NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

The Newsletter of the Cumbria Area Prescribing Committee

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Clinical policy and Formulary news	Recommendations on new medicines	News from the MHRA	NICE Guidance
Co-proxamol JEXT® Probiotics Denosumab Magnesium aspartate Domicilary care staff and assistance with medicines	Budesonide capsules for treatment of collagenous colitis Mirabegron tablets for treatment of symptoms of overactive bladder Medroxyprogesterone (subcutaneous) for long-acting injectable contraception Ursodeoxycholic acid tablets for the dissolution of gallstones Linaclotide for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation. 5-aminolaevulinic acid gel for the treatment of actinic keratosis	Metoclopramide – new restrictions on the prescribing indications and duration. Nitrofurantoin – not to be used for patients with renal impairment (creatinine clearance less than 60mL/min).	TA295 – everolimus + exemestane for the treatment of HER -ve, hormone receptor +ve breast cancer CG167 – Myocardial infarction with ST-segment elevation CG168 – Varicose veins in the legs CG169 – Acute kidney injury CG170 – Autism CG171 – Urinary incontinence in women

Clinical Policy and Formulary News

Co-proxamol	Co-proxamol was, for many years, the most popular analgesic for mild to moderate pain. It is a combination of paracetamol (325mg) and dextropropoxyphene (32.5mg). The use of co-proxamol has decreased due to concerns over the benefits and toxicity of the preparation. On three occasions, (September 2005, June 2009 and January 2011) the MHRA have published adverse data on co-proxamol regarding its risk in overdose and cardiotoxicity. The MHRA recommends that co-proxamol should no longer be used. For a small group of patients who have found it very difficult to change from co-proxamol, when alternatives appear not to be effective or suitable, an unlicensed product remains available. A fuller briefing on the risks and benefits of co-proxamol may be found here (Note that you will require access to NHS Networks to access this document).
JEXT®	The Area Prescribing Committee recently recommended the use of JEXT for the treatment of anaphylaxis. Unfortunately, the manufacturers have reported supply problems that may not be solved until the middle of December.
Probiotics	Probiotics have been suggested as both a preventative and treatment option for reducing the risk of *Clostridium difficile* diarrhoea that is associated with the use of broad-spectrum antibiotics. New evidence suggests that such benefit is now unlikely. A Cochrane review concluded that there was 'moderate quality evidence to suggest that probiotics are both safe and effective for preventing *Clostridium difficile* associated diarrhoea'. This study included 21 trials, including 4213 patients. A variety of different probiotics are tested. The incidence of *C.difficile* diarrhoea in the probiotic group was 12.6% and in the 12.7% in the placebo group. A recent UK study trialed a probiotic vs. in older in-patients who were receiving oral or intravenous antibiotics. This trial included over 17,000 patients. *C.difficile* diarrhoea occurred in 12 (0.8%) patients receiving the probiotic and 17 (1.2%) receiving the placebo. Overall, the benefit was not statistically beneficial (RR 0.71; 95% CI, 0.34 to 1.47). Similarly, the incidence of antibiotic-associated diarrhoea was not significantly affected (159 vs. 153. RR 1.04, CI, 0.84 to 1.28). There is a large disparity in the incidence of *C.difficile* diarrhoea between the meta-analysis and the randomised controlled trial. It is therefore unlikely that there is any benefit in administering a probiotic with an antibiotic to reduce the risk of developing *C.difficile* diarrhoea, so their use is not recommended.

<table>
<tr>
<td>Denosumab</td>
<td>Denosumab is a monoclonal antibody, for the prevention/treatment of osteoporosis. It should not be seen as purely a replacement for alendronate, if oral tolerability is a problem. NICE TA274 recommends its use, in patients who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments
AND
who have a combination of T-score, age and number of independent clinical risk factors for fracture as indicated in the following table.

<table>
<tr><th></th><th colspan="3">Number of independent clinical risk factors for fracture</th></tr>
<tr><th>Age (years)</th><th>0</th><th>1</th><th>2</th></tr>
<tr><td>65-69</td><td>Not recommended</td><td>-4.5</td><td>-4.0</td></tr>
<tr><td>70-74</td><td>-4.5</td><td>-4.0</td><td>-3.5</td></tr>
<tr><td>75 or older</td><td>-4.0</td><td>-4.0</td><td>-3.0</td></tr>
</table>

The clinical risk factors for fracture are:
• parental history of hip fracture
• alcohol intake of 4 or more units per day
• rheumatoid arthritis.</td>
</tr>
<tr>
<td>Magnesium aspartate</td>
<td>The APC recommends magnesium aspartate sachets as the preferred magnesium supplement. It contains 10mmol of magnesium per sachet, compared with 4mmol in the commonly used glycerophosphate tablets. The aspartate seems to be more consistently priced than the glycerophosphate tablets.

Details of the aspartate preparation are available in the BNF for Children (BNFc 2013-14, p475). The proprietary name is Magnaspartate®.

It should be noted that hypomagnesaemia is a recognised side effect of proton pump inhibitor therapy. If this occurs, it would be prudent, as a first step, to consider the need for continuing proton pump inhibitor therapy.</td>
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<tr>
<td>Domiciliary care staff and assistance with medicines</td>
<td>Domiciliary care staff in Cumbria assist service users with medicines taking as part of a package of care commissioned by Adult Social Care. The level of support the service user receives will have been determined by completion of a risk assessment by ASC or health staff. Support for the service user does not automatically include use of a monitored dosage system (dosette box, blister pack or other compliance aid), there are many other possible solutions to medicines related problems (eg large print labels, reminder services). A pharmacist should assess the service user to establish if a compliance aid is an appropriate adjustment to support them to maintain their independence with their medication.</td>
</tr>
</table>

If the risk assessment identifies the service user needs support with medicines, it will also identify the level of support needed (Category 1,2 or 3)

Category 1: General Support (Service user had capacity).

The exact task the carer can perform are detailed in the Service Provision Order (03BMM) and the carer should never be asked to perform any task which is not on the order. They should never pass the person loose tablets from containers filled by anyone other than a pharmacist or doctor, including family members. They must have been trained to complete any task they are expected to perform. They must not do any Category 2 tasks. They must not assist a person who has a degree of mental frailty (these people are supported under category 2)

Support may include

- Requesting repeat prescriptions and collecting them from the pharmacy or dispensing practice.
- Disposing of unwanted medication by returning to the pharmacy
- Ensuring medication is stored safely
- Manipulation of a container eg popping out tablets or opening a bottle at the request of the service user
- Short term impairment of mental capacity may mean care staff need to temporarily give verbal reminders or prompt to take medication, and give physical assistance eg removing tablets from a container and passing to the service user. This requires an additional risk assessment which must be regularly reviewed(Persistent need for reminders may indicate a need for category 2 support) and additional training.

Category 2: Administering Medication

- Care staff can select and prepare medicines for immediate administration. (this might include selection from original packs and/or a compliance aid)
- Only staff that that have had appropriate training should be asked to support individuals needing category 2 support.
- Care staff should not administer medication if the service user appears to be unwell, they will contact their Home Care Manager for advice.
- Care staff will not administer medication if there are no directions on the label. GPs should be aware of this when prescribing and include specific instructions on prescriptions for service users, which the pharmacist will then put on the label (eg apply sparingly twice a day to rash on thigh)
- Care staff must not be expected to make a judgement when to give “when required” medication, the circumstances should be clearly documented and included on the label, with a maximum daily dose and time lapse between administrations.
- If a service user refuses to take their medication, care staff can offer a degree of encouragement but can never force a service user to take their medication. Refusal is documented. Medication must never be hidden in food or otherwise disguised to force a service user to take it against their wishes.
- If a service user appears to be intoxicated or under the influence of alcohol or illicit substances, the care staff will refuse to help with medication and will contact their manager for advice.
- Support may include physically selecting the medication and giving it to the service user, and may include placing the

	medication in the service user's mouth. • Support can include administration of eye/ear/nose drops, eye ointments, creams, powders, lotions and transdermal patches, with the service user's consent. • Consent must be documented in the service delivery plan. If the patient is unable to communicate informed consent, the prescriber must provide written confirmation to the care manager that the treatment is in the best interest of the individual. • Care staff should never be asked to administer medication in such a way as to render it unlicensed eg cut a transdermal patch or crush a tablet. **Category 3: Administration of medication – Specialised Techniques**. Can only be commissioned following a full risk assessment supported by clinical supervision and training from a healthcare professional. • Rectal administration • Insulin by injection, including testing of blood glucose • Administration via a Percutaneous Endoscopic Gastrostomy (PEG) For further advice contact Hazel Smith or any member of the Medicines Optimisation Team.

↑ Return to page 1

Recommendations on New Medicines

The following drugs have been recommended as suitable for use:	Budesonide 3, 9mg gastro-resistant capsule (Budenofalk®)	Symptomatic relief of chronic diarrhoea due to collagenous colitis.	**Included** as a first choice drug, for the indication in question. **GREEN**
	Mirabegron 25, 50mg prolonged-release tablets (Betmiga®)	Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.	**Included** on the LJF as a prescribing note. Recommended as an option by NICE (TA290) 'only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects' **GREEN**
	Medroxyprogesterone acetate 104mg/0.65mL injection (Sayana® Press)	Long-term female contraception. Each **subcutaneous** injection prevents ovulation and provides contraception for at least 13 weeks (+/- 1 week). However, it should be taken into consideration that the return to fertility (ovulation) may be delayed for up to one year.	**Included** in the LJF for the indication in question. **GREEN**
	Ursodeoxycholic acid 500mg tablets (Ursofalk®)	Dissolution of cholesterol gallstones in the gall bladder. The gallstones must not show as shadows on X-ray images and should not exceed 15mm in diameter. The gall bladder must be functioning despite the gallstone(s).	**Included** on the Additional List for the indication in question. **AMBER**
	Linaclotide 290 micrograms capsules (Constella®)	Symptomatic treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C) in adults.	**Included** on the Additional List for the indication in question. **AMBER**
	5-aminolaevulinic acid gel (Ameluz®)	Treatment of actinic keratosis of mild to moderate intensity on the face and scalp (Olsen grade 1 to 2).	**Included** on the Additional List for the indication in question. **RED**

↑ Return to page 1

News from the MHRA

Metoclopramide	The European Medicines Agency's Committee on Medicinal Products for Human Use has reviewed the benefits and risks of metoclopramide. The review has confirmed the well-known risks of neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia. The conclusion was that these risks outweigh the benefits in long-term or high-dose treatment. In adults, metoclopramide remains indicated for: • Prevention of postoperative nausea and vomiting • Radiotherapy-induced nausea and vomiting • Delayed (but not acute) chemotherapy-induced nausea and vomiting • Symptomatic treatment of nausea and vomiting, including that associated with acute migraine (where it may also be used to improve absorption of oral analgesics) In children (age 1 to 18 years), metoclopramide should only be used: • as a second-line option for prevention of delayed chemotherapy-induced nausea and vomiting • for treatment of established post-operative nausea and vomiting Use of metoclopramide is contra-indicated in children younger than 1 year. **Metoclopramide should only be prescribed for short-term use, up to 5 days.** One area that was not addressed in the MHRA guidance was the use of metoclopramide in patients receiving palliative care. It is widely used in this group of patients and it would be sensible to assess the risks and benefit on an individual basis. Useful guidance is available here to guide prescribers on the alternatives that may be considered. (Note that you will require access to NHS Networks to access this document).
Nitrofurantoin	Use of nitrofurantoin is contra-indicated in patients with creatinine clearance less than 60mL/min. The efficacy of nitrofurantoin depends on the renal secretion of the drug into the urinary tract. In patients with renal impairment, renal secretion of nitrofurantoin is reduced to the point where insufficient quantities of nitrofurantoin are present to have an antibacterial effect. In addition, there is an increased risk of nausea, vomiting, diarrhoea and acute and chronic pulmonary reactions Many elderly patients are likely to have a clearance less than 60mL/min, so use of nitrofurantoin in this patient group should be considered very carefully.

↑ Return to page 1

NICE guidance

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

	Drug	Condition	Decision
TA295	**Everolimus (+ exemestane)**	Postmenopausal women with advanced human epidermal growth factor receptor 2 (HER2) negative hormone-receptor positive breast cancer that has recurred or progressed following treatment with a non-steroidal aromatase inhibitor.	Not recommended

CG167	**Myocardial infarction with ST-segment elevation**	Guidance furthers the use of PCI for patients with acute STEMI. Fibrinolysis only recommended if PCI cannot be given in a timely manner. Ticagrelor in combination with low-dose aspirin is recommended for up to 12 months as a treatment option in people with STEMI – defined as ST elevation or new left bundle branch block on electrocardiogram – that cardiologists intend to treat with primary PCI. Bivalirudin in combination with aspirin and clopidogrel is recommended for the treatment of adults with STEMI undergoing primary PCI.
CG168	**Varicose veins in the legs**	No pharmacologically relevant recommendations made.
CG169	**Acute kidney injury**	Identifies risk of acute kidney injury, including the use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic.
CG170	**Autism – management of autism in children and young people**	Consider antipsychotic medication for managing behaviour that challenges in children and young people with autism when psychosocial or other interventions are insufficient or could not be delivered because of the severity of the behaviour. Antipsychotic medication should be initially prescribed and monitored by a paediatrician or psychiatrist who should: • identify the target behaviour • decide on an appropriate measure to monitor effectiveness, including frequency and severity of the behaviour and a measure of global impact • review the effectiveness and any side effects of the medication after 3–4 weeks • stop treatment if there is no indication of a clinically important response at 6 weeks.

CG171	**Urinary incontinence in women**	Bladder training is the first-line treatment of urgency or mixed urinary incontinence. When choosing a drug, offer one of the following choices first to women with overactive bladder (OAB) or mixed urinary incontinence (UI): - oxybutynin (immediate release), or - tolterodine (immediate release), or - darifenacin (once daily preparation). If the first treatment for OAB or mixed UI is not effective or well-tolerated, offer another drug with the lowest acquisition cost. The use of desmopressin may be considered specifically to reduce nocturia in women with UI or OAB who find it a troublesome symptom. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. Do not use duloxetine as a first-line treatment for women with predominant stress UI. Do not routinely offer duloxetine as a second-line treatment for women with stress UI, although it may be offered as second-line therapy if women prefer pharmacological to surgical treatment or are not suitable for surgical treatment. If duloxetine is prescribed, counsel women about its adverse effects. After an MDT review, offer bladder wall injection with botulinum toxin A to women with OAB caused by proven detrusor overactivity that has not responded to conservative management (including 2 OAB drugs).