NHS
Devon
Clinical Commissioning Group

NICE Update Bulletin: February 2022

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

1. **COVID-19 rapid guideline: managing COVID-19 NG191 (UPDATE)**
2. **Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies TA772**
3. **Daratumumab with bortezomib, melphalan and prednisone for untreated multiple myeloma *(terminated appraisal)* TA771**
4. **Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer TA770**
5. **Palforzia for treating peanut allergy in children and young people TA769**
6. **Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs TA768**
7. **Ponesimod for treating relapsing–remitting multiple sclerosis TA767**
8. **Pembrolizumab for adjuvant treatment of completely resected stage 3 melanoma TA766**
9. **Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable TA765**
10. **Fremanezumab for preventing migraine TA764**
11. **Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable TA763**
12. **Olaparib for treating BRCA mutation-positive HER2-negative metastatic breast cancer after chemotherapy *(terminated appraisal)* TA762**
13. **Odevixibat for treating progressive familial intrahepatic cholestasis (PFIC) HST17**
14. **Type 2 diabetes in adults: management NG28 (UPDATE)**
15. **Microwave ablation for primary or metastatic cancer in the lung IPG716**
16. **Stereotactic radiosurgery for trigeminal neuralgia IPG715**
17. **PredictSURE IBD and IBDX to guide treatment of Crohn's disease DG45**
18. **EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules DG46**
19. **Colorectal cancer QS20 (UPDATE)**
20. **Current NICE Consultations**

NICE Rapid COVID-19 Guidelines

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

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

February 2022: NICE added recommendations on molnupiravir and remdesivir for people with COVID-19 who do not need supplemental oxygen.

Technology Appraisals (TAs)

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies TA772

Recommendations

Pembrolizumab is **recommended** as an option for treating relapsed or refractory classical Hodgkin lymphoma in people aged 3 and older. It is recommended if they have had an autologous stem cell transplant that has not worked or they have had at least 2 previous therapies and an autologous stem cell transplant is not an option, and only if:

- they have not had brentuximab vedotin and
- the company provides pembrolizumab according to the commercial arrangement.

The Technology

Hodgkin lymphoma is a cancer of the lymphatic system. It can be classified into 2 main groups; the classical types, and the nodular lymphocyte predominant type. Classical Hodgkin lymphomas contain the Reed-Sternberg cells (which are cancerous B lymphocyte cells). The initial symptom of Hodgkin lymphoma is often swelling of the lymph nodes in the neck, armpit or groin. Other symptoms include recurring fever, night sweats, weight loss, cough, breathlessness, abdominal pain, and itching.

Hodgkin lymphoma accounts for around 20% of all diagnosed lymphomas. The age-specific incidence of Hodgkin lymphoma shows two peaks, one in people aged 20 to 24 years and the second in people aged over 75 years.

Current first-line treatment for Hodgkin lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Up to 5-10% of patients are refractory with these therapies and 10-30% will relapse after achieving initial remission. For these people, high-dose chemotherapy followed by autologous stem cell transplant is a potentially curative treatment that is effective in about 50% of people. However, autologous stem cell transplant may not be an option in some circumstances; for example, when the disease is refractory to chemotherapy, or when the person's age or co-morbidities prohibit this intervention.

Pembrolizumab is a humanised, antiprogrammed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

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 technology is a further treatment option and the overall cost of treatment will be similar and is a cost-effective use of NHS resources.

Pembrolizumab and the other treatment options in the pathway (nivolumab, and brentuximab vedotin) have discounts that are commercial in confidence.

Daratumumab with bortezomib, melphalan and prednisone for untreated multiple myeloma *(terminated appraisal)* TA771

NICE is **unable to make a recommendation** on daratumumab with bortezomib, melphalan and prednisone for untreated multiple myeloma because Janssen did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer TA770

This guidance updates and replaces TA600 which was available through the Cancer Drugs Fund (published September 2019).

Recommendations

Pembrolizumab with carboplatin and paclitaxel is **recommended** as an option for untreated metastatic squamous non-small-cell lung cancer (NSCLC) in adults, only if

- their tumours express PD-L1 with a tumour proportion score of 0% to 49%
- their tumours express PD-L1 with a tumour proportion score of 50% or more and they need urgent clinical intervention
- it is stopped at 2 years of uninterrupted treatment or earlier if their disease progresses and
- the company provides pembrolizumab according to the commercial arrangement.

This recommendation is not intended to affect treatment with pembrolizumab plus carboplatin and paclitaxel that was started in the Cancer Drugs Fund before this guidance was published. For those people, pembrolizumab plus carboplatin and paclitaxel will be funded by the company until the patient and their NHS clinician consider it appropriate to stop.

The Technology

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC) and 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 (locally advanced disease; stage 3) or to other parts of the body (metastatic disease; stage 4).

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers, histology and previous treatment experience

NICE NG122 recommends platinum-based chemotherapy as an option for people with previously untreated stage III or IV NSCLC and good performance status.

NICE TA531 recommends pembrolizumab monotherapy as an option for untreated PD-L1-positive metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score and has no EGFR- or ALK-positive mutations.

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

Financial Factors

This technology is commissioned by NHS England.

Additional evidence collected as part of the Cancer Drugs Fund managed access agreement has now been reviewed and NICE have made the following cost-effectiveness estimates:

The cost-effectiveness estimates in people whose tumours express PD-L1 with a tumour proportion score of 0% to 49% were within what NICE considers a good use of NHS resources. For people whose tumours have a PD-L1 tumour proportion score of 50% or more and who need an urgent clinical intervention (for example, because their cancer may cause major airway blockage), the cost-effectiveness estimates were not certain. However, they are likely to be within what NICE considers a good use of NHS resources.

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

Palforzia for treating peanut allergy in children and young people TA769

Recommendations

Palforzia is **recommended**, within its marketing authorisation, as an option for treating peanut allergy in children aged 4 to 17. It can be continued in people who turn 18 while on treatment. Palforzia should be used with a peanut-avoidant diet.

The Technology

Food allergy is an adverse immune response to food allergens. Peanut allergy is Immunoglobulin E-mediated and one of the most common food allergies. Symptoms of an allergic reaction to peanuts are acute and have rapid onset. Allergic reactions may be characterised by facial swelling, asthma or other respiratory symptoms, conjunctivitis, oral allergy syndrome, inflammation of the nose, blotchy red rash. Reactions may also become severe and life-threatening.

Peanut allergy is often present in children, though some may grow out of it over time. It can have a great impact on people and their families because the constant vigilance required to avoid peanuts and potentially other tree nuts and a constant fear of an allergic reaction.

Current management of peanut allergy is focused on avoidance of peanuts through education and vigilance with checking food labelling. In the event of an allergic reaction, mild events are treated with oral antihistamines and severe events are treated with adrenaline (auto-injector pens).

Palzorzia is an oral immunotherapy that aims to desensitise people with peanut allergy and reduce the chance of severe allergic reactions including anaphylaxis that may occur with accidental exposure to peanuts. The treatment involves taking a small dose of Palforzia initially but gradually increasing under clinical supervision over approximately 6 months until a maintenance dose level is achieved.

Financial Factors

This technology is commissioned by CCGs.

The most likely cost-effectiveness estimates are within the range that NICE normally considers an acceptable use of NHS resources. Also, additional benefits of Palforzia may not have been captured in the cost-effectiveness results.

NICE estimate that in Devon, the eligible population for receiving Palforzia is 2,695 children. At year five, NICE estimate that of the 57 children that start treatment with Palforzia, 9 will discontinue treatment after six months and 47 will continue after their first six months of treatment. NICE anticipate that treatment with Palforzia will cost just over £1.2 million at year five in Devon, this is an increase of £610,000 compared with current practice. It is expected that this figure will also be impacted by costs associated with additional monitoring for children dietary peanut after

stopping Palforzia treatment, however, NICE are unable to model this at a local level and therefore this resource impact is currently unknown.

Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs TA768

Recommendations

Upadacitinib, alone or with methotrexate, is **recommended** as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them. It is recommended only if they have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints and:

- they have had 2 conventional DMARDs and at least 1 biological DMARD or
- TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE's technology appraisal on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis TA199).

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

Assess the response to upadacitinib after 12 weeks of treatment. Only continue treatment if there is clear evidence of response. This is defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC), 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria. If PsARC response does not justify continuing treatment but there is a Psoriasis Area and Severity Index (PASI) 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response.

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

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

These recommendations are not intended to affect treatment with upadacitinib 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

Psoriatic arthritis (also called psoriatic arthropathy) is an inflammatory arthritis closely associated with psoriasis. Men and women are equally likely to develop psoriatic arthritis with the peak onset being between the ages of 30 and 50 years.

Although psoriatic arthritis is a chronic condition that progresses in the joints, its course may be erratic, with flare-ups and remissions. Arthritis symptoms can range from inflammation of the

synovial membrane surrounding a joint, ligaments and tendons, and inflammation of digits to severe progressive erosion of the joints.

The aim of treatment is to suppress joint, tendon and ligament inflammation, and to manage the skin symptoms of the disease. Current practice involves early diagnosis and early use of non-biological DMARDs. Non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy and intraarticular corticosteroid injections may also be used.

In addition, biological tumour necrosis factor (TNF)-alpha inhibitors and other nonconventional DMARDs (such as Janus kinase inhibitors and IL-17 inhibitors) may be used for treating people with active psoriatic arthritis.

Upadacitinib is a selective and reversible Janus-kinase (JAK) 1 inhibitor that blocks the JAK-signal transducer and activator of transcription (STAT) pathway and inflammatory responses. It is administered orally.

Financial Factors

This technology is commissioned by CCGs.

NICE estimate that in Devon the prevalence of active psoriatic arthritis is 1,853. The proportion of people suitable for biological treatment is 371. Of these people, 41 will be eligible for treatment following unsuccessful treatment with two conventional DMARDS and at least one other biological DMARD. Because there are several further biological treatment options available, NICE is unable to estimate how many of the 41 people eligible for treatment in Devon will go on to receive upadacitinib.

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

Upadacitinib has a commercial arrangement. This makes upadacitinib available to the NHS with a discount.

Ponesimod for treating relapsing–remitting multiple sclerosis TA767

Recommendations

Ponesimod is **recommended** for treating relapsing–remitting multiple sclerosis with active disease defined by clinical or imaging features in adults, only if the company provides ponesimod according to the commercial arrangement.

This recommendation is not intended to affect treatment with ponesimod 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

Multiple sclerosis is a chronic, neurological condition which affects the brain, optic nerves, and spinal cord. It often results in progressive neurological impairment and severe disability. Multiple sclerosis has an unpredictable course which varies in severity and rate of progression. Symptoms can include pain, disturbance to muscle tone including weakness or spasticity, chronic fatigue, unsteady gait, speech problems, incontinence, visual disturbance and cognitive impairment.

Relapsing–remitting multiple sclerosis is the most common clinical form of multiple sclerosis. It is characterised by periods of remission followed by relapses. Relapsing–remitting multiple sclerosis can progress to secondary progressive multiple sclerosis. This is characterised by more persistent or gradually increasing disability; some people with secondary progressive disease continue to have relapses. A small number of people are diagnosed with secondary progressive multiple sclerosis without a previous diagnosis of relapsing–remitting multiple sclerosis.

Current pharmacological management of multiple sclerosis includes disease modifying agents to reduce the frequency and severity of relapses and the rate of disease progression. Treatments for relapsing–remitting multiple sclerosis are also used for people with active secondary progressive multiple sclerosis, as evidenced by relapses.

Ponesimod is a selective sphigosine-1 phosphate type 1 (S1P-1) receptor modulator and can be classed as an immunomodulatory drug. Ponesimod acts by preventing lymphocytes from crossing the blood-brain barrier into the central nervous system and causing damage to the myelin sheath around nerve cells. 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 technology is a further treatment option and the overall cost of treatment will be similar.

The use of ponesimod is not expected to result in additional service requirements. It is a further oral treatment option which can increase convenience for people who use it and may save costs. The use of ponesimod may also free up healthcare professional capacity compared to treatments administered by intravenous infusions in hospital. However, any savings as a result are not expected to be significant at a national level.

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

Pembrolizumab for adjuvant treatment of completely resected stage 3 melanoma TA766

This guidance replaces NICE TA553 on pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence (published December 2018).

Recommendations

Pembrolizumab is **recommended**, within its marketing authorisation, as an option for the adjuvant treatment of completely resected stage 3 melanoma with lymph node involvement in adults. It is recommended only if the company provides pembrolizumab according to the commercial arrangement.

The Technology

Cutaneous melanoma is a cancer of the skin. In its early stages, melanoma is normally asymptomatic and can often be cured by surgery (resection). However, it can spread or metastasise to nearby lymph nodes or to other parts of the body. Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, intermittent sun exposure and sunburn.

The stage of melanoma describes how deeply it has grown into the skin, and whether it has spread. Stage III melanoma means that the melanoma cells have spread into skin, lymph vessels, or lymph glands close to the melanoma. Stage III melanomas are considered intermediate to high risk as they more likely to spread to other distant parts of the body (stage IV melanoma) than in earlier melanoma stages.

Surgery is the main treatment for early (stage I) and medium stage (stage II and III) melanoma. Adjuvant chemotherapy and immunotherapy following tumour removal was not widely used in UK practice, but NICE has since published three technology appraisals in this area TA544, TA553, TA684.

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

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 technology is a further treatment option and the overall treatment cost will be similar.

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

Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable TA765

Recommendations

Venetoclax with azacitidine is **recommended**, within its marketing authorisation, as an option for untreated acute myeloid leukaemia (AML) in adults when intensive chemotherapy is unsuitable. It is recommended only if the company provides venetoclax according to the commercial arrangement.

The Technology

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

The aim of treatment for AML is to cure it. For people with good general health, the treatment options are intensive chemotherapy and allogeneic haematopoietic stem cell transplant (HSCT). There are alternative treatment options for people for whom intensive chemotherapy is considered not suitable. Treatments include low dose cytarabine and azacitidine. NICE TA218 recommends azacitidine for adults who are not eligible for HSCT and have AML with 20 to 30% blasts and multilineage dysplasia, according to the World Health Organization classification. NICE TA399 does not recommend azacitidine for treating AML with more than 30% bone marrow blasts in people who are not eligible for HSCT.

Venetoclax is a selective blocker of B-cell lymphoma-2 (BCL-2) a protein that allows cancer cells to stay alive. Venetoclax is administered orally.

Financial Factors

This technology is commissioned by NHS England.

Venetoclax with azacitidine meets NICE's criteria for a life-extending treatment at the end of life. The cost-effectiveness results are uncertain because it is not clear how many people who have venetoclax plus azacitidine might be considered cured. However, the likely cost-effectiveness estimates are within the range that NICE normally considers an acceptable use of NHS resources. The company has a commercial arrangement. This makes venetoclax available to the NHS with a discount.

NICE estimate that, in Devon, the incidence of AML (aged 18 and over) is 69 people. Of these 69 people, 14 will be unsuitable for low dose chemotherapy and therefore eligible for other treatment. NICE estimate that the uptake of people receiving venetoclax with azacytidine will be 12 after five years.

Fremanezumab for preventing migraine TA764

This guidance updates and replaces TA631 (published June 2020).

Recommendations

Fremanezumab 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 fremanezumab 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%

These recommendations are not intended to affect treatment with fremanezumab 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 sound, and/or other sensory stimuli. Migraine can have significant impacts on quality of life and ability to carry out normal activities.

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

- Episodic migraine is defined as the occurrence of headaches on less than 15 days per month.
- Chronic migraine is defined by the International Classification of Headache Disorders 3rd edition (ICHD-3). It is described as headache occurring on 15 or more days a month, which, on at least 8 days a month, has the features of migraine headache.

There are 3 broad approaches to managing migraine: lifestyle and trigger management, acute treatments and preventive treatments.

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.

Fremanezumab is a fully humanised monoclonal antibody that inhibits the action of calcitonin generelated peptide (CGRP) which is believed to transmit signals that can cause severe pain. Fremanezumab is administered by subcutaneous injection.

Financial Factors

This technology is commissioned by CCGs.

NICE do not expect this guidance to have a significant impact on resources, this is because the technology is a further treatment option and the overall cost will be similar.

For chronic migraine (assuming fremanezumab works better than botulinum toxin type A), the most likely cost-effectiveness estimates are within the range NICE normally considers an acceptable use of NHS resources. For episodic migraine, the estimates of cost effectiveness are even lower.

NICE estimate that in Devon after 5 years, 3,195 people with episodic migraine will be eligible for treatment with erenumab, fremanezumab or galcanezumb. Of these, 64 people will receive treatment with fremanezumab. Of the 1,312 eligible people with chronic migraine, 92 people will receive treatment with fremanezumab.

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

Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable TA763

Recommendations

Daratumumab plus bortezomib, thalidomide and dexamethasone is **recommended**, within its marketing authorisation, as induction and consolidation treatment for untreated multiple myeloma in adults, when an autologous stem cell transplant is suitable. It is recommended only if the company provides daratumumab according to the commercial arrangement.

The Technology

Multiple myeloma is a form of cancer that arises from plasma cells (a type of white blood cell) in the bone marrow. Myeloma cells produce large quantities of an abnormal antibody, known as paraprotein. Unlike normal antibodies, paraprotein has no useful function and lacks the capacity to fight infection. Myeloma cells suppress the development of normal blood cells that are responsible for fighting infection (white blood cells), carrying oxygen around the body (red blood cells) and blood clotting (platelets).

The term multiple myeloma refers to the presence of more than one site of affected bone at the time of diagnosis. People with multiple myeloma can experience bone pain, bone fractures, tiredness (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

Treatment aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. Autologous stem cell transplantation may be an option for some people with multiple myeloma. Before having an autologous stem cell transplant, most people with untreated multiple myeloma have bortezomib plus thalidomide and dexamethasone as the first treatment

Daratumumab is a humanised monoclonal antibody that kills multiple myeloma cells, targeting the CD38 protein. It is administered intravenously or subcutaneously.

Financial Factors

This technology is commissioned by NHS England.

Clinical trial results show that, compared with bortezomib plus thalidomide and dexamethasone, daratumumab in combination increases how long people live and extends the time before the condition worsens.

NICE estimate that in Devon, 36 people will be eligible for treatment with daratumumab in combination after 5 years. Of these 36, it is estimated that 33 people will receive daratumumab, bortezomib, thalidomide and dexamethasone.

The cost-effectiveness estimates are within what NICE considers acceptable. The company has a commercial arrangement. This makes daratumumab available to the NHS with a discount. The size of the discount is commercial in confidence

Olaparib for treating BRCA mutation-positive HER2-negative metastatic breast cancer after chemotherapy *(terminated appraisal)* TA762

NICE is **unable to make a recommendation** on olaparib (Lynparza) for treating BRCA mutation-positive HER2-negative metastatic breast cancer after chemotherapy. This is because AstraZeneca did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Highly Specialised Technology Guidance (HSTs)

Odevixibat for treating progressive familial intrahepatic cholestasis (PFIC) HST17

Recommendations

Odevixibat is **recommended**, within its marketing authorisation, as an option for treating progressive familial intrahepatic cholestasis (PFIC) in people 6 months and older. It is recommended only if the company provides odevixibat according to the commercial arrangement.

The Technology

Progressive familial intrahepatic cholestasis (PFIC) is a rare and serious genetic condition and is the name given to a group of genetic disorders that affect the liver. They result in the flow of bile from the liver to the gastrointestinal tract being reduced or stopping completely. This causes bile to accumulate in the liver cells (cholestasis), which start to die and are replaced with scar tissue. This leads to cirrhosis (severe scarring) and liver failure. PFIC is caused by mutations in the genes that encode the proteins involved in transporting bile out of the liver, adversely affecting their function.

People with PFIC have a wide range of symptoms and the condition is characterised by severe pruritus (itching), jaundice and raised serum bile acid levels. Diagnosis is primarily clinical. Other symptoms occurring outside the liver include diarrhoea, fat-soluble vitamin deficiencies and poor growth.

There are no licensed medicines for PFIC. Initial management includes off-label medicines (for example, ursodeoxycholic acid, rifampicin, cholestyramine). The aim with these is to control the cholestatic pruritus. They are often given in combination and used alongside nutritional management, such as vitamin supplements to optimise nutrient absorption and promote growth. Surgical options are used when pruritus persists despite these off-label medicines. A liver transplant is needed by most people with PFIC.

Odevixibat is a selective inhibitor of the ileal bile acid transporter (IBAT). Odevixibat stops the recycling of bile acids, increasing their excretion through the colon and lowering hepatic and serum bile acid levels. Odevixibat is administered daily as a capsule or sprinkled on food.

Financial Factors

This technology is commissioned by NHS England.

The company's cost-effectiveness estimates are above what NICE usually considers acceptable for HSTs. However, several assumptions in the company's economic model are uncertain and possibly conservative. When taking all of these assumptions into account, the cost effectiveness of odevixibat is likely to be lower than the company's estimate. Also, the model does not capture:

- health-related benefits from delaying or stopping lifelong immunosuppression after a liver transplant
- the effect on quality of life for carers of people with PFIC
- the invasive nature of other treatments
- the young age at which PFIC can develop
- the innovative nature of odevixibat.

After consideration of this, NICE determined that odevixibat is recommended for use in the NHS for PFIC.

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

NICE Guidelines (NGs)

Type 2 diabetes in adults: management NG28 (UPDATE)

This guideline covers care and management for adults (aged 18 and over) with type 2 diabetes. It focuses on patient education, dietary advice, managing cardiovascular risk, managing blood glucose levels, and identifying and managing long-term complications.

February 2022: NICE have reviewed the evidence and made new recommendations on drug treatment for adults with type 2 diabetes. These recommendations are marked [2022].

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)

Microwave ablation for primary or metastatic cancer in the lung IPG716

This guidance replaces NICE IPG469 on microwave ablation for treating primary lung cancer and metastases in the lung (published November 2013).

Recommendations

Evidence on the safety of microwave ablation for treating primary lung cancer and metastases in the lung is adequate but shows it can cause infrequent serious complications. Evidence on its efficacy shows it reduces tumour size. But the evidence on improvement in survival, long-term outcomes and quality of life is limited in quantity and quality. Therefore, this procedure **should only be used with special arrangements** for clinical governance, consent, and audit or research.

Further research should be randomised controlled trials or disease registry studies. It should report patient selection, disease progression and quality of life, and take account of the effectiveness of managing oligometastatic disease in patients.

Clinicians who want to use microwave ablation to treat primary lung cancer and metastases in the lung should:

- Inform the clinical governance leads in their healthcare organisation.
- Give patients (and their families and carers as appropriate) clear written information to support shared decision making, including NICE's information for the public.
- Make sure that patients (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Audit and review clinical outcomes of all patients having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).
- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

Healthcare organisations should:

- Make sure 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.

People with primary or metastatic lung cancer should be referred to an appropriately constituted multidisciplinary team.

The procedure should only be done in specialist centres by clinicians with specific training in this procedure.

The Condition

Lung cancer is one of the most common types of cancer. The symptoms often do not appear until the disease is at an advanced stage and the prognosis is generally poor. Cancer that begins in the lungs is called primary lung cancer. There are two main types of primary lung cancer: small-cell lung cancer (which is fast growing and can spread quickly) and non-small-cell lung cancer (NSCLC, which usually grows and spreads slowly; this includes squamous cell carcinoma, adenocarcinoma and large-cell carcinoma).

Cancer that starts in one part of the body and spreads via the blood stream to the lungs is known as secondary lung cancer (also called metastatic lung cancer or lung metastasis).

NICE's guideline on lung cancer (NG122) describes the treatment of non-small-cell and small-cell lung cancer. The choice of treatment for primary or metastatic cancer in the lung depends on the type, size, position and stage of the cancer, and the patient's overall health. Common treatments for primary or metastatic cancer in the lung include surgery, chemotherapy, radiotherapy, or a

combination of these. Other treatments include photodynamic therapy, thermal ablation, immunotherapy and biological therapy.

The Procedure

The procedure is usually done using general anaesthesia, and occasionally using local anaesthesia and sedation. Under imaging guidance, a small probe is advanced through the chest wall and into each targeted lesion. It delivers high-frequency microwave energy to rapidly agitate water molecules in the tissues. This converts energy into heat, which causes tumour necrosis. Patients with larger tumours or multiple lesions may have multiple pulses of energy delivered within a treatment session or have a staged treatment with multiple sessions.

This procedure aims to destroy tumour cells and create localised areas of tissue necrosis with minimal damage to surrounding normal tissues. Microwave ablation is a minimally invasive procedure. It usually lasts 1 to 2 hours with only 5 to 10 minutes of active ablation time.

Stereotactic radiosurgery for trigeminal neuralgia IPG715

This guidance replaces NICE IPG85 on stereotactic radiosurgery for trigeminal neuralgia using the gamma knife (published August 2004).

Recommendations

Evidence on the safety and efficacy of stereotactic radiosurgery for trigeminal neuralgia is adequate to support using this procedure provided that **standard arrangements** are in place for clinical governance, consent and audit.

For auditing the outcomes of this 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).

Patient selection should be done by a multidisciplinary team experienced in managing trigeminal neuralgia.

The procedure should only be done in specialist centres.

The Condition

Trigeminal neuralgia is a chronic pain condition that affects the trigeminal (fifth) cranial nerve, one of the most widely distributed nerves in the head. The pain occurs in areas supplied by the trigeminal nerve: the cheeks, jaw, teeth, gums, lips and around the eye or forehead.

The typical form, type 1, causes sudden and severe facial pain, usually affecting 1 side of the face and lasting for a few seconds or minutes. It may be triggered by touch, talking, eating or brushing teeth.

Atypical trigeminal neuralgia (type 2) is characterised by constant aching, burning, or stabbing pain of lower intensity than type 1. Some people have both types.

Trigeminal neuralgia can be idiopathic or may be caused by pressure on the trigeminal nerve from an artery or a vein (primary trigeminal neuralgia). It can also result from a medical condition such as a tumour, multiple sclerosis or injury (secondary trigeminal neuralgia).

Medication is the first-line treatment for trigeminal neuralgia. Other treatment options are considered for people who experience severe pain despite medication, or who have side effects from medication. Percutaneous treatments include glycerol injection, radiofrequency lesioning and balloon micro compression. The aim is to damage the trigeminal nerve and stop the transmission of pain signals. Recurrence rates of trigeminal neuralgia after these procedures are typically high.

Microvascular decompression is a more invasive procedure involving opening the skull to relieve the pressure on the trigeminal nerve. This can provide longer lasting relief but carries a risk of potentially serious complications such as facial numbness, hearing loss, stroke and death.

The Procedure

Stereotactic radiosurgery for trigeminal neuralgia uses precisely focused multiple beams of ionising radiation aimed at the trigeminal nerve where it enters the brainstem, to deliver a high dose in a single treatment session. It does not require open surgery, needle insertion or general anaesthesia. The aim is to damage the trigeminal nerve and stop the transmission of pain signals as with other percutaneous techniques.

There are different systems available for stereotactic radiosurgery and details of the techniques vary. It can take a few weeks or months for the patient to notice any change after stereotactic radiosurgery.

Medical Technologies Guidance (MTGs)

None published this month.

Diagnostic Guidance (DGs)

PredictSURE IBD and IBDX to guide treatment of Crohn's disease DG45

Recommendations

NICE has **not recommended** the use of the PredictSURE IBD and IBDX tests as there is not enough evidence to recommend it. They should only be used in the **context of research** to help identify people at high risk of a severe course of Crohn's disease and guide treatment.

Further research is recommended to:

- assess how accurate the tests are for identifying a low or high risk of a severe course of Crohn's disease
- understand how the tests affect decisions about treatment

- assess the clinical outcomes and costs associated with different treatment strategies
- assess how the tests affect clinical outcomes.

The Tests

Crohn's disease is a chronic condition that causes inflammation of the gastrointestinal tract, particularly the large intestine and the last section of the small intestine. This condition is characterised by recurring periods of active symptoms (flares). At other times health is generally good (remission). Complications of Crohn's disease include intestinal strictures, fistulas and perforation. Children may also have growth problems because of poor absorption of nutrients.

Crohn's disease has no cure. The goal of treatment is to induce remission by controlling symptoms and maintain remission to prevent relapse. Current standard care is a 'step-up' strategy, which starts with corticosteroids, then immunosuppressants, then biological therapies if the disease does not respond, or loses response, to treatment

An alternative approach not currently recommended as standard care is the top-down strategy, which reverses the order of treatment in the step-up strategy, starting with biologics such as tumour necrosis factor (TNF)-alpha inhibitors. It has been suggested that for some people with Crohn's disease, the top-down strategy could achieve a faster and higher rate of mucosal healing. This could potentially modify the natural disease course and allow people with a severe disease course to control it better. Biologics are more clinically effective but are also associated with more side effects.

PredictSURE IBD and IBDX tests could identify people at a higher risk of a severe course of Crohn's disease, potentially guiding more personalised disease management.

PredictSURE IBD is a whole blood-based biomarker prognostic laboratory-based test combined with a proprietary algorithm to categorise people into a high or low risk of a severe course of Crohn's disease. The test is based on detecting CD8+ T-cell exhaustion. The test involves isolating mRNA from the whole blood sample using the PAXgene Blood RNA kit, followed by quantitative polymerase chain reaction with reverse transcription (RT-qPCR) to assess expression of 15 target genes and 2 controls. RT-qPCR is a 2-step process: cDNA synthesis in the reverse transcription reaction, and then a qPCR on a 384-well plate. A maximum of 4 samples may be analysed per plate because cDNA derived from each RNA sample is run in triplicate.

IBDX is a panel of 6 indirect solid-phase enzyme-linked immunosorbent assay (ELISA) kits, each of which detects serum levels of specific antiglycan antibodies. Antiglycan antibodies are serological biomarkers thought to be highly specific for Crohn's disease and associated with a severe disease course.

Financial Factors

NICE state that the cost-effectiveness estimates are very uncertain and lack face validity (that is, the results are unexpected). More research is needed to resolve the clinical uncertainties. Therefore, these tests are not recommended for routine use in the NHS.

EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules DG46

Recommendations

NICE has **not recommended** the routine use of EarlyCDT Lung for assessing the risk of lung cancer in solid lung nodules as there is not enough evidence.

Further research is recommended on:

- the diagnostic accuracy of EarlyCDT Lung, its performance when used with existing risk models and its effect on clinical management decisions
- patient and nodule characteristics that may relate to the prevalence of malignant disease and disease progression
- current practice for managing intermediate-risk lung nodules
- the clinical consequences of CT surveillance
- the likelihood and impact of overtreatment of benign and indolent nodules.

The Tests

Lung cancer is the third most common cancer in England and is the leading cause of cancer death. There are many risk factors for lung cancer, including age, genetics, lifestyle (especially smoking) and occupation. Lung cancer has 2 main types: non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). NSCLC is the most common type of lung cancer, accounting for 87% of cases. NSCLCs can be broken down into 2 major sub-types: adenocarcinoma and squamous cell carcinoma.

Pulmonary nodules are small growths found inside the lung. They may not lead to symptoms and often are found during tests to diagnose another condition. While most pulmonary nodules are benign and are small, some may develop into cancerous tumours. These are associated with both SCLC and NSCLC. Pulmonary nodules can grow over time, causing breathing problems and other symptoms.

In the NHS, people with nodules below 5 mm in diameter or 80 mm^3 in volume are discharged without follow up. CT surveillance is offered for nodules between 5 mm and 8 mm in diameter or 80 mm^3 and 300 m^3 in volume. For nodules over 8 mm in diameter or 300 m^3 in volume, the Brock model is used to calculate risk of malignancy. CT surveillance is offered to people with nodules that are below a 10% risk score using the Brock model.

EarlyCDT Lung could help identify malignant lung nodules that need immediate treatment or a biopsy. This could result in treatment being offered earlier, potentially giving improved patient outcomes. It could also reduce the number of people on CT surveillance, patient waiting times and radiologist time

EarlyCDT Lung is a blood test to assess the malignancy risk of solid lung nodules found by chest CT or X-ray. EarlyCDT Lung measures the presence of autoantibodies to a panel of 7 lung cancer associated antigens. After blood collection, the test is carried out in a laboratory in a secondary healthcare setting. Positive results are reported as 'positive-moderate' if at least 1 of the 7 autoantibodies is elevated above a predetermined 'low' threshold, but all are below the 'high' threshold. If at least 1 of the 7 autoantibodies is elevated above the 'high' predetermined threshold, the test is reported as 'positive-high'.

EarlyCDT Lung is proposed as a 'rule-in' test to be used in addition to standard care for the detection of lung cancer

Financial Factors

NICE have stated that due to the limited clinical evidence, the cost effectiveness of EarlyCDT Lung was not assessed and therefore it has not been recommended. Further research is needed on both the EarlyCDT Lung test and on the impact of current lung nodule management. Without more data on current management, it would be difficult to quantify the impact of EarlyCDT Lung and other new tests for assessing lung nodules.

NICE Quality Standards

Colorectal cancer QS20 (UPDATE)

This quality standard covers the management of colorectal (bowel) cancer in adults. It includes managing local disease and secondary tumours (metastatic disease). It describes high-quality care in priority areas for improvement.

February 2022: NICE updated or replaced the statements prioritised in 2012. The topic of colorectal cancer was identified for update following the annual review of quality standards. The update quality standard now includes two new statements and two updated statements.

Current NICE Consultations

Title / link	End date of consultation
Self-harm: assessment, management and preventing recurrence	01/03/22
Adrenal insufficiency: acute and long-term management	01/03/22
Vertebral body tethering for idiopathic scoliosis in children and young people	01/03/22
Regional nerve graft to restore corneal sensation	01/03/22
Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer	01/03/22
Semaglutide for managing overweight and obesity [ID3850]	01/03/22
Menopause: diagnosis and management	08/03/22
Transperineal biopsy for diagnosing prostate cancer	08/03/22
GID-MT562 FibroScan for assessing liver fibrosis and cirrhosis outside secondary and specialist care	09/03/22
Melanoma: assessment and management	11/03/22
Preterm labour and birth	17/03/22
Aortic remodelling hybrid stent insertion during surgical repair of an acute type A aortic dissection	17/03/22
Transcatheter tricuspid valve annuloplasty for tricuspid regurgitation	17/03/22
Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation	17/03/22
Bioresorbable stent implantation for treating coronary artery disease	17/03/22
Superfcial vein arterialisation and selective venous embolisation for critical limb ischaemia	24/03/22
Focal articular prosthetic resurfacing for treating articular cartilage defects in the knee	24/03/22
Neurostimulation of lumbar muscles for refractory non-specific chronic low back pain	24/03/22

Produced by the Clinical Effectiveness Team, NHS Devon CCG for distribution
D-CCG.ClinicalEffectiveness@nhs.net