NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

The Newsletter of the Cumbria Area Prescribing Committee

November 2015 No. 38

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Cisclosporin Shared Care Guideline Fludrocortisone & Midodrine Coenzyme Q10 Revised Just in Case sheet Liothyronine Branded Oxycodone prescribing Anticholinergic drugs for urinary incontinence	Nothing this month	Proton Pump Inhibitors Pseudoephedrine & Ephedrine	See relevant page

All Medicines Optimisation guidance, Shared Care Guidelines, PGDs and other resources can now be found on the NECS Medicines Optimisation Website.
http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/

Clinical Policy and Formulary News

Ciclosporin

An updated version of the Shared Care Protocol for Ciclosporin has now been agreed. This is in the new format which does not include a patient details section. Secondary care clinicians will request GPs to prescribe under the SCP and GPs should access the latest version here: http://medicines.necsu.nhs.uk/cumbria-shared-care-protocols/

Changes: Unlicensed use in severe ulcerative colitis is now included

Stable dose and stable bloods are now defined.

Secondary care clinicians are responsible for checking for absence of pregnancy in women of childbearing age and ensuring the patient understands the importance of contraception.

Primary care clinicians are responsible for referring any female patient who discovers they are pregnant whilst taking ciclosporin back to secondary care immediately.

There are changes to the monitoring schedule. All patients taking ciclosporin should be reviewed to ensure monitoring is in line with new schedule.

Fludrocortisone & Midodrine – RAG list status review due to changes in licensing

Fludrocortisone RAG status is confirmed **GREEN**. Fludrocortisone remains 1st line for the treatment of Orthostatic hypotension due to autonomic dysfunction in line with the European Neurological Society guidelines.
http://www.eaneurology.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2011_Orthostatic_hypotension.pdf

Midodrine is now licensed for the treatment of Orthostatic hypotension due to autonomic dysfunction. Status now **AMBER** for the treatment of Orthostatic hypotension due to autonomic dysfunction.

Coenzyme Q10 (ubiquinone, ubidecareone)

The APC reviewed the evidence base for Coenzyme Q10 and allocated RAG status **BLACK**

Coenzyme Q10 (ubiquinone, ubidecarenone) is a naturally occurring quinine found in the cellular membrane. Half of the body's coenzyme Q10 comes from dietary sources, the rest is made endogenously. Coenzyme Q10 plays an important role in oxidative phosphorylation in mitochondria, protects against oxidative stress produced by free radicals and regenerates antioxidants. Deficiency of coenzyme Q10 can lead to severe deficits in mitochondrial energy metabolism, which can present as myopathy with exercise intolerance and recurrent episodes of rhabdomyolysis and myoglobinuria.

Coenzyme Q10 preparations are not licensed drugs under the Medicines Act, so have not undergone the stringent testing laid down by the regulatory authorities to confirm their safety, quality and efficacy, and there is no summary of product characteristics (SPC) for prescribers to consult.

Revised Just in Case (JIC) Sheet for palliative care

An updated version of the Just in Case Authorisation Sheet was launched in Sept 2015 to coincide with the introduction of the new Community Nursing forms, the JiC changes are as follows:

OLD	NEW	Indication
Morphine	No change; Morphine remains first line opioid analgesic	PAIN (Low doses may also be used for BREATHLESSNESS)
Cyclizine	EITHER: CYCLIZINE 50mg every 8 hours prn	NAUSEA or VOMITING
	OR: LEVOMEPROMAZINE 2.5mg-5mg every 6 hours prn	
Hyoscine Hydrobromide (HBr)	GLYCOPYRRONIUM 200micrograms every 4 hours prn	EXCESSIVE SECRETIONS
Midazolam	No change; Midazolam 10mg in 2ml 2.5mg-5mg up to every hour prn	TERMINAL AGITATION (Low doses may also be used for BREATHLESSNESS)

The changes have been made to reflect national trends and for the following reasons:

Cyclizine – is contra-indicated in patients with severe heart failure + "caution" in those with renal or hepatic impairment. However it is still a useful option for many patients

Levomepromazine is a broader spectrum anti-emetic now being used more widely. It can be sedating even at low doses and the usual dose range is 2.5mg – 5mg SC stat every 6 hours (or 2.5mg -12.5mg/24hours by CSCI) Note ampoules are 25mg in 1ml

Hyoscine Hydrobromide is sedating but can cause paradoxical agitation, for this reason Glycoprronium is preferred.

Glycopyrronium is non-sedating and is increasingly being used as first line nationally. The usual dose is 200micrograms stat every 4 hours followed by 600micrograms – 1.2mg over 24 hours via CSCI.

Five ampoules of each of the Just in Case drugs, together with five 10ml ampoules of Water for Injections costs less than £25 making it a cost effective intervention when CHOC calls and admissions can be avoided. Please remember that the Just in Case (JiC) sheet is an authorisation for the Community Nurses to administer, it is NOT the prescription – an FP10 is still needed.

Liothyronine

The cost of liothyronine prescribed in Cumbria CCG has doubled over the last 24 months from £36.2K in Q1 13-14 to £71K in Q4 14-15, despite a small fall in items from 350 to 332. Total spend for the financial year 14-15 was £264K. Further analysis revealed that most prescribing is in Furness and South Lakes locality and that most prescribing is historical. The APC reviewed the evidence base for liothyronine and allocated RAG status **RED** for cancer patients and **BLACK** for all other indications.
Support will be available to practices to review patients.

Branded Oxycodone prescribing

In November 2010 following a recommendation from the Cumbria Palliative Care Medicines Management Group, Cumbria APC agreed to support branded prescribing of opioids following an MHRA safety alert, and specified brand choice:

- Modified release 12 hourly Morphine Sulphate preferred brand = **Zomorph®** (with MST for the 5mg and 15mg strengths as before)
- Fentanyl patches preferred brand = **Matrifen®**

A similar review of oxycodone prescribing has been carried out and the APC have now approved a recommendation from the Palliative Care Medicines Management Group that prescribing of Oxycodone for Palliative Care patients be aligned with prescribing of Morphine; ie that the first line products are the twice daily Modified Release tablets (**Longtec® MR tablets**) with the oral liquid, rather than immediate release capsules, for breakthrough doses. This aims to avoid confusion between the IR capsule and MR tablet forms.
There are several generic Oxycodone liquids available but there is no financial gain from prescribing generically as the current drug tariff price is still based on Oxynorm®, so until a Shortec liquid is available consider prescribing **Oxynorm® liquid** for consistent appearance to avoid confusion. For patients already taking IR capsules for their breakthrough pain, **Shortec®** is now the preferred brand.

Anticholinergic drugs for urinary incontinence

In August 2014 the Cumbria guidance Treatment of Overactive Bladder (OAB) in Women was ratified by the APC. This was produced following publication of NICE GC 171 : Urinary incontinence: The management of urinary incontinence in women in September 2013. A Care Bundle was also developed which included use of a bladder diary, lifestyle modifications and bladder training in line with NICE CG171.

The Cumbria guidance contained recommendation for treatment choices:
First line medication:
Tolterodine 1mg twice daily
Tolterodine 2mg twice daily
If the first line option is not effective or well tolerated, offer another drug with the lowest acquisition cost.
Second line medication:
Darifenacin 7.5mg daily
Darifenacin 15mg daily
Third line medication:
Trospium MR 60mg caps daily
If above options contraindicated, clinically ineffective or unacceptable side effects, consider:
Mirabegron 50 mg daily (25 mg in renal and hepatic impairment)

(continued)

A review of prescribing of drugs for incontinence was presented to the APC. Many practices have adopted the first and second line treatment choices, however a considerable proportion of tolteridone is still prescribed as Modified Release preparations. There continue to be requests to GPs to prescribe outwith the recommended drug choices.
The APC endorsed the drug treatment choices decision made in August 2014 and additionally agreed that Mirabegron, when prescribed in combination with other anticholinergics has RAG status **RED**

The use of immediate release Tolteridone over modified release preparations is also recommended.

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News from the MHRA

Proton pump inhibitors: very low risk of subacute cutaneous lupus erythematosus (Drug Safety Update September 2015)

Proton pump inhibitors (PPIs) are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE), a non-scarring dermatosis that can develop in sun-exposed areas.

If a patient treated with a PPI develops lesions—especially in sun-exposed areas of the skin—and it is accompanied by arthralgia:

- Advise them to avoid exposing the skin to sunlight
- Consider SCLE as a possible diagnosis
- Consider stopping use of the PPI unless it is imperative for a serious acid-related condition. A patient who develops SCLE with a particular PPI may be at risk of the same reaction with another
- In most cases, symptoms resolve on PPI withdrawal. Topical or systemic steroids might be necessary for treatment of SCLE only if there are no signs of remission after a few weeks or months

Pseudoephedrine and ephedrine: update on managing risk of misuse (Drug Safety Update September 2015)

Implementation of measures to regulate sales, together with the additional voluntary actions overseen by the pharmacy profession, has made an important contribution to managing the risk of misuse of pseudoephedrine and ephedrine in the UK.

Pseudoephedrine and ephedrine are medicines used as nasal decongestants, which are available from pharmacies. Between 2007 and 2008, the MHRA introduced restrictions on their use because of concern that medicines containing these active substances could be used in the illicit manufacture of the Class A controlled drug methylamphetamine.

Since April 2008, the following sales restrictions have been in place to manage the risk of misuse of pseudoephedrine and ephedrine:

- It is illegal to sell or supply any product that contains more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription
- It is illegal to sell or supply a combination of products that between them add up to more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription
- It is illegal to sell or supply a product that contains pseudoephedrine and a product that contains ephedrine in one transaction

Furthermore, the Royal Pharmaceutical Society advises that the sale and supply of these products must be made by a pharmacist or suitably trained pharmacy staff under the supervision of a pharmacist

Impact of restrictions: 2015 review

Between June 2013 and March 2015 there have been a few reports from pharmacies of suspicious behaviour, which have been addressed according to established procedures. There has been no evidence of methylamphetamine manufacture from medicines. The evidence suggests that the restrictions are continuing to help manage the risk of misuse. Further information is available in our report: Pseudoephedrine and ephedrine: managing the risk of medicines misuse – September 2015.

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NICE guidance

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

	Drug	Condition	Summary
TA352	Vedolizumab	For treating moderately to severely active Crohn's disease after prior therapy.	Vedolizumab (Entyvio) is recommended. It is a possible option for adults with moderate to severe Crohn's disease if a type of treatment called a tumour necrosis factor (TNF)-alpha inhibitor isn't suitable or hasn't worked well enough. **RED**
TA354	Edoxaban	For treating and preventing recurrent deep vein thrombosis or pulmonary embolism.	Edoxaban (Lixiana) is recommended as an option for treating and preventing recurrent deep vein thrombosis or pulmonary embolism. Edoxaban (Lixiana, Daiichi Sankyo) is an anticoagulant that directly inhibits factor X (factor Xa), which is a key component in the formation of blood clots. It is administered orally. The recommended dosage of edoxaban is 60 mg once daily, or 30 mg once daily in specific patient groups (people with renal impairment, low body weight [60 kg or less], or concomitant use of potent permeability glycoprotein [P-glycoprotein] inhibitors), following treatment with a parenteral anticoagulant for at least 5 days. **GREEN**
TA355	Edoxaban	Edoxaban (Lixiana) is recommended as an option for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation who have one or more risk factors.	Edoxaban (Lixiana) is recommended as an option for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation who have one or more risk factors, such as • heart failure, high blood pressure or diabetes • had a stroke or transient ischaemic attack before • aged 75 years or older. . **GREEN**

TA357	Pembrolizumab	This drug is a possible treatment for melanoma in certain situations.	Pembrolizumab (Keytruda) is recommended. This drug is a possible treatment for adults with melanoma that: • can't be completely removed by surgery or has spread to other parts of the body • has been treated with ipilimumab (melanoma that is BRAF V600 mutation-positive must also have had treatment with vemurafenib, dabrafenib, or trametinib). **RED**

	Condition	Recommendations
NG15	Antimicrobial Stewardship	This guideline covers the effective use of antimicrobials (including antibiotics) in children, young people and adults. It aims to change prescribing practice to help slow the emergence of antimicrobial resistance and ensure that antimicrobials remain an effective treatment for infection.
NG17	Type 1 Diabetes in adults, diagnosis and management	This guideline covers the care and treatment of adults (aged 18 and over) with type 1 diabetes. This guideline updates and replaces the sections for adults in NICE guideline CG15.
NG18	Diabetes (type 1 and type 2) in children and young people: diagnosis and management	This guideline covers the diagnosis and management of type 1 and type 2 diabetes in children and young people aged under 18. The guideline recommends strict targets for blood glucose control to reduce the long-term risks associated with diabetes.
NG20	Coeliac disease: recognition, assessment and management.	This guideline covers the recognition, assessment and management of coeliac disease in children, young people and adults. It updates and replaces NICE guideline CG86.

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