NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

The Newsletter of the Cumbria Area Prescribing Committee

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Due to circumstances beyond our control, many users have been unable to access the Medicines Optimisation website on NHS Networks. Agreement has now been reached to host all documents on the NECS Medicines Optimisation Website. http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/

Clinical Policy and Formulary News

Colesevelam	Colesevelam is a bile acid sequestrant that is licensed to reduce levels of total cholesterol and low-density lipoprotein cholesterol in people with primary hypercholesterolaemia. It has also been observed (in two small case studies) to improve diarrhoea and gastrointestinal symptoms associated with bile acid malabsorption, although this is an unlicensed indication. Colesevelam appears to be well tolerated; the most frequent adverse effects are flatulence and constipation. It is recommended as 2nd line for patients who do not respond to colestyramine or for whom colestyramine is considered unsuitable 1st line in patients who prefer a tablet formulation. **AMBER**
Disulfiram	A shared care protocol for disulfiram has now been agreed with the drug dependency services. The service will supply the drug for the first six to eight weeks until the dose is established before primary care will be asked to continue supply. **AMBER** Available at http://medicines.necsu.nhs.uk/cumbria-shared-care-protocols/
Dosulepin	The use of dosulepin has been raised before in Prescription Pad. In 2007, the MHRA advised that dosulepin should not be prescribed to new patients and in 2009 NICE depression guideline they stated: **Do not switch to, or start, dosulepin because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.** Dosulepin prescribing guidelines have been developed in conjunction with CPFT which contain guidance for stopping and changing dosulepin to other antidepressants available. http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/
Phosphodiesterase type-5 (PDE-5) inhibitors for erectile dysfunction	Since the patent for sildenafil expired, there has been a significant decrease in the cost of drugs for the treatment of erectile dysfunction. Sildenafil accounts for 63% of the prescribing of PDE-5 inhibitor drugs, but only 8% of the cost. Tadalafil and vardenafil are significantly more expensive, but appear to be no more effective or better tolerated than sildenafil. The patents for tadalafil and vardenafil do not expire until 2017 and 2018 respectively. The Drug Tariff states that the SLS restrictions apply to all the PDE-5 inhibitors other than generic sildenafil. **It is recommended that prescribers consider changing appropriate patients taking tadalafil or vardenafil to generic sildenafil.** Prescribing guidance is available at http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/

Vitamin D guideline	A new algorithm with recommendations for the treatment of vitamin D deficiency has been developed. This includes recommendations for the use of the recommended licensed high dose product, Invita D3®. Available at http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/
Headache	The North West Clinical Network has produced guidelines on the diagnosis and management of headache. Copies are available at http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/
Low molecular weight heparin bridging	Patients receiving warfarin for long-term conditions are often transferred onto an injectable low molecular weight heparin (LMWH) such as enoxaparin over the perioperative period. The decision to change the patient from warfarin to a LMWH is made at the pre-assessment clinic and it is the responsibility of the surgical team to implement the regime and to supply sufficient LMWH and sharps bins. Errors have occurred due to poor communication between secondary and primary care, so GPs should not be asked to prescribe in this situation. One possible exception may be when patients have a delayed operation. Rather than putting the patient back on warfarin and then starting a LMWH again, it may be preferable to maintain patients on an LMWH. This should be done after discussion between the surgeon and the GP.
Oral contraceptives and acne	After a request for information, we have produced a brief review on the benefit of preventing and treating acne using combined oral contraceptives (COC). A Cochrane review concluded that there was a benefit of using oral contraceptives, but there is no evidence of superiority of any one preparation. A significant factor in the choice of a COC is the risk of venous thromboembolism. While the risk is low, there are some differences in the risk. This has been highlighted in a recent warning from the MHRA and has been confirmed by a recent study in the BMJ. The review is available at http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/

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Recommendations on New Medicines

	Drug	Licensed indication	Recommendation
The following drugs were <u>not approved</u> by LJF as no submission was made by the manufacturers	Collagenase *clostridium histolyticum* injection, 900 micrograms (Xiapex®)	Treatment of Peyronie's disease.	**Not included** on the LJF because the holders of the marketing authorisation has not made a submission to SMC **BLACK**
	Insulin degludec injection, 100 & 200 units/ml (Tresiba®)	Treatment of diabetes mellitus in adults, adolescents and children from the age of 1 year.	
The following drugs were <u>not approved</u> by LJF as no case for inclusion was made by local specialists	Brimonidine gel, 3.3mg/g (0.33%) (Mirvaso®)	Symptomatic treatment of facial erythema of rosacea in adult patients.	**Not included** on the LJF because clinicians have not responded to an invitation to apply for formulary inclusion for this medicine **BLACK**
	Olodaterol Inhaler, 2.5 microgram (Striverdi®)	Maintenance bronchodilator treatment in patients with COPD (long-acting beta$_2$ agonist).	
	Umeclidinium/Vilanterol inhaler, 55 micrograms, 22 micrograms (Anoro®)	Maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD.	
	Aclidinium/Formoterol inhaler, 340 micrograms, 12 micrograms (Duaklir Genuair®)	Maintenance bronchodilator to relieve symptoms in adult patients with COPD.	

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News from the MHRA

Tiotropium

Previous studies of tiotropium suggested that more people died while using tiotropium Respimat® compared with placebo and with tiotropium HandiHaler®. Previous advice was to use tiotropium Respimat® with caution in patients with known cardiac rhythm disorders.

The TIOSPIR clinical trial compared the safety and efficacy of tiotropium delivered via Respimat® with tiotropium delivered via HandiHaler®. TIOSPIR included 17,135 participants with COPD who were followed up for a mean of 2.3 years. The primary safety outcome was the time to death from any cause, which was used to calculate the relative risk of death between groups. The primary efficacy outcome was time to first exacerbation of COPD. Cardiovascular safety was also assessed.

There was no significant difference in the risk of death from any cause between tiotropium Respimat® compared with tiotropium HandiHaler®. The incidences of different causes of death (including death due to cardiovascular events) and incidences of major cardiovascular adverse events were similar in all groups There was no significant difference in the risk of the first exacerbation of COPD.

When using tiotropium delivered via Respimat® or Handihaler® to treat COPD:

- take the risk of cardiovascular side effects into account for patients with conditions that may be affected by the anticholinergic action of tiotropium, including:
    - o myocardial infarction in the last 6 months
    - o unstable or life threatening cardiac arrhythmia
    - o cardiac arrhythmia requiring intervention or a change in drug therapy in the past year
    - o hospitalisation for heart failure (NYHA Class III or IV) within the past year
- tell these patients to report any worsening of cardiac symptoms after starting tiotropium; patients with these conditions were excluded from clinical trials of tiotropium, including TIOSPIR
- review the treatment of all patients already taking tiotropium as part of the comprehensive management plan to ensure that it remains appropriate for them; regularly review treatment of patients at high risk of cardiovascular events
- remind patients not to exceed the recommended once daily dose

Corticosteroids e-learning module now available from MHRA.

The new module helps clinicians understand how to identify, manage and avoid the important side effects of these valuable and widely prescribed medicines—vital knowledge for optimising the use of corticosteroids.

The interactive module is presented on the MHRA dedicated platform for tracking and organising learning. Designed for clinical practitioners, the module covers:

- recognition of commonly used corticosteroids
- important corticosteroid adverse effects
- factors that increase the risk of adverse effects

- how clinicians and patients can reduce the risk
- specific treatment of the adverse effect

Used with authoritative clinical information and treatment guidelines, this module is a key practical aid to doctors, pharmacists and nurses. The module incorporates interactive knowledge-check exercises to consolidate learning. You will be able to download evidence of your learning on successfully completing an assessed quiz.

The learning module on corticosteroids has been approved for up to two continuing professional development (CPD) credits by the Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the United Kingdom.

The module is available at: https://www.gov.uk/government/publications/e-learning-modules-medicines-and-medical-devices/e-learning-modules-medicines-and-medical-devices

Hydroxyzine

The MHRA have issued additional precautions. A European review of the safety and efficacy of hydroxyzine has been undertaken following concerns of heart rhythm abnormalities. The review concluded that hydroxyzine is associated with a small risk of QT interval prolongation and Torsade de Pointes. Such events are most likely to occur in patients who already have risk factors for QT prolongation, such as:

- concomitant use of medicines that prolong the QT interval
- cardiovascular disease
- family history of sudden cardiac death
- significant electrolyte imbalance (low potassium or magnesium levels)
- significant bradycardia

So, when using hydroxyzine:

- do not prescribe hydroxyzine to people with a prolonged QT interval or who have risk factors for QT interval prolongation
- avoid use in the elderly - they are more susceptible than younger patients to the side effects of hydroxyzine
- consider the risks of QT interval prolongation and Torsade de Pointes before prescribing to patients taking medicines that lower heart rate or potassium levels
- the maximum daily dose is now
    - 100mg for adults
    - 50mg for the elderly (if use cannot be avoided)
    - 2mg per kg body weight for children up to 40 kg in weight
- prescribe the lowest effective dose for as short a time as possible

Use of codeine in children under 12 years	When prescribing or dispensing codeine-containing medicines for cough and cold, consider that codeine is contra-indicated in: • children younger than 12 years old • patients of any age known to be CYP2D6 ultra-rapid metabolisers • breastfeeding mothers • codeine is not recommended for adolescents (12 to 18) who have problems with breathing
Availability of Drug Safety Update	Note that the MHRA have now made Drug Safety Update newsletter available from their website: https://www.gov.uk/government/publications/drug-safety-update-monthly-newsletter . This includes an archive of previous editions. You can also sign up for a monthly e-mail at: https://www.gov.uk/drug-device-alerts/email-signup

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NICE guidance

These are brief summaries. The complete guidance should be consulted (www.nice.org.uk)

	Drug	Condition	Summary
TA329	Infliximab, adalimumab and golimumab	Ulcerative colitis, moderate to severely active, after failure of conventional therapy	Recommended as possible treatments for adults with moderate to severe ulcerative colitis if conventional therapy hasn't worked or isn't suitable. **RED**
TA330	Sofosbuvir	Hepatitis C	Recommended as a possible treatment for adults with some types (called genotypes) of chronic hepatitis C. It is taken with other drugs (peginterferon alfa and ribavirin, or ribavirin alone. **RED** (Note that this implemented from 31st July).
TA331	Simprevir	Hepatitis C, in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4	Recommended as an option for treating genotype 1 and 4 chronic hepatitis C in adults. **RED**
TA332	Sipuleucel-T	Prostate cancer, asymptomatic or minimally symptomatic metastatic hormone-relapsed	**Not** recommended for treating adults who have asymptomatic or minimally symptomatic metastatic non-visceral hormone-relapsed prostate cancer for which chemotherapy is not yet clinically indicated. **BLACK**
TA333	Axitinib	Renal cell carcinoma, advanced disease after failure of prior systemic treatment	Recommended as an option for treating adults with advanced renal cell carcinoma after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine. **RED**
TA334	Regorafenib	Colorectal cancer, metastatic	Unable to make a recommendation because no evidence submission was received from the manufacturers. **BLACK**
TA335	Rivaroxaban	Acute coronary syndrome, acute management	Recommended as an option within its marketing authorisation, in combination with aspirin plus clopidogrel or aspirin alone, for preventing atherothrombotic events in people who have had an acute coronary syndrome with elevated cardiac biomarkers. **AMBER**

TA336	Empagliflozin	Diabetes mellitus, type 2	Recommended as a treatment for type 2 diabetes when taken with metformin, only if the patient: • cannot take a sulfonylurea or • is at significant risk of hypoglycaemia or its consequences. If 3 antidiabetic drugs are required, empagliflozin is recommended when taken with either • metformin and a sulfonylurea, or • metformin and pioglitazone. Empagliflozin is also recommended when taken with insulin, with or without other antidiabetic drugs. **AMBER**
TA337	Rifaximin	Hepatic encephalopathy	Recommended as an option for reducing the recurrence of episodes of overt hepatic encephalopathy in people aged 18 years or older. **AMBER**
TA338	Pomalidomide	Multiple myeloma, relapsed and refractory, previously treated with lenalidomide and bortezomib	**Not** recommended. **BLACK**
TA339	Omalizumab	Previously treated chronic spontaneous urticaria	Recommended as a possible treatment for people aged 12 years and over with severe chronic spontaneous urticaria if: • a doctor has objectively diagnosed the condition as severe • the condition has not improved with standard treatment with H_1-antihistamines or leukotriene receptor antagonists • the drug is stopped at or before the fourth dose if the condition has not responded • the drug is stopped at the end of a course of treatment (6 doses) if the condition has responded, and is only restarted if the condition comes back • the drug is given by a secondary care specialist in dermatology, immunology or allergy. **RED**
TA340	Ustekinumab	Active psoriatic arthritis	Recommended as a possible treatment, alone or with methotrexate, for adults with active psoriatic arthritis when treatment with non-biological DMARDS has not worked well enough if: • treatment with TNF-alpha inhibitors is not suitable for them, or

			• the person has had an TNF alpha inhibitor before. Treatment with ustekinumab should be stopped after 24 weeks if it is not working well enough. RED
TA341	Apixaban	Treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism	Recommended as an option for treating and preventing recurrent deep vein thrombosis or pulmonary embolism. GREEN
TA342	Vedolizumab	Moderate to severe ulcerative colitis	Recommended as a possible treatment for adults with moderate to severe ulcerative colitis. RED
TA343	Obinutuzumab	Untreated chronic lymphocytic leukaemia (in combination with chlorambucil)	Recommended as a possible treatment for adults with untreated chronic lymphocytic leukaemia only if: • they have other conditions that make full-dose fludarabine unsuitable for them and • bendamustine is not suitable for them. RED
TA344	Ofatumumab	Untreated chronic lymphocytic leukaemia (in combination with chlorambucil or bendamustine)	Recommended as a possible treatment for people with untreated chronic lymphocytic leukaemia if treatments containing fludarabine or bendamustine are not suitable. RED

	Condition	**Recommendations**
CG61	Irritable bowel syndrome in adults, diagnosis and management in primary care	Gives recommendations on diagnosis of irritable bowel syndrome (IBS). It makes recommendations about • 'red flag' symptoms which should be urgently referred to secondary care • dietary recommendations: Consider prescribing antispasmodic agents for people with IBS. These should be taken as required, alongside dietary and lifestyle advice. Laxatives should be considered for the treatment of constipation in people with IBS, but people should be discouraged from taking lactulose. Consider linaclotide for people with IBS only if:

		• optimal or maximum tolerated doses of previous laxatives from different classes have not helped and • they have had constipation for at least 12 months. Follow up people taking linaclotide after 3 months. Loperamide should be the first choice of antimotility agent for diarrhoea in people with IBS.
NG2	Bladder cancer, diagnosis and management	Makes recommendations about the specialist management of bladder cancer.
NG3	Diabetes in pregnancy: pre-conception to postnatal period	Recommendations on the management of women with diabetes, before, during and after pregnancy and the baby after birth.
NG5	Medicines optimisation	Systems for identifying, reporting and learning from medicines-related patient safety incidents: • medicines-related communication systems when patients move from one care setting to another • medicines reconciliation • medication review • self-management plans • patient decision aids used in consultations involving medicines • clinical decision support • medicines-related models of organisational and cross-sector working
CG28	Depression in children and young people	The NICE clinical guideline on depression in children and young people covers: • the care children and young people with depression can expect to get from their doctor, nurse or counsellor • the information they can expect to be given • what they can expect from treatment • the kinds of services that can help young people and children with depression, including GP, school health staff and specialists in clinics or hospitals Antidepressant medication should not be used for the initial treatment of children and young people with mild depression. Consider combined therapy (fluoxetine and psychological therapy) for initial treatment of moderate to severe depression in young people (12–18 years), as an alternative to psychological therapy followed by combined therapy. Fluoxetine as this is the only antidepressant for which clinical trial evidence shows that the benefits outweigh the risks.

		If an antidepressant is to be prescribed this should only be following assessment and diagnosis by a child and adolescent psychiatrist.
NG10	Violence and aggression: short-term management in mental health, health and community settings	Makes recommendations on reducing the risk of violence and aggression by anticipating risk, adequate staff training and management of situations. There are recommendations on an individualised pharmacological strategy to reduce the risk of violence and aggression. A multidisciplinary team that includes a psychiatrist and a specialist pharmacist should develop and document an individualised pharmacological strategy for using routine and p.r.n. medication to calm, relax, tranquillise or sedate service users who are at risk of violence and aggression as soon as possible after admission to an inpatient psychiatric unit.
NG11	Challenging behaviour and learning disabilities: prevention and interventions for people with learning disabilities whose behaviour challenges	Gives recommendations on identification and support for patients and carers. Consider medication, or optimise existing medication (in line with the NICE guideline on medicines optimisation), for coexisting mental or physical health problems identified as a factor in the development and maintenance of behaviour that challenges shown by children, young people and adults with a learning disability. Consider antipsychotic medication to manage behaviour that challenges only if: • psychological or other interventions alone do not produce change within an agreed time or • treatment for any coexisting mental or physical health problem has not led to a reduction in the behaviour or • the risk to the person or others is very severe (for example, because of violence, aggression or self-injury). It then goes on to make recommendations according to response to this recommended treatment.
NG9	Bronchiolitis in children	Recommendations on assessment and diagnosis, when to refer and admit. Do not use any of the following to treat bronchiolitis in children: • antibiotics • hypertonic saline

- adrenaline (nebulised)
- salbutamol
- montelukast
- ipratropium bromide
- systemic or inhaled corticosteroids
- a combination of systemic corticosteroids and nebulised adrenaline.

CG97 Lower urinary tract symptoms in men: assessment and management

Offers guidance on the diagnosis, treatment and surgical options for treatment of lower urinary tract symptoms in men. With regards the use of medicines, the following guidance is given:

Indication	**Treatment**	**Review (assess symptoms and effect of the drugs on QoL, and ask about side effects)**
Moderate to severe lower urinary tract symptoms	Offer an α-blocker 1. Alfuzosin m/r 2. Doxazosin)	At 4 to 6 weeks, then every 6 to 12 months
Overactive bladder	Offer an anticholinergic 1. Darifenacin	At 4 to 6 weeks, then every 6 to 12 months
	Mirabegron is recommended as an option only for people in whom antimuscarinics: • are contra-indicated or • are clinically ineffective, or • have unacceptable side effects	
Lower urinary tract symptoms and a prostate estimated to be larger than 30 grams or PSA > 1.4ng/ml and a high risk of progression	Offer a 5-α reductase inhibitor 1. Finasteride 2. Dutasteride	At 3 to 6 months, then every 6 to 12 months
Bothersome moderate to severe lower urinary tract symptoms and a prostate estimated to be larger than 30 grams or PSA > 1.4ng/ml	Consider an α-blocker plus a 5-α reductase inhibitor	

NG8	Anaemia management in people with chronic kidney disease	Fundamentally unchanged from 2006 and 2011 guidance. Recommendations on the investigation of anaemia in renal disease

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