NHS Devon

NICE Update Bulletin: October 2024

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

1. **Quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive acute myeloid leukaemia TA1013**
2. **Belzutifan for treating tumours associated with von Hippel-Lindau disease TA1011**
3. **Danicopan with ravulizumab or eculizumab for treating paroxysmal nocturnal haemoglobinuria TA1010**
4. **Latanaoprost-netarsudil for previously treated primary open-angle glaucoma or ocular hypertension TA1009**
5. **Acute kidney injury: prevention, detection and management NG148 (UPDATE)**
6. **Heart failure algorithms for remote monitoring in people with cardiac implantable electronic devices DG61**
7. **Digital technologies for assessing attention deficit hyperactivity disorder (ADHD) DG60**
8. **Current NICE Consultations**

Technology Appraisals (TAs)

Quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive acute myeloid leukaemia TA1013

Recommendations

Quizartinib is **recommended**, within its marketing authorisation, as an option for newly diagnosed FLT3-ITD-positive acute myeloid leukaemia (AML) in adults, when used:

- with standard cytarabine and anthracycline chemotherapy as induction treatment, then
- with standard cytarabine chemotherapy as consolidation treatment, then
- alone as maintenance treatment.

Quizartinib is only recommended if the company provides it 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 over production of early immature myeloid white blood cells (blasts). The abnormal cells build up in the bone marrow and blood and interfere with normal blood cell production. AML progresses quickly over weeks or months and is fatal if not treated. Anaemia, bleeding problems and serious infections are common symptoms of AML. People with AML also feel fatigued which can impact daily life.

FLT3-ITD-positive is a term used to describe AML cells that have an internal tandem duplication (ITD) mutation in the FLT3 gene. The FLT3 gene plays a role in cell growth and division. FLT3-ITD-positive AML is associated with poor prognosis, with people having a lower chance of achieving remission and shorter overall survival.

The aim of treatment for AML is to cure it. For people who are fit enough, intensive treatment is available. It is conducted in two phases: induction therapy to achieve remission, followed by consolidation therapy to reduce risk of relapse.

NICE has published the following related guidance:

- **TA523** midostaurin for untreated acute myeloid leukaemia
- **TA552** liposomal cytarabine-daunorubicin for untreated acute myeloid leukaemia

People may be offered haematopoietic stem cell transplantation if they are in good health.

Following the intensive treatment stage, people who are in complete remission may be offered long-term maintenance therapy to prevent recurrence of a new episode. Treatment options include monotherapy with midostaurin (**TA523**) or oral azacitidine (**TA827**).

Financial Factors

This technology is commissioned by NHS England.

Evidence from a clinical trial show that quizartinib plus standard chemotherapy increases how long people live compared with placebo plus standard chemotherapy. Quizartinib has not been directly compared in a clinical trial with midostaurin. Results from indirect comparisons mostly suggest there is no difference in how long people having quizartinib live, or how likely it is that their AML will come back, compared with midostaurin. But these results are uncertain because:

- the people in the midostaurin trial were younger than the people who would have quizartinib in the NHS and clinical practice has changed since the trial was done.
- some important characteristics between people in the trials could not be compared.

Because of the uncertainties in the clinical evidence, the cost-effectiveness estimates are uncertain. But the most likely estimates are within the range that NICE considers an acceptable use of NHS resources. Therefore, quizartinib is recommended.

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

NICE estimate that in Devon at year 5, the incidence of AML will be 55 people, of which 15 people will have an FLT3-ITD mutation. The eligible population for treatment with quizartinib will be 9 people.

Belzutifan for treating tumours associated with von Hippel-Lindau disease TA1011

Recommendations

Belzutifan is **recommended** with **managed access** as an option for treating von Hippel-Lindau (VHL) disease in adults:

- who need treatment for VHL-associated renal cell carcinoma, central nervous system hemangioblastomas or pancreatic neuroendocrine tumours and
- when localised procedures are unsuitable or undesirable.

It is only recommended if the conditions in the managed access agreement for belzutifan are followed.

This recommendation is not intended to affect treatment with belzutifan 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

Von Hippel-Lindau (VHL) is a rare disorder caused by a faulty gene. Tumours develop in one or more parts of the body and may be benign or malignant. Many of these tumours involve the abnormal growth of blood vessels in parts of the body which are particularly rich in blood vessels. Areas most frequently affected are the eyes, the back of the brain (cerebellum), the spinal cord, the kidneys, the adrenal glands and the pancreas. Multiple tumours can present in the same or different organs/systems at the same time. Disease management involves regular and lifelong screening to identify new or changed tumours. VHL treatment aims to balance preserving organ function and preventing tumour metastasis.

Kidney cancer affects around 24% to 45% of people with VHL. People with VHL are offered a scan of the kidneys every year to check for tumours. If they are found, they are monitored carefully so people may have treatment at an appropriate time.

Central nervous system (CNS) haemangioblastomas are found in the brain and spinal cord. These are the most common tumour type in VHL affecting around 70% of people. These tumours are benign but can cause significant morbidity and mortality.

Pancreatic neuroendocrine tumours (PNETs) affect around 15% of people with VHL. Treatment depends on the size of the tumour.

With regular screening, most tumours associated with VHL are detected at an early stage. However, for some people, tumours cannot be managed through localised procedures. For people with advanced or metastatic tumours, systemic treatments are similar to those for patients with cancers unrelated to VHL.

Financial Factors

This technology is commissioned by NHS England.

Clinical-effectiveness evidence from a small study suggests that belzutifan reduces tumour size. It also suggests that it increases the amount of time people have before their condition gets worse, but by how much is uncertain.

There are also uncertainties in the economic model, as well as assumptions that likely favour belzutifan. It is not clear what the most likely cost-effectiveness estimates are for belzutifan and it cannot be recommended for routine use.

Belzutifan has the potential to be cost effective, but more evidence is needed to reduce the uncertainties. More evidence is needed to reduce the uncertainties. More evidence from the trial and NHS practice could help address these. Therefore, belzutifan is recommended for use with managed access.

Danicopan with ravulizumab or eculizumab for treating paroxysmal nocturnal haemoglobinuria TA1010

Recommendations

Danicopan is **recommended**, as an add-on to ravulizumab or eculizumab as an option for treating paroxysmal nocturnal haemoglobinuria (PNH) in adults who have residual haemolytic anaemia, only if:

- They have clinically significant extravascular haemolysis while on treatment with a complement component 5 inhibitor (C5 inhibitor) and
- The company provides it according to the commercial arrangement

This recommendation is not intended to affect treatment with danicopan 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

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare blood condition in which red blood cells are attacked by the body's immune system. It is characterised by intravascular haemolysis (rupturing of red blood cells) with resultant anaemia often leading to transfusion dependence, severe disabling symptoms of haemolysis and thrombosis (blood clotting). People with PNH may also experience extravascular haemolysis (EVH; haemolysis taking place in the liver, spleen, bone marrow and lymph nodes), which can be clinically significant and lead to symptomatic anaemia and ongoing transfusion dependence.

The severity of PNH is varied and not everyone with the condition will need treatment. The National PNH service is commissioned by NHS England as a specialist service. Clinical management includes treatment with complement inhibitors, although some people will experience haemolysis despite treatment with complement inhibitors:

- eculizumab, a C5 inhibitor, is commissioned for PNH with high disease activity.
- ravulizumab, a C5 inhibitor, is recommended for adults with haemolysis with clinical symptoms suggesting high disease activity, or whose disease is clinically stable after having eculizumab for at least 6 months (**TA698**)
- pegcetacoplan, a C3 inhibitor, is recommended for adults who have anaemia after at least 3 months of treatment with a C5 inhibitor (**TA778**)

Allogeneic stem cell transplantation may be curative but is associated with significant risks and is only considered for patients with severe bone marrow failure. Other interventions, notably red blood cell transfusions, folic acid, iron tablets and anti-coagulant treatments are offered to prevent or treat complications.

Financial Factors

This technology is commissioned by NHS England.

Evidence from clinical trials shows that danicopan with a C5 inhibitor increases haemoglobin levels and reduces the need for blood transfusions more than a C5 inhibitor alone. There is no direct evidence comparing danicopan with pegcetacoplan and the results from an indirect comparison are uncertain.

The economic evidence for danicopan add-on treatment has some uncertainties, including long-term breakthrough haemolysis rates and around some of the assumptions used to estimate cost effectiveness. But the most likely cost-effectiveness estimates are within the range usually considered a cost-effective use of NHS resources. Therefore, danicopan is recommended.

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

Latanaoprost-netarsudil for previously treated primary open-angle glaucoma or ocular hypertension TA1009

Recommendations

Latanoprost-netarsudil is **recommended** as an option for reducing intraocular pressure (IOP) in adults with primary open-angle glaucoma or ocular hypertension when a prostaglandin analogue alone has not reduced IOP enough, only if:

- they have then tried a fixed-dose combination treatment and it has not reduced IOP enough, or
- a fixed-dose combination treatment containing beta-blockers is unsuitable

This recommendation is not intended to affect treatment with latanoprost-netarsudil 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

Glaucoma refers to a group of eye conditions characterised by progressive damage to the optic nerve. It can lead to impaired peripheral vision and eventually total loss of sight, if it is not detected and treated early. Glaucoma is usually associated with an increase in pressure within the eye. This can be caused by either the production of too much aqueous humour by the ciliary body or decreased outflow (drainage) of the fluid.

Primary, or chronic, open-angle glaucoma (POAG) accounts for over 70% of all glaucoma cases. It develops slowly over many years and does not cause any noticeable symptoms until irreversible

damage has occurred to the optic nerve. The peripheral vision is affected first and without treatment, central vision may also be lost resulting in loss of visual acuity.

Ocular hypertension (OHT) is the term used to describe elevated intraocular pressure (IOP; OHT is IOP greater than 21 mmHg) in the absence of optic nerve damage or visual field loss. It can be present for many years without the development of glaucoma, however sustained elevation of IOP causes damage to the optic nerve head and is a major risk factor for the development of glaucoma. Lowering OHT has been shown to lower the risk of developing glaucoma.

NG81 (Diagnosis and management of glaucoma) recommends a generic prostaglandin analogue as ongoing treatment for people with IOP of 24 mmHg or more if they are at risk of visual impairment within their lifetime.

For those that cannot tolerate their current treatment, an alternative generic prostaglandin analogue should be offered and if this is not tolerated, a beta-blocker. If none of these options are tolerated (or not reducing IOP sufficiently), non-generic prostaglandin analogues, carbonic anhydrase inhibitors, sympathomimetics, miotics or a combination of treatments should be offered. People whose IOP cannot be reduced sufficiently with pharmacological treatment should be referred to a consultant ophthalmologist to discuss other options.

A generic prostaglandin analogue is offered to people with confirmed POAG. For people with advanced POAG, surgery with pharmacological augmentation is offered. If adherence and eye drop instillation technique are satisfactory but IOP has not been reduced sufficiently to prevent the risk of progression to sight loss despite pharmacological treatment, or the drug is not tolerated, a drug from another therapeutic class can be offered and topical drugs from different therapeutic classes may be needed at the same time to control IOP. Alternatively, laser trabeculoplasty or other glaucoma surgery can be offered.

Netarsudil-latanoprost is an eye drop that contains a fixed dose of netarsudil with latanoprost.

Financial Factors

This technology is commissioned by ICBs.

A cost comparison suggests that latanoprost-netarsudil has similar or lower costs than most branded fixed dose combination treatments. These are usually used after a fixed-dose combination treatment has not reduced IOP enough. Latanoprost-netarsudil also has similar or lower costs compared with some generic fixed-dose combination treatment. Therefore, latanoprost-netarsudil is recommended.

NICE estimate that at year 5 in Devon, 2,243 people with primary open-angle glaucoma and 1,570 people with ocular hypertension will be eligible for treatment. NICE estimate that latanoprost-netarsudil will have 5% of the market share, representing 191 people in total.

Highly Specialised Technology Guidance (HSTs)

None published this month.

NICE Guidelines (NGs)

Acute kidney injury: prevention, detection and management NG148 (UPDATE)

This guideline covers preventing, detecting and managing acute kidney injury in children, young people and adults. It aims to improve assessment and detection by non-specialists and specifies when people should be referred to specialist services. This will improve early recognition and treatment and reduce the risk of complications in people with acute kidney injury.

October 2024: NICE have reviewed the evidence and made new and updated recommendations, and a recommendation for research, on risk factors for acute kidney injury in adults having iodine-based contrast media.

The eGFR for adults with chronic kidney disease was changed from less than 40 ml/min/1.73 m^2 to less than 30 ml/min/1.73 m^2 for consistency with the rest of the guideline.

The term 'contrast-induced kidney injury' was updated to 'contrast-associated acute kidney injury' in line with current terminology.

NICE Rapid COVID-19 Guidelines

None published this month

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)

None published this month.

Medical Technologies Guidance (MTGs)

None published this month

Diagnostics Guidance (DGs)

Heart failure algorithms for remote monitoring in people with cardiac implantable electronic devices DG61

Recommendations

Use as an option

For people with heart failure

Use **HeartLogic** and **TriageHF** as options for algorithm-based remote monitoring in people with cardiac implantable electronic devices (CIEDs) who have heart failure. They should be used as part of a specialist multidisciplinary heart failure service with alerts reviewed and acted on by specialist healthcare professionals.

Can only be used in research

For people with heart failure

More research is needed on **HeartInsight** for algorithm-based remote monitoring in people with CIEDs who are at risk of developing heart failure, before they can be routinely used in the NHS.

For people at risk of developing heart failure

More research is needed on **HeartInsight**, **HeartLogic** and **TriageHF** for algorithm-based remote monitoring in people with CIEDs who are at risk of developing heart failure, before they can be routinely used in the NHS.

More research

More research for the technologies listed above is needed in the populations outlined. This research is needed on:

- Prognostic accuracy
- Rates of false positives or unexplained alerts
- Hospitalisation rates
- Hear-failure-related mortality rates
- Rates of emergency department or primary care visits
- Patient-reported outcomes

Access to the technologies listed above in the populations outlined should be through company, research or non-core NHS funding and clinical or financial risks should be appropriately managed.

Do not use

CorVue should not be used for algorithm-based remote monitoring in people with CIEDs who have or are at risk of developing heart failure.

The Technology

Heart failure is a clinical syndrome caused by any structural or functional cardiac disorder that impairs the heart's ability to efficiently pump blood around the body. The most common symptoms of heart failure are breathlessness, fatigue and oedema. Conditions that cause heart failure include:

- coronary heart disease
- high blood pressure
- heart rhythm or valve abnormalities and
- conditions affecting the heart muscle (cardiomyopathies and myocarditis)

Cardiac implantable electronic devices (CIEDs) are recommended as treatment options for some people who have or are at high risk of heart failure. The different types of CIEDs are pacemakers, Implantable cardiovascular defibrillators and cardiac resynchronisation therapy devices.

Remote monitoring is the ability for a CIED to communicate wirelessly with a remote monitoring system. People who have CIEDs must be followed up by hospitals for regular technical reviews of how their device is working. **NG106** recommends that reviews are offered every 6 months for people whose condition is stable, but clinical experts highlighted that in practice most people would have a review annually. Sometimes clinical reviews are only triggered if the person with the CIED reports worsening symptoms.

Some CIEDs have algorithm-based remote monitoring incorporated in the device. Heart failure algorithms analyse and collate different clinical data recorded by the device to detect gradual worsening of heart failure. The system can send alerts to healthcare professionals to prompt a review of the stored data. This enables proactive investigation into the cause of the suspected decompensation, potentially before the person even feels symptomatic. This could ensure that people have appropriate treatment as early as possible, reducing the number of unnecessary hospital visits.

Financial Factors

These technologies are commissioned by ICBs.

Evidence for **HeartLogic** and **TriageHF** shows that they can detect the signs of worsening heart failure that could lead to hospitalisation or an unscheduled clinic visit (referred to as heart failure events). Evidence shows that CIEDs used with **HeartLogic** or **TriageHF** reduce hospitalisations compared with CIEDs used with remote monitoring only.

It is uncertain whether the **HeartInsight** algorithm can detect early signs of worsening heart failure. There is also no evidence to show how well CEIDs that use **HeartInsight** reduce heart failure events. **HeartInsight** may be better at predicting worsening heart failure and reducing hospitalisations than CIEDs without algorithms, so more research is recommended.

More research is also recommended for **HeartInsight**, **HeartLogic** and **TriageHF** in people at risk of developing heart failure because there is very limited evidence in this population.

CorVue collects only intrathoracic impedance data, while other algorithms monitor additional factors. Clinical trial evidence suggests that **CorVue** fails to detect some signs of worsening heart failure and has a high rate of false-positive alerts. Therefore, **CorVue** is not recommended for use in the NHS.

NICE estimate that in Devon, the number of people with an electronic device who would potentially benefit from the technology is 558.

Digital technologies for assessing attention deficit hyperactivity disorder (ADHD) DG60

Recommendations

Use as an option

Use QbTest as an option to help **diagnose** attention deficit hyperactivity disorder (ADHD) in people aged 6 to 17 years. It should only be used with standard clinical assessment by a healthcare professional

Can only be used in research

For people with suspected ADHD

More research is needed on using the following digital technologies to help **diagnose** ADHD:

- QbTest in people 18 years and over
- EFSim Test
- EFSim Test Web Version
- Nesplora Attention Adults Aquarium
- Nesplora Attention Kids Aula
- QbCheck

For people with ADHD

More research is needed on using the following digital technologies to **evaluate** response to treatment:

- QbTest
- EFSim Test
- EFSim Test Web Version
- Nesplora Attention Adults Aquarium
- Nesplora Attention Kids Aula
- QbCheck

More research

More research is needed on:

- how the digital technologies are used in and their impact on, decision making in ADHD diagnosis, including for more complex cases
- the impact of the digital technologies for people with suspected ADHD when used to help diagnose ADHD
- the impact of the digital technologies for people with a diagnosis of ADHD when used:
    - during dose titration
    - as part of longer-term treatment monitoring

Access to the digital technologies for the uses described should be through company, research, or non-core NHS funding and clinical or financial risks should be appropriately managed.

The Technology

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition characterised by a persistent pattern of hyperactivity, impulsivity and inattention that interferes with daily and occupational functioning.

This may manifest as: wandering off-task; having difficulty sustaining focus; being disorganised; excessive motor activity when it is not appropriate; excessive fidgeting, tapping and talkativeness; social intrusiveness and making important decisions without considering the long-term consequences. People with ADHD may make hasty actions that occur in the moment without forethought and have a high potential for harm to the individual.

ADHD is associated with psychiatric disorders including oppositional defiant disorder, conduct disorder, substance misuse and mood disorders such as depression and mania. Autism spectrum

disorder, dyslexia, dyscalculia and dyspraxia commonly co-occur in people with ADHD. Overall prognosis may depend on the severity and management of any comorbid disorders.

Treatment for ADHD may be non-pharmacological, including psychoeducation, ADHD coaching, parent training, or environmental changes. Pharmacological treatment may include stimulant or non-stimulant medication. Medication doses are titrated against symptoms and adverse effects until dose optimisation is achieved.

Standard clinical assessment for ADHD is based on diagnostic criteria that require training and experience to apply correctly and require clinical judgement, relying on information obtained from a range of sources. Information from these sources may often be incomplete or contradictory, requiring multiple clinic visits or observations to reach a diagnostic decision. Diagnosis of ADHD is further complicated by similarities in presentation and overlap with other neurodevelopmental disorders and mental health conditions, which may lead to difficulties and delays in decision making.

Digital technologies that combine measures of cognition and motor (physical) activity may help healthcare professionals when considering a diagnosis of ADHD, by providing additional objective information. This could reduce the number or length of clinical appointments needed to reach a diagnosis, reducing patient waiting lists and freeing up NHS resources. It may also provide people with quicker access to appropriate further care or assessment.

Financial Factors

These technologies are commissioned by ICBs.

The clinical trial evidence suggests that information from QbTest helps to reduce the time it takes for people aged 6 to 17 years to get a diagnostic decision compared with standard clinical assessment by a healthcare professional. Economic modelling using data from this trial suggests the QbTest is cost effective compared with standard clinical assessment for these people.

For people under 18, there is limited evidence for technologies other than QbTest. The other technologies are different to QbTest in how they measure ADHD traits, so it is unclear whether they would have a similar impact. Therefore, it was not possible to assess the cost effectiveness of the technologies other than QbTest when used to help diagnose ADHD for people aged 6 to 17 years and further research is needed.

For adults, there is limited evidence for any of the technologies and the evidence from people under 18 is not generalisable to adults, therefore more research is needed in this group.

After an ADHD diagnosis, the technologies could also be used to help evaluate response to treatment, which may aid decisions about continuing or changing treatment. Little evidence is available on whether any technologies are clinically or cost effective for evaluating response to treatment. More research is needed to help assess this.

NICE estimate that in Devon, at year five, the eligible population for QbTest to help diagnose ADHD in 6–17-year-olds would be 6,433.

Health Technology Evaluations (HTE)

None published this month.

NICE Quality Standards

None published this month.

Current NICE Consultations

Title/link	End date of consultation
Artificial intelligence technologies to help detect fractures on X-rays in urgent care	05/11/2024
Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease	20/11/2024
Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer	20/11/2024
Leniolisib for activated phosphoinositide 3-kinase delta syndrome in people 12 years and over	21/11/2024
Falls: assessment and prevention in older people and people 50 and over at higher risk (update)	28/11/2024