TAYSIDE PRESCRIBER

Tayside D&TC Supplement No. 35

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Produced by Tayside New Medicines Implementation Panel (NMIP)

In this issue:

A Strengthened Role for the Scottish Medicines Consortium (SMC)

The following arrangements have been announced by the Scottish Executive to strengthen the role of the SMC to ensure the national implementation of innovative new drugs.

"Drugs to be reviewed by the SMC will be placed in one of the following categories:

i. unique drugs for specific conditions which, if approved by SMC, will be introduced into NHS Scotland to an agreed national programme, and

ii. drugs for conditions where alternative drug treatments already exists which, if approved by SMC, the implementation of which will be subject to local NHS Board decision.

"Unique category drugs recommended by the SMC must be made available uniformly across Scotland. An executive cohort on SMC will agree a national implementation plan for these products. Normally, these drugs will be provided to meet clinical need within 3 months of publication of SMC advice.

"Experience suggests that each year the unique category of drugs will include one or two innovative new drugs which offer a major clinical impact, but at high cost.

"NHS Boards will be required to fund the cost of SMC recommendations from within their general allocation".

SMC Advice Issued January 2004

Memantine (Ebixa®) – Alzheimer's disease

SMC recommendation

Advice: following a resubmission.
Not recommended for use within NHS Scotland. This is currently the only agent licensed in UK for use in moderately severe to severe Alzheimer's disease. There is only one pivotal trial and it involves 252 patients. It showed a statistically significant benefit over placebo of 0.3 in the Clinician's Interview Based Impression of Change (CIBIC+) on a scale of 1-7, which includes care givers' views. It also showed a reduction in the Alzheimer's Disease Co-operative Study Activities of Daily Living Inventory (ADCS-ADL) of 3.4 on a 54 point range. These results show that the magnitude of any

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Memantine continued
effect is small, the clinical importance of which is unclear. No target sub-group of the population could be identified as potential responders, nor was there evidence of an optimal duration of treatment. The economic case submitted by the manufacturer, does not support a recommendation that use of this drug would be cost-effective relative to standard practice in Scotland.

Tayside recommendation

Not recommended

Points for consideration:
- In a recent memantine review (Oct 2003), the Drug & Therapeutics Bulletin also questioned whether the small reduction in the rate of deterioration in global, functional and cognitive scales shown in clinical trials translates into important changes in quality of life.
- Memantine is not stocked by the hospital pharmacy.

Stalevo® (levodopa/carbidopa/entacapone) – Parkinson's disease

SMC recommendation

Advice: following an abbreviated submission.
Accepted for use in NHS Scotland. Stavelo® for the treatment of patients with Parkinson's disease and end of dose motor fluctuations not stabilised on levodopa/dopa decarboxylase inhibitor treatment. This combination preparation allows administration of a single tablet incorporating ingredients that are routinely combined for the indication above. This may improve convenience to the patient. Depending on the doses and formulations being replaced, conversion to the combination, may result in a modest increase in cost or (less commonly) a cost saving.

Tayside recommendation

Not currently recommended – pending formulary decision

Points for consideration:
- **The place of Stavelo in relation to separate levodopa/carbidopa and entacapone preparations, will be addressed by the Formulary Committee**. **Prescribers are advised to await the outcome of the formulary decision.**

Topiramate (Topamax®) – epilepsy

SMC recommendation

Advice: following a full submission.
Topiramate is accepted for restricted use within NHS Scotland for its extended (monotherapy) indication. It should be initiated only by physicians who have appropriate experience in the treatment of epilepsy. Topiramate should be used principally in patients who have not found benefit from treatment with an older anti-convulsant drug such as carbamazepine or sodium valproate, or for whom these drugs are unsuitable because of contra-indications, interactions or poor tolerance. Its use for second-line therapy in epilepsy is unaffected by this recommendation.

Tayside recommendation

Not currently recommended – pending agreed specialist treatment pathway

Points for consideration:
- The original second-line indication for topiramate is as an adjunctive therapy.
- Topiramate monotherapy shows similar time to first seizure as carbamazepine and sodium valproate in patients recently diagnosed with partial or generalised epilepsy or tonic-clonic seizures.

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Topiramate continued

- Comparative data versus carbamazepine and valproate show that topiramate is associated with fewer treatment-limiting adverse effects and a relatively high incidence of weight loss.
- Comparative data are lacking versus other newer first-line agents eg lamotrigine and oxcarbazepine.
- Topiramate is more expensive than both carbamazepine and sodium valproate given as monotherapy, and slightly less expensive than lamotrigine.
- Topiramate adjunctive therapy is licensed in adults and children over 2 years, monotherapy is limited to children over 6 years.
- Refer to SIGN guideline "Diagnosis and management of epilepsy in adults" for further information on the use of anti-epileptic drugs.

The following recommendations relate to HOSPITAL ONLY medicines

Caspofungin (Cancidas®) – invasive candidiasis

SMC recommendation

Advice: following a full submission.
Recommended for restricted use within NHS Scotland. Caspofungin provides an additional agent for the treatment of invasive candidiasis. Its use should be restricted to patients with fluconazole-resistant *Candida* infection who do not respond to, or cannot tolerate amphotericin B therapy or who are at an increased risk of serious side effects with amphotericin (eg transplant patients, especially those receiving bone marrow transplants.)

Tayside recommendations

Not currently recommended – pending TUH antifungal policy decision

Points for consideration:

- Caspofungin is also licensed for the treatment of invasive aspergillosis in patients refractory to, or intolerant of amphotericin B (AmB) and/or itraconazole. The above SMC recommendation relates only to the treatment of invasive candidiasis.
- Caspofungin demonstrates similar response rates to conventional AmB in adults with invasive candidiasis.
- Comparative data show that caspofungin treatment is associated with a lower rate of infusion-related events and nephrotoxicity than conventional AmB.
- No comparative data are available versus other antifungal agents (fluconazole, itraconazole, lipid formulations of AmB, voriconazole or flucytosine) in the treatment of invasive candidiasis.
- The cost of caspofungin is similar to lipid formulations of AmB.
- **Local policy on the use of antifungal drugs is currently under discussion by the TUH Anti-Infectives Committee. Prescribers are advised to await the outcome of the antifungal policy decision.**

Pegylated Liposomal doxorubicin (Caelyx®) – metastatic breast cancer

SMC recommendations

Advice: following a full submission
Not recommended for use within NHS Scotland. This pegylated liposomal formulation of doxorubicin hydrochloride is now licensed as monotherapy for the treatment of metastatic breast cancer where there is an increased cardiac risk. An inconclusive study has suggested that it was not inferior to conventional doxorubicin in terms of progression-free survival. It was less cardiotoxic than conventional doxorubicin, but was associated with other troublesome adverse events, particularly

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Pegylated liposomal doxorubicin continued
palmar-plantar erythrodysesthesia. The product is significantly more expensive than the standard preparation and its cost-effectiveness in managing metastatic breast cancer has not been addressed by the company in their submission.

Tayside recommendation

Not recommended

Points for consideration:

- Caelyx® is also licensed for the treatment of AIDS-related Kaposi's sarcoma, and advanced ovarian cancer. Myocet® is a further pegylated liposomal formulation of doxorubicin, licensed for use with cyclophosphamide in the treatment of metastatic breast cancer. The above SMC recommendation relates only to the use of Caelyx in metastatic breast cancer.

Propofol 1% MCT-LCT (Propofol Lipuro®) – anaesthesia

SMC recommendation

Advice: following a full submission
Accepted for use within NHS Scotland. Propofol MCT-LCT emulsion 1% is a new formulation of an existing product. It is as effective as alternative formulations of propofol. Pain on injection is significantly reduced in frequency and intensity compared with alternative formulations, though not totally eliminated. The major advantage of this formulation will be realised when co-administration of lignocaine is unnecessary. This advice is based on the assumption that the product will be available through contract at a price that is competitive with available formulations of propofol.

Tayside recommendations

Not currently recommended – pending agreed specialist protocol

Points for consideration:

- Propofol is an anaesthetic used for the induction and maintenance of anaesthesia
- Propofol is an emulsion with long-chain triglycerides (LCT). Propofol Lipuro contains both long and medium chain triglycerides (MCT) in a 1:1 ratio. This reduces the proportion of free propofol in the aqueous phase.
- Propofol Lipuro is competitively priced versus branded propofol LCT emulsion.
- Propofol Lipuro os not currently stocked by the hospital pharmacy.

Teriparatide (Forsteo®) – severe osteoporosis

SMC recommendation

Advice: following a full submission.
Teriparatide (Forsteo®) is accepted for restricted use within NHS Scotland for the treatment of established severe osteoporosis in post-menopausal women. This medicine should be restricted to initiation by specialists experienced in the treatment of osteoporosis following assessment of fracture risk including measurement of BMD. It is the first product to be licensed specifically for established (severe) post-menopausal osteoporosis. It has shown efficacy in reducing vertebral and non-vertebral fractures, particularly in a sub-group with documented severe osteoporosis. At the recommended daily dose it is expensive but appears to be cost-effective in women with proven osteoporosis who have developed fractures.

Tayside recommendation

Recommended for use within agreed specialist treatment pathway

Points for consideration:

- Teriparatide is recombinant parathyroid hormone. It acts by stimulating bone growth rather than by reducing bone loss.

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Teriparatide continued

- Adverse events reported in clinical studies appear similar to placebo.
- 18 months is currently the maximum recommended duration of treatment within licence. Long-term follow-up indicates that beneficial effects persist for at least a further 18 months.
- The cost of teriparatide is £3,444 per patient per year.
- Teriparatide is currently available only as a subcutaneous injection, administered daily.
- Women receiving teriparatide should also receive supplemental calcium and vitamin D if dietary intake is inadequate.
- Eli Lilly has commissioned Healthcare at Home to provide a package of care for each patient receiving teriparatide. This package will include home visits for training in self-injection, monitoring of compliance with treatment, medicines management including safe storage and a patient help line.
- A local protocol for the use of teriparatide has been developed by the bone clinic.
- **Teriparatide is restricted to the bone clinic for treatment of postmenopausal women with WHO defined osteoporosis ie T-score <-2.5 and:**
  - **at least 2 fragility fractures with a Z-score <-2.0 (ie severe osteoporosis), or**
  - **fragility fractures despite bisphosphonate treatment for at least 12 months.**
- Refer to SIGN guideline No 71 for further information on the management of osteoporosis**.**

Zoledronic acid (Zometa®) – prevention of SREs in advanced prostate cancer

SMC recommendation

Advice: following an Independent Review Panel consideration
Zoledronic acid (Zometa®) is not recommended for use within NHS Scotland for the prevention of skeletal related events (SREs) in patients with advanced prostate cancer involving bone. Although zoledronic acid demonstrated a reduction in SREs compared with placebo in these patients, the absolute reduction was small and the study requires caution in accepting this as sufficient evidence to introduce zoledronic acid into standard practice for the treatment of patients with metastatic prostate cancer. An economic case was submitted by the manufacturer, but its quality was not judged to be sufficient to support a recommendation that the drug is cost-effective relative to standard practice in Scotland for this particular indication.

Tayside recommendation

Not recommended

Points for consideration:

- Zoledronic acid is licensed for the treatment of tumour-induced hypercalcaemia and the prevention of SREs in patients with advanced malignancies involving bone. The above SMC recommendation relates only to the prevention of SREs in patients with advanced prostate cancer.
- The SMC approved zoledronic acid for the prevention of SREs associated with breast cancer and multiple melanoma in May 2003. Use in patients with prostate cancer or other solid tumours was not recommended due to insufficient economic evidence.

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 Tayside.