Lincolnshire NHS

Prescribing and Clinical Effectiveness Bulletin

Volume 1; Number 6 **November 2007**

CONTENTS

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: NOVEMBER UPDATE

Drug	Indication	Traffic Light Status
Cinacalcet (Mimpara)	**Secondary hyperparathyroidism in patients with end stage renal disease on dialysis**	**AMBER (New shared care guideline now available)**
Donepezil (Aricept/ Aricept Evess)	**Mild to moderate dementia in Alzheimer's disease**	**RED-RED for mild AD. AMBER for AD of moderate severity (NB Specialist initiation and six monthly review required)**
Fulvestrant (Faslodex)	**Treatment of oestrogen-receptor-positive metastatic or locally advanced breast cancer**	**AMBER (New shared care guideline now available)**
Galantamine (Reminyl/Reminyl XL)	**Mild to moderate dementia in Alzheimer's disease**	**RED-RED for mild AD. AMBER for AD of moderate**

		severity (NB Specialist initiation and six monthly review required)
Ibandronic acid (Bondronat)	**Reduction of bone damage in bone metastases in breast cancer**	**AMBER (New shared care guideline now available)**
Lanthanum (Fosrenol)	**Hyperphosphataemia in patients on haemodialysis or continuous ambulatory peritoneal dialysis**	**AMBER (New shared care guideline now available)**
Memantine (Ebixa)	**Moderate to severe dementia in Alzheimer's disease**	**RED-RED**
Paliperidone (Invega)	**A new antipsychotic agent licensed for the treatment of schizophrenia**	**RED-RED**
Penfluridol	**An unlicensed once weekly oral antipsychotic agent used for the treatment of schizophrenia**	**RED (only to be initiated and prescribed by LPT clinicians)**
Rivastigmine (Exelon)	**Mild to moderate dementia in Alzheimer's disease**	**RED-RED for mild AD. AMBER for AD of moderate severity (NB Specialist initiation and six monthly review required)**
Sevelamer (Renagel)	**Hyperphosphataemia in patients on haemodialysis**	**AMBER (New shared care guideline now available)**
Symbicort SMART (100/6 and 200/6 Turbohalers)	**Combination inhaled steroid and LABA inhaler licensed as *both* maintenance and reliever therapy in adult asthmatics (over 18 years old) *not controlled* at BTS/SIGN asthma guidelines step 3.**	**GREEN (Subject to restrictions detailed on page 4)**
Tiotropium bromide (Spiriva Respimat)	**An inhaled antimuscarinic bronchodilator licensed for maintenance treatment of chronic obstructive airways disease**	**GREEN (N.B. Take care to prescribe by brand to avoid confusion between the Respimat and the HandiHaler)**

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

PALIPERIDONE (INVEGA)

Paliperidone (Invega) is a new antipsychotic agent from Jannssen-Cilag licensed for the treatment of schizophrenia. Chemically, it is also known as 9-hydroxyrisperidone and is an active metabolite of risperidone itself. Only two clinical trials involving paliperidone have been published to date; both favourably compare the active drug to placebo confirming superiority in the treatment of acute exacerbations of schizophrenia and the prevention of symptom relapse. There are no published studies comparing paliperidone with any alternative antipsychotic agent at this stage. There are also no studies confirming long-term efficacy, long-term safety or comparative cost-effectiveness to other alternatives. Without more published trial data the place of paliperidone in therapy is difficult to judge. With the patent of risperidone due to expire in December 2007 and with the imminent likelihood of lower-cost generic risperidone following soon afterwards, it is difficult to justify the use of paliperidone at this time.

PACEF Recommendation:
PACEF remain unconvinced of the benefits of paliperidone beyond its parent drug risperidone. Published trial data of any kind is sparse and specifically lacking in the areas of comparative safety and efficacy to other antipsychotic agents, long-term efficacy, long-term safety, patient orientated outcomes and cost-effectiveness. As a result of this, paliperidone has been designated RED-RED. Prescribers should also be mindful of the imminent patent expiry of risperidone and ensure that all remaining branded risperidone prescriptions are genericised in preparation.

PENFLURIDOL

Penfluridol is an antipsychotic drug with novel pharmacokinetics resulting in a plasma half-life of around 70 hours; this allows an unusual once weekly oral dosage regime. The drug was developed by Janssen in the 1970s and is in use in a variety of countries worldwide. However, it has never been licensed or marketed in the UK and is only available as an import.

PACEF Recommendation:
Penfluridol has been approved for use within Lincolnshire Partnership Trust for a small number of service users who for various reasons have difficulties coping with depot antipsychotic injections. The drug is designated as RED and can be prescribed only from within LPT.

NEW FORMULATION ASSESSMENT

TIOTROPIUM BROMIDE (SPIRIVA RESPIMAT)

Tiotropium bromide (Spiriva), a long-acting antimuscarinic bronchodilator traditionally delivered through the HandiHaler device, is well established as an effective treatment for the management of chronic obstructive pulmonary disease (COPD). Spiriva Respimat provides an alternative CFC free delivery system for tiotopium. The device relies on a spring mechanism to deliver an aqueous solution of tiotropium to the lungs without the use of a propellant. Dose comparison studies have demonstrated that two 2.5mcg puffs once daily from a Spiriva Respimat are equivalent to a single Spiriva 18mcg capsule as used in the Handihaler. The lower inhaled dose with the

Respimat is possible due to improved deposition rates in the lungs; this also helps to reduce deposition in the mouth and throat compared to the HandiHaler. Both devices are comparably priced: a 60 dose Spiriva Respimat and a Spiriva Handihaler (plus 30 capsules) both cost £37.62. A refill of 30 capsules for the Handihaler device costs £34.40, less than a replacement Respimat.

PACEF Recommendation:
The Spiriva Respimat device is approved for use: designation GREEN. In order to avoid confusion, it is recommended that both the Spiriva Handihaler and the Spiriva Respimat are specified by brand on each prescription.

NEW INDICATION ASSESSMENT

SYMBICORT SMART (SYMBICORT FOR MAINTENANCE AND RELIEF THERAPY)

Symbicort Turbohaler is a well established combination product containing budesonide, an inhaled corticosteroid, and formoterol, a long acting $beta_2$ agonist (LABA), formulated in a breath activated device. Symbicort 100/6 and 200/6 strengths are licensed for the regular treatment of asthma where use of a combination inhaled corticosteroid and long acting $beta_2$-agonist is appropriate. Recent studies have investigated the use of Symbicort as a single treatment for both maintenance and reliever therapy; this overall approach to treatment has been marketed by AstraZeneca as Symbicort SMART and has resulted in a license extension for the product. The main clinical advantage demonstrated by the trials has been fewer exacerbations compared with conventional combination treatment.
The licensed dosage for maintenance and reliever therapy for both Symbicort 100/6 and Symbicort 200/6 is:

- 2 puffs daily in one to two divided doses (for maintenance); for the Symbicort 200/6 only the maintenance dose can be increased if necessary to 2 puffs twice daily.
- plus, for the relief of symptoms, 1 puff as needed up to a maximum of six puffs at a time and eight puffs daily; up to 12 puffs can be used for a limited time but medical assessment should be considered.

The advantage of the SMART dosage regime is that it combines maintenance and reliever therapy through a single inhaler allowing patients to increase the dose of Symbicort when their asthma worsens and avoiding the need for multiple inhalers. A typical dose would be: one inhalation twice daily plus as needed. Studies suggest that it is unusual for patients to require more than an average of 3 puffs a day. The new licensed indication is for adult asthmatics (over 18 years old) not controlled at step 3 of the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) asthma guidelines.

PACEF Recommendation:
Following a review of the trial evidence, PACEF are satisfied that Symbicort SMART is an effective approach to asthma management for patients at Step 3 of the BTS/SIGN asthma guidelines. Prescribing of Symbicort SMART should be confined to licensed indications; this means adult asthmatics (over 18 years old) *not controlled* at BTS/SIGN asthma guidelines step 3. 'Not controlled' can be defined as patients experiencing frequent day or night symptoms, requiring reliever medication or those with past exacerbations requiring medical intervention. Patients with good asthma control, even if already prescribed

Symbicort, should NOT be changed to the SMART regimen. Patients requiring high doses of inhaled steroid (defined as >800mcg daily of conventional beclometasone) may not be appropriate for the SMART approach either.
At present, only Symbicort 100/6 and 200/6 Turbohalers are licensed for this indication. Prescribers are reminded that the SMART licence does not allow for the use of Symbicort solely as needed for the relief of symptoms; use as a reliever must only be in addition to regular maintenance therapy. All asthmatics prescribed Symbicort SMART should have a suitable asthma action plan; appropriate training on SMART and the monitoring of inhaler use should be provided. A Patient Support Programme provided by NHS Direct in association with AstraZeneca is available to all patients who have been prescribed Symbicort SMART. The service is free of charge and will help to ensure that patients understand and correctly utilize the SMART treatment regime. Further details are available on (01924) 877914 or E-mail stephen.littler@wyorkshire.nhsdirect.nhs.uk.

NICE UPDATE

NICE TECHNOLOGY APPRAISAL 111: DONEPEZIL, GALANTAMINE, RIVASTIGMINE AND MEMANTINE FOR THE TREATMENT OF ALZHEIMER'S DISEASE

The key recommendations are as follows:

- Donepezil, galantamine and rivastigmine are recommended as options in the management of Alzheimer's disease (AD) of **moderate severity only** (Mini Mental State Examination (MMSE) score between 10 and 20 points).
- Only **specialists** in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists and physicians specialising in the care of the elderly) should **initiate treatment**.
- Patients who continue on the drug should be **reviewed every 6 months** by MMSE score and global, functional and behavioural assessment.
- The drug should only be continued while the patient's MMSE score remains at or above 10 points and their global, functional and behavioural condition remains at a level where the drug is considered to be having a worthwhile effect.
- Review involving MMSE should be undertaken by an appropriate specialist team, unless there are locally agreed protocols for shared care.
- Where acetylcholinesterase inhibitor therapy is indicated, therapy should be initiated with the **drug of lowest acquisition cost**. Alternatives can be used with regard to adverse event profile, concordance issues, co-morbidities, drug interactions etc.
- **Memantine is not recommended** as a treatment for moderate to severe AD, except as part of well designed clinical studies.
- Patients with mild AD currently receiving donepezil, galantamine or rivastigmine may be continued on therapy until they, their carers or specialist consider it appropriate to stop.
- Patients with moderately severe or severe AD currently receiving memantine may be continued on therapy until they, their carers or specialist consider it appropriate to stop.

PACEF Recommendations:
Donepezil, galantamine and rivastigmine will retain AMBER status on the Traffic Lights List, but prescribing will be restricted to AD of moderate severity only. All other indications are designated RED-RED. Local shared care guidelines will be updated to reflect the need for specialist initiation and six monthly review of all patients. PACEF have reviewed the comparative costs of all three of these drugs and concluded that there is no clear drug of lowest acquisition cost to recommend first line. As a result, first line treatment selection should be based on the needs of the patient. Memantine remains RED-RED for all indications.

NICE CLINICAL GUIDELINES 51 AND 52: DRUG MISUSE: PSYCHOSOCIAL INTERVENTIONS AND OPIOID DETOXIFICATION

The key recommendations are as follows:

- Opportunistic brief interventions focused on motivation should be offered to people in limited contact with drug services (e.g. those using needle-syringe exchange).
- Information about self-help groups should be provided.
- Drug services should introduce contingency management programmes. These should aim at reducing illicit drug use for those on methadone maintenance or those who primarily misuse stimulants. Incentives (e.g. vouchers with a cash value or privileges such as take-home methadone doses) should be used to incentivise continuous periods of abstinence. Incentives may also be used to improve physical healthcare in those at risk of physical health problems (e.g. hepatitis B and C, HIV and tuberculosis).
- Detoxification should be a readily available treatment option. Detailed information about detoxification and associated risks should be available to service users (e.g. physical and psychological aspects of opioid withdrawal, non-pharmacological approaches, loss of opioid tolerance after detoxification with increased risk of overdose and death, importance of continued support).
- Community based detoxification programmes are preferred, although exceptions include those who have not benefited from previous community-based detoxification, those with significant co-morbid physical or mental health problems, those requiring complex poly-drug detoxification and those with significant social problems.
- Methadone and buprenorphine should be offered as first-line treatment in opioid detoxification. Choice should take into account maintenance medication and the preference of the service user.
- Lofexidine may be considered for people who have made an informed and clinically appropriate decision not to use methadone or buprenorphine for detoxification and who wish to detoxify over a short time period. Lofexidine can also be used in mild or uncertain dependence (including young people).
- Clonidine and dihydrocodeine should not be routinely used.

NICE CLINICAL GUIDELINE 53: CHRONIC FATIGUE SYNDROME/ MYALGIC ENCEPHALOMYELITIS (OR ENCEPHALOPATHY)

The key recommendations are as follows:

- The reality and impact of the condition should be acknowledged by the healthcare professional. Information should be provided on interventions and management strategies, possible causes, nature and course of the disease,

returning to work or education, local and national self-help groups and support groups. Examples of symptom management include minimising nausea, exclusion diets and dietary advice, sleep management advice, use of rest periods and relaxation techniques.

- Advice on symptom management should not be delayed until diagnosis is established. Symptom management should be tailored to the individual and aimed at minimising impact on daily life and activities.
- A diagnosis should be made after other possible causes have been excluded and symptoms have persisted for 4 months in an adult and 3 months in a child or young person; diagnosis in a child should be confirmed by a paediatrician.
- An individualised, person centred programme should be offered to people with CFS/ME. The programme should aspire to sustain or gradually extend the person's physical, emotional and cognitive capacity and manage the physical and emotional impact of their symptoms.
- Cognitive behavioural therapy and/or graded exercise therapy should be offered to people with mild to moderate CFS/ME.
- The following strategies should not be offered to people with CFS/ME: unsupervised or unstructured vigorous exercise (may worsen symptoms), prolonged or complete rest or extended periods of daytime rest, imposed rigid schedule of activity and rest.
- There is no known pharmacological treatment or cure for CFS/ME.
- There is no evidence that people with CFS/ME are more intolerant of drug treatment than others, although, if patients are concerned, lower starting doses than in usual clinical practice may be considered.
- Specific drug treatment for children and young people with CFS/ME should be started by a paediatrician, but can be continued in primary care.
- Nausea should be managed conventionally by eating little and often, snacking on dry starch foods and sipping fluids. Anti-emetic drugs should only be considered where nausea is severe.
- The following drugs should not be used for CFS/ME: monoamine oxidase inhibitors, glucocorticoids (e.g. hydrocortisone), mineralocorticoids (e.g. fludrocortisone), dexamphetamine, methylphenidate, thyroxine, antiviral agents.
- Complementary therapies are not recommended due to insufficient evidence (e.g. vitamin B12, vitamin C, co-enzyme Q10, magnesium, nicotinamide adenine dinucleotide (NAD), multivitamins and minerals).

PACEF Recommendation:
When treating patients with CFS/ME, prescribers should ensure that they do not prescribe either the conventional medicines or the complementary therapies that are not recommended by NICE.

SHARED CARE GUIDELINES: FULVESTRANT, IBANDRONIC ACID, CINACALCET, LANTHANUM AND SEVELAMER

The following shared care guidelines have been approved by PACEF for use within the Lincolnshire Healthcare Community:

- Fulvestrant in the management of postmenopausal women with oestrogen-receptor positive locally advanced or metastatic breast cancer.
- Ibandronic acid for the prevention of skeletal events in patients with bone metastases from breast cancer.

- Cinacalcet in the management of secondary hyperparathyroidism in adult patients with end-stage renal disease on dialysis.
- Sevelamer in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis and for the unlicensed use of controlling hyperphosphataemia associated with chronic kidney disease.
- Lanthanum in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis who did not respond to or were unable to tolerate sevelamer.

Copies of these shared care guidelines are available to download now from nww.ulh.nhs.uk. All approaches from secondary care to participate in shared care relating to these drugs should be accompanied with a copy of the relevant shared care guideline.

PATIENT SELF-FUNDING OF DRUGS AND TREATMENTS

Prescribers are reminded of the *Code of Conduct for Private Practice: Guidance for NHS Medical Staff* issued in 2003. In this document the following principles were emphasized:

- All patients are entitled to NHS treatment free at the point of delivery.
- If a patient wishes to become a private patient, he/she cannot be a private patient and an NHS patient for the treatment of one condition during a single visit to an NHS organisation.
- Following receipt of private treatment, a patient can change his/her status to that of an NHS patient since he/she remains entitled to NHS care.
- On change of status, the patient should join the waiting list as though they were an NHS patient. It is up to the NHS clinician to assess the patient and decide on his/her priority status and the point at which he/she joins the waiting list.

PACEF Recommendation:
On the basis of this guidance, patients cannot purchase certain components of their care (i.e. medicines) or make co-payments or top-up payments for part of that care while at the same time receiving NHS care for the same condition. Private and NHS healthcare provision must remain separated.

Stephen Gibson
Head of Prescribing and Medicines Management
Lincolnshire PCT
steve.gibson@lpct.nhs.uk

8th November 2007