NICE Update Bulletin October 2015 issued 29th October 2015

Hyperlinks to the relevant NICE web page are included, to activate link left click on your mouse. Details are also available from the NICE website (**http://www.nice.org.uk**)

Type	Guidance title and reference number
Technology Appraisals (TAs)	**Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab TA357** **Recommendations** 1.1 Pembrolizumab is recommended as an option for treating advanced (unresectable or metastatic) melanoma in adults only: •after the disease has progressed with ipilimumab and, for BRAF V600 mutation-positive disease, a BRAF or MEK inhibitor and •when the company provides pembrolizumab with the discount agreed in the patient access scheme **The technology** Pembrolizumab is a humanised monoclonal antibody. It acts on the programmed cell death protein-1 immune checkpoint receptor pathway. It has a marketing authorisation in the UK as monotherapy 'for the treatment of advanced (unresectable or metastatic) melanoma in adults'. Previously, pembrolizumab was available in the NHS through the early access to medicines schemes from the UK Medicines and Healthcare products Regulatory Agency. Pembrolizumab is administered intravenously for 30 minutes at a dose of 2 mg/kg every 3 weeks until disease progression or unacceptable toxicity. **Financial factors** The acquisition cost of pembrolizumab is £1,315 per 50-mg vial (excluding VAT; company's submission). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of pembrolizumab with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. **Tolvaptan for treating autosomal dominant polycystic kidney disease TA358** **Recommendations** 1.1 Tolvaptan is recommended as an option for treating autosomal dominant polycystic kidney disease in adults to slow the progression of cyst development and renal insufficiency only if: • they have chronic kidney disease stage 2 or 3 at the start of treatment • there is evidence of rapidly progressing disease and • the company provides it with the discount agreed in the patient access scheme. 1.2 People whose treatment with tolvaptan is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop. **The technology** Tolvaptan is a selective vasopressin antagonist. By inhibiting the binding of vasopressin to the V2 receptors, tolvaptan reduces cell proliferation, cyst formation and fluid excretion. This reduces kidney growth and protects kidney function. Tolvaptan has a marketing authorisation in the UK 'to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with CKD stage 1 to 3 at initiation of treatment with evidence of rapidly progressing disease'.

Financial factors

Tolvaptan is taken orally, twice daily as a split dose. Doses can be titrated according to tolerability up to a maximum total daily dose of 120 mg. It is available as 15 mg, 30 mg, 60 mg and 90 mg tablets, in 28-day packs of split-dose tablets, at a flat net price of £1,208.20, equating to £43.15 per day, regardless of dose. The company provided these costs to NICE because the British National Formulary (BNF) had not listed the price at the time of producing this guidance. The annual cost of tolvaptan is estimated by the company to be £15,750 per person. The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of tolvaptan, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.

According to the NICE costing report around 2,300 people in England may be eligible for treatment with tolvaptan for ADPKD. This equates to 4 people per 100,000 population.

Idelalisib for treating chronic lymphocytic leukaemia TA359

Recommendations

1.1 Idelalisib, in combination with rituximab, is recommended:

- for untreated chronic lymphocytic leukaemia in adults with a 17p deletion or TP53 mutation or
- for chronic lymphocytic leukaemia in adults when the disease has been treated but has relapsed within 24 months.

Idelalisib is recommended only if the company provides the drug with the discount agreed in the simple discount agreement.

1.2 People whose treatment with idelalisib is not recommended in this NICE guidance but was started within the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

The technology

Idelalisib is a first-in-class inhibitor of enzymes that regulate important cellular functions including proliferation, cell death and migration. It has a marketing authorisation in the UK for use 'in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia who have received at least 1 prior therapy, or as first-line treatment in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy'.

Financial factors

Idelalisib is priced at £3,114.75 for 60 150-mg tablets (British National Formulary 2015). The mean cost of a 1-year treatment course for idelalisib is £37,922. The company has a simple discount agreement that provides a discount to the list price of idelalisib. The level of the discount is commercial in confidence.

Paclitaxel as albumin-bound nanoparticles in combination with gemcitabine for previously untreated metastatic pancreatic cancer TA360

Recommendations

1.1 Paclitaxel as albumin-bound nanoparticles in combination with gemcitabine **is not recommended** within its marketing authorisation for adults with previously untreated metastatic adenocarcinoma of the pancreas.

1.2 People whose treatment with paclitaxel as albumin-bound nanoparticles, in combination with gemcitabine, was started within the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

The technology

Paclitaxel formulated as albumin-bound nanoparticles has a UK marketing authorisation in combination with gemcitabine for the first-line treatment of adults with metastatic adenocarcinoma of the pancreas. Paclitaxel inhibits cancer growth by blocking cell

	division and promoting cell death. The formulation contains albumin to help transport paclitaxel through the walls of blood vessels. This is thought to increase the amount of paclitaxel in the area of the tumour. **Financial factors** The list price of nab-paclitaxel is £246 per 100 mg vial (excluding VAT; British National Formulary [BNF] edition 67). The company estimated the average cost of a 28-day cycle of treatment of nab-paclitaxel to be £1481 (excluding VAT). Median time on treatment with nab-paclitaxel from the CA046 study was 3.4 months, equating to a cost of approximately £5,035 per patient (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts. **Simeprevir in combination with sofosbuvir for treating genotype 1 or 4 chronic hepatitis C (terminated appraisal) TA361** NICE is unable to make a recommendation about the use in the NHS of simeprevir in combination with sofosbuvir for treating genotype 1 or 4 chronic hepatitis C because no evidence submission was received from Janssen for the technology. **Paclitaxel as albumin-bound nanoparticles with carboplatin for untreated non-small-cell lung cancer (terminated appraisal) TA362** NICE is unable to make a recommendation about the use in the NHS of paclitaxel as albumin-bound nanoparticles with carboplatin for adults with untreated non-small-cell lung cancer when potentially curative surgery or radiation therapy or both are unsuitable, because no evidence submission was received from Celgene technology.
Highly specialized technology guidance (HSTs)	**None published so far this month**

Note: From January 2015 NICE has decided to use a single set of methods and processes to develop all NICE guidelines, whether they are clinical, public health, social care, safe staffing or medicines practice.

Technology appraisals, interventional procedures, medical technologies and diagnostics guidance; and quality standards and advice products, are unaffected by this change.

NICE Guidelines (NGs)	**Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset NG16** **Background** This guideline makes recommendations on approaches in mid-life to delay or prevent the onset of dementia, disability and frailty in later life. These terms describe sets of symptoms and outcomes that can be caused by a wide range of conditions. The risk of dementia, disability and frailty will sometimes be determined by factors that can't be changed, such as inherited conditions or injury. But changing specific risk factors and behaviours can reduce the risk of dementia, disability and frailty for many people. These changeable factors – smoking, lack of physical activity, alcohol consumption, poor diet and being overweight – are the focus of this guideline. **Recommendations** 1 Encouraging healthy behaviours 2 Integrating dementia risk reduction prevention policies 3 Raising awareness of risk of dementia, disability and frailty 4 Producing information on reducing the risks of dementia, disability and frailty

	5 Preventing tobacco use 6 Improving the environment to promote physical activity 7 Reducing alcohol-related risk 8 Supporting people to eat healthily 9 Delivering services to promote behaviour change 10 Providing accessible services 11 Providing advice on reducing the risks of dementia, disability and frailty at every appropriate opportunity 12 Providing physical activity opportunities 13 Provide training 14 Leading by example in the public sector 15 Providing support in the workplace
Interventional Procedures Guidance (IPGs)	**Implanting a baroreceptor stimulation device for resistant hypertension IPG533** **Recommendations** 1.1 Current evidence on the safety and efficacy of implanting a baroreceptor stimulation device for resistant hypertension is inadequate. **Therefore, this procedure should only be used in the context of research.** 1.2 Further research on implanting a baroreceptor stimulation device for resistant hypertension should document patient selection in detail and should specify the devices and techniques used, and any adjunctive therapies. It should describe the changes in blood pressure that are considered to result from baroreceptor stimulation, and those that might be caused by other factors. Outcomes should include the duration of effect of baroreceptor stimulation; device durability; and the complications of hypertension, such as myocardial infarction and stroke. **The procedure** The device consists of an electrode placed on 1 of the carotid sinuses and a battery-powered implantable generator. Implanting a baroreceptor stimulation device for resistant hypertension aims to lower blood pressure by electrically stimulating the carotid baroreflex, which controls blood pressure by regulating autonomic nervous activity. The device is usually activated about a month after implantation. Clinic staff adjust therapy settings, such as the frequency, amplitude and pulse-width of stimulation, using wireless communication when the patient attends hospital for follow-up appointments.
Medical Technologies Guidance	None published so far this month
Diagnostics Guidance	**Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) DG18** **Recommendations** 1.1 The procalcitonin tests (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) show promise but there is currently insufficient evidence to recommend their routine adoption in the NHS. Further research on procalcitonin tests is recommended for guiding decisions to: • stop antibiotic treatment in people with confirmed or highly suspected sepsis in the intensive care unit or • start and stop antibiotic treatment in people with suspected bacterial infection presenting to the emergency department.

	Centres currently using procalcitonin tests to guide these decisions are encouraged to participate in research and data collection. **The Technology** Procalcitonin is involved in maintaining calcium levels in the blood and is an indirect biomarker of infection. It is released into the circulation in response to pro-inflammatory stimuli, especially those originating from bacteria. Procalcitonin testing can be used to help clinicians to diagnose bacterial infection (that can cause sepsis) and guide decisions on starting antibiotic treatment. Procalcitonin levels are usually low in people with viral infections, chronic inflammatory disorders or autoimmune processes. **Background** The most common type of bacterial infection in people attending the emergency department is respiratory tract infection. Lower respiratory tract infection includes: acute bronchitis; acute exacerbations of chronic obstructive pulmonary disease or asthma; and pneumonia. It is a major cause of sepsis in children and adults. In addition to the lungs, the most common sites of bacterial infection leading to sepsis are the urinary tract, abdomen and pelvis. Sepsis can also result from skin infections (such as cellulitis), post-surgical infections and infections of the nervous system (such as meningitis or encephalitis).
NICE Quality Standards	**Learning disabilities: challenging behaviour QS101** NICE quality standards describe high-priority areas for quality improvement in a defined care or service area. Each standard consists of a prioritised set of specific, concise and measurable statements. They draw on existing guidance, which provides an underpinning, comprehensive set of recommendations, and are designed to support the measurement of improvement. This quality standard covers the care of children, young people and adults with a learning disability and behaviour that challenges. **List of quality statements** Statement 1. People with a learning disability have a comprehensive annual health assessment from their GP. Statement 2. People with a learning disability and behaviour that challenges have an initial assessment to identify possible triggers, environmental factors and function of the behaviour. Statement 3. People with a learning disability and behaviour that challenges have a designated person responsible for coordinating the behaviour support plan and ensuring that it is reviewed. Statement 4. People with a learning disability and behaviour that challenges take part in personalised daily activities. Statement 5. People with a learning disability and behaviour that challenges have a documented review every time a restrictive intervention is used. Statement 6. People with a learning disability and behaviour that challenges only receive antipsychotic medication as part of treatment that includes psychosocial interventions. Statement 7. People with a learning disability and behaviour that challenges have a multidisciplinary review of their antipsychotic medication 12 weeks after starting treatment and then at least every 6 months. Statement 8. Parents or carers of children aged under 12 years with a learning disability and behaviour that challenges are offered a parent-training programme. **Bipolar disorder, psychosis and schizophrenia in children and young people QS102** This quality standard covers the recognition, early intervention and management of

	bipolar disorder, psychosis and schizophrenia (including related psychotic disorders such as schizoaffective disorder, schizophreniform disorder and delusional disorder) in children and young people under 18. **List of quality statements** Statement 1. Children and young people who are referred to a specialist mental health service with a first episode of psychosis start assessment within 2 weeks. Statement 2. Children and young people with a first episode of psychosis and their family members are offered family intervention. Statement 3. Children and young people newly diagnosed with bipolar depression or a first episode of psychosis are offered a psychological intervention. Statement 4. Parents and carers of children and young people newly diagnosed with bipolar disorder, psychosis or schizophrenia are given information about carer-focused education and support. Statement 5. Children and young people with bipolar disorder, psychosis or schizophrenia are given healthy lifestyle advice at diagnosis and at annual review. Statement 6. Children and young people with bipolar disorder, psychosis or schizophrenia prescribed antipsychotic medication have their treatment monitored for side effects. Statement 7 (developmental). Children and young people with bipolar disorder, psychosis or schizophrenia who are in crisis are offered home treatment if it is suitable. Statement 8. Children and young people with bipolar disorder, psychosis and schizophrenia have arrangements for accessing education or employment-related training included in their care plan.
Commissioning Guides	**Nalmefene HTTA325** Technology appraisal support This resource has been developed to provide practical information and advice on NICE technology appraisal guidance on nalmefene for reducing alcohol consumption in people with alcohol dependence. It is intended to be used by both clinical and non-clinical staff when implementing this NICE guidance at a local level. It may be of particular interest to Health and Wellbeing Boards. NICE's Adoption and Impact Programme worked with local authorities and NHS organisations to share their learning and experiences of putting nalmefene into their alcohol care pathway. The information presented in this resource is intended for the sole purpose of supporting the decisions that are made around the introduction of nalmefene. It summarises the issues that are considered to be of significance to local authorities and the NHS, but is not NICE guidance. The information presented has not been assessed by the Evidence Review Group and was not considered by the Technology Appraisal Committee when it considered the consultation comments and developed its final recommendations on nalmefene for reducing alcohol consumption in people with alcohol dependence.
Public health briefings for local government	**None published so far this month**

Current NICE consultations with links and start and finish dates for stakeholders to make contribution

Title / link	Start date of consultation	End date of consultation
Diabetes in adults QS (update) : Topic engagement	16/10/2015	30/10/2015
Bladder cancer : Topic engagement	16/10/2015	30/10/2015
Diagnostic services: the scope	05/10/2015	02/11/2015
Food allergy and anaphylaxis: quality standard consultation	05/10/2015	02/11/2015
Medicines optimisation : Quality Standard consultation	05/10/2015	02/11/2015
Preventing excess winter deaths and morbidity: quality standard consultation	07/10/2015	04/11/2015
Skin cancer : Topic engagement	22/10/2015	05/11/2015
Coeliac disease : Topic engagement	22/10/2015	05/11/2015
Duchenne muscular dystrophy (nonsense mutation) - ataluren [ID428] : Evaluation consultation	16/10/2015	06/11/2015
Air pollution - outdoor air quality and health : Call for evidence	12/10/2015	09/11/2015
Hypercholesterolaemia - ezetimibe (review TA132) [ID627] : Appraisal consultation	21/10/2015	10/11/2015
Myelofibrosis (splenomegaly, symptoms) - ruxolitinib (review TA289) [ID831] : Appraisal consultation	21/10/2015	10/11/2015
Spectra Optia Apheresis System for automated red blood cell exchange in patients with sickle cell disease : Draft guidance	19/10/2015	16/11/2015
Angioplasty and/or stenting to treat peripheral arterial disease causing refractory erectile dysfunction : Interventional procedure consultation	23/10/2015	20/11/2015
Endovascular aneurysm sealing for abdominal aortic aneurysm : Interventional procedure consultation	23/10/2015	20/11/2015
Mechanical clot retrieval for treating acute ischaemic stroke : Interventional procedure consultation	23/10/2015	20/11/2015
Normothermic ex-vivo preservation of hearts from brainstem dead donors for clinical transplantation : Interventional procedure consultation	23/10/2015	20/11/2015
Preoperative tests (update) : Draft guidance consultation	12/10/2015	23/11/2015
The safe use and management of controlled drugs : Draft guidance consultation	28/10/2015	25/11/2015

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