NHS Devon

NICE Update Bulletin: May 2024

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

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2. **Alemtuzumab for treating highly active relapsing-remitting multiple sclerosis TA312 (UPDATE)**
3. **Cladribine for treating relapsing-remitting multiple sclerosis TA616 (UPDATE)**
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5. **Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion TA283 (UPDATE)**
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Technology Appraisals (TAs)

Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis TA127 (UPDATE)

Recommendations

Natalizumab (branded or biosimilar) is **recommended** as an option for the treatment only of rapidly evolving severe relapsing-remitting multiple sclerosis (RES-RRMS) in adults. RES-RRMS is defined by 2 or more relapses in the previous year and baseline MRI evidence of disease activity.

This recommendation is not intended to affect treatment with natalizumab that was started in the NHS before this guidance was published. People having treatment outside of this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

May 2024: NICE updated the wording in the recommendation to address concerns raised by the clinical community and company that the previously used definition of rapidly evolving severe multiple sclerosis (RES) was overly restrictive. This is because the requirement for 2 MRI scans places significant burden on a limited diagnostic and monitoring resource. The wording has now been changed to better reflect clinical practice.

Alemtuzumab for treating highly active relapsing-remitting multiple sclerosis TA312 (UPDATE)

Recommendations

Alemtuzumab is **recommended** as an option, within its marketing authorisation, for treating highly active relapsing-remitting multiple sclerosis in adults with:

- highly active disease despite a full and adequate course of treatment with at least 1 disease-modifying therapy, or
- rapidly evolving severe relapsing-remitting multiple sclerosis defined by 2 or more relapses in the previous year and baseline MRI evidence of disease activity.

May 2024: NICE updated the wording in the recommendation to address concerns raised by the clinical community and company that the previously used definition of rapidly evolving severe multiple sclerosis (RES) was overly restrictive. This is because the requirement for 2 MRI scans places significant burden on a limited diagnostic and monitoring resource. The wording has now been changed to better reflect clinical practice.

Cladribine for treating relapsing-remitting multiple sclerosis TA616 (UPDATE)

Recommendations

Cladribine is **recommended** as an option for treating highly active multiple sclerosis in adults, only if the person has:

- rapidly evolving severe relapsing-remitting multiple sclerosis, defined by 2 or more relapses in the previous year and baseline MRI evidence of disease activity, or
- relapsing-remitting multiple sclerosis that has responded inadequately to treatment with disease-modifying therapy, defined as 1 relapse in the previous year and MRI evidence of disease activity.

This recommendation is not intended to affect treatment with cladribine that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

May 2024: NICE updated the wording in the recommendation to address concerns raised by the clinical community and company that the previously used definition of rapidly evolving severe multiple sclerosis (RES) was overly restrictive. This is because the requirement for 2 MRI scans places significant burden on a limited diagnostic and monitoring resource. The wording has now been changed to better reflect clinical practice.

Ranibizumab and pegaptanib for the treatment of age-related macular degeneration TA155 (UPDATE)

Recommendations

Ranibizumab, within its marketing authorisation, is **recommended** as an option for the treatment of wet age-related macular degeneration if:

- all of the following circumstances apply in the eye to be treated:
  - the best-corrected visual acuity is between 6/12 and 6/96
  - there is no permanent structural damage to the central fovea
  - the lesion size is less than or equal to 12 disc areas in greatest linear dimension
  - there is evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes) **and**
- the manufacturers of ranibizumab (branded or biosimilar) only provide it at a discount level no lower than the discount agreed in the patient access scheme.

It is recommended that treatment with ranibizumab should be continued only in people who maintain adequate response to therapy. Criteria for discontinuation should include persistent

deterioration in visual acuity and identification of anatomical changes in the retina that indicate inadequate response to therapy. It is recommended that a national protocol specifying criteria for discontinuation is developed.

Pegaptanib is **not recommended** for the treatment of wet age-related macular degeneration.

People who are currently receiving pegaptanib for any lesion type should have the option to continue therapy until they and their clinician consider it appropriate to stop.

May 2024: NICE updated the wording of the recommendation describing the patient access scheme to include procurement information about ranibizumab biosimilars.

Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion TA283 (UPDATE)

Recommendations

Ranibizumab is **recommended** as an option for treating visual impairment caused by macular oedema:

- following central retinal vein occlusion or
- following branch retinal vein occlusion only if treatment with laser photocoagulation has not been beneficial, or when laser photocoagulation is not suitable because of the extent of macular haemorrhage and
- only if the manufacturers of ranibizumab (branded or biosimilar) provide it at a discount level no lower than the discount agreed in the patient access scheme.

People currently receiving ranibizumab whose disease does not meet the criteria above should be able to continue treatment until they and their clinician consider it appropriate to stop.

May 2024: NICE updated the wording of the recommendation describing the patient access scheme to include procurement information about ranibizumab biosimilars.

Ranibizumab for treating choroidal neovascularisation associated with pathological myopia TA298 (UPDATE)

Recommendations

Ranibizumab is **recommended** as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia only if the manufacturers of ranibizumab (branded or biosimilar) provide it at a discount level no lower than the discount agreed in the patient access scheme.

May 2024: NICE updated the wording of the recommendation describing the patient access scheme to include procurement information about ranibizumab biosimilars.

Zanubrutinib with obinutuzumab for treating relapsed or refractory B-cell follicular lymphoma after 2 or more treatments TA978 (*terminated appraisal*)

NICE is **unable to make a recommendation** on zanubrutinib with obinutuzumab for treating relapsed or refractory B-cell follicular lymphoma in adults after 2 or more treatments. This is because the company has requested a delay to the evidence submission. NICE will review this decision if the company decides to make a submission.

Dabrafenib with trametinib for treating BRAF V600E mutation-positive glioma in children and young people aged 1 year and over TA977

Recommendations

Dabrafenib with trametinib is **recommended**, within its marketing authorisation, as an option for treating:

- low-grade glioma (LGG) with a BRAF V600E mutation in children and young people aged 1 year and over who need systemic treatment.
- high-grade glioma (HGG) with a BRAF V600E mutation in children and young people aged 1 year and over after at least 1 radiation or chemotherapy treatment.

  Dabrafenib with trametinib is only recommended if the company provides it according to the commercial arrangements.

The Technology

Gilomas are the most common type of primary brain tumour. They develop from the glial cells that support the nerve cells of the brain and spinal cord. Grade 1 or 2 tumours are considered 'low-grade,' are slow growing and may rarely spread to other areas of the brain. Grade 3 and 4 tumours, known as 'high-grade,' are malignant and have a worse prognosis. The types of glioma are further identified by the cells they develop from and increasingly, by a range of genetic markers including BRAF mutation status.

The symptoms of glioma in children and young people are often general and non-specific and may include headaches, nausea or vomiting, double vision and seizures. Other symptoms depend on where the glioma is in the brain. Glioma is associated with wide reaching impacts on quality of life, including loneliness, difficulty doing activities outside the house and difficulty concentrating and processing information.

Treatment for glioma depends on the grade of the tumour, where the tumour is in the brain, if it is possible to remove the tumour with surgery, age and if symptoms are present.

LGG is usually treated with surgery, if possible, which may achieve either complete or partial macroscopic resection of the tumour. After surgery, radiotherapy or proton beam therapy, with or without chemotherapy may be used. Chemotherapy may also be used alone.

HGG is also usually treated with surgery. Depending on age, some children and young people may be given radiotherapy with or without chemotherapy after surgery. Some children may be given chemotherapy only.

Financial Factors

This technology is commissioned by NHS England.

When considering the condition's severity and its effect on quality and length of life, the most likely cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. Therefore, dabrafenib plus trametinib is recommended.

NICE estimate that in Devon, 1 person with LGG will be eligible for treatment, but there will be no one with HGG eligible for treatment.

The company has a commercial arrangement for each medicine. This makes dabrafenib plus trametinib available to the NHS with a discount.

Trastuzumab deruxtecan for treating HER2-mutated advanced non-small-cell lung cancer after platinum based chemotherapyTA976 (*terminated appraisal*)

NICE is **unable to make a recommendation** on trastuzumab deruxtecan for treating HER2-mutated advanced non-small-cell lung cancer in adults after platinum-based chemotherapy. This is because the company did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people 25 years and under TA975

This guidance updates and replaces TA554 (published December 2018).

Recommendations

Tisagenlecleucel is **recommended**, within its marketing authorisation, as an option for people 25 years and under for treating B-cell acute lymphoblastic leukaemia that is:

- relapsed after a transplant, or
- relapsed for a second or later time, or
- refractory

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

The Technology

Acute lymphoblastic leukaemia (ALL) is a cancer of the lymphocyte-producing cells. Lymphocytes are white blood cells that are vital for the body's immune system In ALL there is an excess production of immature lymphocyte-precursor cells, called lymphoblasts or blast cells, in the bone marrow. This affects the production of normal blood cells and there is a reduction in the numbers of red cells, white cells and platelets in the blood. ALL can be classified into 3 groups based on immunophenotyping:

1. B-precursor ALL (also known as precursor-B-cell ALL)
2. mature B-cell ALL
3. T-cell ALL

B-precursor ALL is characterised by the presence of cytoplasmic immunoglobulins and CD10, CD19, CD22 and CD79a expression.

ALL is most common in children, adolescents and young adults, with around 65% of cases diagnosed in people aged under 25.

The aim of treatment in ALL is to achieve a cure. Treatment for newly diagnosed ALL can take up to 3 years to complete and is generally divided into 3 phases:

1. induction- newly diagnosed ALL in children and adults is generally treated with chemotherapy combinations including vincristine, an anthracycline and asparaginase.
2. consolidation- treatment typically includes intensified chemotherapy. For high risk ALL, stem cell transplantation may also be used as consolidation therapy.
3. maintenance- low dose chemotherapy.

There is no universally accepted treatment approach for relapsed or refractory ALL. Treatment may include conventional combination chemotherapy. In adults with relapsed or refractory disease, NICE TAs recommend targeted treatments; **TA450**, **TA451** and **TA541**. NICE also recommends chimeric antigen receptor T-cell (CAR-T) therapies, immunotherapies that uses a patient's own immune cells that have been genetically modified to treat their cancer (**TA893**.)

Other treatment options may include stem cell transplantation if a suitable donor can be found, or best supportive care (including palliative care).

Tisagenlecleucel-T is administered intravenously as a single infusion.

Financial Factors

This technology is commissioned by NHS England.

NICE estimate that less than 100 children and young people in England are eligible for treatment with tisagenlecleucel.

When considering the condition's severity and its effect on quality and length of life, the most likely cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. Therefore, tisagenlecleucel is recommended for routine use in the NHS.

Tisagenlecleucel is a chimeric antigen receptor (CAR) T-cell therapy that has been available in the NHS since 2018 through the Cancer Drugs Fund. As a result, there is unlikely to be a substantial shift in treatment as a result of this guidance.

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

Selinexor with bortezomib and dexamethasone for previously treated multiple myeloma TA974

This guidance partially updates and replaces TA700 (terminated appraisal, published May 2021)

Recommendations

Selinexor plus bortezomib and dexamethasone is **recommended** as an option for treating multiple myeloma in adults, only if:

- they have had 1 previous line of treatment and their condition is refractory to both daratumumab and lenalidomide, or
- they have only had 2 previous lines of treatment and their condition is refractory to lenalidomide.

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

This recommendation is not intended to affect treatment with selinexor plus bortezomib and dexamethasone that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

The Technology

Multiple myeloma is a form of cancer that arises from plasma cells 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, carrying oxygen around the body and blood clotting. 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, tiredness, infections, hypercalcaemia and kidney problems.

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

For people whose disease is relapsed or refractory after at least 1 prior treatment NICE recommends: **TA129**, **TA586**, **TA695**, **TA657** and **TA897**.

For people whose condition is relapsed or refractory after at least 2 prior treatments, NICE recommends: **TA171**, **TA870** and **TA380**.

For people whose condition is relapsed or refractory after at least 3 prior treatments, NICE recommends: **TA427**, **TA783**, **TA658**.

Financial Factors

This technology is commissioned by NHS England.

The cost-effectiveness estimates for selinexor combination compared with carfilzomib plus dexamethasone at second line and with panobinostat combination at third line are within the range that NICE considers an acceptable use of NHS resources. Therefore, Selinexor combination is only recommended as a second-line treatment for multiple myeloma that is refractory to both daratumumab and lenalidomide, or as a third-line treatment for multiple myeloma that is refractory to lenalidomide.

NICE estimate that in Devon, 50 people will be eligible to second line treatment and 44 people will be eligible for third line treatment.

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

Atogepant for preventing migraine TA973

Recommendations

Atogepant is **recommended** as an option for preventing migraine in adults who have at least 4 migraine days per month, only if at least 3 preventative medicines have failed.

Stop atogepant after 12 weeks if the frequency of migraines does not reduce by:

- at least 50 % in episodic migraine (defined as fewer than 15 headache days per month)
- at least 30 % in chronic migraine (defined as 15 or more headache days per month, with at least 8 of those having features of migraine).

If people with the condition and their healthcare professional consider atogepant to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use

the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

This recommendation is not intended to affect treatment with atogepant that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

The Technology

A migraine is primarily a headache disorder which manifests as a throbbing head pain. It may be accompanied by nausea, vomiting and sensitivity to light, sound or other sensory stimuli. Migraine attacks usually last from 4 to 72 hours. Some people experience disturbances known as aura, which precede the headache and other symptoms, but the most common type of migraine is without aura.

The exact cause of migraines is unknown, but it is thought to be linked to changes in brain activity which temporarily affects nerve signals, chemicals and blood vessels in the brain. Factors that can trigger these changes include stress, changes in sleep pattern, overtiredness, menstruation or environmental triggers such as bright lights or specific medicines.

There are three broad approaches to managing migraine: lifestyle and trigger management, acute treatments and preventative treatments. Preventative 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.

NG150 recommends offering topiramate or propranolol and considering amitriptyline for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events.

Financial Factors

This technology is commissioned by ICBs.

Usual preventative medicines for people who have already had 3 preventative medicines that have not worked include, erenumab (**TA682**), fremanezumab (**TA764**), galcanezumab (**TA659**), eptinezumab (**TA871**), rimegepant (**TA906**, for episodic migraine only) or botulinum toxin type A (**TA260**, for chronic migraine only).

Clinical trial evidence shows that atogepant reduces monthly migraine days more than placebo, but there is no clinical trial evidence directly comparing it with other preventative medicines. The results from indirect comparisons are uncertain and it is unclear how well atogepant works compared with other preventative medicines for episodic or chronic migraine.

For episodic migraine, the most relevant comparator is rimegepant because it is also an oral preventative medicine. The most likely cost-effectiveness estimates for atogepant compared with rimegepant is within the range that NICE normally considers an acceptable use of NHS resources.

For chronic migraine, it is not clear whether atogepant is better or worse than the other preventative medicines, but it has lower costs. Therefore, atogepant is recommended for preventing episodic and chronic migraine after 3 or more preventative medicines.

NICE estimate that in Devon, 9 people with episodic migraine will be eligible for treatment and that 363 people with chronic migraine will be eligible for treatment.

Sirolimus for treating facial angiofibroma caused by tuberous sclerosis complex in people 6 years and over TA972 (*terminated appraisal*)

NICE is **unable to make a recommendation** on sirolimus for treating facial angiofibroma caused by tuberous sclerosis complex in people 6 years and over. This is because the company did not provide an evidence submission. NICE will review this decision if the company decides to make a submission.

Remdesivir and tixagevimab plus cilgavimab for treating COVID-19 TA971

This guidance updates recommendations on remdesivir and tixagevimab plus cilgavimab in NG191.

Recommendations

Remdesivir is **recommended** as an option for treating COVID-19 in hospitals in:

- adults, only if they have a high risk of serious illness (risk factors as defined in section 5 of **TA878**)
- babies, children and young people, only if they:
    - are aged 4 weeks to 17 years and weigh at least 3 kg and:
        - have pneumonia and
        - need supplemental oxygen, or
    - weigh at least 40 kg and have a high risk of serious illness (risk factors as defined in section 5 of **TA878**

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

Tixagevimab plus cilgavimab is **not recommended**, within its marketing authorisation for treating COVID-19 in adults who do not need supplemental oxygen and who have an increased risk of progression to severe COVID-19.

The Technology

COVID-19 is predominantly an acute respiratory illness caused by infection with 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.

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.

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

Post-COVID-19 syndrome (also known as long COVID) also has a significant burden for some people, including longer-term effects on breathing, pain and variations in heart rate. It is defined as any symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis.

Currently, established clinical management for most people in hospital with COVID-19 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. **NG191** also recommends therapeutics for treating COVID-19 for people in hospital.

Remdesivir is a viral RNA polymerase inhibitor. It is administered intravenously.

Tixagevimab and cilgavimab are mABs used in combination. They are administered as two separate intramuscular injections at two different muscles sites.

Financial Factors

These technologies are commissioned by ICBs.

Most of the clinical evidence for remdesivir and tixagevimab plus cilgavimab is highly uncertain because it comes from studies done before the dominant Omicron variants of SARS-CoV-2. Also, some evidence does not reflect clinical practice at the time of this evaluation.

The cost-effectiveness estimates are highly dependent on how well each treatment works compared with standard care and hospitalisation and mortality rates. Hospitalisation and mortality rates are lower with Omicron variants than earlier variants in the pandemic. These lower rates increase the cost-effectiveness estimates.

Remdesivir in adults

Clinical evidence suggests remdesivir is effective for treating mild COVID-19 in adults. Clinical evidence on remdesivir for treating COVID-19 in adults in hospital is highly uncertain. But it suggests that remdesivir can increase how long adults needing low-flow supplemental oxygen live compared with standard care.

The cost-effectiveness estimates for remdesivir are only likely to be within what NICE considers an acceptable use of NHS resources for adults in hospital who have a high risk of serious illness. Therefore, remdesivir is recommended for treating COVID-19 in this group.

Remdesivir in babies, children and young people

There is limited clinical evidence comparing remdesivir with standard care for treating severe COVID-19 in the groups of babies, children and young people as defined in the recommendations above. Therefore, the cost-effectiveness estimates are highly uncertain. But there are limited treatment options licensed for these groups and the number who would have remdesivir is very small. Therefore, remdesivir is recommended for treating COVID-19 in these groups.

Tixagevimab plus cilgavimab in adults

Evidence suggests that it is highly uncertain that tixagevimab plus cilgavimab is effective against Omicron variants of COVID-19. Because of this, it is not possible to reliably estimate its cost effectiveness, therefore it is not recommended.

Selinexor with dexamethasone for treating relapsed or refractory multiple myeloma after 4 or more treatmentsTA970

This guidance partially updates TA700 (terminated appraisal, published May 2021)

Recommendations

Selinexor plus dexamethasone is **recommended**, within its marketing authorisation, for treating multiple myeloma in adults when:

- they have had 4 or more treatments, and
- the condition is refractory to at least 2 proteasome inhibitors, 2 immunomodulatory agents and an anti-CD38 monoclonal antibody (penta-refractory), and
- the condition has progressed on the last treatment, and
- the company provides it according to the commercial arrangement.

The Technology

Multiple myeloma is a form of cancer that arises from plasma cells 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, carrying oxygen around the body and blood clotting. 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, tiredness, infections, hypercalcaemia and kidney problems.

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

For people whose disease is relapsed or refractory after at least 1 prior treatment NICE recommends: **TA129**, **TA586**, **TA695**, **TA657** and **TA897**.

For people whose condition is relapsed or refractory after at least 2 prior treatments, NICE recommends: **TA171**, **TA870** and **TA380**.

For people whose condition is relapsed or refractory after at least 3 prior treatments, NICE recommends: **TA427**, **TA783**, **TA658**.

Financial Factors

This technology is commissioned by NHS England.

Standard care for relapsed or refractory multiple myeloma after 4 or more treatments is best supportive care (BSC).

There is no direct clinical trial evidence that compares selinexor plus dexamethasone with BSC. But evidence from indirect comparisons suggests that it increases how long people live compared with BSC.

There is uncertainty in the economic model for selinexor plus dexamethasone. But, when considering the condition's severity and effect on quality and length of life, the most likely cost-effectiveness estimates are below what NICE considers to be a cost-effective use of NHS resources. Therefore, selinexor plus dexamethasone is recommended.

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over TA967

This guidance partially updates TA540 (published September 2018)

Recommendations

Pembrolizumab is **recommended** as an option for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over who have had at least 2 previous treatments and cannot have an autologous stem cell transplant (ASCT). It is recommended only if:

- they have already had brentuximab vedotin and
- pembrolizumab is stopped after 2 years of treatment or earlier if the person has a stem cell transplant or the disease progresses and
- the company provides it 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
- the nodular lymphocyte-predominant type.

Classical Hodgkin lymphomas contain the Reed-Sternberg cells (which are cancerous B lymphocyte cells).

Nodular lymphocyte-predominant lymphoma contains lymphocyte-predominant cells, a variant of Reed-Sternberg cells.

The most common 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.

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. However, autologous stem cell transplant may not be an option in some circumstances, for example, then the disease is refractory to chemotherapy, or when the person's age or co-morbidities prohibit this intervention.

NICE recommends the following TAs for Hodgkin lymphoma: **TA524**, **TA462** and **TA772**.

Financial Factors

This technology is commissioned by NHS England.

This evaluation reviews the evidence for pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people who have had brentuximab vedotin and cannot have an ASCT (**TA540**). It also reviews new data collected as part of the managed access agreement. The new evidence includes data from clinical trials and from people having treatment in the NHS in England.

When people with relapsed or refractory classical Hodgkin lymphoma cannot have an ASCT, they can have brentuximab vedotin. After that, they have standard care, which included chemotherapy and radiotherapy. Pembrolizumab would be offered instead of standard care and stopped after 2 years or earlier if the person's condition gets worse or they are able to have a stem cell transplant. This is in line with how people had pembrolizumab in the clinical trials and during the managed access period.

There is no evidence directly comparing pembrolizumab with standard care. But indirect comparisons suggest that people who have pembrolizumab live longer.

When considering the conditions severity and its effect on quality and length of life, the most likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources, therefore, pembrolizumab is recommended.

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma TA540 (UPDATE)

May 2024: Recommendation 1.2 was updated and replaced by TA967 on pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over (see above).

Recommendations

Pembrolizumab is **not recommended** for treating relapsed or refractory classical Hodgkin lymphoma in adults who have had autologous stem cell transplant and brentuximab vedotin.

This recommendation is not intended to affect treatment with pembrolizumab 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

See detail above for **TA967** Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over.

Financial Factors

This technology is commissioned by NHS England.

The marketing authorisation for pembrolizumab includes 2 subpopulations of people with relapsed or refractory classical Hodgkin lymphoma:

- people who have had an autologous stem cell transplant and brentuximab vedotin and
- people who have had brentuximab vedotin but cannot have autologous stem cell transplant.

There is no evidence directly comparing pembrolizumab with current standard care in either of the subpopulations. Indirect analyses suggest that having pembrolizumab after brentuximab vedotin may lead to longer progression-free survival than current treatment. This would increase the number of people who can have curative allogeneic stem cell transplant. It is uncertain how many people having pembrolizumab will be able to have allogeneic stem cell transplant and their long-term outcomes compared with those having standard care and this is a key driver of cost effectiveness.

Pembrolizumab meets NICE's criteria to be considered a life-extending treatment at the end of life.

Because of the uncertainties in the clinical effectiveness and the modelling, the cost-effectiveness estimates are uncertain. Because of this, pembrolizumab cannot be recommended for treating relapsed or refractory classical Hodgkin lymphoma in adults who have had *an autologous stem cell transplant and brentuximab vedotin*.

There is an unmet treatment need for people who have *had brentuximab vedotin and cannot have autologous stem cell transplant*. There are no licensed immunotherapies for this subpopulation.

In May 2024, NICE reviewed new evidence for pembrolizumab in this subpopulation submitted by the company and evidence collected as part of the Cancer Drugs Fund managed access agreement. NICE has therefore published new recommendations on pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over (**TA967**).

Highly Specialised Technology Guidance (HSTs)

Setmelanotide for treating obesity and hyperphagia in Barder-Biedl syndrome HST21

Recommendations

Setmelanotide is **recommended** as an option for treating obesity and hyperphagia in genetically confirmed Bardet-Biedl syndrome (BBS) in people aged 6 years and over, only if they are aged between 6 and 17 years when treatment starts. These people can carry on having setmelanotide as adults until they need to stop. Setmelanotide is only recommended if the company provided it according to the commercial arrangement.

This recommendation is not intended to affect treatment with setmelanotide that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop. For children or young people, this decision should be made jointly by them, their healthcare professional and their parents or carers.

The Technology

Obesity is a chronic condition characterised by increased body fat. People who are obese are at an increased risk of developing cardiovascular disease, type 2 diabetes, atherosclerosis, hypertension and dyslipidaemia. The most common method for measuring obesity is body mass index (BMI) which is calculated as a ration of weight to height squared. In adults, obesity is typically defined by a BMI of 30 kg/m^2 or more. In childhood, obesity is usually defined as a BMI at or above the 95^{th} percentile for individuals of the same age and sex.

BBS is a rare, recessively inherited condition caused by genetic mutations. Symptoms experienced vary but obesity is a key symptom due to the patient's increased appetite, caused by impairment of an area of the brain that controls appetite, the melanocortin-4 receptor (MC4R) pathway. Problems with weight management may further complicate issues with heart and blood vessels common in patients with BBS. Other symptoms may include cognitive impairment, polydactyly, renal anomalies, hypogonadism and visual impairment.

Standard management of overweight and obesity includes dietary and lifestyle advice, behaviour modification, pharmacological treatments and surgical intervention. Specialist multidisciplinary weight management interventions are also used in current practice.

Setmelanotide is a MC4R agonist with the potential to restore lost activity in the MC4R pathway and re-establish weight and appetite control in people with BBS. It is administered via subcutaneous injection.

Financial Factors

This technology is commissioned by NHS England.

In the population of children, young people and adults (which reflects the current population in the NHS), the uncertainties in the evidence mean that the cost-effectiveness estimates for setmelanotide are higher than what NICE normally considers an acceptable use of NHS resources within the context of a highly specialised technology. But setmelanotide is estimated to be cost effective in people who start taking it aged between 6 and 17 years. Therefore, setmelanotide is recommended for these people.

The eligible population for setmelanotide is around 150 per year in England in year 2024/25 rising to around 160 per year in 2028/29 after adjusting for expected population growth.

NICE estimate that in Devon, 4 people will be eligible for treatment. The company has a commercial arrangement. This makes setmelanotide available to the NHS with a discount.

NICE Guidelines (NGs)

None published this month

NICE Rapid COVID-19 Guidelines

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

This guideline covers managing COVID-19 in babies, children, young people and adults in community and hospital settings. It includes recommendations on communication, assessment, therapeutics for COVID-19, non-invasive respiratory support, preventing and managing acute complications, and identifying and managing co-infections.

May 2024: NICE updated the guidance on remdesivir and added a new recommendation on tixagevimab plus cilgavimab in line with NICE's technology appraisal guidance on remdesivir and tixagevimab plus cilgavimab for treating COVID-19 (TA971).

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)

Image-guided percutaneous laser ablation for primary and secondary liver tumours IPG788

Recommendations

Image-guided percutaneous laser ablation for primary and secondary liver cancers can be used in the NHS while more evidence is generated. It can only be used with **special arrangements** in place for clinical governance, informed consent and audit.

Clinicians wanting to do image-guided percutaneous laser ablation for primary and secondary liver tumours 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 advice shared decision making, including 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

Patient selection should be done by a multidisciplinary team experienced in managing primary and secondary liver tumours.

More research

More research is needed on:

- patient selection
- ablation success
- longer-term outcomes

The Condition

The most common type of primary liver cancer is hepatocellular carcinoma (HCC). Secondary cancer in the liver can arise from any primary site, but it most commonly spreads from cancers of the bowel, breast, lung, pancreas, stomach, ovary and neuroendocrine tumours.

Treatment for primary liver cancer depends on several factors, including the exact location and stage of the cancer, the person's liver function and any patient-related comorbidities. The treatment options include:

- surgical excision
- chemotherapy (conventional or hepatic artery infusion)
- transarterial chemoembolization (TACE)
- selective internal radiation therapy
- percutaneous ethanol injection
- local ablation techniques such as cryotherapy, radiofrequency and microwave ablation.

  A liver transplant (with curative intent) may be appropriate for some people

Treatment for secondary liver cancer depends on the site of the primary cancer, which parts of the liver are affected and whether the cancer has metastasised further. The most common treatment is chemotherapy, but other treatments include surgery, hormonal therapies, targeted therapies, ablation and embolization treatments.

The Procedure

Image guided percutaneous laser ablation is done under general anaesthesia or local anaesthesia with sedation. Depending on the size of the tumour, 1 or more (usually up to 4) optical fibres are percutaneously inserted into the liver using a small introducer needle. The fibre distance and energy deliver laser energy per fibre are adjusted to shape the area to be ablated. The fibres deliver laser energy for several minutes to heat the tissue until it is destroyed with a sufficient safety margin. The fibres work simultaneously to amplify the ablation volume. Image guidance is used to check the positioning of the fibres, monitor the treatment and verify the effective ablation area. The aim is to destroy the tumour.

Endoscopic duodenal mucosal resurfacing for insulin resistance in type 2 diabetes IPG787

Recommendations

More research is needed on endoscopic duodenal mucosal resurfacing for insulin resistance in type 2 diabetes.

This procedure should only be done as part of a **formal research study** and a research ethics committee needs to have approved its use.

More research

More research, which should ideally be adequately powered randomised controlled trials, analysis of registry data or other suitably designed studies, is needed on:

- patient selection
- procedure used
- quality of life
- blood sugar control
- change in antidiabetic medication (including insulin)
- complications
- long term outcomes

The Condition

Type 2 diabetes is a chronic, progressive metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in hyper glycaemia. The condition is commonly associated with obesity, physical inactivity, raised blood pressure, periodontitis, disturbed blood lipid levels and a tendency to develop thrombosis. It is recognised to lead to an increased cardiovascular and stroke risk.

Dietary control is the mainstay of type 2 diabetes treatment. Weight loss and being active are also recommended to help manage the condition. In addition to lifestyle modification, type 2 diabetes is controlled using metformin, insulin or other medicines, with the aim of keeping a person's blood sugar levels within a healthy range. These treatments have varying efficacy and can sometimes cause side effects, including hypoglycaemia. **NG28** describes its management.

The Procedure

Endoscopic duodenal mucosal resurfacing is a minimally invasive procedure. It involves endoscopic exploration under general anaesthesia or deep sedation. This is followed by submucosal expansion with saline and then the hydrothermal ablation of the duodenal mucosa under direct vision with fluoroscopic guidance. The aim is for mucosal regeneration and so to treat the duodenal dysfunction that is thought to contribute to insulin resistance.

Selective internal radiation therapy for neuroendocrine tumours that have metastasised to the liver IPG786

Recommendations

Use selective internal radiation therapy (SIRT) as an option for neuroendocrine tumours that have metastasised to the liver, with **standard arrangements** in place for clinical governance, consent and audit.

Patient selection should be done by a multidisciplinary team with experience in managing neuroendocrine tumours.

The procedure should only be done in specialist centres by clinicians trained and experienced in delivering SIRT.

Clinicians should enter details about everyone having this procedure into an appropriate registry.

The Condition

Neuroendocrine tumours grow in many organs of the body. The tumours start in cells that release hormones into the blood stream (neuroendocrine cells). The tumours commonly spread from other organs to the liver, where it may not be possible to remove them with surgery. Some metastatic symptoms of carcinoid syndrome are flushing of the skin, diarrhoea, fast heart rate and breathlessness. Some people with uncontrolled carcinoid syndrome may develop carcinoid heart disease and mesenteric fibrosis. This can reduce quality of life and prognosis and limit what treatments can be offered.

Current treatment options depend on the history and the clinical and histological presentation of the metastatic neuroendocrine tumours. They include:

- surgical resection
- percutaneous ablation
- systemic chemotherapy
- systemic somatostatin analogues
- peptide receptor radiation therapy

- other intra-arterial therapies such as:
    - transarterial bland embolization
    - transarterial chemoembolization
    - trug-eluting-bead transarterial chemoembolization.

The Procedure

In selective internal radiation therapy (SIRT), microspheres containing sources of beta radiation are infused through the hepatic artery and carried by blood flow to the vessels that supply the tumour. Infusion through this route minimises damage to health liver tissues because they are mainly supplied by the portal vein, whereas the tumours are mainly supplied by hepatic arteries.

The procedure is done in 2 stages. First, the work-up is done to assess blood supply to the tumour, assess lung shunt, exclude extrahepatic uptake and plan personalised dosimetry. Then, during SIRT, the microspheres containing the radionuclide are infused through a catheter placed in the hepatic artery. Catheterisation is done under local anaesthetic.

Medical Technologies Guidance (MTGs)

None published this month

Diagnostics Guidance (DGs)

Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer DG58

This guidance replaces DG34 (published December 2018)

Recommendations

Lymph node-positive early breast cancer

Can be used

Use EndoPredict, Oncotype DX or Prosigna as options alongside consideration of clinical risk factors to guide adjuvant chemotherapy decisions for treating oestrogen receptor (ER)- or progesterone receptor (PR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer with 1 to 3 positive lymph nodes for:

- women who have been through the menopause
- men
- trans, non-binary or intersex people, depending on their hormonal profile.

Use clinical judgement to determine if testing is suitable for men, trans or non-binary or intersex people.

Should not be used

For women who have not been through the menopause, EndoPredict, Oncotype DX and Prosigna **should not be used** to guide adjuvant chemotherapy decisions for ER- or PR-positive, HER2-negative early breast cancer with 1 to 3 positive lymph nodes.

MammaPrint **should not be used** to guide adjuvant chemotherapy decisions for people with ER- or PR-positive, HER2-negative early breast cancer with 1 to 3 positive lymph nodes.

Lymph node-negative and micrometastatic early breast cancer

Can be used with evidence generation

EndoPredict, Oncotype DX or Prosigna **can be used** in the NHS while more evidence is generated, to guide adjuvant chemotherapy decisions for people with ER- or PR-positive, HER2-negative and lymph node (LN)-negative (including micrometastatic disease) early breast cancer, only if:

- they have an intermediate risk of distant recurrence using a validated tool such as Predict or the Nottingham Prognostic Index
- clinicians and companies make timely, complete and linkable record-level test data available to the National Cancer Registration and Analysis Service.

Should not be used

MammaPrint and IHC4+C **should not be used** to guide adjuvant chemotherapy decisions for people with ER- or PR-positive, HER2-negative and LN-negative early breast cancer.

Conditions for use

Use EndoPredict, Oncotype DX or Prosigna to guide adjuvant chemotherapy decisions for ER- or PR-positive, HER2-negative early breast cancer only if:

- the person having the test will use the results to help them choose, with their healthcare professional, whether or not to have adjuvant chemotherapy
- the tests are used within their intended purpose:
    - EndoPredict (ER-positive, or both ER- and PR-positive)
    - Oncotype DX (ER- or PR-positive, or both)
    - Prosigna (ER- or PR-positive, or both; only for women who have been through the menopause)

- the companies provide the tests to the NHS with the discounts agreed in the access proposals
- laboratories processing the tests take part in a UK national external quality assurance scheme.

Use the test and results alongside NICE's guideline on shared decision making (**NG197**). An oncologist should explain to the person what their tumour profiling test results mean, and the risks and benefits of treatment options based on all available risk factors.

The Technology

Breast cancer is the most common cancer in the UK. Early breast cancer is cancer that has not spread beyond the breast or lymph nodes in armpit on the same side of the body. Early breast cancer can be locally advanced; this means that the cancer has spread to the surrounding areas such as the nearby lymph nodes, skin or chest muscle, but not to distant parts of the body.

When cancer cells have been detected, further tests are done to provide more information on the characteristics of the tumour. The results of these tests are used to classify the cancer and to determine which types of treatment it is most likely to respond to. Typically, tests determine oestrogen receptor (ER), progesterone receptor (PR) and HER2 status.

NG101 describes the care pathway. Surgery is often the initial treatment for ER- or PR-positive, HER2-negative early and locally advanced breast cancer. After surgery, further treatment (adjuvant treatment) might be recommended and this can include:

- radiotherapy
- chemotherapy
- endocrine therapy
- targeted therapy

Some people may have treatment before surgery (neoadjuvant treatment).

Tumour profiling tests provide information on the expression of genes in tumour samples from people with early breast cancer. The test results provide a risk profile of an individual’s breast cancer. This can be considered with other clinical risk factors, such as nodule status and tumour size, to better predict the risk of disease recurrence in the future. Some tests may also predict how beneficial chemotherapy may be for the person.

Financial Factors

These diagnostic tests are commissioned by NHS England.

Some NHS trusts are already offering tumour profiling tests to inform chemotherapy decisions for people with LN positive early breast cancer. Many began doing so during the COVID-19 pandemic to help relieve pressure on infusion services. The recommendations may lead to savings at a local level from a reduction in the number of people receiving chemotherapy treatment.

Depending on current local practice, areas which may require additional resources and result in additional costs include:

- time to prepare and submit the number of additional samples for testing.
- additional capacity in laboratories to perform the additional tumour profiling tests using EndoPredict or Prosigna.
- time for the reporting and discussing of results.

Implementing the guideline may:

- reduce the number of chemotherapy treatments for people with oestrogen receptor (ER)- or progesterone receptor (PR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer with 1 to 3 positive lymph nodes. The reduction in chemotherapy treatment recommendations will be dependent on the test used.
- identify people who are most likely to benefit from chemotherapy treatment. These people can be prioritized for treatment, while people who are less likely to benefit can avoid unnecessary treatments.
- lead to improved consistency of best practice across the country.
- lead to better health outcomes and care experience.

NICE estimate that in Devon, 74 people will be eligible for testing.

Artificial intelligence (AI)-derived software to help clinical decision making in stroke DG57 UPDATE

May 2024: This guidance was updated to include Viz in recommendation 1.1, because it now has a high enough class of CE mark to be included in the recommendations:

The following artificial intelligence (AI)-derived software **can be used** in the NHS while more evidence is generated, to support review and reporting of CT brain scans for people who have had a suspected stroke:

- e-Stroke
- RapidAI
- Viz.

  These technologies can only be used once they have appropriate Digital Technology Assessment Criteria (DTAC) approval.

Health Technology Evaluations (HTE)

None published this month

NICE Quality Standards

None published this month.

Current NICE Consultations

Title/link	End date of consultation
Heart failure algorithms for remote monitoring in people with cardiac implantable electronic device	04/06/2024
Novel home-testing devices for diagnosing obstructive sleep apnoea/ hypopnoea syndrome	05/06/2024
Efanesoctocog alfa for treating and preventing bleeding episodes in haemophillia A [ID6170]	10/06/2024
Danicopan as an add-on treatment to a C5 inhibitor for treating extravascular haemolysis in adults with paroxysmal nocturnal haemoglobinuria [ID5088]	19/06/2024
Endoscopic bipolar radiofrequency ablation for malignant biliary obstruction	28/06/2024
Direct skeletal fixation of limb or digit prostheses using intraosseous transcutaneous implants	28/06/2024