NHS Devon

NICE Update Bulletin: March 2023

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Technology Appraisals (TAs)

Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 TA878

Recommendations

Nirmatrelvir plus ritonavir is **recommended** as an option for treating COVID-19 in adults, only if they:

- do not need supplemental oxygen for COVID-19 and
- have an increased risk for progression to severe COVID-19, as defined in the independent advisory group report commissioned by the Department of Health and Social Care.

Sotrovimab is **recommended** as an option for treating COVID-19 in adults and young people aged 12 years and over and weighing at least 40 kg, only if:

- they do not need supplemental oxygen for COVID-19 and
- they have an increased risk for progression to severe COVID-19, as defined in the independent advisory group report commissioned by the Department of Health and Social Care and
- nirmatrelvir plus ritonavir is contraindicated or unsuitable.

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

Tocilizumab is **recommended**, within its marketing authorisation, as an option for treating COVID-19 in adults who:

- are having systemic corticosteroids and
- need supplemental oxygen or mechanical ventilation.

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

Casirivimab plus imdevimab is **not recommended**, within its marketing authorisation, for treating acute COVID-19 in adults.

The Technology

COVID-19 is predominantly an acute respiratory illness caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease refers to any symptom resulting from the infection and these can vary widely in clinical severity. People who become critically ill may develop acute respiratory distress syndrome (ARDS), the leading cause of mortality among patients with COVID-19.

The COVID-19 pandemic rapidly evolved globally, with countries facing different stages of the spread of disease. The gradual mutation of SARS-CoV-2 has led to various variants of concern, each with different transmissibility, morbidity, and mortality effects. Data from the UK suggest that mortality due to COVID-19 is strongly associated with older age, male gender, deprivation and Black, Asian and minority ethnic family background. Disabled people and people with a learning disability have a higher risk of dying from COVID19. People with pre-existing conditions, including people with dementia and Alzheimer's disease, diabetes, heart disease or obesity, are also more at risk from dying from COVID-19.

COVID-19 has a diverse range of clinical manifestations, ranging from mild infection to severe disease accompanied by high mortality. It begins with infection, or the viral replication phase, with symptoms such as cough, fever and breathlessness. This disease stage is when viral shedding occurs and people are at the peak of infectiousness. At this stage anti-viral treatments and neutralising monoclonal antibodies (mABs) are expected to be more beneficial because they inhibit viral replication, which may reduce severity of symptoms. If the disease is not adequately controlled, excessive immune response can lead to more severe complications. This is part of the inflammatory phase of the disease, with symptoms that include ARDS, other organ failure and exacerbation of co-morbid conditions. At this stage, anti-inflammatory treatments and immunomodulatory mAbs, which target responses to the inflammatory pathway, may be more beneficial to reduce inflammation and avoid these hyperinflammatory complications.

Anti-viral treatments can also be useful during the inflammatory stage of the disease, to reduce ongoing viral replication.

Currently, established clinical management for most people in hospital with COVID19 is an appropriate level of respiratory support which may range from oxygen delivered by face mask or nasal canula to invasive mechanical ventilation and organ support. NG191 recommends corticosteroids, including dexamethasone, or either hydrocortisone or prednisolone if dexamethasone cannot be used or is unsuitable, for people with COVID-19 who need supplemental oxygen.

Nirmatrelvir and ritonavir is an antiviral medication. Ritonavir is a protease inhibitor. Nirmatrelvir and ritonavir are administered orally, consecutively. Sotrovimab is a mAb. It is administered intravenously. Tocilizumab is a mAb. It can be administered by subcutaneous injection or intravenously. Casirivimab and imdevimab are mAbs, used in combination. Casirivimab and imdevimab can be administered intravenously, together.

Financial Factors

These technologies are commissioned by ICBs.

Nirmatrelvir plus ritonavir and *tocilizumab* are recommended because the likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. The cost-effectiveness estimates for *sotrovimab* are also within what NICE considers an acceptable use of NHS resources, but only for people for whom *nirmatrelvir plus ritonavir* is contraindicated or unsuitable. So, sotrovimab is recommended in this group.

Casirivimab plus imdevimab is not recommended because it is unlikely to be effective at treating COVID-19 and it is not possible to reliably estimate its cost effectiveness.

Finerenone for treating chronic kidney disease in type 2 diabetes TA877

Recommendations

Finerenone is **recommended** as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults. It is recommended only if:

- it is an add-on to optimised standard care; this should include, unless they are unsuitable, the highest tolerated licensed doses of:
    - angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) **and**
    - sodium–glucose cotransporter-2 (SGLT2) inhibitors **and**
- the person has an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m^2 or more.

This recommendation is not intended to affect treatment with finerenone 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

Chronic kidney disease (CKD) is a condition where the kidneys do not work as well as they should and is linked with adverse outcomes including cardiovascular disease. It is common in people who have diabetes because people with diabetes have too much glucose in their blood and this can damage the tiny filters in the kidneys. People with CKD do not usually have symptoms during the early stages of the disease but symptoms including weight loss and poor appetite, swollen ankles, feet or hands, shortness of breath, tiredness, feeling sick and itchy skin can develop as the disease progresses.

The severity of CKD is determined by the estimated glomerular filtration rate (eGFR) of which there are 6 categories:

1. normal
2. mild reduction
3. mild to moderate reduction
4. moderate to severe reduction
5. severe reduction
6. kidney failure

The severity of CKD is also determined by albumin to creatinine ratio (ACR) with 3 categories:

1. normal to mild increase
2. moderate increase
3. severe increase

An ACR of more than 3 mg/mmol is an indicator for albuminuria, when urine protein levels are increased, resulting from damage within the kidneys.

Around 20% of people with diabetes will need treatment for kidney disease during their lifetime. More than 1 in 3 people who need kidney dialysis, or a transplant have diabetes. End-stage renal disease is associated with significant impact on quality of life for people with the condition and their families and diabetes with early kidney involvement may be associated with shorter life expectancy.

Lifestyle changes are usually recommended for people with kidney disease, including stopping smoking, eating a healthy diet and regular exercise. There is no medicine specifically for CKD, but treatment can help control many of the associated problems such as high blood pressure, high cholesterol and anaemia. For people with CKD and diabetes, CG182 recommends aiming to keep systolic blood pressure below 130 mmHg and the diastolic blood pressure below 80 mmHg. To control blood pressure, CG182 recommends a drug that blocks or inhibits the renin-angiotensin system including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs) and direct renin inhibitors if there is an ACR of 3 mg/mmol or more. People with severely reduced kidney function may need dialysis or a kidney transplant.

Finerenone is a selective non-steroidal mineralocorticoid receptor inhibitor which reduces the activity of aldosterone and cortisol. Finerenone blocks the over-activation of this receptor. It is administered orally.

Financial Factors

This technology is commissioned by ICBs.

The cost-effectiveness estimates are uncertain, but they are all within the range that NICE considers an acceptable use of NHS resources. Because finerenone has not been compared directly with SGLT2 inhibitors as an add-on to standard care (without SGLT2 inhibitors), it cannot be recommended instead of them. Therefore, finerenone is recommended as an add-on to standard care, when standard care includes SGLT2 inhibitors.

NICE have stated that they do not expect this guidance to have a significant impact on resources. Part of the cost of treatment with finerenone is expected to be offset by savings and benefits. The clinical evidence suggests that finerenone plus standard care can improve kidney function and helps to slow the worsening of disease.

Nivolumab with chemotherapy for neoadjuvant treatment of resectable non-small-cell lung cancer TA876

Recommendations

Nivolumab with chemotherapy is **recommended**, within its marketing authorisation, as an option for the neoadjuvant treatment of resectable (tumours at least 4 cm or node positive) non-small-cell lung cancer (NSCLC) in adults. It is only recommended if the company provides it according to the commercial arrangement.

The Technology

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK. Up to 85% of lung cancers are non-small-cell lung cancers (NSCLC).

Most lung cancers are diagnosed at an advanced stage when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage III) or to other parts of the body (metastatic disease; stage IV). Less than 30% of lung cancers are diagnosed at an early stage (stage I or II).

NG122 recommends surgery, radiotherapy, chemotherapy or a combination of these for early-stage disease.

Neoadjuvant chemotherapy (before surgical removal of cancerous tumour) has shown equivalent outcomes in terms of survival to adjuvant chemotherapy.5For stage III NSCLC, surgery is carried out if the surgeon deems the tumour to be excisable. Before surgery, chemoradiotherapy may be given or surgery may potentially be followed by chemotherapy. If surgery is not possible, patients may undergo treatments including chemoradiotherapy which may be followed by immunotherapy. If well enough, people may be offered a cisplatin-based chemotherapy (adjuvant treatment) after surgery.

Despite the curative intent of treatment for early-stage lung cancer, survival is poor, with only about 57% people with stage I, 34% with stage II and 13% with stage III surviving for 5 years after diagnosis.

It is estimated that over half of all NSCLCs express the programmed cell death ligand-1 (PD-L1) biomarker.7 Cancer cells expressing PD-L1 are believed to suppress certain immune responses and cause increased tumour aggressiveness.

Financial Factors

This technology is commissioned by NHS England.

The cost-effectiveness estimates for neoadjuvant nivolumab with chemotherapy compared with standard care are within the range NICE normally considers an acceptable use of NHS resources. Therefore, neoadjuvant nivolumab with chemotherapy is recommended.

NICE estimate that 108 people in Devon will be eligible for treatment with nivolumab with chemotherapy.

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

Semaglutide for managing overweight and obesity TA875

Recommendations

Semaglutide is **recommended** as an option for weight management, including weight loss and weight maintenance, alongside a reduced-calorie diet and increased physical activity in adults, only if:

- it is used for a maximum of 2 years, and within a specialist weight management service providing multidisciplinary management of overweight or obesity (including but not limited to tiers 3 and 4), and
- they have at least 1 weight-related comorbidity and:
    - a body mass index (BMI) of at least 35.0 kg/m^2, or
    - a BMI of 30.0 kg/m^2 to 34.9 kg/m^2 and meet the criteria for referral to specialist weight management services in NICE's guideline on obesity: identification, assessment and management.

    Use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family backgrounds.

Consider stopping semaglutide if less than 5% of the initial weight has been lost after 6 months of treatment.

These recommendations are not intended to affect treatment with semaglutide 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

Overweight and obesity is a chronic condition characterised by increased body fat. People living with overweight or obesity are at an increased risk of developing cardiovascular disease, type 2 diabetes, atherosclerosis, hypertension and dyslipidaemia. Other conditions associated with obesity are non-alcoholic fatty liver disease, non-diabetic hyperglycaemia, subfertility, osteoarthritis, dyslipidaemia, obstructive sleep apnoea and idiopathic intracranial hypertension. The most common method for measuring obesity is body mass index (BMI) which is calculated as the ratio of weight to height squared. Overweight is typically defined by a BMI of 25 kg/m^2 to <30 kg/m^2 and obesity by a BMI of 30 kg/m^2 or more. Some ethnic groups may be at increased risk of some ill health conditions at lower BMI than people of European family origin.

CG189 states multicomponent interventions are the treatment of choice. Weight management programmes include behaviour change strategies to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the person's diet, and reduce energy intake. Pharmacological treatments are usually considered only after dietary, exercise and behavioural approaches have been started and evaluated.

If dietary and lifestyle advice, behaviour modification and drug treatments are unsuccessful, the CG189 recommends bariatric surgery for people meeting certain criteria.

TA664 recommends liraglutide as an option for managing overweight and obesity alongside a reduced-calorie diet and increased activity in adults if they have a BMI of at least 35 kg/m^2.

Semaglutide binds to and activates the glucagonlike peptide-1 (GLP-1) receptor in order to increase insulin levels and suppress glucagon secretion. This action leads to the slowing of glucose absorption and lower post-meal blood glucose levels. It is administered by subcutaneous injection.

Financial Factors

This technology is commissioned by ICBs.

For people who have at least 1 weight-related comorbidity and a BMI of at least 35 kg/m^2 or a BMI of 30 kg/m^2 to 34.9 kg/m^2 and also meet the NICE criteria for referral to a specialist weight management service, the cost-effectiveness estimates for semaglutide are likely to be within what is normally considered a cost-effective use of NHS resources. For these groups, semaglutide is recommended alongside lifestyle interventions in an appropriate multidisciplinary setting.

NICE estimate that in Devon, 93,441 people will be eligible for treatment and that 620 people will choose treatment with semaglutide in year and that 469 people will continue with semaglutide in year 2. To note, NICE estimate that 91,909 people will choose diet and exercise.

Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma TA874

Recommendations

Polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone (R-CHP) is **recommended** for untreated diffuse large B-cell lymphoma (DLBCL) in adults, only if

- they have an International Prognostic Index (IPI) score of 2 to 5
- the company provides it according to the commercial arrangement.

This recommendation is not intended to affect treatment with polatuzumab vedotin with R-CHP 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

Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Lymphomas are divided into Hodgkin lymphoma and non-Hodgkin lymphoma.

Non-Hodgkin lymphomas (NHL) are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease. The most common B-cell lymphomas are follicular lymphoma which is a slow growing, low grade form of NHL and diffuse large B-cell lymphomas (DLBCL), a fast growing, high grade form of NHL.

Some follicular lymphomas transform into high grade DLBCL (transformed high grade follicular lymphoma). The symptoms differ depending on which organ or tissues are affected by the lymphoma. NHL often presents as painless lumps in the neck, armpit or groin but sometimes may start in other parts of the body such as the stomach or bowel. People may also have loss of appetite, tiredness or night sweats.

There are two biologically distinct subtypes of DLBCL, germinal centre B-cell (which arises in secondary lymphoid organs such as lymph node and spleen) and post-germinal centre (also known as activated B-cell lymphoma) which differ in prognosis. They are distinguished by immunohistochemical testing of gene expression profiling.

Current first-line treatment is combination chemotherapy with rituximab. The most widely used first-line chemoimmunotherapy is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone).

Polatuzumab vedotin is an antibody drug conjugate which is a monoclonal antibody combined with a cytotoxic agent called monomethyl auristatin E (MMAE). It acts by selectively binding to CD79b, a protein which is found on the surface of B-cells, resulting in the death of B-cells. It is administered as an intravenous infusion.

Financial Factors

This technology is commissioned by NHS England.

The cost-effectiveness estimates for polatuzumab vedotin with R-CHP are likely to be within what NICE considers an acceptable use of NHS resources. Therefore, polatuzumab vedotin with R-CHP is recommended for people with an IPI score of 2 to 5.

NICE estimate that in Devon, 41 people will be eligible for treatment and 37 will receive treatment with polatuzumab vedotin with R-CHP.

Cannabidiol for treating seizures caused by tuberous sclerosis complex TA873

Recommendations

Cannabidiol is **recommended** as an add-on treatment option for seizures caused by tuberous sclerosis complex in people aged 2 years and over, only if:

- their seizures are not controlled well enough by 2 or more antiseizure medications (either used alone or in combination) or these treatments were not tolerated
- seizure frequency is checked every 6 months, and cannabidiol is stopped if the frequency has not fallen by at least 30% compared with the 6 months before starting treatment
- the company provides cannabidiol according to the commercial arrangement.

These recommendations are not intended to affect treatment with cannabidiol that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. For children, this decision should be made jointly by the clinician and the child and/or the child's parents or carers.

The Technology

Tuberous sclerosis or tuberous sclerosis complex is a rare genetic condition that causes mainly non-cancerous tumours to develop in different parts of the body. The tumours most often affect the brain, kidneys, heart, lungs, eyes and skin.

Two disease causing genes have been identified: TSC1 and TSC2. Tuberous sclerosis is present from birth, although symptoms may not appear immediately. People with *tuberous sclerosis complex* present at different ages with a variety of clinical manifestations.

The effect of tuberous sclerosis complex on the brain can cause epilepsy, a condition that causes seizures. Seizures can progress to become refractory, which is when the seizures no longer respond to anti-epileptic medication. In UK clinical practice, this means that 2 different anti-epileptic drugs have failed to control a person's seizures. Refractory epilepsy associated with

tuberous sclerosis complex is associated with risks including sudden unexpected death in epilepsy, potentially fatal prolonged seizures and adverse impact on neurodevelopment.

Seizures are the most common presenting sign of tuberous sclerosis Complex. Although there is no curative treatment for tuberous sclerosis, current treatment can help to manage symptoms. Anti-seizure medications such as vigabatrin are administered to control seizures. Everolimus may also be used to reduce the frequency of seizures, which are closely linked to issues with development in infants and children. Early management is important in preventing and reducing the cognitive, neurological and psychiatric consequences for people with tuberous sclerosis complex.

Cannabidiol is a small-molecule cannabinoid compound extracted from the Cannabis sativa plant. The precise mechanism of action of cannabidiol is unknown, although it is thought to act on the GPR55 and TRPV1 protein channels, which is expected to have an effect on epileptic activity in the brain. It is administered orally.

Financial Factors

This technology is commissioned by NHS England.

NICE do not expect this guidance to have a significant impact on resources. This is because the population size is small, and part of the cost of cannabidiol is likely to be offset by savings in management costs and delays to more expensive treatments.

The use of cannabidiol plus usual care may reduce seizure frequency and increases the number of seizure-free days compared with usual care alone.

Eptinezumab for preventing migraine TA871

Recommendations

Eptinezumab is **recommended** as an option for preventing migraine in adults, only if:

- they have 4 or more migraine days a month
- at least 3 preventive drug treatments have failed and
- the company provides it according to the commercial arrangement.

Stop eptinezumab after 12 weeks of treatment if:

- in episodic migraine (fewer than 15 headache days a month), the frequency does not reduce by at least 50%
- in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine), the frequency does not reduce by at least 30%.

If people with the condition and their clinicians consider eptinezumab to be 1 of a range of suitable treatments (including erenumab, fremanezumab and galcanezumab), discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

These recommendations are not intended to affect treatment with eptinezumab 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

Migraine is primarily a headache disorder manifesting as recurring attacks usually lasting between 4 and 72 hours involving throbbing head pain of moderate to severe intensity. It is often accompanied by nausea, sometimes vomiting, sensitivity to light, sensitivity to sounds, and/or other sensory stimuli. Migraine can have significant impacts on quality of life and ability to carry out normal activities. Some people can have warning symptoms called an aura, before the start of a headache. Factors that can trigger attacks in people susceptible to migraines include stress, change in sleep pattern, overtiredness, menstruation, consumption of caffeine or alcohol, climatic conditions and use of visual display units.

Migraine is on a continuum and it is possible for people to move between episodic and chronic migraine.

There are 3 broad approaches to managing migraine: lifestyle and trigger management, acute treatments and preventive treatments. Preventive treatment of migraines can take many forms including nutritional supplements, lifestyle alterations such as increased exercise and avoidance of migraine triggers. It can also include medications, which are generally considered for people depending on their disease burden and frequency of attacks.

CG150 recommends offering topiramate or propranolol and considering amitriptyline, for preventing migraine according to the person's preference, comorbidities and risk of adverse events.

TA764, TA682 and TA659 recommend fremanezumab, erenumab and galcanezumab respectively for preventing migraine in adults who experience 4 or more migraine days per month and at least 3 preventive drug treatments have failed. TA260 recommends botulinum toxin type A for preventing headaches in adults with chronic migraine that has not responded to at least 3 prior pharmacological prophylaxis therapies and whose condition is appropriately managed for medication overuse.

Eptinezumab is a humanised monoclonal antibody. It inhibits the action of calcitonin gene-related peptide (CGRP) which is believed to transmit signals that can cause severe pain. Eptinezumab is administered every 12 weeks by intravenous infusion.

Financial Factors

This technology is commissioned by ICBs.

NICE do not expect this guidance to have a significant impact on resources. This is because eptinezumab is another treatment option that works in a similar way to other calcitonin gene-related peptide (CGRP) inhibitors but is administered as an infusion into a vein. NICE do not think practice will change substantially as a result of this guidance. Therefore, the overall incremental cost of treatment is low.

NICE estimate that in Devon, 106 people with episodic migraine will be eligible for treatment and 10 of these will access CGRPs or BOTx. NICE estimate that in Devon. 3,616 people with chronic migraine will be eligible for treatment and 333 of these will access CGRP inhibitors.

Highly Specialised Technology Guidance (HSTs)

Asfotase alfa for treating paediatric-onset hypophosphatasia HST23

This guidance updates and replaces HST6 (published August 2017).

Recommendations

Asfotase alfa is **recommended** as an option for treating paediatric-onset hypophosphatasia if the person's symptoms started before or at birth (perinatal onset) or between the ages of 0 and 6 months (infantile onset). It is also recommended for people whose symptoms started between the ages of 6 months and 17 years (juvenile onset) only if:

- they are aged 1 year to 4 years and have:
    - not reached expected developmental gross motor milestones for their age or
    - continuing or recurring significant musculoskeletal pain that affects daily activities and quality of life, and has not improved after 2 different types of painkiller recommended by a national pain specialist
- they are aged 5 years to 18 years and have:
    - limited mobility assessed by a specialist using the modified Bleck Ambulation Efficiency Score and a Bleck score between 1 and 6 or
    - continuing or recurring significant musculoskeletal pain that affects daily activities and quality of life, and has not improved after 2 different types of painkiller recommended by a national pain specialist

- they are over 18 years and have 2 or more of the following:
    - current fractures with a history of non-traumatic, recurring or non- or poorly healing fractures
    - limited mobility assessed by a specialist using the modified Bleck Ambulation Efficiency Score and a Bleck score between 1 and 6
    - continuing or recurring significant musculoskeletal pain that affects daily activities and quality of life and has not improved after 2 different types of painkiller recommended by a national pain specialist.

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

The Technology

Hypophosphatasia is a genetic disorder caused by mutations in the TNSALP gene which reduce the activity of the enzyme tissue nonspecific alkaline phosphatase. Over 375 different mutations of this gene leading to hypophosphatasia have been identified. The reduction of this enzyme's activity disrupts mineralisation, a process in which calcium and phosphorous are deposited in developing bones and teeth. This leads to ricket-like symptoms, softening and weakening of the bones, bone deformity and a greater incidence of fractures. Fractures are particularly common in adults but less common in children. Hypophosphatasia can also lead to generalised seizures because of vitamin B6 deficiency, as well as renal and respiratory complications.

The signs and symptoms of hypophosphatasia vary widely and can appear anytime from before birth to adulthood. Six clinical forms are currently recognised:

1. perinatal (lethal)
2. perinatal (benign [non-lethal])
3. infantile (where symptoms start within 6 months after birth)
4. childhood
5. adult
6. odontohypophosphatasia (which only affects the teeth).

The most severe hypophosphatasia tends to present before birth and in early infancy. Infants with hypophosphatasia are born with short limbs, craniosynostosis and soft skull bones, vitamin B6-responsive seizures and an abnormally shaped chest which can lead to further complications. Additional complications in infancy include poor feeding and a failure to gain weight, respiratory problems and high levels of calcium in the blood, which can lead to recurrent vomiting and kidney problems. These complications can be life threatening.

Infants who present with hypophosphatasia in the first 6 months of life have a high mortality rate, around half of infants dying within the first year of life primarily due to respiratory failure. Hypophosphatasia that manifests later in childhood or in adults is typically less severe than hypophosphatasia manifesting in infancy.

Children may have short stature with bowed legs or knock knees, enlarged wrist and ankle joints, and an abnormal skull shape causing musculoskeletal pain, fatigue, exhaustion and decreased mobility. Adult forms of hypophosphatasia are characterised by a softening of the bones, premature loss of secondary (adult) teeth and increased risk of fractures in the foot and thigh bones, bone pain, joint pain, decreased mobility, fatigue, exhaustion and inflammation. Physical symptoms can severely impact quality of life.

Diagnosis is made on the basis of physical and radiographic findings consistent with hypophosphatasia and low or abnormal serum alkaline phosphatase. There is no standardised diagnostic algorithm. There is currently no treatment for hypophosphatasia. Medical management is aimed at monitoring and alleviating symptoms and decreasing morbidity. Vitamin B6 may also be given to reduce seizures.

Asfotase alfa is a recombinant fusion protein that includes the catalytic domain of human tissue non-specific alkaline phosphatase and a peptide that targets the enzyme to bone. It is a targeted enzyme replacement therapy designed to restore the regulation of metabolic processes in the bones and teeth and reduce complications of dysregulated bone mineral metabolism. It is administered by subcutaneous injection.

Financial Factors

This technology is commissioned by NHS England.

In perinatal- or infantile-onset hypophosphatasia, asfotase alfa is likely to increase how long people live before needing a ventilator and how long people live overall compared with best supportive care. In juvenile-onset hypophosphatasia, asfotase alfa is likely to improve outcomes including mobility, pain and health-related quality of life compared with best supportive care.

In perinatal- and infantile-onset populations, the cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources, therefore, asfotase alfa is recommended for all people in these groups.

In juvenile-onset populations, the cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources when symptoms are more severe, therefore, asfotase alfa is only recommended for juvenile-onset hypophosphatasia with severe symptoms.

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

NICE Guidelines (NGs)

Lung cancer: diagnosis and management NG122 (UPDATE)

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 2023: NICE added the technology appraisal guidance on mobocertinib (TA855) to the systemic anti-cancer therapy treatment pathways for advanced non-small-cell lung cancer.

NICE Rapid COVID-19 Guidelines

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

This guideline covers the management of COVID-19 for babies, children, young people and adults in all care settings. It brings together our existing 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.

March 2023: In the section on therapeutics for COVID-19 NICE updated recommendations on baricitinib and remdesivir, updated recommendations on casirivimab plus imdevimab, nirmatrelvir plus ritonavir, and tocilizumab and replaced the recommendations on neutralising monoclonal antibodies and sarilumab with recommendations on sotrovimab and tocilizumab, in line with TA878 (published March 2023).

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)

Percutaneous transluminal renal sympathetic denervation for resistant hypertension IPG754

This guidance replaces IPG418 (published January 2012).

Recommendations

Percutaneous transluminal renal sympathetic denervation for resistant hypertension should only be used with **special arrangements** for clinical governance, consent, and audit or research.

Clinicians wanting to do percutaneous transluminal renal sympathetic denervation for resistant hypertension should:

- Inform the clinical governance leads in their healthcare organisation.
- Ensure that people (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Take account of NICE's guidance on shared decision making (NG197), and NICE's information for the public.
- Audit and review clinical outcomes of everyone 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 everyone having this procedure.
- Regularly review data on outcomes and safety for this procedure.

Further research should include randomised controlled trials or analysis of registry data. It should report details of patient selection, technique used and long-term outcomes.

Patient selection should be done by a multidisciplinary team including experts in managing hypertension and potential complications, and clinicians with specific training in this procedure.

The Condition

Hypertension is a major risk factor for cardiovascular disease and chronic kidney disease. Hypertension can be primary or secondary. Primary hypertension does not have a single known cause, whereas secondary hypertension develops because of an underlying medical condition or disease. Hypertension is considered resistant if it is not controlled after treatment with at least 3 antihypertensive medications from different classes.

NICE's guideline on hypertension in adults (NG136) describes diagnosing and managing hypertension, including resistant hypertension. Current treatments for hypertension include lifestyle modifications and antihypertensive medications. Blood pressure and treatment are regularly monitored, and treatment is adjusted as needed. For resistant hypertension, additional medications and device-based antihypertensive therapies (for example renal denervation and carotid baroreceptor stimulation) can be considered.

The Procedure

This procedure is usually done using local anaesthesia, with sedation and anticoagulation. A catheter is introduced through the femoral artery and advanced into each renal artery under fluoroscopic guidance. The catheter is connected to a generator which delivers radiofrequency or ultrasound energy from the distal to proximal end of each renal artery. This ablates the renal nerves leading to the kidney, with the aim of disrupting neurogenic reflexes involved in blood pressure control. There are different systems with different technologies in use for renal sympathetic denervation.

Endoluminal gastroplication for gastro-oesophageal reflux disease IPG753

This guidance replaces IPG404 (published July 2011).

Recommendations

Evidence on the safety of endoluminal gastroplication for gastro-oesophageal reflux disease is adequate. However, evidence on its efficacy is inadequate in quality, particularly in terms of patient selection and long-term outcomes. Therefore, this procedure should be used only in **research**.

Further research should include suitably powered randomised controlled trials with details of patient selection, physiological measurements, and long-term outcomes.

The Condition

Gastro-oesophageal reflux disease (GORD) is a common condition caused by failure of the sphincter mechanism at the lower end of the oesophagus. Symptoms of GORD can be broadly grouped into those directly related to reflux episodes, such as heartburn, regurgitation, chest pain and nausea, and those symptoms caused by complications of reflux disease, including problems swallowing (dysphagia) and respiratory symptoms. Repeat episodes of GORD can damage the

lining of the oesophagus and lead to oesophageal ulceration, oesophageal stricture, and Barrett's oesophagus.

NICE's guideline on the investigation and management of gastro-oesophageal reflux disease and dyspepsia in adults (CG184) makes recommendations for treatment. The standard treatments for symptomatic GORD are lifestyle modification and drug therapy. Drug therapy includes acid-lowering agents such as H2 receptor antagonists and proton pump inhibitors (PPIs). People with reflux symptoms that do not respond to medical treatment or who develop intolerance to medication may have anti-reflux surgery.

Surgical or laparoscopic fundoplication may be used and minimally invasive treatments such as endoscopic radiofrequency ablation or endoscopic injection of bulking agents are available.

The Procedure

Different devices have been used for this procedure and exact details of the technique vary. The procedure is usually done with the patient under general anaesthesia. An endoscopic fastening device is inserted through the mouth and into the stomach, along with an endoscope for constant visualisation. The device is used to attach the fundus to the anterior and left lateral wall of the distal oesophagus slightly above the oesophagogastric junction.

With 1 of the devices, polypropylene fasteners are delivered through apposed layers of oesophageal and fundus tissue to anchor the repair. About 20 fasteners are implanted during the procedure to create a full thickness, partial circumference, gastro-oesophageal fundoplication. The aim is to recreate a valve and form a barrier to reflux. Endoluminal gastroplication for gastro-oesophageal reflux disease aims to reduce the morbidity associated with open or laparoscopic fundoplication.

Medical Technologies Guidance (MTGs)

None published this month.

Diagnostics Guidance (DGs)

None published this month.

Health Technology Evaluations (HTE)

Genedrive MT-RNR1 ID Kit for detecting a genetic variant to guide antibiotic use and prevent hearing loss in babies: early value assessment HTE6

Recommendations

The Genedrive MT-RNR1 ID Kit **can be used** while further evidence is generated as an option for detecting the genetic variant m.1555A>G to guide antibiotic (aminoglycoside) use and prevent hearing loss in newborns who are being considered for treatment with aminoglycosides.

Healthcare professionals should tell parents about the possible implications of positive test results for their baby and their family at an appropriate time and give support and information.

Positive results should be confirmed by laboratory testing.

The recommendation is conditional on further evidence being generated on:

- how the test affects time to antibiotics
- how the test result affects antibiotic prescribing decisions
- the technical performance and accuracy of the test.

The Technology

Neonatal bacterial infection is a significant cause of death and illness in newborn babies. NICE's guideline on neonatal infection (NG195) recommends treating suspected early-onset infection in babies with benzylpenicillin with gentamicin and that this should be given as soon as possible and always within 1 hour of the decision to treat.

Babies with a genetic variant in the mitochondrial MT-RNR1 gene (m.1555A>G) are at an increased risk of profound bilateral deafness caused by damage to the ear (ototoxicity) if they have treatment with the aminoglycoside family of antibiotics, which includes gentamicin.

Currently available laboratory testing for m.1555A>G cannot provide results quickly enough to inform antibiotic prescribing in babies with a suspected infection that needs to be treated within 1 hour.

The Genedrive MT-RNR1 ID Kit is a qualitative in vitro molecular diagnostic test for detecting the MT-RNR1 m.1555A>G variant. It is intended to be used by healthcare professionals in a near patient setting using a buccal swab sample. The company says that the kit provides a result within about 26 minutes. This could help ensure that babies who have the m.1555A>G variant have alternative antibiotics and avoid irreversible, lifelong hearing loss caused by ototoxicity.

Financial Factors

This technology is commissioned by NHS England.

NICE state that depending on current local practice, areas which may impact resources include:

- Costs of the technologies (Genedrive system and Bluetooth printer). Upfront costs of implementing the Genedrive test should be carefully considered by providers and commissioners. It noted that where possible, purchase options not associated with large capital investment costs should be explored for any conditional recommendation and real-world data collection.
- Staff workload may be increased if all babies who are going to be treated with antibiotics, or who are likely to be treated, are offered the point-of-care test. Staff will also need to be trained on how to use the test.

Implementing the guidance may have the following benefits:

- Preventing hearing loss will mean newborn babies will not require lifelong use of cochlear implants, would not experience the lifelong impacts of hearing loss, and would not require surgeries associated with treating severe or profound hearing loss.
- The costs associated with treating people with damage to their ears caused by antibiotics could be reduced.
- Better health outcomes and care experience.
- Hospitals currently not following recommendations from the NICE guideline on neonatal infection (NG195) to use benzylpenicillin with gentamicin because of the risk of deafness now have a way to manage this risk and become compliant.

ProKnow cloud-based system for radiotherapy data storage, communication and management: early value assessment HTE5

Recommendations

ProKnow **can be used** while further evidence is generated. This includes use of all 3 ProKnow modules:

- ProKnow DS – a database used for importing, analysing and storing patient data
- ProKnow CA – a contouring accuracy tool to practise, study and improve anatomical contouring
- ProKnow PS – a platform for creating and comparing radiotherapy treatment plans.

Further evidence should be generated on:

- the impact on quality assurance for radiotherapy treatment planning, including surrogate, qualitative, and quantitative measures such as:
    - changes to radiotherapy treatment plans
    - dose prescription changes
    - dose volume distributions
    - scorecards.
- healthcare professionals' experience of using ProKnow, including usability
- ease of retrieving and storing patient data
- radiotherapy treatment planning time (including difference in time to start of treatment)
- changes in the number of internal and external peer reviews
- the impact on staffing and treatment planning resources
- the impact on clinical oncology training for healthcare professionals who contribute to radiotherapy treatment planning
- the ability for data linkage to national registries (including change in the number of treatment plans added to national registries)
- changes in inequality of access.

The Technology

ProKnow is a system used in radiotherapy offering a cloud-based data repository, communication tools and analytics software. The technology is used for people having image-guided 3D planned radiotherapy and allows centres to compare radiotherapy plans and collect images and dosimetric data.

ProKnow can be used to view treatment plan information, visualise images and the structures they contain and inspect dosimetric data, such as dose volume histograms and dose distributions. Custom treatment plan quality metrics can be extracted, such as data on local radiotherapy control, survivorship, and side effects. ProKnow allows teams to work together to mark the areas of interest on images, in a process known as contouring. This can be done from any computer without the need for a dedicated workstation, so it allows collaboration and peer review of treatment plans between centres that are using ProKnow. At present, ProKnow is not used for brachytherapy, radionuclide therapy or 4D datasets.

The comparator is standard care, which varies across centres. Most radiotherapy departments have local radiotherapy protocols specifying the technique and dose for each tumour site. Treatment planning involves clinical oncologists, radiographers, dosimetrists and medical physicists, with the qualified clinical oncologist taking overall responsibility for planning and final sign-off. Peer review is an important step in treatment planning to ensure the proposed plan will deliver safe and effective treatment, and to identify issues that could affect quality of care. The peer review process is also intended to improve standardisation and reduce variation in practice and improve knowledge sharing between healthcare professionals involved in treatment planning.

Financial Factors

This technology is commissioned by NHS England.

NHS England commissioned a pilot of ProKnow (including all 3 modules) in March 2022 across 49 specialist cancer centres, with funding provided until March 2025. The pilot is part of the Radiotherapy Transformation Programme, aiming to improve the quality and reduce variability of radiotherapy service delivery. Data collected by NHS radiotherapy centres using ProKnow under the NHSE-commissioned pilot scheme will help generate evidence.

Using ProKnow within the NHS may enable greater adherence to national guidance and local peer review protocols. It may also result in higher-quality radiotherapy treatment plans because of the increased number of peer reviews performed, including re-review (either internally or externally). It may also increase flexibility to peer review as it allows peer review collaboration across radiotherapy services.

Using ProKnow may also improve standardisation and training across radiotherapy services. It may support wider adoption of more complex treatment modalities and improve outcomes at smaller radiotherapy sites by facilitating access to oncologists across radiotherapy services. However, clinical experts noted that ProKnow is unlikely to have any direct effect on patient outcomes but facilitates peer review and training, which may have a direct effect. Also, the committee concluded that there is very limited evidence to support the benefits of ProKnow.

Experts highlighted that the key parameters impacting resource use are the technology cost and the length of peer review activity. The cost of ProKnow is commercial in confidence.

Due to a lack of robust data on current practice and the variation across organisations and services, the size of the resource impact will need to be determined at a local level.

CaRi-Heart for predicting cardiac risk in suspected coronary artery disease early value assessment HTE4

Recommendations

CaRi-Heart is **not recommended** for use in the NHS while further evidence is generated. It should only be used in research to predict cardiac risk in people with suspected coronary artery disease (CAD), while treatment strategies to reduce coronary inflammation and cardiac death are identified.

Further research is recommended on:

- how clinical outcomes might change for people with suspected CAD who have had CaRi-Heart testing and appropriate treatment
- how CaRi-Heart results affect clinical decision making compared with UK standard clinical practice
- the costs to the NHS of using CaRi-Heart
- how well CaRi-Heart predicts cardiac risk to validate it in a UK population; in particular, data should be generated in the following groups: women, people from different ethnic backgrounds, and people who do not have CAD identified on CT coronary angiography (CTCA).

The Technology

Coronary artery disease (CAD) affects the arteries that supply blood to the heart muscle. Fatty plaques can build up on the walls of these arteries, narrowing them. This reduces blood flow and can result in angina and heart attack. Heart attack risk is also linked to inflammation in the wall of the artery. This can cause plaque to form and rupture, which can block an artery, leading to acute coronary syndrome or sudden death.

In current standard practice people with recent-onset chest pain are referred to have a CTCA, which is non-invasive and visualises coronary arteries to identify abnormalities such as plaque build-up and narrowing. But CTCA scans do not identify inflammation in coronary arteries.

CaRi-Heart can identify inflammation and its extent, by analysing images from CTCA scans. It aims to identify risk of cardiac mortality with greater discrimination than the currently used clinical risk-factor based models and improve outcomes by personalising prevention and treatment.

Financial Factors

This technology is commissioned by ICBs.

Clinical evidence shows that CaRi-Heart improves cardiac risk prediction compared with using a model based on traditional clinical risk factors, but it is uncertain how CaRi-Heart would perform compared with UK standard clinical practice.

CaRi-Heart's cost to the NHS is unknown because the company has not yet specified the NHS price and no data was identified on the costs or resource use associated with implementing CaRi-Heart. Based on the list price and the number of people who could be offered it, the costs to the NHS could be substantial if it were implemented while evidence is generated to demonstrate its value.

Due to the uncertainty around its benefits and costs, CaRi-Heart cannot be recommended for routine use in the NHS. Because it might more accurately identify people at risk of heart attack or cardiac death than the standard risk assessment alone, therefore, further research is recommended to see if CaRi-Heart testing can lead to effective treatment strategies to improve outcomes for people with cardiac risk.

NICE Quality Standards

Type 2 diabetes in adults QS209

This quality standard updates and replaces QS6 (published March 2011).

This quality standard covers prevention of type 2 diabetes in adults (aged 18 and over) and care and treatment for adults with type 2 diabetes. It describes high-quality care in priority areas for improvement. It does not cover diabetes in children and young people, diabetes in pregnancy and other types of diabetes in adults. These are covered by other quality standards.

Type 1 diabetes in adults QS208

This quality standard updates and replaces QS6 (published March 2011).

This quality standard covers care and treatment for adults (aged 18 and over) with type 1 diabetes. It describes high-quality care in priority areas for improvement. It does not cover diabetes in children and young people, diabetes in pregnancy or other types of diabetes in adults. These are covered by other quality standards.

Acute kidney injury QS76 (UPDATE)

This quality standard covers preventing, detecting and managing acute kidney injury in adults, young people and children. It describes high-quality care in priority areas for improvement.

March 2023: NICE updated and replaced the previous version published in 2014. The topic was identified for update following discussion with NHS England's Renal Services Transformation Programme and the UK Kidney Association, which identified changes in the priority areas for improvement.

Current NICE Consultations

Title/link	End date of consultation
Neonatal infection update	03/04/2023
Atopic eczema in under 12s: diagnosis and management (update)	04/04/2023
Stroke and transient ischaemic attack in over 16s	11/04/2023
Targeted temperature management to improve neurological outcomes after cardiac arrest	18/04/2023
Aortic valve reconstruction with glutaraldehyde-treated autologous pericardium	18/04/2023
Metastatic spinal cord compression in adults: risk assessment, diagnosis and management	19/04/2023
Suspected Sepsis: recognition, diagnosis and early management (update)	21/04/2023
Percutaneous deep venous arterialisation for chronic limb-threatening ischaemia	24/04/2023