NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

The Newsletter of the Cumbria Area Prescribing Committee

September 2013 No. 26

Click here to find more ➢

Clinical policy and Formulary news	Recommendations on new medicines	News from the MHRA	NICE Guidance
Melatonin for children – shared care protocol LJF changes Website migration 'Prescribing infant formula in cows' milk protein allergy and lactose intolerance' Shortage of hyoscine tablets (Kwells®)	Lisdexamfetamine capsules (Elvanse®) Latanoprost unit dose vials (Monoprost®) Ulipristal tablets (Esmya®) Mirabegron tablets (Betmiga®) Nomegestrol/estradiol tablets (Zoely®)	Diclofenac - new contraindications and warnings after a review of cardiovascular safety Cyproterone acetate with ethinyloestradiol (co-cyprindiol) - balance of benefits and risks remains positive; updated prescribing advice Oral retinoids (acetretin, alitretinoin and isotretinoin) - pregnancy prevention, reminder of measures to minimise teratogenic risk Codeine for analgesia: restricted use in children due to reports of morphine toxicity	TA287 – Rivaroxaban, pulmonary embolism & recurrent thromboembolism TA288 – Dapagliflozin combination therapy, type 2 diabetes TA289 – Ruxolitinib, myelofibrosis TA290 – Mirabegron, overactive bladder TA291 – Pegloticase, gout TA293 – Eltrombopag, thrombocytopenic purpura TA294 – Aflibercept, age-related macular degeneration CG161 – Falls CG262 – Idiopathic pulmonary fibrosis CG164 – Familial breast cancer CG165 – Hepatitis B (chronic) CG166 – Ulcerative colitis

Clinical Policy and Formulary News

Melatonin for children – shared care protocol

A shared care protocol for the prescribing of melatonin for children has been agreed. It will use the product, Circadin®. Circadin® is only licensed for the treatment of insomnia in adults aged 55 or over, but it is likely to be better 'quality assured' than some of the special products being used.

For patients already receiving melatonin, a straight change from the present dose of melatonin to Circadin® can be made by the GP, but if necessary 'odd' doses may be rounded down to the nearest convenient dose, e.g., 3mg > 2mg. Alternatively, the change can be carried out at the patients next secondary care appointment.

Liquid preparations of melatonin should only be prescribed by the secondary care specialist.

The shared protocol can be found here .

A patient information leaflet, explaining the use of melatonin children is available from:
http://www.medicinesforchildren.org.uk/download.php?id=85&type=leaflet

LJF changes

Changes have been made to the contraception section, Section 7.3.

Some of the key points are:

- Expanded information on drug interactions has been included with a link to Faculty of Sexual and Reproductive Healthcare guidance.
- Transdermal contraceptives - additional information has been added on VTE risk, with possible increased risk with transdermal contraceptives compared to oral contraceptives.
- Norgeston® removed as second choice progestogen-only contraceptive (POP).
- Generic versions of Cerazette® (desogestrel) are now available. Cerelle® is now the second choice POP. (It is approximately half the price of Cerazette®).
- New note added advising review after 2 years Depo-Provera® use in women of all ages.
- Ortho® diaphragms have been discontinued therefore Omniflex® added as second choice.

Website migration

We will shortly be moving to a new internet and intranet site. Apologies in the interim, but will let you know when we have these up and running.

'Prescribing infant formula in cows' milk protein allergy and lactose intolerance'	The current guidelines have been revised to include two new preparations, Similac Alimentum® and Althera®. The guidelines can be found here.
Shortage of Kwells®	There is a shortage of Kwells® and other hyoscine-containing tablets. These are sometimes prescribed for patients with some neurological conditions and also for some patients receiving clozapine when hypersalivation is a problem. If there is a supply problem, please contact the consultant concerned for advice on alternatives. The shortage is imminent and will last 6 to 9 months.

↑ Return to page 1

Recommendations on New Medicines

The following drugs have been recommended as suitable for use:	Lisdexamfetamine capsules (Elvanse®)	As part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.	Approved **AMBER**
	Latanoprost UDV eye drops (Monoprost®)	Reduction of elevated intraocular pressure in patients with open angle glaucoma and ocular hypertension.	Approved for use in patients who have proven sensitivity to the preservative benzalkonium chloride **GREEN**
	Ulipristal tablets (Esmya®)	Pre-operative treatment of moderate-to-severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment is limited to three months.	Approved, first month of treatment will be supplied by secondary care **AMBER**
	Mirabegron (Betmiga®)	Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.	NICE TA290, recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects **GREEN**
The following drugs were <u>not approved</u> by SMC and LJF, on the basis that a cost-effectiveness case was not submitted by the manufacturer:	Nomegestrol/estradiol tablets (Zoely®)	Oral contraception.	**BLACK**

↑ Return to page 1

News from the MHRA

Diclofenac: new contraindications and warnings after a review of cardiovascular safety

Diclofenac is now contraindicated in patients with established:

- ischaemic heart disease
- peripheral arterial disease
- cerebrovascular disease
- congestive heart failure (New York Heart Association [NYHA] classification II–IV)

Patients with these conditions should be switched to an alternative treatment at their next routine appointment. Diclofenac treatment should only be initiated after careful consideration for patients with significant risk factors for cardiovascular events (e.g., hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Reminder of existing advice for all NSAIDs

- The decision to prescribe an NSAID should be based on an assessment of a patient's individual risk factors, including any history of cardiovascular and gastrointestinal illness

- Naproxen and low-dose ibuprofen are considered to have the most favourable thrombotic cardiovascular safety profiles of all non-selective NSAIDs

For patients with cardiovascular and cerebrovascular disease, current evidence suggests that the risk of heart failure is increased with all NSAIDs. The risk of myocardial infarction is also increased with most NSAIDs, with the possible exception of naproxen. The risk of stroke is increased with most NSAIDs with the possible exception of low dose (<200mg daily) celecoxib.

Cyproterone acetate with ethinyloestradiol (co-cyprindiol)—balance of benefits and risks remains positive; updated prescribing advice is provided

The benefits of co-cyprindiol outweigh the risks in women of reproductive age for the treatment of:

- skin conditions related to androgen sensitivity (e.g., severe acne with or without seborrhoea)
- hirsutism

Co-cyprindiol provides effective contraception in these women. An additional hormonal contraceptive should not be used in combination with co-cyprindiol. The need to continue treatment should be evaluated periodically by the treating physician

The risk of VTE is rare but this remains an important side effect, and healthcare professionals should themselves be vigilant for signs and counsel patients to remain vigilant for signs and symptoms. These include:

- DVT—unusual leg pain (usually in the calf), which may be accompanied by tenderness or swelling in the leg; increased warmth, redness, or discolouration of skin
- PE—sudden sharp chest pains (which may increase with breathing in); shortness of breath (which can come on suddenly or

	gradually); sudden coughing for no apparent reason; severe light-headedness, dizziness or fainting
Oral retinoids (acetretin, Alitretinoin and isotretinoin): pregnancy prevention—reminder of measures to minimise teratogenic risk	All women should be made aware of the teratogenic risks before starting treatment. • Pregnancy must be excluded before treatment with oral retinoids • Pregnancy test results (with a minimum sensitivity of 25mIU/mL) must be documented 3 days or less before the prescription is issued • Women of childbearing potential should be on at least one, or preferably two, complementary forms of effective contraception (e.g., barrier and hormonal) • Contraception should start 1 month before treatment, and should continue throughout oral retinoid treatment and after until the retinoids have left the patient's system—i.e.: o At least 1 month after stopping treatment with isotretinoin or alitretinoin o At least 2 years after stopping treatment with acitretin Females should undergo a pregnancy assessment every 4 weeks at follow-up appointments. Specialist advice from a physician specialised in teratology must be sought immediately if a pregnancy occurs. Prescription of oral retinoids should be limited to 30 days' treatment. The prescription must be dispensed within 7 days of issue. Available data suggest that maternal exposure from the semen of patients receiving an oral retinoid is not associated with teratogenic effects. The choice of contraception is particularly important for acitretin because it must be used throughout the treatment period and for at least 2 years after the patient has completed her course. These patients must also have regular follow-up appointments with their dermatology prescriber every 3 months during the 2-year period after treatment with acitretin has stopped to ensure patients are continuing to use contraception effectively.
Codeine for analgesia: restricted use in children due to reports of morphine toxicity	Codeine is metabolised in the liver to morphine. The rate of conversion varies due to genetic variations of the responsible enzyme. A proportion of patients may be classified as ultra-rapid metabolisers, which may lead to high morphine levels, which may be critical in children. Codeine should only be used to relieve acute moderate pain in children older than 12 years and only if it cannot be relieved by other pain killers such as Paracetamol and ibuprofen. Codeine is contraindicated in all children (i.e., younger than 18 years) who undergo tonsillectomy or adenoidectomy (or both) for obstructive sleep apnoea. Codeine is not recommended for use in children whose breathing might be compromised, including those with neuromuscular disorders,

severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures.

In children age 12-18 years, the maximum daily dose should not exceed 240mg. This may be taken in divided doses, up to four times a day at intervals of no less than 6 hours. Duration of treatment should be limited to 3 days and if no effective pain relief is achieved, treatment should be reviewed by a physician.

↑ Return to page 1

NICE guidance

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

	Drug	Condition	Resume
TA287	Rivaroxaban	Pulmonary embolism and recurrent thromboembolism	Recommended as an option for treating pulmonary embolism and preventing recurrent deep vein thrombosis and pulmonary embolism in adults. **GREEN**
TA288	Dapagliflozin combination therapy	Type 2 diabetes	**Recommended** in combination with metformin as an option for treating type 2 diabetes as an alternative to dipeptidyl peptidase-4 (DPP-4) inhibitors. **AMBER** **Recommended** in combination with insulin with or without other antidiabetic drugs.**AMBER** **Not recommended** in combination with metformin and a sulfonylurea, except as part of a clinical trial. **BLACK**
TA289	Ruxolitinib	Myelofibrosis (splenomegaly symptoms)	**Not recommended**. **BLACK**
TA290	Mirabegron	Overactive bladder	**Recommended** as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contra-indicated or clinically ineffective, or have unacceptable side effects. The formulary first choice remains either oxybutynin or solifenacin. **GREEN**
TA291	Pegloticase	Gout (tophaceous, severe, debilitating, chronic)	**Not recommended**. **BLACK**
TA293	Eltrombopag	Thrombocytopenic purpura	**Recommended** as an option for treating adults with chronic immune (idiopathic) thrombocytopenic purpura, within its marketing authorisation (that is, in adults who have had a splenectomy and whose condition is refractory to other treatments, or as a second-line treatment in adults who have not had a splenectomy because surgery is contraindicated), only if: - their condition is refractory to standard active treatments and rescue therapies, or - they have severe disease and a high risk of bleeding that needs frequent courses of rescue therapies. **RED**

			Subject to Patient Access Discount Scheme
TA294	Aflibercept	Age-related macular degeneration (wet)	**Recommended** as an option for treating wet age-related macular degeneration only if it is used in accordance with the recommendations for ranibizumab in NICE TA155 (re-issued in May 2012), i.e., all of the following circumstances apply in the eye to be treated: – the best-corrected visual acuity is between 6/12 and 6/96 – there is no permanent structural damage to the central fovea – the lesion size is less than or equal to 12 disc areas in greatest linear dimension – there is evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes) RED Subject to Patient Access Discount Scheme
CG161	Falls	Covers assessment and prevention of falls in all individuals over 65 years and people aged over 50 years who are admitted to hospital with a fall or have a condition predisposing them to falls. From a pharmacological point of view, medication review should form part of a multifactorial assessment. Older people on psychotropic medications should have their medication reviewed, with specialist input if appropriate, and discontinued if possible to reduce their risk of falling. A guide, Medicines and Falls in Hospital: Guidance Sheet provides useful advice about the risk of falls with various drugs.	
CG162	Stroke rehabilitation	Guidance relates to physical therapies only.	
CG163	Idiopathic pulmonary fibrosis	The mainstay of pharmacological treatment is perfenidone. This has been assessed by NICE (TA282). This will be managed by tertiary care centres. Azathioprine and prednisolone were formerly used (in conjunction with acetylcysteine), but this is no longer recommended. The benefit of acetylcysteine is uncertain. In addition, oxygen therapy may be indicated in advanced disease.	
CG164	Familial breast cancer	Offers evidence-based advice on the classification and care of people at risk of familial breast cancer. It also makes recommendations on genetic testing thresholds, surveillance and risk reduction and treatment strategies for people with a diagnosis of breast cancer and a family history of breast, ovarian or a related cancer.	

CG165	Hepatitis B (chronic)	• Recommends a 48-week course of peginterferon alfa-2a as first-line treatment in adults with HBeAg-**positive** chronic hepatitis B and compensated liver disease. • Recommends tenofovir disoproxil as second-line treatment to people who do not undergo HBeAg seroconversion or who relapse (revert to being HBeAg positive following seroconversion) after first-line treatment with peginterferon alfa-2a. • Recommends entecavir as an alternative second-line treatment to people who cannot tolerate tenofovir disoproxil or if it is contraindicated. • Recommends a 48-week course of peginterferon alfa-2a as first-line treatment in adults with HBeAg-**negative** chronic hepatitis B and compensated liver disease. Recommends entecavir or tenofovir disoproxil as second-line treatment to people with detectable HBV DNA after first-line treatment with peginterferon alfa-2a.
CG166	Ulcerative colitis	***Inducing remission: Step 1 therapy for mild to moderate ulcerative colitis*** To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis: • offer a topical aminosalicylate alone (suppository or enema, taking into account the person's preferences) **or** • consider adding an oral aminosalicylate to a topical aminosalicylate **or** • consider an oral aminosalicylate alone, taking into account the person's preferences and explaining that this is not as effective as a topical aminosalicylate alone or combined treatment. • If aminosalicylates are not tolerated, offer a topical corticosteroid **or** consider oral prednisolone To induce remission in adults with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis: • offer a high induction dose of an oral aminosalicylate • consider adding a topical aminosalicylate or oral beclometasone dipropionate, taking into account the person's preferences. To induce remission in children and young people with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis: • offer an oral aminosalicylate • consider adding a topical aminosalicylate or oral beclometasone dipropionate, taking into account the person's preferences (and those of their parents or carers as appropriate). To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis who cannot tolerate or who decline aminosalicylates, in whom aminosalicylates are contraindicated or who have subacute ulcerative colitis, offer oral prednisolone.

Inducing remission: Step 2 therapy for mild to moderate ulcerative colitis

Consider adding oral prednisolone to aminosalicylate therapy to induce remission in people with mild to moderate ulcerative colitis if there is no improvement within 4 weeks of starting step 1 aminosalicylate therapy or if symptoms worsen despite treatment. Stop beclometasone dipropionate if adding oral prednisolone.

Consider adding oral tacrolimus to oral prednisolone to induce remission in people with mild to moderate ulcerative colitis if there is an inadequate response to oral prednisolone after 2–4 weeks.

Inducing remission: therapy for acute severe ulcerative colitis

For people admitted to hospital with acute severe ulcerative colitis (either a first presentation or an inflammatory exacerbation):

- offer intravenous corticosteroids to induce remission **and**
- assess the likelihood that the person will need surgery

Consider adding intravenous ciclosporin to intravenous corticosteroids or consider surgery for people:

- who have little or no improvement within 72 hours of starting intravenous corticosteroids **or**
- whose symptoms worsen at any time despite corticosteroid treatment.

Maintaining remission

Consider a once-daily dosing regimen for oral aminosalicylates when used for maintaining remission. Take into account the person's preferences, and explain that once-daily dosing can be more effective, but may result in more side effects.

↑ Return to page 1