company provides it according to the commercial arrangement.

The Technology

Acute myeloid leukaemia (AML) is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid cells. AML progresses quickly over weeks or months and is fatal if not treated. Anaemia, bleeding problems and serious infections are common symptoms of AML. People with AML also feel fatigued, which can affect daily life.

The aim of treatment for AML is to cure it. People who are fit enough can have intensive treatment. It is done in 2 phases: induction chemotherapy to reduce the number of blast cells, then consolidation chemotherapy to reduce the risk of recurrence. For people with good general health, the treatment options are intensive chemotherapy and allogeneic haematopoietic stem cell transplant (HSCT).

Over half of patients with AML are ineligible for intensive chemotherapy and stem cell transplants because of factors such as age or comorbidities. Other treatment options for these people include azacytidine, low dose cytarabine and venetoclax.

NICE has published the following technology appraisals for the treatment of AML; **TA218**, **TA765**, **TA787**.

Financial Factors

This technology is commissioned by NHS England.

Usual treatment for newly diagnosed AML with IDH1 R132 mutation in adults who cannot have standard intensive induction chemotherapy is venetoclax plus azacytidine.

Ivosidenib plus azacytidine has not been directly compared in a clinical trial with venetoclax plus azacitidine. An indirect comparison suggests that ivosidenib plus azacytidine increases how long people live and how long they have before their condition gets worse compared with venetoclax plus azacytidine.

The most likely cost-effectiveness estimates for ivosidenib plus azacytidine are within the range that NICE considers an acceptable use of NHS resources, therefore, it is recommended.

NICE estimate that in Devon, 2 people will be eligible for treatment.

The company has a commercial arrangement. This makes ivosidenib available to the NHS with a discount.

Highly Specialised Technology Guidance (HSTs)

None published this month

NICE Guidelines (NGs)

None published this month

NICE Rapid COVID-19 Guidelines

None published this month

Public Health Guidelines

None published this month.

Antimicrobial Prescribing Guidelines

None published this month.

Social Care Guidelines

None published this month.

Interventional Procedures Guidance (IPGs)

Minimally invasive percutaneous surgical techniques with internal fixation for correcting hallux valgus IPG789

Recommendations

Use of minimally invasive percutaneous surgical techniques with internal fixation as an option for correcting hallux valgus with **standard arrangements** in place for clinical governance, consent and audit.

These challenging techniques should only be done by a clinician with specific training and specialist experience in the procedure techniques

Clinicians should enter details about everyone having these procedures onto a registry, which could include the BOFAS registry. This should include:

- details of patient selection
- the techniques used
- the type of implant used
- short- and longer-term patient reported outcomes.

The Condition

Hallux valgus (HV) is more commonly known as a bunion. The big toe is deviated towards the other toes resulting in a bony protrusion. This deviation occurs at the first metatarsal phalangeal joint. The small sesamoid bones found beneath the first metatarsal also becomes displaced as the first metatarsal bone drifts away from its normal position, weakening the big toe. Symptoms include damage to the skin over the bunion, pain and weakness of the forefoot when walking, cosmetic concerns and difficulty with footwear.

In a small number of people, bunion development is associated with underlying genetic conditions affecting the structure of the foot. But in most people the aetiology is not clear. Chronic trivial injury to the joint may be the cause. The condition is most common in women and in middle and later life.

Current treatment options include exercises, orthoses, spacers between the toes to keep them in the correct position, shoe alterations and analgesics to relieve symptoms. Open surgery is considered as standard care when conservative treatments have failed and severe pain and deformity cause functional impairment. Many different surgical operations are used for treating HV, depending on the nature and extent of the deformity. One commonly used open surgical procedure is distal first metatarsal osteotomy, which divides and repositions the bone of the big toe near to the joint to correct the deformity.

The Procedure

Surgical correction of HV using minimally invasive percutaneous surgical techniques with internal fixation is done as a day case under local or general anaesthesia and in supine position. Low dose x-ray monitoring or endoscopic images are used. One or more small incisions are made close to the hallux metatarsophalangeal joint of the affected toe. The bunion is then removed and the metatarsal is divided surgically.

Motorised high torque low speed burrs and surgical jigs aid the complex reduction and fixation steps of the procedure and implant insertion. Temporary wires may be used to toggle the separated parts of the divided bone into the desired position. The bone fragments are then stabilised using plates, specialised screws, or wires. The temporary wires used for toggling pieces of bone are removed. The small incisions are closed and a dressing applied. After surgery, a dressing or plaster may be used to support the foot in the corrected position until the divided bones heal. People are usually allowed to put weight on the foot immediately.

The proposed advantages of minimally invasive techniques are shorter operation time, quicker recovery, less pain, fewer complications, shorter hospital stay, earlier weight bearing and smaller scars.

Medical Technologies Guidance (MTGs)

None published this month

Diagnostics Guidance (DGs)

None published this month

Health Technology Evaluations (HTE)

None published this month

NICE Quality Standards

None published this month.

Current NICE Consultations

Title/link	End date of consultation
Digital supported self-management technologies for adults with chronic obstructive pulmonary disease: early value assessment	08/07/2024
12 SQ-HDM SLIT for treating allergic rhinitis and allergic asthma caused by house dust mites (review of TA834) [ID6280]	17/07/2024
Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (Review of TA761) [ID5120]	18/07/2024
Meningitis (bacterial) and meningococcal disease update	23/07/2024
Asthma: diagnosis, monitoring and chronic asthma management	30/07/2024