Lincolnshire NHS

Prescribing and Clinical Effectiveness Bulletin

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This bulletin has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Steps will be taken to ensure the widest possible distribution across Lincolnshire PCT and within United Lincolnshire Hospitals Trust and Lincolnshire Partnership Trust. Both paper and electronic copies will be circulated initially with a view to evolving into complete electronic distribution as soon as we are confident that all key stakeholders can access E-mail. There are also plans to make all bulletins, guidelines, formularies, new product assessments, care pathways and other PACEF publications available through the LPCT website.

SUMMARY OF PACEF DECISIONS: APRIL UPDATE

Drug	Indication	Traffic Light Status
Coconut oil compound ointment (Sebco)	**Licensed as an adjunctive treatment of common scaly scalp disorders such as psoriasis, eczema, seborrhoeic dermatitis and dandruff.**	**GREEN**
Exenatide (Byetta)	**Licensed for the treatment of Type 2 diabetes mellitus in combination with metformin and sulphonylureas where adequate glycaemic control has not been achieved on maximally tolerated doses of these**	**GREEN** **Treatment should primarily be initiated by a diabetologist or a GP with a Specialist Interest in diabetes (GPSI), although the GREEN status allows for broader GP initiation. Exenatide should only be**

	agents alone.	**considered within the context of the draft NICE initiation criteria (see below)**

RED-RED: This signifies that a product is **not recommended** for prescribing in **both** primary and secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within ULHT and/or LPT **only** and has **no role in primary care**.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; in the coming months PACEF will be working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care**. Specialist initiation and shared care guidelines are not considered necessary.

NEW DRUG ASSESSMENTS

EXENATIDE (BYETTA) REVIEW

Exenatide (Byetta) is a new twice daily sub-cutaneous injection licensed for the treatment of Type 2 diabetes mellitus in combination with metformin and sulphonylureas where adequate glycaemic control has not been achieved on maximally tolerated doses of these agents alone. PACEF reviewed the trial data in September 2007 and designated the product as RED-RED. Among our concerns were the lack of comparative data against glitazones, the lack of outcome data (we do not know how exenatide effects macrovascular or microvascular complications), the incidence of gastrointestinal side effects, the lack of evidence of cost-effectiveness and the relatively high cost in comparison to alternative therapies.

ULHT Diabetologists recently appealed against this decision. They presented evidence to support a limited role for the drug, particularly in overweight or obese Type 2 diabetic patients who might otherwise require insulin; in this patient group further weight gain linked to the initiation of insulin can further complicate management. While gastrointestinal intolerance can be a significant problem in the early stages of therapy (trials suggest that 33 to 57% of patients will experience mild to moderate nausea), PACEF were reassured that in many patients these effects resolve in the first few weeks of treatment. The draft NICE Clinical Guideline on the management of type 2 diabetes (due for publication shortly) acknowledged a role for exenatide, but stated that the drug should not be recommended for routine use. The following initiation criteria were proposed:

- A BMI over 35kg/m^2
- Specific problems of a psychological, biochemical or physical nature arising from high body weight.
- Inadequate blood glucose control (HbA1c>7.5% on conventional oral therapy after trial of metformin and a sulfonylurea)
- Where other high cost medications such as glitazones or insulin would otherwise be started.

Prescribers are reminded that the special warnings and precautions section of the exenatide (Byetta) Summary of Product Characteristics (SPC) specifically warns against use in type 1 diabetes and in type 2 diabetic patients on insulin.

PACEF Recommendation:
Exenatide (Byetta) is reclassified as GREEN. Treatment should primarily be initiated by a diabetologist or a GP with a Specialist Interest in diabetes (GPSI), although the GREEN status allows for broader GP initiation. Exenatide initiation should only be considered within the context of the draft NICE initiation criteria as detailed above. These criteria will be reviewed once the final version of the NICE CG is published.

FURTHER ADVICE ON GLITAZONE USE

Following a recent review meeting with ULHT Diabetologists, a number of additional recommendations have been added to existing PACEF advice on the use of glitazones:

- Prescribers are reminded that glitazones are advocated by NICE as third line agents in the treatment of type 2 diabetes and that this is likely to be reinforced in the updated NICE clinical guideline due for publication shortly. Glitazones should only be utilized in patients unable to tolerate metformin and sulphonylurea combination therapy or in those for whom either metformin or a sulphonylurea are contra-indicated or inappropriate.
- **Where a glitazone is indicated, pioglitazone should be initiated. Local diabetologist advice is that rosiglitazone should no longer be initiated due to rising concerns over cardiovascular safety.**
- All patients currently taking rosiglitazone and pioglitazone should be reviewed to ensure that they are fully aware of the cardiovascular safety risks and that these risks are minimized. Both pioglitazone and rosiglitazone are contra-indicated in patients with cardiac failure or a history of cardiac failure.
- The European Medicines Agency (EMEA) have recommended that, in patients with ischaemic heart disease, rosiglitazone should only be used after careful evaluation of each patient's individual risk.
- Fluid retention is well documented with glitazones and may exacerbate or precipitate heart failure, particularly in patients at risk (e.g. those with a prior MI or symptomatic coronary artery disease, the elderly, those with mild to moderate renal failure, those on concurrent NSAID or insulin therapy). Patients should be monitored closely during treatment for signs and symptoms of fluid retention, including weight gain or oedema. Treatment should be stopped if any deterioration in cardiac status occurs. People who are at particular risk of heart failure should start rosiglitazone or pioglitazone at the lowest available dose; any dose increases should be done gradually.
- The incidence of heart failure is increased when either rosiglitazone or pioglitazone is combined with insulin. Clinical trials have recorded an increased risk of cardiac ischaemia for rosiglitazone combined with insulin. Therefore this combination should only be used in exceptional circumstances and under close supervision.
- The increased fracture risk with both of the glitazones necessitates the need for caution in those at risk.

RAPID ASSESSMENT: SEBCO OINTMENT

Sebco is a coconut oil compound ointment licensed as an adjunctive treatment of common scaly scalp disorders such as psoriasis, eczema, seborrhoeic dermatitis and dandruff. It is available as a 40g or 100g tube with an applicator and is lower in price than alternative identical formulations.

PACEF Recommendation:
Coconut oil compound ointment (Sebco) is designated GREEN.

NICE TECHNOLOGY APPRAISAL 138: INHALED CORTICOSTEROIDS FOR THE TREATMENT OF CHRONIC ASTHMA IN ADULTS AND IN CHILDREN AGED 12 YEARS AND OVER (MARCH 2008)

The key recommendations are as follows:

- For adults and in children aged 12 years and over with chronic asthma where an inhaled corticosteroid is considered appropriate, the **least costly product** that is suitable for an individual, within its marketing authorisation, is recommended.
- For adults and in children aged 12 years and over with chronic asthma where an ICS and long-acting beta-2 agonist (LABA) is considered appropriate, the following apply: (1) the use of a combination device within its marketing authorisation is recommended as an option; (2) the decision to use a combination device or the two agents in separate devices should be made on an individual basis, taking into consideration therapeutic need and likelihood of treatment adherence; and (3) if a combination device is chosen then the **least costly device** that is suitable for an individual is recommended.

PACEF Recommendations:
Beclometasone dipropionate
Beclometasone dipropionate (BDP) is currently the recommended first choice ICS for children and adults. This recommendation is based on the wide range of inhaler devices available, known safety at recommended doses, no lower age limit for the generic pMDI and cost. A BDP CFC free pMDI is recommended as the first line device (Clenil Modulite remains significantly lower in cost than a generic CFC containing beclometasone pMDI). Where a breath operated MDI is indicated, both Aerobec and Beclazone Easi-Breathe are appropriate alternatives; both are reasonably priced in comparison to BDP pMDIs. Dry powder devices such as Asmabec Clickhaler, Becodisks, Cyclocaps and Pulvinal are all more expensive than pMDIs and should not be routinely used first line.
Alternative Inhaled Corticosteroids
Of the alternative ICSs indicated for adults and children, budesonide and fluticasone offer no convincing evidence of superiority to BDP in terms of either safety or efficacy. Clinically, the three drugs are interchangeable; budesonide is dose equivalent with BDP, fluticasone is equivalent to half the daily dose of BDP. Where budesonide is indicated, the pMDI is recommended first line; this is more expensive than a BDP pMDI. Where a budesonide DPI is indicated, the Easyhaler represents the least costly device. Where fluticasone is indicated, the pMDI (Flixotide Evohaler) is recommended first line; this is more expensive than a BDP pMDI. Where a fluticasone DPI is indicated, the Flixotide Accuhaler represents the least costly device.

ICS/LABA Combination Inhalers

NICE state that a combination device is almost always cheaper than the components prescribed as separate inhalers. Of the two ICS/LABA combination products they reviewed (Seretide and Symbicort), they suggest that Seretide Evohaler (CFC free pMDI) emerges as the least costly device. The Fostair inhaler has been launched recently and was not included as part of this TA. PACEF guidance on the use of Fostair is as follows: Fostair currently represents a lower cost inhaled corticosteroid/LABA combination inhaler than any of the alternative branded products at equivalent doses. However, the 'extrafine particle' formulation means that there is no dose-for-dose equivalence between this product and other inhaled corticosteroid/ LABA formulations and transfer between one preparation and another could give rise to confusion. Additionally, the Fostair MDI is only stable for three months after dispensing. Despite these reservations, Fostair MDI is designated as GREEN. It should only be used for the management of asthma as it is not licensed for the management of Chronic Obstructive Pulmonary Disease (COPD). For practices interested in using the device, it should be reserved for new patients only; it is not recommended for therapeutic switching due to the lack of dose equivalence with existing combination ICS/LABA inhalers. More detailed coverage of current issues relating to BDP pMDIs and the original PACEF review of the Fostair inhaler appears in the *PACE Bulletin* Vol 2, No 3 (April 2008).

NICE TECHNOLOGY APPRAISAL 139: CONTINUOUS POSITIVE AIRWAY PRESSURE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNOEA/HYPOPNOEA SYNDROME (MARCH 2008

The key recommendations are as follows:

- **Continuous positive airway pressure (CPAP) is recommended as a treatment option for adults with moderate or severe symptomatic obstructive sleep apnoea/hypopnoea syndrome (OSAHS).**
- CPAP is only recommended as a treatment option for adults with mild OSAHS if: (1) they have symptoms that affect their quality of life and ability to go about their daily activities and (2) lifestyle advice and any other relevant treatment options have been unsuccessful or are considered inappropriate. [Lifestyle management includes helping people to lose weight, stop smoking and/or decrease alcohol consumption. Dental devices are also used to keep the upper airway open during sleep. The efficacy of dental devices has been established in clinical trials; these devices are traditionally viewed as treatment options for mild and moderate OSAHS. Surgery is not routinely used in clinical practice].
- The diagnosis and treatment of OSAHS and the monitoring of the response should be carried out by a specialist service with appropriately trained medical and support staff.

PACEF Recommendations

PACEF understand that a review of the provision of these services is currently underway across the county and the East Midlands.

NICE CLINICAL GUIDELINE 60: SURGICAL MANAGEMENT OF OTITIS MEDIA WITH EFFUSION IN CHILDREN (FEBRUARY 2008)

The key recommendations are as follows:

- Formal assessment of a child with suspected otitis media with effusion (OME) should include: (1) clinical history taking (focusing on poor listening skills, indistinct speech, delayed language development, inattention or behavioural problems, hearing fluctuation, recurrent ear infections or upper respiratory tract infections, balance problems and clumsiness, poor educational progress); (2) clinical examination focusing on otoscopy, upper respiratory health, developmental status; (3) hearing testing; and (4) tympanometry.
- Children with persistent bilateral OME documented over a period of 3 months with a hearing level in the better ear of 25-30 dBHL or worse averaged at 0.5, 1, 2 and 4 kHz should be considered for **surgical intervention**.
- Once a decision to offer surgical intervention has been taken, insertion of ventilation tubes is recommended. Adjuvant adenoidectomy is not recommended in the absence of persistent and/or frequent upper respiratory tract symptoms.
- **As an alternative to surgical intervention where surgery is contra-indicated or not acceptable, hearing aids should be offered to children with persistent bilateral OME and hearing loss.**
- Hearing aids should normally be offered to children with Down's syndrome and OME with hearing loss.
- Insertion of ventilation tubes at primary closure of the cleft palate should be performed only after careful otological and audiological assessment.
- Insertion of ventilation tubes should be offered as an alternative to hearing aids in children with cleft palate who have OME and persistent hearing loss.
- **The following treatments are not recommended for the management of OME: antibiotics, topical or systemic antihistamines, topical or systemic decongestants, topical or systemic steroids, homeopathy, cranial osteopathy, acupuncture, dietary modification, including probiotics, immunostimulants and massage.**

NICE CLINICAL GUIDELINE 61: IRRITABLE BOWEL SYNDROME IN ADULTS – DIAGNOSIS AND MANAGEMENT OF IRRITABLE BOWEL SYNDROME IN PRIMARY CARE (FEBRUARY 2008)

The key recommendations are as follows:

Diagnosis

- Consider assessment for irritable bowel syndrome (IBS) if the person reports any of the following symptoms for at least 6 months: **A**bdominal Pain, **B**loating, **C**hange in bowel habit.
- All people presenting with possible IBS symptoms should be asked if they have any of the following **'red flag' indicators** and **referred to secondary care** if they are present. The 'red flag' indicators are: (1) unintentional and unexplained weight loss, (2) rectal bleeding, (3) a family history of bowel or ovarian cancer and (4) a change in bowel habit to looser and/or more frequent stools persisting for more than 6 weeks in a person aged over 60.
- All people presenting with possible IBS symptoms should be assessed and clinically examined for the following further **'red flag' indicators**: anaemia, abdominal masses, rectal masses, inflammatory markers for inflammatory bowel disease.

- A pelvic examination should be considered in those where there is significant concern that symptoms are suggestive of ovarian cancer.
- A **diagnosis of IBS** should be considered **only** if the person has **abdominal pain or discomfort that is either relieved by defaecation or associated with altered bowel frequency or stool form.** This should be accompanied by at least two of the following four symptoms: (1) altered stool passage (straining, urgency, incomplete evacuation); (2) abdominal bloating (more common in women than men), distension, tension or hardness; (3) symptoms made worse by eating; and (4) passage of mucus.
- Other features common in IBS include lethargy, nausea, backache and bladder symptoms.
- In those who meet the IBS criteria, the following tests should be undertaken to exclude other diagnoses: (1) full blood count; (2) erythrocyte sedimentation rate or plasma viscosity; (3) c-reactive protein; (4) antibody testing for coeliac disease (endomysial antibodies or tissue transglutaminase).

Self-help including general lifestyle, physical activity and diet

- General dietary advice includes: (1) having regular meals and taking time to eat; (2) not missing meals or leaving long gaps between eating; (3) keeping well hydrated (eight cups of fluid a day, especially water); (4) restricting tea or coffee to 3 cups a day; (5) reducing the consumption of alcohol and fizzy drinks; (6) limiting the intake of high fibre food; (7) limiting fresh fruit and vegetables to 3 x 80g portions a day; (8) for diarrhoea, avoid sorbitol (an artificial sweetener) and (9) for wind and bloating increase the intake of oats (e.g. porridge) and linseeds.
- People with IBS should be discouraged from eating insoluble fibre (e.g. bran). If an increase in dietary fibre is advised, it should be soluble fibre (e.g. ispaghula powder or foods high in soluble fibre like oats).

Symptom targeted medication

- **Antispasmodics** should be taken **as required** alongside dietary and lifestyle advice.
- Consider **laxatives for constipation**, but **discourage the use of lactulose.**
- **Loperamide** should be offered as the **first choice antimotility agent for diarrhoea.**
- Doses of laxatives or antimotility agents should be adjusted according to clinical response. The dose should be titrated according to stool consistency with the aim of achieving a soft, well-formed stool.
- **Tricyclic antidepressants** (TCAs) (prescribed for their **analgesic effect**) should be considered **second-line if laxatives, loperamide or antispasmodics have not helped**. Treatment should be initiated at a low dose (5-10mg equivalent of amitriptyline) which should be taken once at night and reviewed regularly. The dose may be increased, but not usually above 30mg. TCAs do not currently hold a UK marketing authorisation for this indication. Consider selective serotonin reuptake inhibitors (SSRIs) only if TCAs are ineffective. Both TCAs and SSRIs have the potential for significant side effects; patients should be followed up after 4 weeks and then every 6 to 12 months.
- If the person wants to try probiotics, advise them to take the dose recommended by the manufacturer for at least 4 weeks while monitoring the effect.
- Discourage the use of aloe vera for IBS.

- For people who do not respond to pharmacotherapy after 12 months and who develop a continuing symptom profile consider referring for cognitive behavioural therapy (CBT), hypnotherapy and psychological therapy.

ADDENDUM: CALCIUM AND VITAMIN D SUPPLEMENTATION

In a recent issue of the *PACE Bulletin* (Volume 2, Number 6), we may have unintentionally given the impression that only calcium and vitamin D formulations that can deliver a daily dose of 1200mg of calcium and 800iu of vitamin D (i.e. Adcal-D3 tablets and Calfovit D3 sachets) should be prescribed. In fact, formulations that can provide 1000mg of calcium and 800iu of vitamin D are also endorsed. The cost comparison table from the original bulletin is reprinted below for reference.

Product	Licensed Indication	Price (28 days)
Adcal –D3 (calcium 600mg/ vit D 400IU) Chewable tablets	**Adjunct in osteoporosis. 1 tablet twice daily**	**£4.06**
Adcal-D3 Dissolve (calcium 600mg/Vit D 400iu) Effervescent tablets	Adjunct in osteoporosis. 1 tablet twice daily	£4.99
Cacit D3 Effervescent granules (calcium 500mg/ Vit D 440IU)	Adjunct in osteoporosis. 1 or 2 sachets daily	£8.05
Calceos Chewable tabs (Calcium 500mg/ Vit D 400IU	**Adjunct in osteoporosis. 1 tablet twice daily**	**£3.59**
Calcichew D3 Forte Chewable tablets (calcium 500mg, Vit D 400IU)	**Adjunct in osteoporosis. 1 tablet twice daily**	**£4.20**
Calfovit D3 Sachets (calcium 1200mg/Vit D3 800IU)	**Adjunct in osteoporosis. 1 sachet daily**	**£4.04**

(Appropriate first line options are highlighted in bold)

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