NICE Update Bulletin July 2014 for guidance issued Wednesday 23rd July 2014

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)	**Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen TA316** **Background** The cause of prostate cancer is thought to be multi-factorial, involving both environmental and genetic factors. The incidence of prostate cancer increases with age and is higher in men of African-Caribbean family origin. In England and Wales, there were around 37,000 people diagnosed with prostate cancer in 2009, and over 9,600 deaths from prostate cancer in 2010. Around 55–65% of people with prostate cancer develop metastatic disease (that is, the cancer spreads to other parts of the body). Over 90% of people with metastatic prostate cancer initially respond to hormonal therapy but eventually become resistant to it. **Recommendations** 1.1 Enzalutamide is recommended within its marketing authorisation as an option for treating metastatic hormone-relapsed prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy, only if the manufacturer provides enzalutamide with the discount agreed in the patient access scheme. 1.2 The use of enzalutamide for treating metastatic hormone-relapsed prostate cancer previously treated with abiraterone is not covered by this guidance. **The technology** Enzalutamide is an oral androgen receptor signalling inhibitor that reduces the proliferation of prostate cancer cells and therefore stops the growth of cancerous tumours. It has a UK marketing authorisation 'for the treatment of adult men with metastatic castrate-resistant prostate cancer whose disease has progressed on or after docetaxel therapy'. The recommended dosage of enzalutamide is 160 mg once daily until disease progression. **Financial factors** Enzalutamide costs £2734.67 for 1 pack of 112 40-mg capsules, (excluding VAT; 'British national formulary' [BNF] website accessed March 2014). Assuming a daily dose of 160 mg and a mean length of treatment of 8.5 months, the manufacturer estimated that the average cost of treatment with enzalutamide, based on the list price, is £25,269. **The commissioner for this technology is NHS England.** NICE does not expect the guidance to have a significant impact on NHS resources. This is because most people who are eligible for treatment with enzalutamide are already eligible for treatment with abiraterone which has a similar cost. **Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of technology appraisal guidance 182) TA317** **Background** Acute coronary syndromes refers to a group of symptoms associated with acute myocardial ischaemia with or without infarction. It encompasses a spectrum of disorders or syndromes including acute myocardial infarction and unstable angina pectoris. Acute coronary syndromes are usually the result of an acute or sub-acute primary reduction of myocardial oxygen supply provoked by disruption of an atherosclerotic plaque (build-up of material in a heart vessel) associated with inflammation, thrombosis, vasoconstriction and microembolisation.

Recommendations

Prasugrel 10 mg in combination with aspirin is recommended as an option within its marketing authorisation, that is, for preventing atherothrombotic events in adults with acute coronary syndrome (unstable angina [UA], non-ST segment elevation myocardial infarction [NSTEMI] or ST segment elevation myocardial infarction [STEMI]) having primary or delayed percutaneous coronary intervention.

The technology

Prasugrel is an oral inhibitor of platelet activation and aggregation. It works by the irreversible binding of its active metabolite to the P2Y12 class of adenosine diphosphate receptors on platelets. It has a marketing authorisation when co-administered with aspirin for the prevention of atherothrombotic events in adults with acute coronary syndrome (that is, unstable angina or non-ST-segment-elevation myocardial infarction [NSTEMI] or ST-segment-elevation myocardial infarction [STEMI]) undergoing primary or delayed percutaneous coronary intervention. The summary of product characteristics for prasugrel states that it should be started with a single 60 mg loading dose and then continued at 10 mg once a day. People taking prasugrel should also take 75 mg to 325 mg aspirin daily. Treatment for up to 12 months is recommended unless stopping prasugrel is clinically indicated.

Financial factors

The price of prasugrel is £47.56 per 28-tab pack (excluding VAT, British National Formulary [BNF] edition 67). The cost of treatment for 12 months is £628.47 (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts. This guidance is unlikely to result in a significant change in resource use in the NHS because prasugrel is an alternative treatment option to clopidogrel or ticagrelor and the population affected is small.

Lubiprostone for treating chronic idiopathic constipation TA318

Background

Chronic constipation is defined as 2 or more of the following symptoms at least a quarter of the time for at least 6 months: straining, lumpy or hard stools, a sensation of incomplete evacuation, a sensation of anorectal obstruction or blockage, and/or less than 3 defecations per week. Constipation may also be the consequence of an underlying condition. However, when constipation cannot be explained by any anatomical, physiological, radiological or histological abnormalities, it is referred to as idiopathic constipation.

Recommendations

1.1 Lubiprostone is recommended as an option for treating chronic idiopathic constipation, that is, for adults in whom treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and for whom invasive treatment for constipation is being considered.

1.2 If treatment with lubiprostone is not effective after 2 weeks, the person should be re-examined and the benefit of continuing treatment reconsidered.

1.3 Lubiprostone should only be prescribed by a clinician with experience of treating chronic idiopathic constipation, who has carefully reviewed the person's previous courses of laxative treatments specified in 1.1.

The technology

Lubiprostone is a prostone that specifically activates a chloride ion channel located in the apical intestinal membrane enhancing the intestinal fluid secretion. It is administered orally. Lubiprostone has a UK marketing authorisation for the 'treatment of chronic idiopathic constipation and associated symptoms in adults when response to diet and non-pharmacological measures (for example, educational measures, physical activity) are inappropriate'. It is given orally at a dose of 24 micrograms twice daily. The summary of product characteristics states that a course of treatment for constipation with lubiprostone is 2 weeks.

Financial factors

The cost of an initial 2-week course of treatment is £29.68, after which response is

	assessed, and those people continuing treatment receive the 56-capsule packs. Costs may vary in different settings because of negotiated procurement discounts. The guidance is unlikely to result in a significant change in resource use in the NHS because the technology is an additional treatment option, and the cost is not significantly different from that of prucalopride which is currently recommended by NICE at a position in the treatment pathway that is alongside that proposed for lubiprostone. **Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma TA319** **Background** Malignant melanoma is a cancer of the skin which in its early stages is normally asymptomatic and, if detected early, before it has spread, can be curable. However, at presentation, approximately 10% of cutaneous melanomas will have metastasised. Melanoma can spread to nearby lymph nodes (stage III, advanced) or to other parts of the body (stage IV, metastatic). The incidence of malignant melanoma is increasing in England and Wales with rates doubling approximately every 10-20 years. There were 10,656 new diagnoses of malignant melanoma and 1,825 deaths registered in England in 2010. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 13% of cases occur in young adults aged between 15 and 39 years old. **Recommendations** Ipilimumab is recommended, within its marketing authorisation, as an option for treating adults with previously untreated advanced (unresectable or metastatic) melanoma, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme. **The technology** Ipilimumab is a fully human antibody that binds to cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), a molecule expressed on T cells that plays a critical role in regulating natural immune responses. Ipilimumab is designed to block the activity of CTLA-4 resulting in augmentation and prolongation of the T-cell immune response, thereby sustaining the immune attack on cancer cells. It has a UK marketing authorisation 'for the treatment of advanced (unresectable or metastatic) melanoma in adults'. The recommended dose of ipilimumab is 3 mg per kilogram of body weight (mg/kg) administered intravenously over a 90-minute period every 3 weeks for a total of 4 doses. **Financial factors** Ipilimumab is priced at £3,750 per 10-ml vial (5 mg/ml) or £15,000 per 40-ml vial (5 mg/ml) (excluding VAT; 'British national formulary' [BNF] edition 67). The manufacturer of ipilimumab has agreed a patient access scheme with the Department of Health. The undiscounted cost of 1 dose for a 75kg patient is £18,750 with 4 doses costing £75,000. **The commissioner for this technology is NHS England.**
Clinical Guidelines (CGs)	**Advanced breast cancer (update): Diagnosis and treatment CG81 (first published November 2009)** **Background information** This 2014 update assesses exercise in people with or at risk of breast-cancer-related lymphoedema. Because of the variation between the exercise programmes in the included studies, it was not possible to define the frequency and intensity of the exercise programmes that may be undertaken. The exercise programmes that were included could reasonably be completed at gyms or similar facilities, or at home. Breast cancer is the most common cancer affecting women in England and Wales, with about 40,500 new cases diagnosed and 10,900 deaths recorded in England and Wales each year. In men breast cancer is rare, with about 260 cases diagnosed and 68 deaths in England and Wales each year. Of these new cases in women and men, a small proportion is diagnosed in the advanced stages, when the tumour has spread significantly within the breast or to other organs of the body. In addition, there are a significant number of women who have been previously treated with curative intent who subsequently develop either a local recurrence or metastases. Over recent years there have been important developments in the investigation and management of patients with advanced breast cancer, including new chemotherapy, and biological and hormonal

agents. There is some evidence of practice variation across the country and of patchy availability of certain treatments and procedures.

The key priorities for implementation are

- Diagnosis and assessment
- Systemic disease-modifying therapy
- Supportive care
- Managing complications

The recommendations in full cover

- Diagnosis and assessment
- Providing information and support for decision making
- Systemic disease-modifying therapy
- Supportive care
- Managing complications

Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease CG181

Background information

This clinical guideline (published July 2014) updates and replaces NICE clinical guideline 67 (published May 2008) and NICE technology appraisal guidance 94 (published January 2006). It offers evidence-based advice on the care and treatment of people at risk of cardiovascular disease and people who have had previous cardiovascular disease. It includes new and updated recommendations on risk assessment, lifestyle modifications and the use of lipid-lowering drugs.

CVD is the leading cause of death in the UK. In 2008 diseases of the circulatory system caused 190,857 deaths in the UK, of which 88,236 were due to coronary heart disease and 43,142 to stroke. The death rate varies with age, gender, socioeconomic status, ethnicity and geographic location. Death rates for CVD peaked in the 1970s and 1980s but have more than halved since then. About 58% of this decline during the 1980s and 1990s is attributable to reductions in major risk factors, principally smoking. Treatment of people at risk, including secondary prevention, accounts for the remaining 42%. CVD is a major cause of morbidity in England, with a prevalence of 13.6% in men and 13.0% in women. Blood lipids, including cholesterol, are a modifiable risk factor for CVD. The risk of CVD is directly related to blood cholesterol levels.

The key priorities for implementation are

- Identifying and assessing cardiovascular disease (CVD) risk
- Lipid modification therapy for the primary and secondary prevention of CVD

The recommendations in full cover

- Identifying and assessing cardiovascular disease (CVD) risk
- Lifestyle modifications for the primary and secondary prevention of CVD
- Lipid modification therapy for the primary and secondary prevention of CVD

Financial factors

Two parts of the guidance will have significant financial cost:

- Offer atorvastatin for the primary prevention of cardiovascular disease (CVD) to people who have a 10% or greater 10-year risk of developing CVD. Previously the threshold for treatment was 20%
- Switching patients from a medium intensity statin to a high intensity low cost statin (atorvastatin)

CVD has significant cost implications and was estimated to cost the NHS in England almost £6,940 million in 2003, rising to £7,880 million in 2010.

	Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care CG182 **Background information** Chronic kidney disease (CKD) describes abnormal kidney function and/or structure. It is common, frequently unrecognised and often exists together with other conditions (such as cardiovascular disease and diabetes). Moderate to severe CKD is also associated with an increased risk of other significant adverse outcomes such as acute kidney injury, falls, frailty and mortality. The risk of developing CKD increases with age. As kidney dysfunction progresses, some coexisting conditions become more common and increase in severity. CKD can progress to end-stage kidney disease in a small but significant percentage of people. **The key priorities for implementation are** • Investigations for chronic kidney disease • Classification of chronic kidney disease • Table 1 Classification of chronic kidney disease using glomerular filtration rate (GFR) and albumin:creatinine ratio (ACR) categories • Frequency of monitoring • Table 2 Frequency of monitoring of GFR (number of times per year, by GFR and ACR category) for people with, or at risk of, CKD **The recommendations in full cover** • 1.1 Investigations for chronic kidney disease • 1.2 Classification of chronic kidney disease • 1.3 Frequency of monitoring • 1.4 Information and education • 1.5 Referral criteria • 1.6 Pharmacotherapy • 1.7 Other complications **Financial factors** The use of ACR and cystatin C testing is anticipated to improve the diagnosis of people with CKD by more accurate classification. Increased costs are expected at a local level as result of this change. The improved classification of people with CKD is expected to reduce the number people requiring treatment and monitoring. Savings are expected at a local level as a result of this change. Overall this guidance is expected to present cost saving opportunities but this cannot be estimated with any degree of certainty.
Public Health Guidance	**None published so far this month**
Medical Technologies Guidance	**None published so far this month**
NICE Quality Standards	**None published so far this month**
Safe staffing guideline	**Safe staffing for nursing in adult inpatient wards in acute hospitals SG1** **Background information** This is the first guideline for this new NICE work programme. It makes recommendations on safe staffing for nursing in adult inpatient wards in acute hospitals, based on the best available evidence. The guideline focuses on wards that provide overnight care for adult patients in acute hospitals. It does not cover intensive care, high dependency, maternity, mental health, acute admission or assessment units or wards, or inpatient wards in community hospitals.

	Recommendations • 1.1 Organisational strategy • 1.2 Principles for determining nursing staff requirements • 1.3 Setting the ward nursing staff establishment • 1.4 Assessing if nursing staff available on the day meet patients' nursing needs • 1.5 Monitor and evaluate ward nursing staff establishments
Interventional Procedures Guidance (IPGs)	**Endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia or no dysplasia IPG 496** **Recommendations** 1.1 Current evidence on the efficacy of endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia is adequate provided that patients are followed up in the long term. There are no major safety concerns. Therefore, this procedure may be used in patients with Barrett's oesophagus with low-grade dysplasia with normal arrangements for clinical governance, consent and audit or research. 1.2 Current evidence on the efficacy and safety of endoscopic radiofrequency ablation for Barrett's oesophagus with no dysplasia is limited in quality and quantity. Therefore, this procedure should only be used in patients with no dysplasia in the context of research. 1.3 Patient selection for endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia should be done by a multidisciplinary team experienced in managing Barrett's oesophagus, as described in the British Society of Gastroenterology guidelines. 1.4 Endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia should only be done by endoscopists experienced in treating Barrett's oesophagus, as described in the British Society of Gastroenterology guidelines. 1. 5 Clinicians should enter details of all patients undergoing endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia or no dysplasia onto the UK National HALO Patient Registry, and review clinical outcomes locally. 1. 6 NICE encourages further research into endoscopic radiofrequency ablation for Barrett's oesophagus with no dysplasia. Studies should define clearly the policies used for histological diagnosis. Outcomes should include complete resolution of Barrett's oesophagus, change and progression to low-grade dysplasia, high-grade dysplasia or cancer. All complications should be reported, particularly development of strictures. Comparative studies against surveillance would be useful. **The procedure** The procedure is usually carried out with the patient under conscious sedation, in an outpatient setting. Using endoscopic visualisation, an appropriately sized radiofrequency ablation probe attached to the endoscope is inserted into the oesophagus, and advanced to the target area. Controlled pulses of radiofrequency energy are delivered, which cause thermal ablation of a thin layer of epithelium in the affected areas. A circumferential ablation catheter is usually used for primary treatment, whereas a focal ablation catheter can be used for remaining patches of Barrett's epithelium in any subsequent treatments. Radiofrequency ablation can also be used after doing endoscopic resection to remove larger, superficial abnormal areas. **Endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus IPG497** **Recommendations** 1.1 Current evidence on the efficacy of endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus is inadequate in quality and quantity. With regard to safety, there are well-recognised complications, particularly oesophageal strictures. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake endoscopic radiofrequency ablation for squamous

	dysplasia of the oesophagus should take the following actions. • Inform the clinical governance leads in their NHS trusts. • Ensure that patients understand the uncertainties about the procedure's safety and efficacy, inform them about alternative treatment options and provide them with clear written information. In addition, the use of NICE's information for the public is recommended. 1.3 Patient selection for endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus should be done by a multidisciplinary team experienced in the management of oesophageal dysplasia. 1.4 Endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus should only be done by endoscopists experienced in treating oesophageal dysplasia. 1.5 NICE encourages further research into endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus, including observational data collection. Studies should clearly define patient selection. Outcomes should include completeness of ablation, resolution of squamous dysplasia, progression to cancer and quality of life. All complications should be reported, particularly development of oesophageal strictures. 1.6 Clinicians should enter details about all patients undergoing endoscopic radiofrequency ablation for squamous dysplasia of the oesophagus onto the UK National HALO patient register, and review clinical outcomes locally. **The procedure** The procedure is usually carried out with the patient under conscious sedation, in an outpatient setting. The area of squamous dysplasia is visualised using an endoscope. Spraying the oesophageal lining with Lugol's iodine identifies areas of dysplasia that can otherwise be difficult to find. An appropriately sized radiofrequency ablation probe attached to the endoscope is inserted into the oesophagus, and advanced to the target area. Controlled pulses of radiofrequency energy are delivered, which cause thermal ablation of a thin layer of cells in the affected areas. A circumferential ablation catheter is usually used for primary treatment, whereas a focal ablation catheter can be used for remaining patches of squamous dysplasia in any subsequent treatments. Radiofrequency ablation can also be used after doing endoscopic mucosal resection to remove larger, superficial abnormal areas. **Powered microdebrider turbinoplasty for inferior turbinate hypertrophy** **Recommendations** Current evidence on the efficacy and safety of powered microdebrider turbinoplasty for inferior turbinate hypertrophy is adequate to support the use of this procedure with normal arrangements for clinical governance, consent and audit or research. **The procedure** Inferior turbinates are ridges inside the nose, covered by mucous membrane, which increase the surface area within the nose and help to filter and humidify inspired air. Inflammation of the mucous membrane (rhinitis) can cause inferior turbinates to swell (turbinate hypertrophy). This narrows the nasal passage, and may cause complete nasal obstruction. Symptoms include breathing difficulties, excessive mucous secretion (rhinorrhoea), postnasal drip, facial discomfort or pain and mid-facial headaches. Powered microdebrider turbinoplasty aims to reduce the size of inferior turbinates. It removes submucosal vascular stromal tissue, while preserving overlying respiratory mucosa, using a cutting tool with irrigation and suction functions.
NICE Pathways	These pathways are not guidance in themselves but a way of displaying online the various guidance that exists around a subject.
Commissioning Guides	**None published so far this month**
Diagnostics Guidance	**None published so far this month**

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	Finish date of consultation
Urinary tract infection in adults: topic engagement exercise	10/07/2014	24/07/2014
CG105 Motor neurone disease: surveillance review proposal	14/07/2014	25/07/2014
Excess winter deaths and illnesses: guideline consultation	13/06/2014	25/07/2014
Alcohol - preventing harmful alcohol use in the community: quality standard consultation	01/07/2014	29/07/2014
Antibiotics for neonatal infection: quality standard consultation	01/07/2014	29/07/2014
Nalmefene for reducing alcohol consumption in people with alcohol dependence: appraisal consultation	09/07/2014	29/07/2014
Pneumonia: guideline consultation	18/06/2014	30/07/2014
Maternal and child nutrition: review proposal consultation	17/07/2014	31/07/2014
Telemetric adjustable pulmonary artery banding for reducing pulmonary hypertension in infants with congenital heart defects: guidance consultation	20/06/2014	31/07/2014
Post-natal care (update): addendum consultation	03/07/2014	31/07/2014
Cyanoacrylate glue ablation for the treatment of varicose veins: guidance consultation	20/06/2014	31/07/2014
Insertion of an annular disc implant at lumbar discectomy: guidance consultation	20/06/2014	31/07/2014
Open reduction of slipped capital femoral epiphysis: guidance consultation	20/06/2014	31/07/2014
Preventing type 2 diabetes - population and community-level interventions: review proposal consultation	18/07/2014	01/08/2014
Cerebral Palsy: scope consultation	07/07/2014	04/08/2014
Obesity - prevention and lifestyle management in children: quality standard consultation	10/07/2014	07/08/2014
Obesity (update): guideline consultation	11/07/2014	08/08/2014
VibraTip for testing vibration perception to detect diabetic peripheral neuropathy: medical technologies consultation	11/07/2014	08/08/2014
Child abuse and neglect: scope consultation	23/07/2014	20/08/2014
Accreditation process manual update for consultation	02/06/2014	26/08/2014
Antenatal and postnatal mental health (update): guideline consultation	16/07/2014	27/08/2014
NICE quality standards - the process guide	10/06/2014	03/09/2014
Disability, dementia and frailty in later life - mid-life approaches to prevention: guideline consultation	14/07/2014	05/09/2014

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