Lincolnshire Prescribing and Clinical Effectiveness Bulletin

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Summary of PACEF decisions from October 2017

PACE Short (Vol 11 No 13)

Device, Dressing or Drug	Indication(s)	Traffic Light and *Joint Formulary* Status
Accrete D3 One a Day Chewable Tablets	• For the prevention and treatment of vitamin D and calcium deficiency in the elderly • As vitamin D and calcium supplement as an adjunct to specific osteoporosis treatment of patients who are at risk of vitamin D and calcium deficiency	Green Approved for inclusion on to the Joint Formulary as an option when a calcium and vitamin D product is required.
Gaviscon Advance oral suspension	• Treatment of symptoms resulting from the reflux of acid, bile and pepsin into the oesophagus such as acid regurgitation, heartburn, indigestion	Green Approved as a second line drug, after Peptac restricted for use in patients with laryngeal reflux and those not responding to treatment with Peptac.

Other news

MEDICINES AND HEALTHCARE REGULATORY AGENCY (MHRA): DRUG SAFETY UPDATE (August 2017)

Ibrutinib – there have been reports of ventricular tachyarrhythmia, risk of hepatitis reactivation and opportunistic infections, associated with its use.

Corticosteroids – Risk of serious chorioretinopathy associated with corticosteroids administered by a variety of different routes inhaled, intranasal, epidural, intra-articular, topical, dermal and periocular.

Adrenaline Auto-injectors - Advice has been updated after European Medicines Agency (EMA) review. It is now recommended that patients must carry a minimum of two adrenaline auto-injectors on them at all times.

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Rapid Cost Comparison Accrete D3 One a Day Chewable Tablets

Accrete D3 One a Day chewable tablets are an extension to the Accrete D3 range of calcium and vitamin D products. Each chewable tablet containing 2,500 mg of calcium carbonate (equivalent to 1,000 mg of calcium) and 8.8 mg of colecalciferol concentrate (powder form) (equivalent to 22 micrograms of colecalciferol = 880 IU of vitamin D3).

- Accrete D3 one a day chewable tablets provide the same total daily dose of calcium and colecalciferol as the Accrete D3 tablets which are administered twice daily.
- The cost of a month's treatment is the same for both Accrete products and they are currently one of the lowest cost options.

Cost comparison table (formulary approved products in bold)

product	calcium	Vitamin D3	dose	Cost(£) 28 days
Accrete D3 One a Day	**1gram**	**880IU**	**Once daily**	**£2.76**
Accrete D3 tablets	**600mg**	**400IU**	**Twice daily**	**£2.76**
Adcal D3 chewable tablet	**600mg**	**400IU**	**Twice daily**	**£3.65**
Adcal D3 caplets	**300mg**	**200IU**	**2 tablets twice daily**	**£2.95**
Adcal D3 Dissolve Effervescent tablet	600mg	400IU	Twice daily	£5.99
Cacit D3	500mg	440IU	1 or 2 sachets daily	£7.58
Calceos chewable tablets	**500mg**	**100IU**	**Twice daily**	**£3.62**
Calci-D Chewable tablets	**1gram**	**1000IU**	**Once daily**	**£2.25**

Calcichew D3 Chewable tablets	500mg	200IU	2-3 daily	£6.45
Calcichew D3 Forte Chewable tablets	500mg	400IU	Twice daily	£3.96
Calcichew D3 500mg/400IU caplets	500mg	400IU	Twice daily	£4.16
Calcichew D3 once daily	1 gram	800IU	Once daily	£6.30
Calfovit D3 sachets	1.2gram	800IU	Once daily	£4.04
Evacal D3	**600mg**	**400IU**	**Twice daily**	**£2.75**
Kalcipos D Chewable tablets	500mg	800IU	Once daily	£3.93
Kalcipos D tablets	500mg	800IU	Once daily	£3.93
Natecal D3 Chewable tablets	**600mg**	**400IU**	**1-2 daily**	**£3.39**
TheiCal-D3	**1gram**	**880IU**	**Once daily**	**£2.76**

- PACEF approved Accrete D3 chewable tablets as an option when a calcium and vitamin D product is required. Classed as GREEN

Rapid Cost Comparison Gaviscon Advance

Application came from the ENT service at United Lincolnshire Hospital requesting the use of Gaviscon Advance for patients suffering from laryngeal reflux

- On the Lincolnshire formulary the compound alginate preparation of choice is Peptac. The only Gaviscon product on the formulary are Gaviscon sachets which are reserved for paediatric use only
- Gaviscon Advance has double the amount of active ingredient (per 10ml dose), lower sodium content and longer duration of action compared to Peptac.
- Gaviscon Advance is reported to have duration of action of 4 hours, compared to 2 hours for Peptac.
- Gaviscon Advance is currently classed as Red/Red on Lincolnshire formulary. Despite this classification there is still significant use across the county.
- Historically Gaviscon Advance was prohibitively priced compared to alternative alginate compounds.

Cost comparison table

product	dose	cost	Cost per month (30 days at QDS dosage)
Gaviscon Advance liquid	**5-10mls after meals and at bedtime**	**250ml = £2.65 500ml =£5.12**	**£12.29**
Peptic liquid	**10-20mls after meals and at bedtime**	**500ml= £1.95**	**£9.36**

- PACEF approved Gaviscon Advance as a second line drug, after Peptac restricted for use in patients with laryngeal reflux and those not responding to treatment with Peptac. Classed as GREEN on the formulary

Reviewing use of Asacol switching to Octasa.

PACEF had been asked to provide advice on how to manage a review of patients currently receiving treatment with mesalazine 400mg & 800mg modified release tablets prescribed as the brand Asacol with the potential of switching to the Octasa brand.

- PACEF accept that Asacol 400mg MR tablets, Ipocol tablets 400mg and Octasa 400mg MR tablets are all similar products in terms of formulation, optimal pH for drug release and site of drug release and that there is little difference in clinical efficacy or in licensed indications. However, as Octasa 400mg MR tablets are significantly lower in cost than the two alternatives, it is recommended that Octasa 400mg MR tablets should be used first-line in all new patients where the oral mesalazine 400mg strength is indicated. ULH gastroenterologists will be increasingly initiating Octasa 400mg MR tablets within this context. Existing patients in remission taking alternative preparations would continue on their current treatment.
- A review of mesalazine prescribing in included in the programme of quality and cost saving initiatives offered across the county.
- Historically it was recommended that mesalazine should be prescribed by brand, however the BNF now states that there is no evidence to show any oral preparation is more effective than another; however the delivery characteristics of mesalazine preparations may vary. If it is necessary to switch a patient to a different brand of mesalazine, the patient should be advised to report any changes in symptoms.
- Asacol m.r. and Octasa m.r have very similar pharmacokinetic release characteristics.

Comparison of the release characteristics of the 400mg m.r. tablets
(reproduced from PrescQIPP Bulletin No 79 August 2014)

	Asacol 400 m.r.	Octasa M.r.
pH1.0-1.2 for 2 hours	0% release	0% release
pH 6.4 for 1 hour	<1% released	<1% released
pH 7.2 for 1 hour	˜98% released in 30-60 minutes	˜99% released in 30-60 minutes

- Octasa m.r. 400mg and Asacol 4090mgm.r. have a virtually identical in vitro dissolution profile, optimal pH for release, site of drug release and similar formulations as they both have an enteric coating of Eudragit.
- Octasa 400mg & 800mg the optimal drug release pH is >7 and the drug site of release is the terminal ileum & colon
- Asacol 400mg the optimal drug release pH is >7 and the drug site of release is the terminal ileum & large bowel (colon & rectum)

- Asacol 800mg the optimal drug release pH is >6-7 and the drug site of release is the terminal ileum & large bowel (colon & rectum). The 800mg strength of Asacol is coated with both Eudragit S and Eudragit L.
- The manufacturers of Octasa, Tillotts Pharma UK Limited, have produced patient information leaflets to support switching mesalazine m.r. from the Asacol brand to Octasa m.r. The information leaflet provides assurance on clinical equivalence between the different brands but does advise patients that of they notice a change in their symptoms following a switch they should report these to their doctor.
- PACEF sought advice from ULHT gastroenterology service as to which patients would be suitable for this switch. Patients should only be considered suitable for the switch if their condition has been judged to be well controlled and stable for the past 12 months. All patients need to be made aware of the change to Octasa from Asacol and instructed to report any changes in their symptoms.

MEDICINES AND HEALTH CARE REGULATORY AGENCY (MHRA): DRUG SAFETY UPDATE (August 2017)

Ibrutinib – The MHRA have received reports of ventricular tachyarrhythmia, risk of hepatitis reactivation and opportunistic infections, associated with its use.

Ibrutinib is used for the treatments of types of lymphoma & leukaemia and is classed as a RED hospital only drug.

The MHRA have issued the following advice to healthcare professionals.

- Cases of ventricular tachyarrhythmia have been reported.
- Temporarily discontinue ibrutinib in patients who develop symptoms suggestive of ventricular arrhythmia, including palpitations, chest pain, dyspnoea, dizziness or fainting and assess benefit risk before starting therapy.
- Be aware of the risk of hepatitis B virus reactivation and establish hepatitis b virus status before initiating therapy.
- For patients with positive hepatitis B serology, consultation with a liver disease expert is recommended before start of treatment, monitor and manage patients according to local standards of care to minimise the risk of hepatitis B virus reactivation.
- Consider prophylaxis according to standard of care for patients who are at an increased risk of opportunistic infections

Corticosteroids rare risk of central serous chorioretinopathy with local as well as systemic administration.

Central serous chorioretinopathy is a retinal disorder that has bene linked to the systemic use of corticosteroids. Recently it has also been reported after local administration of corticosteroids via inhaled, intranasal, epidural, intra-articular, topical, dermal and periocular routes.

The MHRA has issued the following advice for health care professionals:

- Advise patients to report any blurred vision or other visual disturbances during corticosteroid treatment.
- Consider referral to an ophthalmologist for evaluation of possible causes if a patient presents with vision problems.
- Report suspected adverse reactions using a yellow card.

Adrenaline auto-injectors: updated advice after European review.

The MHRA has issued the following advice to health care professionals:

- It is recommended that 2 adrenaline auto-injectors are prescribed which patients should carry at all times.

- Ensure that people with allergies and their carers have been trained to sue the particular auto-injector that they have been prescribed – technique varies between the injectors.
- Encourage people with allergies and their carers to obtain and practise using a trainer device (available free from the manufacturer websites)

Advice to give to people with allergies and their carers:

- It is recommended that you carry 2 adrenaline auto-injectors at all times; this is particularly important for people who also have allergic asthma because they are at increased risk of a severe anaphylactic reaction
- Use the adrenaline auto-injector at the first signs of a severe allergic reaction
- Take the following actions immediately after every use of an adrenaline auto-injector.
- 1. Call 999, ask for an ambulance and state anaphylaxis, even if symptoms are improving
- 2. Lie flat with legs raised to maintain blood flow. However if you have breathing difficulties, you may need to sit up to make breathing easier.
- Seek help immediately after using the auto-injector and if at all possible make sure someone stays with you while waiting for an ambulance
- If you do start to feel better, use the second auto-injector 5-15 minutes after the first-one.

NICE Update

NICE Technology Appraisal	Guidance	PACEF recommendation
TA 455 Adalimumab, etanercept and ustekinumab for treating plaque psoriasis in children and young people.	Adalimumab, etanercept and ustekinumab have been approved for use if certain criteria have been met.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication.
NICE TA 456 Ustekinumab for moderately to severely active Crohn's disease after previous treatment.	Ustekinumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active Crohn's disease, that is, for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication.
TA 457 Carfilzomib for previously treated multiple myeloma	Carfilzomib in combination with dexamethasone is recommended as an option for treating multiple myeloma in adults, only if: •they have had only 1 previous therapy, which did not include bortezomib and •the company provides carfilzomib with the discount agreed in the patient access scheme	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication

TA 458 Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane.	**Trastuzumab emtansine is recommended, within its marketing authorisation, as an option for treating human epidermal growth factor receptor 2 (HER2)‑positive, unresectable, locally advanced or metastatic breast cancer in adults who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for locally advanced or metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy. Trastuzumab emtansine is recommended only if the company provides it in line with the commercial access agreement with NHS England**	**Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication**
NICE TA 460 Adalimumab and dexamethasone for treating non-infectious uveitis	Adalimumab and dexamethasone have been approved for use if certain criteria have been met.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication
TA 461 Roflumilast for treating chronic obstructive pulmonary disease	Roflumilast, as an add-on to bronchodilator therapy, is recommended as an option for treating severe chronic obstructive pulmonary disease in adults with chronic bronchitis, only if: •the disease is severe, defined as a forced expiratory volume in 1 second (FEV1) after a bronchodilator of less than 50% of predicted normal, and •the person has had 2 or more exacerbations in the previous 12 months despite triple inhaled therapy with a long-acting muscarinic antagonist, a long-acting beta-2 agonist and an inhaled corticosteroid. 1.2 Treatment with roflumilast should be started by a specialist in respiratory medicine.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication.
NICE TA 462 Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma	Nivolumab is recommended, within its marketing authorisation, as an option for treating relapsed or refractory classical Hodgkin lymphoma in adults after autologous stem cell transplant and treatment with brentuximab vedotin, when the company provides nivolumab with the discount agreed in the patient access scheme.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication.
NICE TA 463 Cabozantinib for previously treated advanced renal cell carcinoma	Cabozantinib is recommended, within its marketing authorisation, as an option for treating advanced renal cell carcinoma in adults after vascular endothelial growth factor (VEGF)-targeted therapy, only if cabozantinib is provided with the discount agreed in the patient access scheme.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication

TA 465 Olaratumab in combination with doxorubicin for treating advanced soft tissue sarcoma	Olaratumab, in combination with doxorubicin, is recommended for use within the Cancer Drugs Fund as an option for advanced soft tissue sarcoma in adults, only if certain criteria are met.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication
TA 466 Baricitinib for moderate to severe rheumatoid arthritis	Baricitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis if certain clinical criteria.	Designated RED and approved for use through the Lincolnshire Joint Formulary for this indication

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