NHS
Devon
Clinical Commissioning Group

NICE Update Bulletin: July 2021

Hyperlinks to the relevant NICE web page are included below.

NICE rapid COVID-19 guidelines

COVID-19 rapid guideline: vaccine-induced immune thrombocytopenia and thrombosis (VITT) NG200

This guideline covers vaccine-induced immune thrombocytopenia and thrombosis (VITT), a syndrome which has been reported in rare cases after COVID-19 vaccination. VITT may also be called vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) or thrombotic thrombocytopenic syndrome (TTS). Because VITT is a new condition, there is limited evidence available to inform clinical management, identification and management of the condition is evolving quickly as the case definition becomes clearer. This guideline was produced to support clinicians to diagnose and manage this newly recognised syndrome.

COVID-19 rapid guideline: haematopoietic stem cell transplantation NG164 (update)

The purpose of this guideline is to maximise the safety of patients who need haemopoietic stem cell transplantation and make the best use of NHS resources, while protecting staff from infection.

July 2021: NICE made changes to recommendations on testing patients for viruses, including SARS-CoV-2 and repeating respiratory review in patients who test positive for, or are suspected of having COVID-19.

Technology Appraisals (TAs)

Secukinumab for treating non-radiographic axial spondyloarthritis TA719

Recommendations

Secukinumab is **recommended** as an option for treating active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) that is not controlled well enough with non-steroidal anti-inflammatory drugs (NSAIDs) in adults. It is recommended only if:

- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough and

- the company provides secukinumab according to the commercial arrangement.

Assess response to secukinumab after 16 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as:

- a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and
- a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more.

Take into account any communication difficulties, or physical, psychological, sensory or learning disabilities that could affect responses to the BASDAI and spinal pain VAS questionnaires, and make any appropriate 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.

The technology

Axial spondyloarthritis belongs to a clinically heterogeneous group of inflammatory rheumatologic diseases which share common genetic, histological and clinical features (also including psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondyloarthritis).

Axial spondyloarthritis involves inflammation of the sacroiliac joints and spine. If inflammation is visible on x-ray (as erosions, thickening of the bone, or fusion of joints), the disease is classified as radiographic axial spondyloarthritis (also known as ankylosing spondylitis). If x-rays of the sacroiliac joints and spine are normal, but there are other objective signs of inflammation (elevated C-reactive protein or evidence on magnetic resonance imaging) the disease is classified as non-radiographic axial spondyloarthritis.

Conventional therapy for non-radiographic axial spondyloarthritis includes anti-inflammatory treatment with NSAIDs and physiotherapy.

Secukinumab is indicated for the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) in adults who have responded inadequately to NSAIDs. It is administered subcutaneously.

Financial factors

This technology is commissioned by CCGs.

NICE does not expect this guidance to have a significant impact on resources because the technology is a further treatment option, the overall cost of treatment will be similar, and they do not think practice will change substantially as a result of this guidance.

Ixekizumab for treating axial spondyloarthritis TA718

Recommendations

Ixekizumab is **recommended** as an option for treating active ankylosing spondylitis that is not controlled well enough with conventional therapy, or active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) that is not controlled well enough with non-steroidal anti-inflammatory drugs (NSAIDs), in adults. It is recommended only if:

- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough, and
- the company provides ixekizumab according to the commercial arrangement.

Assess response to ixekizumab after 16 to 20 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as:

- a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and
- a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more.

Take into account any communication difficulties, or physical, psychological, sensory or learning disabilities that could affect responses to the BASDAI and spinal pain VAS questionnaires, and make any appropriate adjustments.

These recommendations are not intended to affect treatment with ixekizumab 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

Axial spondyloarthritis belongs to a clinically heterogeneous group of inflammatory rheumatologic diseases which share common genetic, histological and clinical features (also including psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondyloarthritis).

Axial spondyloarthritis involves inflammation of the sacroiliac joints and spine. If inflammation is visible on x-ray (as erosions, thickening of the bone, or fusion of joints), the disease is classified as radiographic axial spondyloarthritis (also known as ankylosing spondylitis). If x-rays of the sacroiliac joints and spine are normal, but there are other objective signs of inflammation (elevated C-reactive protein or evidence on magnetic resonance imaging) the disease is classified as non-radiographic axial spondyloarthritis.

Conventional therapy for axial spondyloarthritis includes anti-inflammatory treatment with NSAIDs and physiotherapy.

Ixekizumab is indicated for the treatment of adult patients with active ankylosing spondylitis [radiographic axial spondyloarthritis] who have responded inadequately to conventional therapy, and active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately to NSAIDs. Ixekizumab is administered by subcutaneous injection.

Financial factors

This technology is commissioned by CCGs.

NICE does not expect this guidance to have a significant impact on resources because the technology is a further treatment option, the overall cost of treatment will be similar, and they do not think practice will change substantially as a result of this guidance.

Duvelisib for treating relapsed follicular lymphoma after 2 or more systemic therapies *(terminated appraisal)* TA717

NICE is **unable to make a recommendation** on duvelisib for treating relapsed follicular lymphoma after 2 or more systemic therapies in adults because Secura Bio did not provide an evidence submission. They will review this decision if the company decides to make a submission.

Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency TA716

Recommendations

Nivolumab plus ipilimumab is **recommended**, within its marketing authorisation, as an option for treating metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency after fluoropyrimidine-based combination chemotherapy. It is recommended only if the company provides nivolumab and ipilimumab according to the commercial arrangement.

The technology

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). Metastatic colorectal cancer refers to disease that has spread beyond the large intestine and nearby lymph nodes. This type of cancer often first spreads to the liver, but metastases may also occur in other parts of the body including the lungs, brain and bones.

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. It is administered intravenously.

Ipilimumab is a fully human antibody that binds to and blocks the activity of cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), thereby sustaining the immune attack on cancer cells. It is administered intravenously.

Financial factors

This technology is commissioned by NHS England.

The number of people who are eligible for treatment is expected to be affected by the positive recommendation for Pembrolizumab in TA709 because a large proportion of people in the incident population will now receive pembrolizumab as first line treatment rather than a fluoropyrimidine-based combination chemotherapy. There will be an initial prevalent population who did not receive pembrolizumab at first line and will become eligible for treatment with nivolumab plus ipilimumab.

NICE estimates an annual incidence of 65 people in England with previously treated metastatic colorectal cancer with high MSI or MMR deficiency will be eligible for treatment with nivolumab plus ipilimumab each year. Of these, 48 people will start treatment from year 2022/23 onwards once uptake has reached 73% (company submission).

A further 325 people in the prevalent population will progress to second line treatment with 163 people assumed to start second line treatment in 2021/22 and a further 163 people assumed to start second line treatment in 2022/23. It is estimated that there will be an uptake of 37% in 2021/22 and 119 people will start treatment in 2022/23 once uptake has reached 73%.

Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed TA715

Recommendations

Adalimumab, etanercept and infliximab, all with methotrexate, are **recommended** as options for treating active rheumatoid arthritis in adults, only if:

- intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs) has not controlled the disease well enough and
- disease is moderate (a disease activity score [DAS28] of 3.2 to 5.1) and
- the companies provide adalimumab, etanercept and infliximab at the same or lower prices than those agreed with the Commercial Medicines Unit.

Adalimumab and etanercept can be used as monotherapy when methotrexate is contraindicated or not tolerated, when the criteria above are met.

Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. If this initial response is not maintained at 6 months, stop treatment.

If more than one treatment is suitable, start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.

Take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any appropriate adjustments.

Abatacept with methotrexate is not recommended, within its marketing authorisation, for treating moderate active rheumatoid arthritis in adults when 1 or more DMARDs has not controlled the disease well enough.

The technology

Rheumatoid arthritis is an inflammatory autoimmune disease that typically affects the synovial tissue of the small joints of the hands and feet but can affect any synovial joint, causing swelling, stiffness, pain and progressive joint destruction. It is a systemic disease and can affect the whole body, including the lungs, heart and eyes. Rheumatoid arthritis is usually a chronic relapsing condition which has a pattern of

flare-ups followed by periods of lower disease activity; however, for some people, the disease is constantly progressive.

Severity of disease can be classified into 4 categories, based on the disease activity score (DAS28) scoring system. A DAS28 greater than 5.1 indicates high disease activity or severe disease, between 3.2 and 5.1 indicates moderate disease activity, less than 3.2 indicates low disease activity, and less than 2.6 indicates disease remission.

There is no cure for rheumatoid arthritis and treatment aims to improve quality of life and to prevent or reduce joint damage. The main aim of management in early disease is to suppress disease activity and induce disease remission, prevent loss of function, control joint damage, maintain pain control and enhance self-management.

Adalimumab in combination with methotrexate, is indicated for the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to DMARDs including methotrexate has been inadequate. Adalimumab can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

Etanercept in combination with methotrexate, is indicated for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to DMARDs, including methotrexate (unless contraindicated), has been inadequate. Etanercept can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

Infliximab in combination with methotrexate, is indicated for the reduction of signs and symptoms as well as the improvement in physical function in: adult patients with active disease when the response to DMARDs, including methotrexate, has been inadequate.

Abatacept, in combination with methotrexate, is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who responded inadequately to previous therapy with one or more DMARDs including methotrexate (MTX) or a tumour necrosis factor (TNF)-alpha inhibitor.

Financial factors

This technology is commissioned by CCGs.

The guidance is an update of TA375 and increases the population eligible for treatment to include people with moderate disease.

Until publication of this guidance, filgotinib was the only advanced treatment available for moderate rheumatoid arthritis. Filgotinib is a targeted disease-modifying antirheumatic drug (tsDMARD). The technologies recommended for use in this guidance offer new advanced treatment options for moderate rheumatoid arthritis and are biologic DMARDs (bDMARDs).

NICE estimates that 593 people in Devon with moderate rheumatoid arthritis who respond inadequately to, or are intolerant of, (two or more) conventional DMARDs are eligible for treatment. Of these, 178 people are expected to receive bDMARDs or tsDMARDs once uptake has reached 30%.

149 people in Devon are estimated to receive adalimumab, etanercept or infliximab from year 2023/24 onwards once uptake has reached 84%. This guidance will lead to the overall proportion of the eligible population receiving bDMARDs or tsDMARDs to increase from 15% to 30%.

Dasatinib for treating Philadelphia-chromosome-positive acute lymphoblastic leukaemia *(terminated appraisal)* TA714

NICE is **unable to make a recommendation** on dasatinib for Philadelphia-chromosome-positive acute lymphoblastic leukaemia in children and adults because Bristol Myers Squibb did not provide an evidence submission. They will review this decision if the company decides to make a submission.

Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy TA713

This guidance updates and replaces NICE technology appraisal guidance 484 on nivolumab for previously treated non-squamous non-small-cell lung cancer, which was available through the Cancer Drugs Fund.

Recommendations

Nivolumab is **recommended** as an option for treating locally advanced or metastatic non-squamous non-small-cell lung cancer (NSCLC) in adults after chemotherapy, only if:

- their tumours are PD-L1 positive, and
- it is stopped at 2 years of uninterrupted treatment, or earlier if their disease progresses, and
- they have not had a PD-1 or PD-L1 inhibitor before.

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

The technology

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma.

Most lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest or to other parts of the body. The aims of therapy are to prolong survival and improve quality of life.

Nivolumab is a monoclonal antibody that targets 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.

Financial factors

These technology is commissioned by NHS England.

The guidance constitutes a further review of additional evidence collected as part of the Cancer Drugs Fund managed access agreement for nivolumab for locally advanced or metastatic PD-L1 positive non-squamous NSCLC (TA484).

NICE does not expect this to have a significant impact on resources. Around 800 people are estimated to be eligible for second-line treatment each year. Based on clinical expert opinion, and in line with TA531, the majority of these people would have already received immunotherapy (PD-1 or PD-L1 inhibitor) at first line. Therefore only a small number of people (likely to be less than 100) would receive nivolumab at this stage in the clinical pathway.

Nivolumab has a commercial arrangement (simple discount patient access scheme).

Enzalutamide for treating hormone-sensitive metastatic prostate cancer TA712

Recommendations

Enzalutamide plus androgen deprivation therapy (ADT) is **recommended**, within its marketing authorisation, as an option for treating hormone-sensitive metastatic prostate cancer in adults. It is only recommended if the company provides enzalutamide according to the agreed 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.

Enzalutamide 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. Enzalutamide is administered orally.

Financial factors

This technology is commissioned by NHS England.

NICE estimates that 10,225 people in England with hormone-sensitive metastatic prostate cancer are eligible for treatment with enzalutamide each year

3,070 people will start enzalutamide each year from year 2022/23 onwards once uptake has reached 30%. Around 6,140 people will be receiving subsequent years treatment with enzalutamide by 2024/25.

Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation TA355 (update)

July 2021: NICE updated recommendation 1.2 to include the other anticoagulants approved by NICE.

Recommendations

Edoxaban is recommended, within its marketing authorisation, as an option for preventing stroke and systemic embolism in adults with non-valvular atrial fibrillation with one or more risk factors, including:

- congestive heart failure

- hypertension
- diabetes
- prior stroke or transient ischaemic attack
- age 75 years or older.

Decide whether to start treatment with edoxaban after an informed discussion with the person about its risks and benefits compared with warfarin, apixaban, dabigatran etexilate and rivaroxaban. For people taking warfarin, consider the potential risks and benefits of switching to edoxaban taking into account their level of international normalised ratio (INR) control.

The technology

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia and its main characteristic is an erratic and rapid heartbeat. AF leads to deterioration in the mechanical function of the atria and prevents complete expulsion of blood. Stasis of blood in the atria predisposes to thrombus (blood clot) formation and leads to an increased risk of systemic thromboembolism and stroke.

The risk of stroke in people with AF can be reduced with antithrombotic treatment. The choice of antithrombotic treatment in any individual is based on a balance of the benefits of treatment in terms of a reduction in the risk of stroke and other thromboembolic events versus the increased risk of bleeding associated with anticoagulation or antiplatelet therapy.

Edoxaban is an anticoagulant that directly inhibits factor X (factor Xa), which is a key component in the formation of blood clots. It is administered orally.

Financial factors

This technology is commissioned by CCGs.

NICE has not produced an updated resource impact report in respect of this updated guidance.

Apixaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation TA275 (update)

July 2021: NICE updated recommendation 1.2 to include the other anticoagulants approved by NICE.

Recommendations

Apixaban is recommended as an option for preventing stroke and systemic embolism within its marketing authorisation, that is, in people with non-valvular atrial fibrillation with 1 or more risk factors such as:

- prior stroke or transient ischaemic attack
- age 75 years or older
- hypertension
- diabetes mellitus
- symptomatic heart failure.

Decide whether to start treatment with apixaban after an informed discussion with the person about its risks and benefits compared with warfarin, dabigatran etexilate, edoxaban and rivaroxaban. For people taking warfarin, consider the potential risks and benefits of switching to apixaban taking into account their level of international normalised ratio (INR) control.

The technology

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia and its main characteristic is an erratic and rapid heartbeat. AF leads to deterioration in the mechanical function of the atria and prevents complete expulsion of blood. Stasis of blood in the atria predisposes to thrombus (blood clot) formation and leads to an increased risk of systemic thromboembolism and stroke.

The risk of stroke in people with AF can be reduced with antithrombotic treatment. The choice of antithrombotic treatment in any individual is based on a balance of the benefits of treatment in terms of a reduction in the risk of stroke and other thromboembolic events versus the increased risk of bleeding associated with anticoagulation or antiplatelet therapy.

Apixaban is a direct oral factor Xa inhibitor, which prevents the formation of thrombin and fibrin, the key components in blood clot formation.

Financial factors

This technology is commissioned by CCGs.

NICE has not produced an updated resource impact report in respect of this updated guidance.

Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation TA256 (update)

July 2021: NICE updated recommendation 1.2 to include the other anticoagulants approved by NICE.

Recommendations

Rivaroxaban is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with non-valvular atrial fibrillation with one or more risk factors such as:

- congestive heart failure
- hypertension
- age 75 years or older
- diabetes mellitus
- prior stroke or transient ischaemic attack.

Decide whether to start treatment with rivaroxaban after an informed discussion with the person about its risks and benefits compared with warfarin, apixaban, dabigatran etexilate and edoxaban. For people taking warfarin, consider the potential risks and benefits of switching to rivaroxaban taking into account their level of international normalised ratio (INR) control.

The technology

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia and its main characteristic is an erratic and rapid heartbeat. AF leads to deterioration in the mechanical function of the atria and prevents complete expulsion of blood. Stasis of blood in the atria predisposes to thrombus (blood clot) formation and leads to an increased risk of systemic thromboembolism and stroke.

The risk of stroke in people with AF can be reduced with antithrombotic treatment. The choice of antithrombotic treatment in any individual is based on a balance of the benefits of treatment in terms of a reduction in the risk of stroke and other thromboembolic events versus the increased risk of bleeding associated with anticoagulation or antiplatelet therapy.

Rivaroxaban is an anticoagulant which acts by direct inhibition of activated factor X (factor Xa). Factor Xa is a key component in the formation of blood clots. It is administered orally.

Financial factors

This technology is commissioned by CCGs.

NICE has not produced an updated resource impact report in respect of this updated guidance.

Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation TA249 (update)

July 2021: NICE updated recommendation 1.2 to include the other anticoagulants approved by NICE.

Recommendations

Dabigatran etexilate is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular atrial fibrillation with one or more of the following risk factors:

- previous stroke, transient ischaemic attack or systemic embolism
- left ventricular ejection fraction below 40%
- symptomatic heart failure of New York Heart Association (NYHA) class 2 or above
- age 75 years or older
- age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension.

Decide whether to start treatment with dabigatran etexilate after an informed discussion with the person about its risks and benefits compared with warfarin, apixaban, edoxaban and rivaroxaban. For people taking warfarin, consider the potential risks and benefits of switching to dabigatran etexilate taking into account their level of international normalised ratio (INR) control.

The technology

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia and its main characteristic is an erratic and rapid heartbeat. AF leads to deterioration in the

mechanical function of the atria and prevents complete expulsion of blood. Stasis of blood in the atria predisposes to thrombus (blood clot) formation and leads to an increased risk of systemic thromboembolism and stroke.

The risk of stroke in people with AF can be reduced with antithrombotic treatment. The choice of antithrombotic treatment in any individual is based on a balance of the benefits of treatment in terms of a reduction in the risk of stroke and other thromboembolic events versus the increased risk of bleeding associated with anticoagulation or antiplatelet therapy.

Dabigatran etexilate is an orally administered prodrug (a drug that is administered in an inactive or less active form) which is converted to dabigatran after administration. Dabigatran is an anticoagulant that inhibits the formation of the thrombin enzyme. Thrombin converts fibrinogen into fibrin during the coagulation cascade and is the primary component of thrombus (blood clots). Dabigatran etexilate does not require anticoagulation monitoring.

Financial factors

This technology is commissioned by CCGs.

NICE has not produced an updated resource impact report in respect of this updated guidance.

Highly specialised technology guidance (HSTs)

Onasemnogene abeparvovec for treating spinal muscular atrophy HST15

Recommendations

Onasemnogene abeparvovec is **recommended** as an option for treating 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of type 1 SMA in babies, only if:

- they are 6 months or younger, or
- they are aged 7 to 12 months, and their treatment is agreed by the national multidisciplinary team.

It is only recommended for these groups if:

- permanent ventilation for more than 16 hours per day or a tracheostomy is not needed
- the company provides it according to the commercial arrangement.

For babies aged 7 to 12 months, the national multidisciplinary team should develop auditable criteria to enable onasemnogene abeparvovec to be allocated to babies in whom treatment will give them at least a 70% chance of being able to sit independently.

Onasemnogene abeparvovec is recommended as an option for treating pre-symptomatic 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene in babies. It is recommended only if the conditions in the managed access agreement are followed.

The technology

Spinal muscular atrophy (SMA) is a rare, progressive neuromuscular condition caused by a genetic mutation in the SMN1 gene on chromosome 5q. This causes a lack of survival motor neuron (SMN) protein, which causes motor neurones to malfunction, deteriorate and eventually die. People with the condition have a range of symptoms, including muscle weakness, and have worsening physical disability, mobility loss and respiratory dysfunction.

SMA can be grouped into 5 main types (types 0 to 4), based on the age of onset and the maximum motor function reached. Type 0 SMA, the most severe, affects babies before birth. The babies do not develop any motor skills and often survive for only a few weeks after birth. Babies with type 1 SMA generally develop symptoms before they are 6 months old. They are unable to sit or roll because of severe muscle weakness, which gets worse over time. The muscle weakness also affects swallowing and breathing, and typically results in death within 2 years. In type 2 SMA, the onset of symptoms is between 6 months and 18 months. People with this condition may be able to sit at diagnosis but are likely to lose this ability over time. However, progressive loss of motor function means they have a reduced life expectancy compared with the general population. In type 3 SMA, there are varying degrees of muscle weakness, which appear between 18 months and 10 years. People with this condition can have a normal lifespan, and walk or sit unaided at some point, but many lose mobility over time. Most people with type 2 SMA and a proportion of those with type 3 SMA will develop scoliosis for which surgery will eventually be needed. Type 4 SMA, the least severe, affects adults, who may have only mild motor impairment and a normal lifespan.

Onasemnogene abeparvovec is a gene therapy medicinal product that expresses the human survival motor neuron (SMN) protein. It is a non-replicating recombinant viral vector modified to contain the cDNA of the human SMN gene. When infused, the vector is expected to carry a functional copy of the SMN1 gene into the motor neurons. This provides an alternative source of SMN protein expression in these cells, which is expected to promote the survival and function of the motor neurons that contain the vector.

It is administered as a single-dose intravenous infusion and the effects are thought to be lifelong.

Financial factors

This technology is commissioned by NHS England.

The price for onasemnogene abeparvovec is £1,795,000 (excluding VAT). The company has a commercial arrangement that makes onasemnogene abeparvovec available to the NHS with a discount. The size of the discount is commercial in confidence.

NICE Guidelines (NGs)

Type 1 diabetes in adults: diagnosis and management NG17 (update)

July 2021: NICE reviewed the evidence and updated the recommendations on long-acting insulin therapy.

This guideline covers care and treatment for adults (aged 18 and over) with type 1 diabetes. It includes advice on diagnosis, education and support, blood glucose management, cardiovascular risk, and identifying and managing long-term complications.

Public Health Guidelines

None published this month.

Antimicrobial prescribing guidelines

***Clostridioides difficile* infection: antimicrobial prescribing NG199**

This guideline sets out an antimicrobial prescribing strategy for managing *Clostridioides difficile* infection in adults, young people and children aged 72 hours and over in community and hospital settings. It aims to optimise antibiotic use and reduce antibiotic resistance. The recommendations do not cover diagnosis.

This guideline partially updates NICE's interventional procedures guidance on faecal microbiota transplant for recurrent *Clostridium difficile* infection.

It also updates and replaces technology appraisal TA601 (September 2019).

The guideline contains recommendations on:

- Assessment
- Treating suspected or confirmed C. difficile infection
- Advice
- Reassessment
- Referral
- Choice of antibiotic
- Preventing *C. difficile* infection

Social Care guidelines

None published this month.

Interventional Procedures Guidance (IPGs)

Inducing and maintaining normothermia using temperature modulation devices to improve outcomes after stroke or subarachnoid haemorrhage IPG701

Recommendations

Evidence on the safety and efficacy of inducing and maintaining normothermia using temperature modulation devices to improve outcomes after stroke or subarachnoid

haemorrhage is inadequate in quality and quantity. Therefore, this procedure should only be used in the **context of research**.

Further research should preferably be randomised controlled trials. It should report details of patient selection (including cause of fever, severity of stroke and neurological injury), method and duration of cooling, time from the neurological injury and onset of fever to starting cooling, complications related to the procedure and the device, neurological outcomes assessed using validated measures, and patient-reported outcomes (including quality of life) in the long term.

The condition

Stroke (ischaemic stroke and intracerebral haemorrhage) is an acute neurological event presumed to be vascular in origin and causing cerebral ischaemia, cerebral infarction or cerebral haemorrhage. Subarachnoid haemorrhage (SAH) is a haemorrhage from a cerebral blood vessel, aneurysm or vascular malformation into the subarachnoid space.

Both conditions can interrupt blood flow to the brain, damage brain cells and cause abnormalities of thermoregulation and an abnormally high body temperature (neurogenic fever). The abnormally high temperature may result in secondary neurological injury and is associated with worse outcomes, greater morbidity and mortality.

Current treatments for managing fever after stroke or SAH include identifying and treating a cause, antipyretic medications and standard physical methods of cooling such as fans and cooling blankets to lower body temperature.

The procedure

In this procedure, a temperature modulation device is used to maintain the patient's core temperature within normal limits (37.0±0.5oC). Either surface techniques (such as heat exchange cooling pads) or internal techniques (such as an endovascular cooling device) may be used. Heat is exchanged between the patient and the device to allow the body temperature to be controlled to a pre-set point determined by the clinician.

This procedure aims to reduce brain injury and improve neurological outcomes after stroke or SAH by maintaining normothermia with precise temperature control.

Medical Technologies Guidance (MTGs)

ENDURALIFE powered CRT-D devices for treating heart failure MTG33 (update)

July 2021: NICE updated this guidance to reflect 2020 costs and revise cost-saving estimates.

Recommendations

The case for adopting ENDURALIFE-powered cardiac resynchronisation therapy-defibrillator (CRT-D) devices for treating heart failure is **supported** by the published evidence. Extended battery life is of clinical and patient benefit and associated with fewer replacement procedures.

ENDURALIFE-powered CRT-Ds should be considered as an option in people offered CRT-D devices in line with NICE technology appraisal guidance on implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure.

Cost modelling was based on published data using predecessor devices, and showed that the price and lifespan of the CRT-D have the greatest effect on overall treatment costs. Assuming an average selling price of £15,322, across different devices, using ENDURALIFE-powered CRT-Ds may save between £2,614 and £6,941 per patient using NHS tariff costs and between £2,313 and £6,140 per patient using NHS reference costs over 15 years through a reduction in the need for replacement procedures [2021]. This could save the NHS in England around £6 million in the first 5 years.

The technology

The ENDURALIFE battery technology is designed to extend the battery life of Boston Scientific cardiac resynchronisation therapy-defibrillator (CRT-D) devices. CRT-Ds are a treatment option for heart failure and life-threatening ventricular arrhythmias. ENDURALIFE battery technology uses a lithium manganese dioxide (Li/MnO2) battery chemistry, which is claimed to be less susceptible to the variations in voltage and resistance associated with early battery depletion. CRT-Ds with ENDURALIFE battery technology are also claimed to use less current than other CRT-Ds.

Diagnostics Guidance (DGs)

None published this month.

NICE Quality Standards

None published this month.

Current NICE consultations

Title / link	End date of consultation
Metastatic spinal cord compression in adults: risk assessment, diagnosis and management	02/08/2021
Oral azacitidine for maintenance treatment of acute myeloid leukaemia after induction therapy [ID3892]	02/08/2021
Belimumab for treating lupus nephritis [ID2722]	03/08/2021
SeHCAT (tauroselcholic [75 selenium] acid) for diagnosing bile acid diarrhoea	04/08/2021
Tobacco: preventing uptake, promoting quitting and treating dependence (update)	06/08/2021
Pelvic floor dysfunction: prevention and non-surgical management	09/08/2021

Omburtamab for treating relapsed neuroblastoma [ID1664]	09/08/2021
MT539 3C Patch System for treating diabetic foot ulcers	10/08/2021
GID-MT554 KardiaMobile for the ambulatory detection of atrial fibrillation	12/08/2021
Ectopic pregnancy and miscarriage: diagnosis and initial management (update)	17/08/2021
Endobronchial vagal nerve ablation for chronic obstructive pulmonary disease	19/08/2021
Transanal total mesorectal excision for rectal cancer	19/08/2021
Percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure	19/08/2021
Rehabilitation after traumatic injury	08/09/2021

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