NHS Cumbria Clinical Commissioning Group

PRESCRIPTION PAD

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Clinical Policy and Formulary News

Vitamin D preparations

A new preparation of colecalciferol, Invita D3® is now available. It is available as oral ampoules of liquid, containing 25,000iu in 1ml.

The principal use of Invita D3® is as a loading dose for the treatment of vitamin D deficiency. The recommended dose in adults is 50,000iu once a week for a total of 6 weeks, i.e., 12 ampoules in total.

Prevention of vitamin D deficiency may be offered as either:

Invita D3®, 25,000iu (1 ampoule) once a month (£1.43 a month), or
Fultium-D3® or Desunin®, 800iu daily (£3.60 a month)

Unlicensed preparations should not be used now that licensed preparations are now available.

Barrier preparations

New guidance has been produced for the use of barrier preparations. This is mostly based on that produced by Cumbria Partnerships. The recommended preparation for dry, intact skin is Sorbaderm® barrier cream. It is important to note that the recommended is 'a pea-sized amount', about 2 grams. The barrier film is recommended where skin is moist and/or broken.

Possible second-line products include Conotrane® cream and the Proshield® system. It should be noted that Conotrane should not be used with incontinence pads and Proshield inters with action of adhesive dressings.

The guidance can be found at:
https://www.networks.nhs.uk/nhs-networks/nhs-cumbria-ccg/medicines-management/guidelines-and-other-publications/barrier-creams/file_popview

Aqueous cream

Aqueous cream has been used as an emollient or moisturiser and as a wash off soap substitute to relieve the symptoms of dry skin conditions such as atopic eczema since the 1950's, however it is now only recommended as a wash off soap substitute.

NICE, the BNF and the National Eczema Society report that aqueous cream may be associated with skin reactions, such as burning, stinging, itching and redness, when used as a leave-on emollient and worsen with a longer skin contact time. The reactions, which are not generally serious, usually occur within 20 minutes of application.

Aqueous cream contains emulsifying ointment, purified water and a preservative, plus other excipients. Emulsifying ointment contains the anionic surfactant sodium lauryl sulphate (SLS), which has been shown in research to damage the skin barrier to mimic the effects of skin disease. A 2013 MHRA Drug Safety Update advises that if a patient reports skin irritation with the use of aqueous cream, treatment should be discontinued and an alternative that does not contain SLS should be tried.

Several studies have assessed and confirmed the effect of aqueous cream on skin structure, comparing the effects of Aqueous Cream to other emollients or control. No studies have been conducted to determine if any particular excipient, or any one particular brand of aqueous cream is responsible for the observed skin reactions.

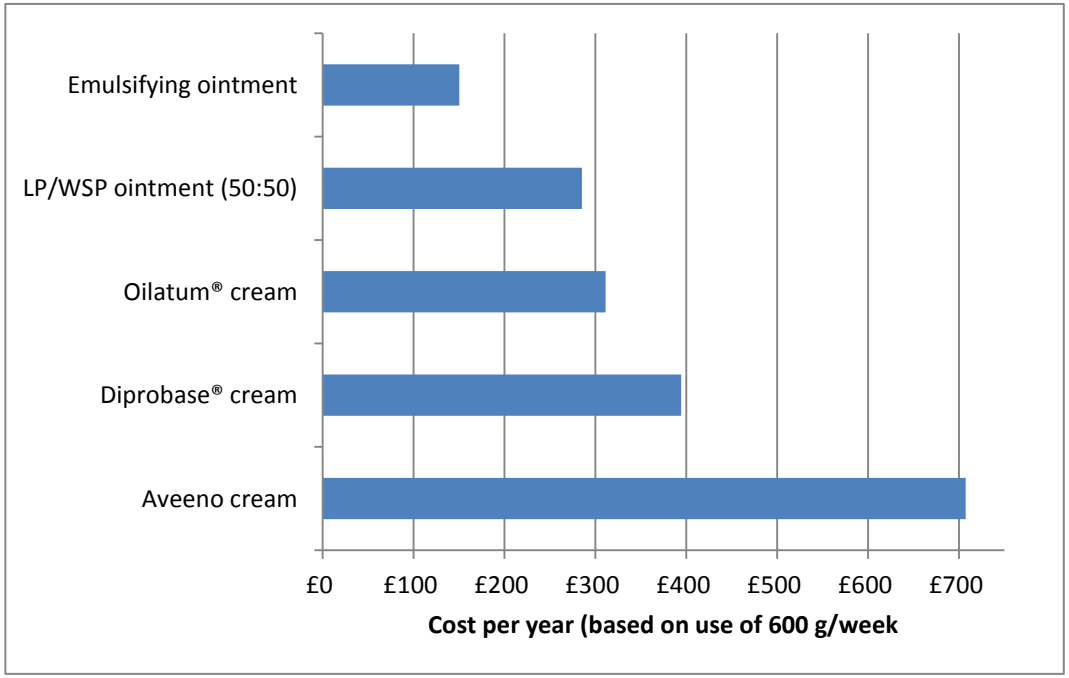
Using aqueous cream as a leave on emollient has the potential to damage skin with increasing evidence for SLS as the causative ingredient. Evidence for damage caused when it is used as a soap substitute is less clear. Ointments, although greasier, are preferable in patients with eczema due to their higher lipid content, although creams may be more socially acceptable. Alternative emollients should be prescribed according to the dryness of the skin and patient preference.

Adapted from UKMI article.

Full UKMI article: http://www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=795103

Lothian Emollient choices:

http://www.ljf.scot.nhs.uk/LothianJointFormularies/Adult/13.0/13.2/13.2.1/Pages/default.aspx



Antibiotic guideline app	This mentioned previously as a forthcoming development. It is now available to download from either the Apple App store or from Android Play, free of charge, searching for MicroGuide. A guide to using the app is available here.
Errors with oxycodone	There have been some recent problems due to the wrong strengths of oxycodone oral solution being given, where the concentrated 10mg/mL solution has been given to patients instead of the intended 5mg/5mL solution. Prescribers and dispensers are advised to double check these prescriptions are correct.

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Recommendations on New Medicines

	Drug	Licensed indication	Recommendation
The following drugs have been recommended as suitable for use:	Clindamycin 1%, tretinoin 0.025% gel (Treclin®)	For the topical treatment of acne vulgaris when comedones, papules and pustules are present in patients 12 years or older.	**Included** on the LJF as a prescribing note, for the indication in question. GREEN
	Colecalciferol oral solution, 25,000 units (Invita D3®)	The prevention and treatment of vitamin D deficiency.	**Included** on the LJF for the indication in question. GREEN Should be included to replace the unlicensed products currently included in the formulary.
	Indacaterol + glycopyrronium inhaler (Ultibro Breezhaler®)	Maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD.	**Included on** the Additional List, for the indication in question. Suitable for patients in whom the combination is an appropriate choice of therapy. GREEN
	Colecalciferol capsules, 3200 units (Fultium-D_3®)	Treatment of vitamin D deficiency.	**Added** to LJF. New strength of preparation already on formulary. GREEN
	Capsaicin patches (Qutenza®)	Treatment of peripheral neuropathic pain in non-diabetic adults either alone or in combination with other medicinal products for pain.	**Added** to the Additional List for treatment in secondary care under the direct supervision of a specialist. RED
The following drug was <u>not approved</u> by LJF as no case for inclusion was made by local specialists	Umeclidinium inhaler (Incruse®)	Maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD.	**Not included** on the LJF because clinicians have not responded to an invitation to apply for formulary inclusion for this medicine. BLACK

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News from the MHRA

Ivabradine in the symptomatic treatment of angina

Ivabradine (Procoralan®) is used to treat chronic heart failure and the symptoms of chronic angina in adults unsuited to or unable to take beta blockers. It can also be used in combination with β-blockers in patients for whom an optimal β-blocker dose is not enough.

In a recent trial there was a small but significant increase in the combined risk of cardiovascular death or non-fatal heart attack with ivabradine compared with placebo (3.4 vs. 2.9% yearly incidence rates). The risk of bradycardia (17.9 vs. 2.1%) and atrial fibrillation (5.3 vs. 3.8%) was also increased in participants taking ivabradine compared with placebo.

The following recommendations are made when using ivabradine to treat the symptoms of chronic angina:

- only start ivabradine if the resting heart rate is at least 70 beats per minute
- do not prescribe ivabradine with other medicines that cause bradycardia, such as verapamil, diltiazem, or strong CYP3A4 inhibitors
- monitor patients regularly for atrial fibrillation. If atrial fibrillation occurs, carefully reconsider whether the benefits of continuing ivabradine treatment outweigh the risks
- consider stopping ivabradine if there is no or only limited symptom improvement after 3 months

In addition:

- ivabradine is indicated to treat symptoms of chronic angina in patients unable to tolerate or with a contra-indication to β-blockers - it can also be used in combination with β-blockers in patients for whom an optimal β-blocker dose is not enough
- the recommended starting dose is 5mg twice daily
- do not exceed the maximum maintenance dose of 7.5mg twice daily
- down-titrate the dose if resting heart rate decreases persistently below 50 beats per minute or if the patient experiences symptoms of bradycardia. The dose can be down-titrated to 2.5mg twice daily if necessary
- stop ivabradine treatment if the resting heart rate remains below 50 beats per minute or symptoms of bradycardia persist

Isotretinoin: reminder of risk of psychiatric disorders

There have been reports of psychiatric disorders in patients taking isotretinoin (e.g., depression, anxiety, and very rarely suicidal ideation and suicide). Ongoing concerns prompted a review the available data.

Due to conflicting study results and the limitations in the data it was not possible to identify a clear increase in risk of psychiatric disorders in people who take isotretinoin compared to those that do not. In addition there was no clear biological mechanism by which isotretinoin would cause psychiatric disorders. Acne itself is associated with some psychiatric disorders. Also, the age at which many patients take isotretinoin is also the age at which some psychiatric disorders are commonly diagnosed.

Healthcare professionals are advised that:

	• isotretinoin should only be prescribed by or under the supervision of a consultant dermatologist with expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risks of isotretinoin therapy and monitoring requirements • warn patients and their family that isotretinoin might cause psychiatric disorders such as depression, anxiety, and in rare cases suicidal thoughts - tell them to watch out for symptoms • when prescribing isotretinoin to patients with a history of depression, carefully consider the balance of benefits of treatment against the possible risk of psychiatric disorders • monitor all patients for signs of depression and refer for appropriate treatment if necessary; stopping isotretinoin may not be enough to alleviate symptoms and further psychiatric or psychological evaluation may be necessary.
Mycophenolate mofetil and mycophenolic acid: risk of hypogammaglobulinaemia and risk of bronchiectasis	A review by European regulators concluded that mycophenolate mofetil in combination with other immunosuppressants can cause hypogammaglobulinaemia in adults and children, which can be associated with recurrent infections. This conclusion was based on published reports, clinical trial data, and reports from clinical practice. Switching from mycophenolate mofetil to an alternative immunosuppressant resulted in serum IgG levels returning to normal in some cases. The review also concluded that mycophenolate mofetil in combination with other immunosuppressants can cause bronchiectasis in adults and children (sometimes years after starting mycophenolate mofetil treatment). The risk of bronchiectasis may be linked to hypogammaglobulinaemia or to a direct effect of mycophenolate on the lungs. Patients who developed bronchiectasis usually presented with a persistent productive cough and, in some cases, recurrent upper or lower respiratory tract infections. The diagnosis was confirmed by high resolution computed tomography of the chest. In some of these cases, switching from mycophenolate mofetil to another immunosuppressant improved respiratory symptoms. Mycophenolate mofetil is also known to cause pulmonary fibrosis. When using mycophenolate mofetil or any other medicine containing mycophenolic acid (MPA) as its active ingredient: • measure serum immunoglobulin levels if recurrent infections develop • in cases of sustained, clinically relevant hypogammaglobulinaemia, consider appropriate clinical action. Take into account the potent cytostatic effects of mycophenolate on B-lymphocytes and T-lymphocytes • consider bronchiectasis or pulmonary fibrosis if patients develop persistent respiratory symptoms, such as cough and dyspnoea • please continue to report suspected adverse drug reactions to mycophenolate mofetil, medicines containing mycophenolate, or any other medicines on a Yellow Card www.gov.uk/yellowcard.

Yellow Card Reporting	Yellow card reporting has now been extended to include devices, counterfeits and defective medicines. This will hopefully simplify the reporting process. You can now report any of the following on a Yellow Card: • suspected adverse drug reactions • medical device incidents • defective medicines • suspected fake medicines Please continue to report all suspected adverse drug reactions that are serious, medically significant, or result in harm - serious reactions are any of the following: • fatal • life-threatening • a congenital abnormality • disabling or incapacitating • those that result in or prolong hospitalisation • associated with new drugs and vaccines (denoted by a ▼) Report via Yellow Card at www.gov.uk/yellowcard.
New arrangements for receiving Drug Safety Update	Drug Safety Update is available as a monthly e-mail. You can sign up to the e-mail at: https://www.gov.uk/drug-safety-update/email-signup . The individual articles from all Drug Safety Updates are available at: https://www.gov.uk/drug-safety-update

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NICE guidance

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

	Drug	Condition	Summary
TA327	Dabigatran	Treatment and secondary prevention of DVT and/or pulmonary embolism	Recommended as an option. Rivaroxaban is already on the formulary for this indication. **GREEN**
TA328	Idelalisib	Follicular lymphoma refractory to two prior treatments	Not recommended, manufacturers did not make a submission to NICE. **BLACK**

	Condition	Recommendations
CG131	Colorectal cancer	Gives guidance on the diagnosis and staging of the condition. Specifically recommends the use of capecitabine or 5-FU, oxaliplatin + folinic acid for adjuvant treatment of stage III (Dukes C) colon cancer, as per previous NICE TA100. Advanced or metastatic colorectal cancer - use of FOLFOX or FOLFIRI or XELOX regimes. Raltitrexed may be offered as an alternative
CG190	Intrapartum care of healthy women and their babies during childbirth	Guidance on the care of pregnant women when giving birth. It recommends the appropriate use of midwife-led delivery units. Use of IV/IM analgesics, regional anaesthesia. Recommends use of oxytocin to promote contractions. Offer second-line treatment for postpartum haemorrhage if needed. No particular uterotonic drug can be recommended over any other; options include repeat bolus of oxytocin (intravenous), ergometrine (intramuscular, or cautiously intravenously), combined oxytocin and ergometrine (intramuscular), misoprostol, oxytocin infusion, carboprost (intramuscular).

CG191	Pneumonia	Makes recommendations about using point-of-care C-reactive protein tests and clinical judgement to guide need for antibiotics. It recommends the use of the CRB65 score to decide on need for hospital treatment • Low severity CAP - amoxicillin for 5 days, alternatives either macrolide or tetracycline. Consider lengthening the to more than 5 days if symptoms do not improve as expected after 3 days • Moderate to severe CAP - dual therapy with amoxicillin + macrolide for 7-10 days • Severe CAP - co-amoxiclav + macrolide Do not routinely offer corticosteroids.
NG1	Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people	Do not offer acid-suppressing drugs, such as PPIs or H2RAs, to treat overt regurgitation in infants and children occurring as an isolated symptom. Consider a 4-week trial of a PPI or H2RA for those who are unable to tell you about their symptoms (for example, infants and young children, and those with a neurodisability associated with expressive communication difficulties) who have overt regurgitation with 1 or more of the following: • unexplained feeding difficulties (for example, refusing feeds, gagging or choking) • distressed behaviour • faltering growth. Consider a 4-week trial of a PPI or H2RA for children and young people with persistent heartburn, retrosternal or epigastric pain. Assess the response to the 4-week trial of the PPI or H2RA, and consider referral to a specialist for possible endoscopy if the symptoms: • do not resolve or • recur after stopping the treatment. When choosing between PPIs and H2RAs, take into account: • the availability of age-appropriate preparations • the preference of the parent (or carer), child or young person (as appropriate) • local procurement costs.

Offer PPI or H2RA treatment to infants, children and young people with endoscopy-proven reflux oesophagitis, and consider repeat endoscopic examinations as necessary to guide subsequent treatment.

Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events.

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