NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

The Newsletter of the Cumbria Area Prescribing Committee

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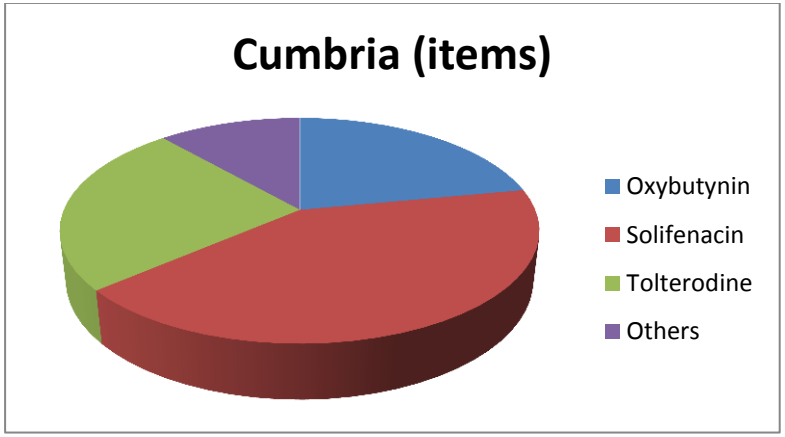
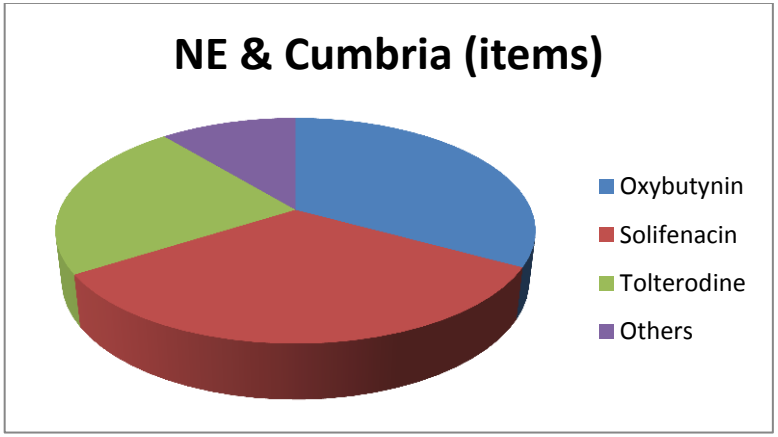
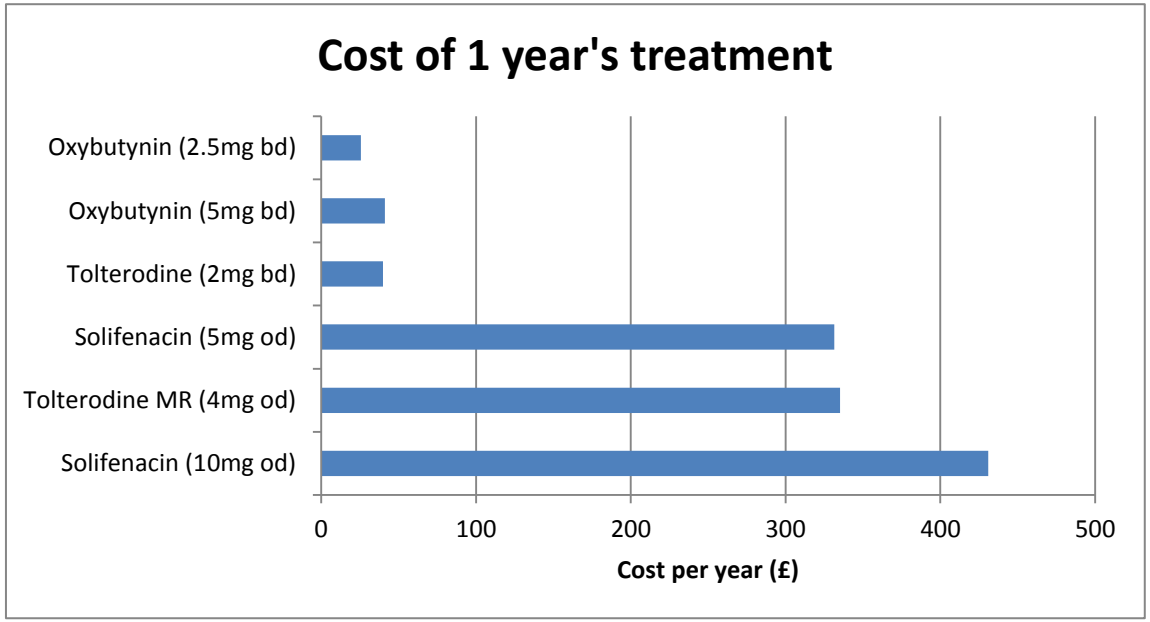
Clinical Policy and Formulary News

Fosfomycin	Fosfomycin is an unlicensed drug (unlicensed in the UK, but is licensed in many European countries), specifically used for the treatment of symptomatic lower UTI in adult men and non-pregnant women where multi-resistant coliforms are identified (e.g., ESBL-positive *E.coli*) from urine culture. It is used for this indication, where the only other option would be the use of intravenous broad-spectrum antibiotics. It should be used only on the recommendation of a consultant microbiologist. The recommended dose for women is 3 grams given as a single dose, while in men, a second 3 gram dose should be taken after 3 days. It is not stocked by community pharmacies and has to be ordered, so there may be a delay in treatment. The cost is approximately £48 for a 3 gram sachet. There is a NICE review on fosfomycin as part of its evidence summaries on unlicensed medicines which is available here.
Guidance for the prescribing of vitamins, minerals, supplements, herbal and homeopathic medicines without a product licence	The APC has now agreed advice for the prescribing of vitamin, minerals, supplements, herbal and homeopathic medicines, where these products do not have a product licence. These preparations should not be prescribed in recognition of the fact that do not have a product licence and are not subject to the same level of trial evidence and good manufacturing practice that is applied to licensed medicines. This does not apply in patients where there is a proven deficiency that is treated with a licensed medicine.
LJF amendments	**Induction of remission/symptomatic relief of chronic diarrhoea in collagenous colitis** - a new section for treatment of collagenous colitis has been included. Budesonide (Budenofalk®) e/c capsules and granules have been approved for treatment for this condition. Treatment is limited to 8 weeks and should be tapered off in the final two weeks. **Injectable progestogen-only contraceptives** - medroxyprogesterone acetate 104mg/0.65ml suspension for injection (Sayana® Press) has been added. This formulation is for **subcutaneous** depot injection. Depo-Provera is still available as an intramuscular alternative. **Urinary frequency due to bladder instability -** mirabegron has been added as a prescribing note for patients who have not responded to two antimuscarinics or in whom antimuscarinics are contra-indicated.

	Incretin mimetics (injectable) - lixisenatide has replaced exenatide as first choice in this section. Exenatide twice daily (Byetta®) should be used in patients with mild renal impairment (CrCl 30-50ml/min) and exenatide once weekly (Bydureon®) is restricted for patients with genuine needle phobia or district nurse administration is necessary.
Mycophenolate mofetil shared care guideline	A shared care protocol has now been agreed for the use of mycophenolate mofetil in a number of rheumatological conditions such as connective tissue diseases with severe / organ threatening manifestations, vasculitidies, as maintenance post-cyclophosphamide in patients for whom azathioprine is contra-indicated or is inappropriate. It should be noted, however, that it is not licensed for these conditions.
Drugs for urinary frequency, enuresis and incontinence	Cumbria has a high cost of drugs used in the treatment of urinary frequency, enuresis and incontinence, the highest of all 13 CCG's in the North East and Cumbria. This is despite being the third lowest prescribing frequency. Examination of the data strongly suggests that this is due to a high use of solifenacin compared with oxybutynin and tolterodine immediate release.   In patients with urinary frequency, enuresis and incontinence, it is recommended that before considering drug treatment, a leaflet from patient.co.uk may give patients an insight into overactive bladder (http://www.patient.co.uk/pdf/4768.pdf). In addition, they produce an incontinence/bladder chart (http://www.patient.co.uk/pdf/4770.pdf), which allows the patient to make a record of their condition, which may be useful for some patients. When starting drug treatment, low doses should be used and then titrated upwards, dependent on efficacy and tolerability. The BNF recommends that antimuscarinic treatment should be reviewed every 4 to 6 weeks until symptoms stabilise, and then every 6 to 12 months.

In the STOP START criteria, it recommends that antimuscarinics should be used with caution in patients with:

- dementia *(risk of increased confusion, agitation)*
- chronic glaucoma *(risk of acute exacerbation of glaucoma)*
- chronic constipation *(risk of exacerbation of constipation)*
- chronic prostatism *(risk of urinary retention)*



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Recommendations on New Medicines

The following drugs have been recommended as suitable for use:	Lixisenatide injection (Lysumia®)	Treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.	**AMBER**
	Fluorouracil and / salicylic acid solution (Actikerall®)	Topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients.	**GREEN**
	Imiquimod cream (Aldara®)	Topical treatment of clinically typical, non-hyperkeratotic, non-hypertrophic actinic keratoses on the face or scalp in immunocompetent adult patients when size or number of lesions limit the efficacy and/or acceptability of cryotherapy and other topical treatment options are contra-indicated or less appropriate**.**	**AMBER**
	Ingenol mebutate gel (Picato®)	Cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults.	**GREEN**
The following drugs were <u>not approved</u> by LJF, as no submission was received from local clinicians	Nalmefene tablets (Selincro®)	Reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level (DRL), without physical withdrawal symptoms and who do not require immediate detoxification.	**BLACK**

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News from the MHRA

New oral anticoagulants – apixaban, dabigatran and rivaroxaban

Haemorrhage is a common adverse effect of all anticoagulants. Although these three new oral anticoagulants have some differing contra-indications due to their different properties, the contra-indications in patients with conditions putting them at significant risk of major bleeding, and those relating to use with other concomitant anticoagulants, now apply to all three of the medicines.

The following contra-indications now apply to all three new oral anticoagulants, for all doses and indications:

- A lesion or condition, if considered a significant risk factor for major bleeding. This may include:
  - current or recent gastrointestinal ulceration
  - presence of malignant neoplasm at high risk of bleeding
  - recent brain or spinal injury
  - recent brain, spinal, or ophthalmic surgery
  - recent intracranial haemorrhage
  - known or suspected oesophageal varices
  - arteriovenous malformation
  - vascular aneurysms, or major intraspinal or intracerebral vascular abnormalities
- Concomitant treatment with any other anticoagulant agent—e.g., unfractionated heparin, low molecular weight heparin, heparin derivatives (such as fondaparinux), or oral anticoagulants (such as warfarin). Exceptions are switching of therapy to or from the medicine, or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter.

Additional advice and information for healthcare professionals:

- Special care should be taken when deciding to prescribe these anticoagulant medicines to patients with other conditions, procedures, and concomitant treatments (e.g., NSAIDs, antiplatelets), which may increase the risk of major bleeding
- Attention should be paid to renal function. Impaired renal function may constitute a contra-indication or recommendation not to use the anticoagulant medicine, or may require a dose reduction; recommendations differ for the three medicines
- The contra-indications, posology, and warnings and precautions for use specific to each medicine, together with the individual's risk factors for bleeding (e.g., renal function), should be considered before prescribing these medicines.

Antiepileptic drugs and consistency of brand

Different antiepileptic drugs (AEDs) vary considerably in their characteristics, which influences the risk of whether switching between different manufacturers' products of a particular drug may cause adverse effects or loss of seizure control. The MHRA have therefore advised, that for **some products, used in the treatment of epilepsy**, that there is continuity of preparation used.

AEDs have been divided into three categories to help healthcare professionals decide whether it is necessary to maintain continuity of supply of a specific manufacturer's product:

Category	Drugs	Advice
1	Carbamazepine Phenobarbital Phenytoin Primidone	Prescribers are advised to ensure that their patient is maintained on a specific manufacturer's product.
2	Clobazam Clonazepam Eslicarbazepine Lamotrigine Oxcarbazepine Perampanel Retigabine Rufinamide Topiramate Valproate Zonisamide	For these products, the need for continued supply of a particular manufacturer's product should be based on clinical judgment and consultation with the patient and/or carer, taking into account factors such as seizure frequency and treatment history.
3	Ethosuximide Gabapentin Lacosamide Levetiracetam Pregabalin Tiagabine Vigabatrin	For these drugs, it is usually unnecessary to ensure that patients are maintained on a specific manufacturer's product unless there are specific reasons such as patient anxiety and risk of confusion or dosing errors.

- If it is felt desirable for a patient to be maintained on a specific manufacturer's product, this should be prescribed either by specifying a brand name, or by using the generic drug name and name of the manufacturer.
- **This advice relates only to anti-epileptics use for treatment of epilepsy; it does not apply to their use in other indications (e.g., mood stabilisation, neuropathic pain).**

Additional advice for pharmacists:

- Dispensing pharmacists should ensure the continuity of supply of a particular product when the prescription specifies it. If the prescribed product is unavailable, it may be necessary to dispense a product from a different manufacturer to maintain continuity of treatment of that AED. Such cases should be discussed and agreed with both the prescriber and patient (or carer)
- Usual dispensing practice can be followed when a specific product is not stated

Mefloquine

Although the potential for neuropsychiatric side effects with mefloquine is a well-established risk, a recent review of the prescribing information has led to strengthened warnings and new measures to help minimise risks. The overall safety profile of mefloquine has also been clarified in the product information.

Updated information and advice for healthcare professionals:

- Psychiatric symptoms associated with use of mefloquine such as nightmares, acute anxiety, depression, restlessness, or confusion should be regarded as potentially prodromal for a more serious event
- Cases of suicide, suicidal thoughts, and self-endangering behaviour such as attempted suicide have been reported in association with use of mefloquine
- Adverse reactions may occur and persist up to several months after discontinuation of mefloquine because of its long half-life. In a small number of patients, dizziness or vertigo and loss of balance have been reported to continue for months after discontinuation of the drug
- To minimise the risk of these adverse reactions, mefloquine must not be used for chemoprophylaxis in patients with active or a history of psychiatric disturbances such as depression, anxiety disorders, schizophrenia, or other psychiatric disorders
- If neuropsychiatric reactions or changes to mental state occur during mefloquine chemoprophylaxis, the patient should be advised to stop taking mefloquine and seek medical advice as soon as possible so that it can be replaced by another medicine for malaria prevention
- Suspected adverse reactions to mefloquine should be reported on a Yellow Card. This includes reports from patients and the public, who can report directly or you can do it on their behalf (www.mhra.gov.uk/yellowcard).

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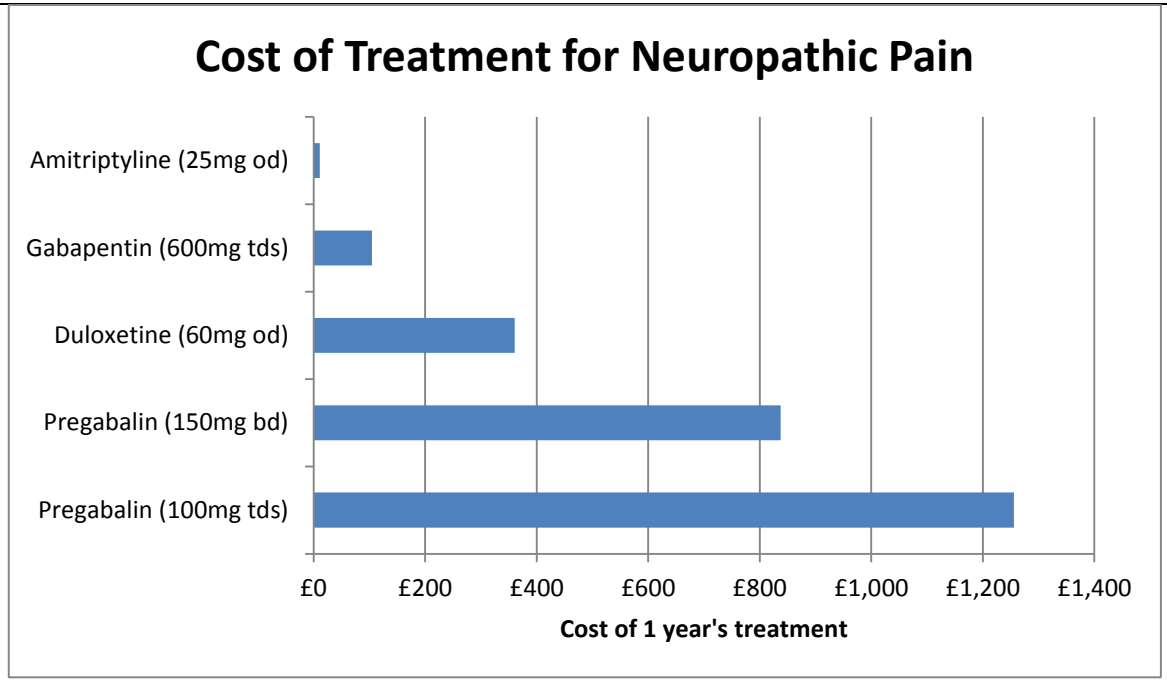
NICE guidance

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

	Drug	Condition	Resume
TA296	**Crizotinib**	Previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene	Not recommended. **BLACK**
TA297	**Ocriplasmin**	Vitreomacular traction	Ocriplasmin is recommended as an option for treating vitreomacular traction in adults, only if: - an epiretinal membrane is not present, and - they have a stage II full-thickness macular hole with a diameter of 400 micrometres or less, and/or - they have severe symptoms. **RED**
TA298	**Ranibizumab**	Choroidal neovascularisation (pathological myopia)	Recommended as an option. Subject to Patient Access Scheme **RED**
TA299	**Bosutinib**	Leukaemia (chronic, myeloid), previously treated	Not recommended for previously treated Philadelphia-chromosome-positive chronic myeloid leukaemia. **BLACK**
TA300	**Peginterferon and ribavirin**	Hepatitis C (children and young people) (Update of TA75 and TA106)	Recommended as an option for treating chronic hepatitis C in children and young people **RED**
TA301	**Fluocinolone intravitreal implant**	Macular oedema (diabetic) (Replaces TA271)	Recommended as an option for treating chronic diabetic macular oedema that is insufficiently responsive to available therapies only if the implant is to be used in an eye with an intraocular (pseudophakic) lens. Subject to Patient Access Scheme **RED**
TA302	**Canakinumab**	Juvenile idiopathic arthritis	No evidence submission was received from the manufacturer of the technology. **BLACK**

CG172	**Myocardial infarction – secondary prevention**	Offer all people who have had an acute MI treatment with the following drugs: - ACE inhibitor. Titrate the ACE inhibitor dose upwards at short intervals (for example, every 12 to 24 hours) before the person leaves hospital until the maximum tolerated or target dose is reached. If it is not possible to complete the titration during this time, it should be completed within 4–6 weeks of hospital discharge - dual antiplatelet therapy (aspirin plus a second antiplatelet agent) - beta-blocker. Communicate plans for titrating beta-blockers up to the maximum tolerated or target dose – for example, in the discharge summary - statin. Do not offer or advise people to use the following to prevent another MI: - omega-3 fatty acid capsules - omega-3 fatty acid supplemented foods. Ticagrelor in combination with low-dose aspirin is recommended for up to 12 months as a treatment option in adults with ACS that is, people: - with STEMI – defined as ST elevation or new left bundle branch block on electrocardiogram, that cardiologists intend to treat with primary PCI or - with NSTEMI. Offer clopidogrel as a treatment option for up to 12 months to: - people who have had an NSTEMI, regardless of treatment - people who have had a STEMI and received a bare-metal or drug-eluting stent. Offer clopidogrel as a treatment option for at least 1 month and consider continuing for up to 12 months to people who have had a STEMI and medical management with or without reperfusion treatment with a fibrinolytic agent. Continue the second antiplatelet agent for up to 12 months in people who have had a STEMI and who received CABG surgery. Do not add a NOAC in combination with dual antiplatelet therapy in people who otherwise need anticoagulation, who have had an MI. Consider using warfarin and discontinuing treatment with a new oral anticoagulant (apixaban, dabigatran or rivaroxaban,) in people who otherwise need anticoagulation and who have had an MI, unless there is a specific clinical indication to continue it.

		Do not routinely offer calcium-channel blockers to reduce cardiovascular risk after an MI. For patients who are stable after an MI, calcium-channel blockers may be used to treat hypertension and/or angina. For patients with heart failure, use amlodipine, and avoid verapamil, diltiazem and short-acting dihydropyridine agents in line with chronic heart failure. For patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, initiate treatment with an aldosterone antagonist licensed for post-MI treatment within 3–14 days of the MI, preferably after ACE inhibitor therapy. Patients who have recently had an acute MI and have clinical heart failure and left ventricular systolic dysfunction, but who are already being treated with an aldosterone antagonist for a concomitant condition (for example, chronic heart failure), should continue with the aldosterone antagonist or an alternative, licensed for early post-MI treatment.
CG173	**Neuropathic pain – pharmacological management**	Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia). If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated. Consider tramadol only if acute rescue therapy is needed. Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments. Trigeminal neuralgia - offer carbamazepine as initial treatment for trigeminal neuralgia. Note that: • *amitriptyline did not have a UK marketing authorisation for this indication* • *duloxetine is licensed for diabetic peripheral neuropathic pain* • *gabapentin is licensed for peripheral neuropathic pain only* • *capsaicin cream is licensed for post-herpetic neuralgia and painful diabetic peripheral polyneuropathy, so use for other conditions would be off-label.* It should be noted that there are significant disparities in the costs:



Doses given do not imply therapeutic equivalence

This is available at the CCG Medicines Management website at:
http://www.cumbriaccg.nhs.uk/about-us/key-policies/medicines-management/index.aspx

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