TAYSIDE PRESCRIBER

Tayside DTC Supplement No 58

May 2006

Produced by NHS Tayside Drug and Therapeutics Committee Medicines Advisory Group (MAG)

In this issue:

SMC Advice Issued May 2006

Advice issued in May 2006 includes a number of products for which the manufacturers have chosen not to submit applications to the Scottish Medicines Consortium (SMC). In the absence of a submission, the SMC is unable to recommend use in NHS Scotland.

Cinacalcet (Mimpara®) – hypercalcaemia in patients with parathyroid carcinoma

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation.

Cinacalcet (Mimpara®) is not recommended for the reduction of hypercalcaemia in patients with parathyroid carcinoma.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Cinacalcet is also licensed for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy – refer to Tayside Prescriber; DTC Supplement No.57, April 2006 for recent SMC advice in this indication.

Choriogonadotropin alfa (Ovitrelle®) – superovulation prior to IVF

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Choriogonadotropin (Ovitrelle®) is not recommended for women undergoing superovulation prior to assisted reproductive techniques such as in vitro fertilisation (IVF).
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Pending NHS Tayside Drug and Therapeutics Committee decision

Choriogonadotropin alfa (Ovitrelle®) – anovulation/oligo-ovulation

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Choriogonadotropin (Ovitrelle®) is not recommended for the treatment of anovulatory/oligo-ovulatory women.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Pending NHS Tayside Drug and Therapeutics Committee decision

Darbepoetin alfa (Aranesp®) – cancer treatment induced anaemia

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Darbepoetin alfa (Aranesp®) is not recommended for the treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration

- NICE guidance "Erythropoietin for anaemia induced by cancer treatment" is anticipated in May 2006.

Darbepoetin alfa (Aranesp®) SureClick – cancer treatment induced anaemia

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Darbepoetin alfa (Aranesp®) SureClick is not recommended for the treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- See above.

Epinastine eye drops (Relestal®) – seasonal allergic conjunctivitis

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation

Epinastine (Relestal®) is not recommended for the treatment of the symptoms of seasonal allergic conjunctivitis.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Olopatadine is an alternative antihistamine eye drop recently accepted by the SMC – refer to Tayside Prescriber; DTC Supplement No.55, February 2006.
- Epinastine eye drops are not stocked by the hospital pharmacy.

Escitalopram (Cipralex®) – generalised anxiety disorder (GAD).

SMC recommendation

Advice: following a full submission

Escitalopram (Cipralex®) is accepted for use for the treatment of generalised anxiety disorder in situations where pharmacological therapy is appropriate. Escitalopram shows similar efficacy to the other selective serotonin re-uptake inhibitor (SSRI) licensed for the treatment of generalised anxiety disorder.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Escitalopram is the second SSRI to be licensed for the treatment of generalised anxiety disorder (GAD).
- Short-term comparative studies of up to 24 weeks duration indicate that escitalopram 10-20mg daily provides similar improvement in anxiety symptoms as paroxetine 20-50mg daily in patients with GAD. Escitalopram appeared to be at least as well tolerated as paroxetine.
- At £15-£25 per 28 days treatment, escitalopram is more expensive than generic paroxetine at current Scottish drug tariff prices (£5 per 28 days paroxetine 20mg daily).
- NICE guideline No. 22 "Anxiety: management of anxiety (panic disorder, with or without agoraphobia, and GAD) in adults in primary, secondary and community care" (December 2004) recommends that any of the following interventions should be offered for the longer-term care of the individuals with GAD; psychological therapy (cognitive behavioural therapy), pharmacological therapy (antidepressant medication), and self-help (bibliotherapy). A SSRI is considered first-choice pharmacological therapy. Venlafaxine XL is reserved for patients in whom significant symptoms remain following two types of interventions (any combination of psychological intervention, medication, or bibliotherapy). Note that treatment with venlafaxine XL should be under specialist advice.
- CSM advice (December 2004) on the use of SSRIs in relation to withdrawal reactions, dose changes and suicidal behaviour is highlighted in the Tayside Area Prescribing Guide (TAPG).
- **Locally, escitalopram may be considered as an alternative to paroxetine for the longer-term treatment of GAD where pharmacological therapy is appropriate. Treatment should be in accordance with NICE Guideline No. 22 on the management of anxiety in adults in primary, secondary and community care.**

Fentanyl 12mcg/hr patch (Durogesic® D Trans) – non-malignant pain

SMC recommendation

Advice: following an abbreviated submission

Transdermal Fentanyl (Durogesic® D Trans) patch 12 mcg/hour is accepted for restricted use for patients with chronic intractable pain due to non-malignant conditions.

It should be considered as a second-line alternative, reserved for patients whose pain has initially been controlled by oral means, the pain being stable. Its use should focus on patients who have difficulty swallowing or have problems with opiate-induced constipation. The new strength allows greater flexibility in dose titration without a substantial impact on price compared with the range of patches previously available. However, it remains significantly more expensive than oral therapy.

SMC has not assessed transdermal fentanyl in its original indication for intractable pain due to cancer.

Tayside recommendation

Non-formulary

Points for consideration:

- The dose range of Durogesic® D Trans patches has been extended to include the 12mcg/hr patch.
- Refer to Tayside Prescriber; DTC Supplement No.52, July 2005 for SMC and local advice on Durogesic® D Trans patches.

Fondaparinux (Arixtra®) – VTE prevention in high risk medical patients

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation

Fondaparinux (Arixtra®) is not recommended for the prevention of venous thromboembolic events (VTE) in medical patients who are judged to be at high risk of VTE and who are immobilised due to acute illness, such as cardiac insufficiency and/or acute respiratory disorders, and/or acute infections or inflammatory disease.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Dalteparin is the low molecular weight heparin of choice locally.
- Fondaparinux is not stocked by the hospital pharmacy.

Fondaparinux (Arixtra®) – acute DVT/PE treatment

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation

Fondaparinux (Arixtra®) is not recommended for the treatment of acute deep vein thrombosis (DVT) and the treatment of acute pulmonary embolism (PE).

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- See above.

Letrozole (Femara®) – initial adjuvant treatment in early breast cancer

SMC recommendation
Advice: following a full submission
Letrozole (Femara®) is accepted for restricted use within NHS Scotland for the adjuvant treatment of postmenopausal women with hormone receptor positive invasive early breast cancer.
Letrozole has shown benefit over standard anti-oestrogen therapy in terms of disease-free survival, although a pre-planned sub-group analysis showed a statistically significant beneficial effect in node-positive patients but not node-negative patients. It offers an alternative to existing treatment and has a different range of adverse effects.
Another aromatase inhibitor is available for the same indication at a lower cost.
Treatment with letrozole should be initiated by a breast cancer specialist.
Click here for SMC link

Tayside recommendation

Pending update of local breast cancer protocol

Points for consideration:

- Letrozole is also licensed for the treatment of advanced breast cancer and more recently for extended adjuvant therapy in early breast cancer following three years of tamoxifen (refer to Tayside Prescriber; DTC Supplement No.49, March 2005).
- The evidence to support the use of letrozole as an initial adjuvant therapy comes from the Breast International Group (BIG) study comparing five years of letrozole to tamoxifen. Five-year estimates, based on a median follow-up of 26 months, show that 84% of women who receive letrozole remain disease free compared to 81% who receive tamoxifen. This represents an absolute risk reduction of 2.6% in favour of letrozole. Overall survival was higher in the letrozole arm, but this failed to reach statistical significance.
- In the BIG study, significantly more letrozole patients experienced bone fractures (6% vs 4%), cardiac failure (0.8% vs 0.4%), hypercholesterolaemia (44% vs 19%), and joint pain (20% vs 12%) compared with tamoxifen recipients. The SPC recommends that during adjuvant treatment with letrozole, women with osteoporosis or at risk of osteoporosis should have their bone mineral density assessed at the start of treatment and at regular intervals thereafter. Treatment for osteoporosis should be initiated as appropriate and carefully monitored.
- No comparative efficacy or safety data versus other aromatase inhibitors used in the adjuvant setting eg anastrozole, are available.
- Longer-term follow-up is required to clarify the benefit of letrozole in patients with node-negative disease and the effects of letrozole on serum lipids and bone resorption.
- Letrozole is slightly more expensive than anastrozole, the other aromatase inhibitor licensed for initial adjuvant use, and considerably more expensive that tamoxifen. (Annual treatment with letrozole 2.5mg daily costs £1,084 versus £894 for anastrozole 1mg and £34 for tamoxifen 20mg).
- **The place of letrozole in the initial adjuvant treatment of postmenopausal HR +ve early invasive breast cancer, and in relation to tamoxifen and other aromatase inhibitors, will be addressed by the Oncology & Haematology Medicines Management Group (OHMMG) in the next review of the local breast cancer protocol.**

Olmesartan/hydrochlorothiazide (Olmetec Plus®) – hypertension

SMC recommendation
Advice: following an abbreviated submission
Olmesartan/hydrochlorothiazide (Olmetec Plus®) is accepted for restricted use for the treatment of hypertension as an alternative in patients unable to tolerate an ACE inhibitor, whose blood pressure is not adequately controlled by olmesartan 20mg monotherapy and for whom the addition of a thiazide diuretic is an appropriate next step.
There is no additional cost compared to administration of olmesartan alone. The combination is competitively priced compared with other combinations of angiotensin II antagonists and thiazide diuretics. Angiotensin II receptor antagonists are an alternative to angiotensin converting enzyme (ACE) inhibitors where the latter are not tolerated. This fixed dose combination is one of a number of options for the treatment of hypertension, many of which are less expensive.

Continued over

Olmesartan/hydrochlorothiazide continued

Tayside recommendation

Non-formulary

Points for consideration:

- Olmetec Plus® is a further angiotensin receptor blocker (ARB)/thiazide combination product.
- Combination products may theoretically improve patient compliance. However, they may limit the flexibility of patients' medication regimens with respect to dose and drug adjustments.
- Candesartan is the first-line ARB recommended for hypertension in the TAPG. Advice on the management of hypertension is available in the Cardiovascular Guidance Notes within the TAPG.

Oxycodone (OxyNorm®) injection – post-operative pain

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Oxycodone (OxyNorm®) injection is not recommended for the treatment of post-operative pain.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Oxycodone injection is also licensed for the treatment of moderate to severe cancer pain – refer to Tayside Prescriber; DTC Supplement No.45, October 2004 for SMC and local advice in this indication.
- Local guidance on post-operative analgesia is available in Section 20 of the TAPG "Drug therapy in relation to anaesthesia".

Palifermin (Kepivance®) – oral mucositis in bone marrow transplantation

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Palifermin (Kepivance®) is not recommended for the treatment of oral mucositis in bone marrow transplantation.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Palifermin is not stocked by the hospital pharmacy.

Pemetrexed (Alimta®) – non-small cell lung cancer (NSCLC)

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation
Pemetrexed (Alimta®) is not recommended for use as monotherapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after prior chemotherapy.
The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- Pemetrexed is also licensed for the treatment of malignant pleural mesothelioma – refer to Tayside Prescriber; DTC Supplement No.53, September 2005 for SMC and local advice in this indication.

Continued over

Pemetrexed continued

- SIGN guidance on the management of patients with lung cancer recommends the use of docetaxel monotherapy for second-line treatment of advanced NSCLC.
- NICE guidance for the use of pemetrexed in NSCLC is anticipated in December 2006.

Pramipexole (Mirapexin®) – moderate to severe restless legs syndrome (RLS)

SMC recommendation

Advice: following a full submission

Pramipexole (Mirapexin®) is accepted for use for the symptomatic treatment of moderate to severe idiopathic Restless Legs Syndrome (RLS). It should only be used in patients with a baseline score of 15 points or more on the International Restless Legs Scale (IRLS).

In three double blind placebo-controlled studies pramipexole was associated with a 4 to 9-point improvement on the patient-administered 40-point IRL scale in comparison with placebo based on the core clinical features of the syndrome.

Click here for SMC link

Tayside recommendation

Specialist treatment pathway (GPs may prescribe under the direction of secondary care)

Points for consideration:

- Restless legs syndrome (RLS) is characterised by a range of uncomfortable and sometimes distressing motor and sensory symptoms during quiet wakefulness and/or sleep eg feelings of burning, tickling, crawling, pain, cramping, numbness, weakness in the lower limbs. It can occur secondary to other factors eg iron deficiency anaemia, pregnancy, renal disease, peripheral neuropathy, diabetes mellitus, and hypothyroidism. Differential diagnoses include nocturnal leg cramps, peripheral neuropathy, peripheral vascular disease, and Parkinson's disease.
- Pramipexole is the first dopamine agonist to be licensed for the treatment of RLS. A similar licence for ropinirole is anticipated shortly.
- Symptom augmentation is the most serious adverse effect of dopaminergic therapy in RLS. This is a relative worsening of symptoms, or an occurrence of symptoms earlier in the day than experienced prior to starting treatment. Pramipexole studies were generally of insufficient duration to adequately capture augmentation phenomena.
- Follow-up studies extend to one-year, longer-term data on the clinical benefits and safety profile of dopamine agonists in the treatment of RLS are unavailable. Likewise, comparative data versus other dopamine agonists eg ropinirole, are also unavailable.
- 28 days treatment with pramipexole 0.25mg-0.75mg daily costs £17-£52.
- The majority of patients presenting with symptoms of RLS may be treated successfully with non-pharmacological self-help methods. These include advice on improving sleep (avoiding caffeine at bedtime), keeping cool (wearing loose clothes), avoiding standing or sitting for long periods, avoiding drugs that exacerbate symptoms (CNS stimulants, diuretics, tricyclic antidepressants, calcium antagonists, phenytoin), and the use of relaxation techniques. Dopamine agonists are considered to be the first-choice pharmacological therapy.
- **Locally, pramipexole is recommended, under the direction of a secondary care physician, for the treatment of moderate to severe RLS in patients with an IRLS score ≥15 whose symptoms persist despite an adequate trial of non-pharmacological methods (see above).**

Triptorelin (Gonapeptyl® depot) – prostate cancer

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation

Gonapeptyl depot is not recommended for the treatment of advanced, hormone-dependent prostate carcinoma. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Continued over

Triptorelin – prostate cancer - continued

Points for consideration:

- Gonapeptyl® depot is also licensed for use in central precocious puberty (CPP) - refer to Tayside Prescriber; DTC Supplement No.50, May 2005 for SMC and local advice in this indication.
- **The alternative triptorelin preparation, Decapeptyl® SR, is recommended for the treatment of advanced prostate cancer within the TAPG.**
- Gonapeptyl® depot is not stocked by the hospital pharmacy.

Triptorelin (Gonapeptyl® depot) - endometriosis

SMC recommendation

Advice: in the absence of a submission from the holder of the marketing authorisation

Gonapeptyl depot is not recommended for symptomatic endometriosis confirmed by laparoscopy when suppression of the ovarian hormonogenesis is indicated to the extent that surgical therapy is not primarily indicated.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.

Tayside recommendation

Not recommended

Points for consideration:

- The alternative triptorelin preparation, Decapeptyl® SR, has recently been accepted by the SMC for the treatment of endometriosis – refer to Tayside Prescriber; DTC Supplement No.54, November 2005.

Daptomycin Update

The April 2006 SMC advice for the use of daptomycin in complicated skin and soft tissue infections was deferred to the Hospital Anti-infectives Committee. See below for final decision:

Tayside recommendation

Recommended within specialist treatment pathway – **HOSPITAL ONLY**

- Daptomycin may be considered as an alternative to linezolid for the second-line treatment of MRSA skin and soft tissue infection. Prior approval of an Infectious Diseases Physician or a Medical Microbiologist is required and treatment must be under the direction of this specialist.

Temocillin Update

The Hospital Anti-infectives Committee recently considered the place of temocillin in the local treatment of extended spectrum beta-lactamase (ESBL) infections. See below for final decision:

Tayside recommendation

Recommended within specialist treatment pathway – **HOSPITAL ONLY**

- Temocillin may be considered as an alternative to carbapenems for ESBL infections. Prior approval of an Infectious Diseases Physician or a Medical Microbiologist is required and treatment must be under the direction of this specialist.

Tayside Prescriber Issue 90 Jan 2006 - amendment

This supplement on anti-obesity agents has been amended and reposted on the DTC intranet pages. The statement relating to the EMEA safety review of sibutramine is outdated and has been removed.

Forthcoming SMC Advice

Gastro-intestinal system
Esomeprazole (Nexium®)
Beclometasone dipropionate 5mg (Clipper®)
Mesalazine (Asacol®)
Cardiovascular system
Perindopril (Coversyl®)
Nebivolol (Nebilet®)
Losartan/hydrochlorothiazide (Cozaar®-Comp)
Respiratory
Omalizumab (Xolair®)
Beclometasone inhaler (Clenil® Modulite®)
Ciclesonide (Alvesco®) Adolescents & children
Budesonide (Novolizer Budesonide®)
Central nervous system
Ropinirole (Adartrel®)
Rivastigmine (Exelon®)
Pregabalin (Lyrica®) - ***IRP***
Zonisamide (Zonegran®)
Topiramate (Topamax®)
Duloxetine (Cymbalta®)
Rotigotine (Neupro®)
Infections
Tigecyclin (Tygacyl®)
Posaconazole (Noxafil®)
Interferon-α-2b/ribavirin (Viraferon/Rebetol®)
Ertapenem (Invanz®) - ***Abbreviated***
Tipranavir (Aptivus®)
Endocrine system
Somatropin (Norditropin SimpleXx®) - ***Abbreviated***
Pioglitazone/metformin - ***Abbreviated***
Inhaled insulin (Exubera®)
Pegvisomant (Somavert®) - ***Resubmission***

Endocrine system (contd)
Testosterone (Testim®) - ***Abbreviated***
Rosiglitazone/metformin (Avandamet®) - ***Abbreviated***
Insulin glulisine (Apridra®)
Desmopressin (Desmomelt®) - ***Abbreviated***
Ibandronic acid (Bonviva®)
Obstetrics, Gynaecology and UTD
Dinoprostone (Propess®) - ***Abbreviated***
Malignant disease & immunosuppression
Lanreotide (Somatuline® LA)
Mitotane (Lysodren®)
Fludarabine (Fludara® Oral)
Sunitinib (Sutent®)
Bevacizumab (Avastin®) - ***Resubmission***
Erlotinib (Tarceva®) - ***Resubmission***
Trastuzumab (Herceptin®)
Cetuximab (Erbitux®)
Nutrition & Blood
Lanthanum carbonate (Fosrenol®)
Paricalcitrol (Zemplar®)
Cinacalcet (Mimpara®) - ***Resubmission***
Carglumic acid (Carbaglu®)
Musculoskeletal and joint diseases
Etoricoxib (Arcoxia®) - ***Abbreviated***
Etanercept (Enbrel®) - ***Abbreviated***
Adalimumab (Humira®)
Eye
Dorzolamide (Trusopt®)
Pegaptanib sodium (Macugen®)
Travoprost/timolol (Duotrav®) - ***Abbreviated***
Skin
Clobetasol propionate (Clarelux®) - ***Abbreviated***
Etanercept (Enbrel®) - ***Abbreviated***

Contact details: Local implementation of SMC recommendations is being taken forward by the Tayside Medicines Unit – contact Jan Jones, Pharmaceutical Prescribing Adviser (jan.jones@tpct.scot.nhs.uk) if you have any queries in relation to the introduction of new drugs within NHS Tayside