NHS
Devon
Clinical Commissioning Group

NICE Update Bulletin: April 2022

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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.

April 2022: NICE added a new recommendation on nirmatrelvir and ritonavir (Paxlovid) for people at high risk of progression to severe COVID-19.

Technology Appraisals (TAs)

Venetoclax with low dose cytarabine for untreated acute myeloid leukaemia (AML) when intensive chemotherapy is unsuitable TA787

Recommendations

Venetoclax with low dose cytarabine is **recommended** as an option for untreated acute myeloid leukaemia in adults when intensive chemotherapy is unsuitable, only if:

- they have over 30% bone marrow blasts
- the company provides venetoclax according to the commercial arrangement.

This is not intended to affect treatment with venetoclax with low dose cytarabine 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

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 who are fit enough, intensive treatment is available. It is conducted in 2 phases: induction chemotherapy to reduce the number of blast cells, followed by consolidation chemotherapy to reduce the risk of recurrence. For people with good general health, the treatment options are intensive chemotherapy and allogeneic haematopoietic stem cell transplant (HSCT).

There are alternative treatment options for people for whom intensive chemotherapy is considered not suitable. Treatments include low dose cytarabine and azacitidine.

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.

NICE do not expect this guidance to have a significant impact on resources. This is because venetoclax with low dose cytarabine is a further treatment option available at a similar price to the current treatment options and the population size is small.

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

Tucatinib with trastuzumab and capecitabine for treating HER2-positive advanced breast cancer after 2 or more anti-HER2 therapies TA786

Recommendations

Tucatinib with trastuzumab and capecitabine is recommended, within its marketing authorisation, as an option for treating HER2-positive locally advanced or metastatic breast cancer in adults after 2 or more anti-HER2 treatment therapies, only if the company provides tucatinib according to the commercial arrangement.

The Technology

Metastatic breast cancer is when the cancer has spread beyond the breast and nearby lymph nodes to other organs in the body. 'Locally advanced' cancer describes tumours that are larger than 5cm in size and may have grown into the skin or muscle of the chest or nearby lymph nodes. Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. Some breast cancer cells have higher than normal levels of HER2 receptors. In this case, the tumour is described as being HER2-positive.

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment depends on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease and previous treatments.

TA509 recommends pertuzumab with trastuzumab and docetaxel as first line treatment for people with HER2-positive unresectable or metastatic breast cancer who have not had previous anti-HER2 treatment or chemotherapy for their metastatic disease.

TA34 recommends trastuzumab with paclitaxel as an option for people with tumours expressing HER2 who have not received chemotherapy for metastatic breast cancer and in whom anthracycline is not appropriate.

TA458 recommends trastuzumab emtansine as an option for treating HER2-positive unresectable, locally advanced or metastatic breast cancer after trastuzumab and a taxane in people whose disease has progressed.

TA423 recommends eribulin for locally advanced or metastatic breast cancer after 2 or more lines of chemotherapy regimens. In addition, lapatinib is a HER2 targeted treatment which in combination with capecitabine or trastuzumab is also licensed for use at this point in the treatment pathway.

Tucatinib is a selective tyrosine kinase inhibitor of the HER2 receptor protein on the surface of the cancer cell. By inhibiting HER2, tucatinib interrupts cell signalling pathways and in turn stops the growth of HER2-positive tumours. It is given orally.

Trastuzumab is a recombinant, humanized monoclonal antibody, which specifically targets the HER2 protein expressed on the cell-surface, inhibiting cell proliferation. It is given intravenously or subcutaneously.

Capecitabine is a fluoropyrimidine carbamate precursor of the chemotherapy drug fluorouracil. Enzymes principally located in the liver and tumour tissue change capecitabine into fluorouracil, which stops cells making and repairing DNA. It is given orally.

Financial Factors

This technology is commissioned by NHS England.

Clinical trial evidence shows that tucatinib combination increases the time people have before their cancer gets worse and how long they live compared with trastuzumab with capecitabine. But trastuzumab with capecitabine is not standard care in the NHS. Comparing tucatinib combination indirectly with chemotherapy suggests it may increase the time people have before their cancer gets worse and how long they live. It is likely that tucatinib combination improves people's quality of life before and after their cancer gets worse compared with chemotherapy.

The economic model does not take into account all of the benefits of tucatinib combination, particularly for people with brain metastases. Taking this into account, the cost-effectiveness estimates for tucatinib combination are likely to be within what NICE normally considers an acceptable use of NHS resources

NICE estimate that in England, 570 people per year will be eligible for treatment with tucatinib with trastuzumab and capecitabine. 170 people in third-line treatment and 90 people in fourth-line treatment will receive tucatinib with trastuzumab and capecitabine from year 3 onwards once uptake has reached 45%. This equates to 4 people receiving tucatinib with trastuzumab and capecitabine as third line treatment and 2 people as fourth line treatment for the Devon population.

Nivolumab with cabozantinib for untreated advanced renal cell carcinoma *(terminated appraisal)* TA785

NICE is unable to make a recommendation on nivolumab with cabozantinib for untreated advanced renal cell carcinoma. This is because the company withdrew the evidence submission. NICE will review this decision if the company decides to make a submission.

Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer TA784

This guidance updates and replaces TA528 (published July 2018) which was available through the Cancer Drugs Fund

Recommendations

Niraparib is **recommended** as an option for treating relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to the most recent course of platinum-based chemotherapy in adults. It is recommended only if:

- they have a BRCA mutation and have had 2 courses of platinum-based chemotherapy, or
- they do not have a BRCA mutation and have had 2 or more courses of platinum-based chemotherapy, and
- the company provides it according to the commercial arrangement.

The Technology

Ovarian cancer is a cancerous growth that occurs in different parts of the ovary or fallopian tubes. The most common type of ovarian cancer, high grade serous type, is thought to arise from the peritoneum or fallopian tube and presents after it has spread to the ovary. Ovarian cancer is classified from stage I to stage IV. Advanced ovarian cancer falls within stages II and IV. In stage II, the disease has grown outside the ovaries but is still within the pelvic area. Stage III denotes disease that is locally advanced and has spread outside the pelvis into the abdominal cavity. Stage IV denotes that distant metastasis to other body organs such as the liver and the pleura has occurred. Some people have gene mutations that may increase the risk of ovarian cancer. Mutated inherited genes that increase the risk of ovarian cancer include BRCA 1 or 2.

Ovarian cancer may be categorised according to the response to initial platinum chemotherapy as follows:

- Platinum-sensitive. Disease responds to platinum-based therapy but relapses after 6 months or more, which can be subdivided into fully and partially platinum-sensitive disease
- Platinum-resistant. Disease which relapses within 6 months of completion of platinum-based chemotherapy.
- Platinum-refractory. Disease does not respond to initial platinum-based chemotherapy.

In people whose disease relapses following initial therapy:

TA389 recommends paclitaxel as monotherapy or in combination with platinum, and pegylated liposomal doxorubicin hydrochloride as monotherapy or in combination with platinum, for treating recurrent ovarian cancer.

TA381 recommends olaparib as an option for maintenance treatment of relapsed, platinum sensitive ovarian, fallopian tube or peritoneal cancer in adults who have BRCA1 or BRCA2 mutations and whose disease has responded to platinum based chemotherapy, if they have had 3 or more courses of platinum based chemotherapy.

Niraparib is a poly-ADP-ribose polymerase (PARP) inhibitor which inhibits PARP-1 and PARP-2 proteins. PARP proteins are involved in DNA repair. Niraparib is administered orally.

Financial Factors

This technology is commissioned by NHS England.

Additional evidence collected as part of the Cancer Drugs Fund managed access agreement (TA528) has been reviewed. Niraparib improves how long people with relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer live before their disease progresses. New evidence collected suggests it may also extend how long these people live. However, it is uncertain if niraparib extends how long people without a BRCA mutation may live.

Cost-effectiveness estimates for niraparib in people with a BRCA mutation whose disease has responded to 2 courses of platinum-based chemotherapy and for people without a BRCA mutation whose disease has responded to 2 or more courses of platinum-based chemotherapy are in the range usually considered a cost-effective use of NHS resources.

NICE estimate that, in England, 80 people with relapsed, platinum-sensitive high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer with a BRCA mutation and 330 people without a BRCA mutation are eligible for treatment with niraparib in the first year and that 250 people will start treatment with niraparib in year 1 onwards and this will reduce as uptake of PARP inhibitors for first-line maintenance increases.

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

Daratumumab monotherapy for treating relapsed and refractory multiple myeloma TA783

This guidance updates and replaces TA510 (published March 2018) which was available through the Cancer Drugs Fund.

Recommendations

Daratumumab monotherapy is **recommended** as an option for treating relapsed and refractory multiple myeloma in adults who have had a proteasome inhibitor and an immunomodulator, and whose disease progressed on the last treatment, only if:

- they have daratumumab after 3 treatments and
- the company provides daratumumab 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. Myeloma cells suppress the development of normal blood cells that are responsible for fighting 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, bone fractures, 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. Following initial treatment, subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

TA129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people who are at first relapse having received 1 prior therapy and who have undergone or are unsuitable for bone marrow transplantation.

TA171 recommends lenalidomide in combination with dexamethasone as a treatment option for people with multiple myeloma who have received at least 2 prior therapies.

TA380 recommends panobinostat in combination with bortezomib and dexamethasone as an option for treating multiple myeloma in adults with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent.

TA427 recommends pomalidomide plus low-dose dexamethasone as a treatment option for adults who have had at least 3 previous treatments including both lenalidomide and bortezomib.

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

Financial Factors

This technology is commissioned by NHS England.

Additional evidence has been collected as part of the Cancer Drugs Fund managed access agreement. The new clinical evidence shows that daratumumab monotherapy increases how long people live compared with pomalidomide plus dexamethasone, but by how much is still uncertain. Because of this uncertainty, the cost-effectiveness estimates vary, but the most likely estimates are within what NICE considers an acceptable use of NHS resources.

NICE estimate that in England approximately 790 people (18 in Devon) will be eligible for treatment with daratumumab monotherapy and that by 2026/27 around 110 people (2 in Devon) will start treatment with daratumumab; 14% of the eligible population.

Highly Specialised Technology Guidance (HSTs)

Elosulfase alfa for treating mucopolysaccharidosis type 4A (MPS 4A) HST19

This guidance updates and replaces HST2 (published December 2015). Elosulfase alfa for treating MPS 4A was previously available as part of a managed access agreement.

Recommendations

Elosulfase alfa is **recommended**, within its marketing authorisation, as an option for treating mucopolysaccharidosis type 4A (MPS 4A) for people of all ages. It is only recommended if the company provides elosulfase alfa according to the commercial arrangement.

The Technology

MPS 4A is an inherited lysosomal storage disorder caused by a lack of the enzyme N-acetylgalactosamine-6-sulfataserare. It is rare and progressive and has a significant effect on the quality of life of people with the condition, and their families and carers. MPS 4A causes a wide spectrum of symptoms including joint and skeletal abnormalities, hearing loss, corneal clouding and heart valve disease. The joint and skeletal abnormalities associated with this condition lead to short stature, difficulties with breathing and movement, spinal instability and spinal cord compression.

Current treatment options are limited. Management of MPS 4A requires a multi-disciplinary approach to treat the symptoms and address the complications. This may include surgery for skeletal problems, respiratory support, drugs to treat heart valve lesions, dental and eye care, pain relief and hearing aids and ventilating tubes to manage deafness and middle ear effusions

Elosulfase alfa is a recombinant form of human Nacetylgalactosamine-6-sulfatase. It is intended to directly replace the lacking N-acetylgalactosamine-6-sulfatase enzyme in people with mucopolysaccharidosis type IVA. It is administered by intravenous infusion.

Financial Factors

This technology is commissioned by NHS England.

Clinical trial evidence, data from the managed access agreement and feedback from patient and carer experience collected suggests that MPS 4A is likely to progress more slowly when treated with elosulfase alfa compared with standard care. The health and quality-of-life benefits of elosulfase alfa are considered to be substantial. Also, data from younger people who may benefit more from elosulfase alfa was not specifically included and additional skeletal benefits may not be fully captured.

Taking these factors into account, the cost-effectiveness estimates are within the range that NICE considers acceptable for highly specialised technologies.

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

NICE Guidelines (NGs)

Epilepsies in children, young people and adults NG217

This guideline updates and replaces CG137 (published January 2012)

This guideline covers diagnosing and managing epilepsy in children, young people and adults in primary and secondary care and referral to tertiary services. It aims to improve diagnosis and treatment for different seizure types and epilepsy syndromes and reduce the risks for people with epilepsy.

Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults NG215

This guideline covers general principles for prescribing and managing withdrawal from opioids, benzodiazepines, gabapentinoids, Z-drugs and antidepressants in primary and secondary care. It does not cover gabapentinoids prescribed for epilepsy, nor opioids prescribed for acute or cancer pain, or at the end of life, nor management of illicit drug dependence.

Stroke and transient ischaemic attack in over 16s: diagnosis and initial management NG128 (UPDATE)

This guideline updates and replaces NICE guideline CG68 (published July 2008).

This guideline covers interventions in the acute stage of a stroke or transient ischaemic attack (TIA). It offers the best clinical advice on the diagnosis and acute management of stroke and TIA in the 48 hours after onset of symptoms.

April 2022: NICE have reviewed the evidence on blood pressure control for people with acute intracerebral haemorrhage and updated recommendations 1.5.4, 1.5.5, 1.5.6 and 1.5.8.

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)

Liposuction for chronic lymphoedema IPG723

This guidance replaces IPG588 (published August 2017).

Recommendations

Evidence on the efficacy and safety of liposuction for chronic lymphoedema is adequate. The evidence on safety shows that the potential risks include venous thromboembolism, fat embolism, and fluid overload. This procedure can be used 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 must be done by a multidisciplinary team with expertise in managing lymphoedema.

The procedure should only be done in specialist centres by clinicians with training and expertise in liposuction for lymphoedema following agreed perioperative protocols.

The Condition

Lymphoedema is the abnormal accumulation of subcutaneous fluid and sometimes fat in body tissues. It leads to chronic swelling that can cause disability, pain, and cosmetic issues. Any part of the body can be affected, but the condition is most common in the arms and legs. Lymphoedema can be complicated by recurrent infection (cellulitis), which further damages the lymphatic vessels and aggravates the condition.

Primary lymphoedema results from a range of conditions that affect how the lymphatic system develops and functions. Secondary lymphoedema results from damage to the lymphatic system or removal of lymph nodes by surgery, radiation, infection, or injury.

Liposuction may be particularly appropriate for select people with primary lymphoedema and for people with cancer-related lymphoedema.

The current conservative treatment for lymphoedema is decongestive lymphatic therapy. This involves compression bandaging, skin care and exercise. For some people, manual lymphatic drainage massage that stimulates lymph to move away from the affected limb may also be helpful. Once decongestive lymphatic therapy sessions are stopped, the person is fitted with a custom-made compression garment, which is worn every day for life.

These techniques aim to reduce the pain and discomfort associated with lymphoedema. Procedures to restore lymphatic flow from the limb, such as lymphovenous anastomosis or lymph node transfer, are less commonly used and are usually reserved for earlier-stage lymphoedema.

The Procedure

Liposuction for chronic lymphoedema is usually done under general anaesthesia but using regional nerve blockade is also possible. A tourniquet is applied to the proximal limb. A few small incisions are made in the limb. Cannulas, connected to a vacuum pump, are inserted into the incisions and oedematous adipose tissue is removed by vacuum aspiration.

Liposuction is done around and all the way along the limb up to the distal border of the tourniquet. The tourniquet is then removed; the proximal limb, which is unable to be controlled by tourniquet, is infused with tumescent solution; and the fat and fluid from this area are aspirated. Immediately after liposuction, a compression bandage is applied to the limb to control any bleeding and to prevent post-surgical oedema.

After the procedure, a custom-made compression garment must be worn for life to maintain the volume reduction. This garment needs to be revised multiple times until the oedema volume has been reduced as much as possible and a steady state has been reached.

Intramedullary distraction for upper limb lengthening IPG722

Recommendations

Evidence on the safety and efficacy of intramedullary distraction for upper limb lengthening is inadequate in quantity and quality. But because this is a rare condition with limited alternative treatments, the procedure can be considered as long as **special arrangements** for clinical governance, consent, and audit or research are in place.

Clinicians wanting to use intramedullary distraction for upper limb lengthening should:

- Inform the clinical governance leads in their healthcare organisation.
- Give people (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 people (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 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:

- 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.

This technically challenging procedure should only be done in specialist centres by surgeons with specific training and experience in upper limb lengthening techniques, using a multidisciplinary approach.

Report any problems with a medical device using the Medicines and Healthcare products Regulatory Agency's Yellow Card Scheme.

Further research, which could be registry data, should report details of patient selection, device selection, technique used, procedural outcomes, long-term outcomes including quality of life, the need for repeat interventions or surgery, and complication rates.

The Condition

People may have different limb lengths caused by trauma or infection or, more rarely, hypoplasia or dysplasia (congenital conditions such as achondroplasia, Ollier's disease, and brachial plexus palsy). The condition can be unilateral or bilateral. Unequal limb lengths can lead to dis ability and limit functional ability.

Lengthening of a short upper limb can be attempted using external fixation devices, which exert force along the long axis of bone to induce new bone formation. The main potential problems with external fixation include infection of the pin tracts, and external frames that are impractical and aesthetically unpleasant. In some people with an underlying bone pathology, once the external fixation is removed, the new bone is augmented by either an internal plate fixation or an intramedullary nail.

The Procedure

Intramedullary distraction systems are intramedullary devices that are similar to intramedullary nails used for managing fractures. Once inserted and fixed, they can be mechanically lengthened over time using different techniques, resulting in a controlled lengthening of the bone. The device can be inserted into the humerus from the top, though this may cause damage to the shoulder muscles, or the lower end.

The device exerts a force along the long axis of the bone, which stimulates new bone formation in the gap, causing bone lengthening. Over a period of days, weeks or months, sequential distractions are used to produce the target limb length. Different devices achieve distraction in different ways. For example, some work mechanically by releasing a preloaded spring or using a motor. Others use an external electromagnetic device.

The intramedullary device remains implanted until bone consolidation is completed. When there is radiological evidence of adequate bone consolidation across the gap, full function and limb use (weight bearing) is permitted. The device can usually be removed using standard surgical techniques or may be left in place indefinitely.

Medical Technologies Guidance (MTGs)

None published this month.

Diagnostic Guidance (DGs)

None published this month.

NICE Quality Standards

None published this month.

Current NICE Consultations

Title / link	End date of consultation
Upadacitinib, abrocitinib and tralokinumab for dermatitis [ID3960]	04/05/22
Antenatal care (update)	10/05/22
Obesity: identification and classification of overweight and obesity (update)	11/05/22
GID-MT566 Faecal microbiota transplant for recurrent Clostridioides difficile infection	11/05/22
Falls in older people: assessing risk and prevention	12/05/22
Extracorporeal shockwave therapy for calcific tendinopathy in the shoulder	24/05/22
Ab interno canaloplasty for open-angle glaucoma	24/05/22

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