TAYSIDE PRESCRIBER

Tayside D&TC Supplement No. 32

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Produced by Tayside New Medicines Implementation Panel (NMIP)

In this issue:

Scottish Medicines Consortium (SMC) Advice Issued in October 2003

Calfovit D3® (Ca 1200mg/colecalciferol 800iu) - calcium and vitamin D deficiency

- Calfovit D3 is licensed for the correction of calcium and vitamin D deficiency in the elderly and as an adjunct to specific therapy for osteoporosis. It is available as a powder for oral suspension for once daily administration.

➢ **Recommendation pending formulary decision**

Points for consideration:

- Adcal D3 and Calcichew D3 Forte are alternative preparations included in the Tayside Area Prescribing Guide (TAPG) – both are chewable with a dose of two tablets daily (equivalent to one sachet of Calfovit D3).
- Calfovit D3 is priced below other calcium and vitamin D supplements (£4.03 for 28 days of Calfovit D3 versus £4.20 for Adcal D3 and £5.32 for Calcichew D3 Forte).
- **The place of Calfovit D3 in relation to other calcium and vitamin D supplements will be addressed by the Formulary Committee. Prescribers are advised to await the outcome of the formulary decision.**

Mirtazapine (Zispin Soltab®) - depressive illness

- Zispin Soltab is a new orodispersible formulation of mirtazapine, an antidepressant with presynaptic α_2-antagonist properties that increases central noradrenergic and serotonergic neurotransmission. It has the same dose and indication (depressive illness) as the standard formulation.

➢ **Recommendation pending formulary decision**

Points for consideration:

- Zispin Soltab is priced slightly below standard mirtazepine (Zisprin).
- Mirtazapine is currently a TAPG option for patients intolerant of SSRI's and where sedation is required.
- **The place of Zisprin Soltabs in relation to the standard formulation of mirtazepine will be addressed by the Formulary Committee. Prescribers are advised to await the outcome of the formulary decision.**

Modafinil (Provigil®) - obstructive sleep apnoea / hypopnoea syndrome (OSAHS)

- Modafinil is a centrally acting non-amphetamine sympathomimetic. It is licensed for the treatment of excessive daytime sleepiness associated with narcolepsy and OSAHS. The precise mechanism of action of modafinil is unknown.
- Modafinil is the only drug on the UK market currently licensed for OSAHS.
- The SMC has made a recommendation only on the new indication for OSAHS.

➢ **Not recommended**

Points for consideration:

- Modafinil has shown small beneficial effects on daytime sleepiness in short-term studies in patients with OSAHS who remained sleepy despite effective use of continuous positive airways pressure (CPAP) therapy.
- SIGN Guideline No. 73 "Management of OSAHS in adults" recommends that pharmacotherapy should **not** be first line therapy for OSAHS. It recognises the small beneficial effects of drugs such as modafinil on daytime sleepiness in some patients who remain sleepy despite good CPAP compliance. However, the guideline expresses concern that drugs may decrease CPAP use and that longer-term studies of their value and risks are needed.
- There is no evidence to suggest that alerting drugs such as modafinil could be used as an alternative to CPAP and they are not a substitute for careful attention to improving CPAP comfort and efficacy.
- The manufacturer failed to provide the SMC with information on the cost-effectiveness of modafinil in the management of OSAHS.

Moxifloxacin (Avelox®) - community acquired pneumonia (CAP)
acute exacerbations of chronic bronchitis (AECB)

- Moxifloxacin is a new fluoroquinolone antibiotic. Its licence includes the treatment of CAP except severe cases, and AECB.
- Moxifloxacin is currently only available in an oral formulation.

➢ **Recommendation pending TUH antibiotic policy decision**

Points for consideration:

Community acquired pneumonia

- Moxifloxacin has similar efficacy and safety to standard first-line antibiotics used in mild to moderate CAP (amoxicillin and/or clarithromycin).
- The side-effect profile of moxifloxacin appears similar to that of other quinolones.
- There is concern that these valuable new antibiotics should not be overused leading to the development of fluoroquinolone-resistant bacteria.
- The current British Thoracic Society (BTS) CAP Guideline states that new fluoroquinolones are not recommended as first-line agents or for community use in pneumonia.
- The BTS CAP Guideline and SIGN Guideline No 59 "Community management of lower respiratory tract infection in adults" advise amoxicillin or a macrolide (erythromycin or clarithromycin) as first-line monotherapy in the community and combined oral therapy with amoxicillin and a macrolide for patients with non-severe CAP who require hospital admission for clinical reasons. The local Primary Care Anti-infective Advisory Notes and the TUH Antibiotic Policy recommend the same strategy.
- New fluoroquinolones may provide a useful alternative in selected hospitalised patients with CAP, eg those intolerant to penicillins or macrolides or where there are local concerns over *C. difficile* associated diarrhoea.
- Levofloxacin is currently the only other fluoroquinolone licensed in the UK specifically for the treatment of CAP. Levofloxacin is available in an IV formulation and is included in TUH Antibiotic Policies as second-line treatment for **severe** CAP in penicillin-allergic patients.
- **The place of moxifloxacin in the local treatment of CAP will be addressed by the TUH Anti-Infectives Committee. Prescribers are advised to await the outcome of the antibiotic policy decision.**
- Moxifloxacin is not currently stocked by the hospital pharmacy.

Acute exacerbations of chronic bronchitis

- Moxifloxacin has similar efficacy and safety to standard second-line antibiotics used in the treatment of AECB (eg clarithromycin, co-amoxiclav).
- The current BTS chronic obstructive pulmonary disease (COPD) Guideline and SIGN Guideline No 59 do not recommend fluoroquinolones for first-line treatment of AECB.
- The local Primary Care Anti-infective Advisory Notes and the TUH Antibiotic Policy recommend amoxicillin first-line (erythromycin if allergic) for the treatment of AECB. Co-amoxiclav and ciprofloxacin are second-line choices.
- **The place of moxifloxacin in the local treatment of AECB will be addressed by the TUH Anti-Infectives Committee. Prescribers are advised to await the outcome of the antibiotic policy decision.**
- Moxifloxacin is not currently stocked by the hospital pharmacy

The following recommendation relates to a HOSPITAL ONLY medicine

Pegfilgrastim (Neulasta®) – cytotoxic-induced neutropenia

- Pegfilgrastim is a polyethylene glycol-conjugated derivative of filgrastim (ie a sustained release formulation of filgrastim – a recombinant human granulocyte-colony stimulating factor (CSF)).
- Pegfilgrastim stimulates the production of neutrophils and is licensed for the reduction in duration of neutropenia and the incidence of febrile neutropenia in patients treated with cytotoxic chemotherapy for malignancy (except chronic myeloid leukaemia and myelodysplastic syndromes). This licence is very limited compared to that of filgrastim or lenograstim.

➢ **Recommended for restricted use**

Points for consideration:

- Unlike filgrastim, which is renally cleared, the elimination of pegfilgrastim is prolonged and is thought to be neutrophil mediated. This allows for a single injection per chemotherapy cycle rather than a course of daily injections with benefits of convenience for both patients and staff.
- Pegfilgrastim shows similar efficacy, in terms of duration of severe neutropenia, and tolerability to filgrastim. However, there is only clinical data available using pegfilgrastim with a limited range of cytotoxics.
- The main side-effect reported in trials is mild to moderate bone pain.
- Excluding administration costs, each pegfilgrastim dose costs the equivalent of over 10 daily doses of filgrastim for patients up to 60kg and over 6 daily doses for patients of 60-96kg and over 10 daily doses of lenograstim in patients up to 1.8m^2 body surface area. As a rough guide, if pegfilgrastim were used in a patient who would have received 8 days of filgrastim in a treatment cycle then the total drug and administration costs of the two drugs are similar.
- Further guidance on the use of CSF's is available in the "2000 update of recommendations for the use of hematopoietic CSFs: evidence based, clinical practice guidelines" produced by the American Society of Clinical Oncology and "Guidelines on the use of CSFs in haematological malignancies" produced by the British Committee for Standards in Haematology.
- **Pegfilgrastim is restricted to secondary care on the recommendation of a haematologist/ oncologist in the context of current practice guidelines for CSF's.**

Named Patient Use of New Medicines Prior to SMC Evaluation/Outwith SMC Recommendation in TUH - revised process

The local process to allow named patient use of new medicines prior to SMC evaluation in exceptional cases of compelling need has been revised since issue of D&TC Supplement No 26, May 2003.

New medicines should not be prescribed in NHS Scotland until they have been evaluated by the SMC and a recommendation for use has been made. If TUH clinicians wish to prescribe a new medicine that has not been evaluated by the SMC or is not recommended by the SMC, they should make a case for exceptional treatment of an individual patient to their Clinical Group by addressing the following points:

- Does this patient represent a case of exceptional life circumstances?
- Is use of this new medicine a good use of resources in relation to the Clinical Group's priorities?
- How robust is the evidence of benefit associated with this new medicine compared to other interventions with proven effectiveness?
- Why should this particular patient receive treatment ahead of others/against national guidance?
- Declaration of interests

The Clinical Group will then consider whether there are overriding factors that make prescribing reasonable in the particular circumstances.

Prescribing approved by the Clinical Group should remain the responsibility of secondary care specialists, ie such new medicines should be supplied from hospital. This process applies to both in-patient and out-patient care.

A pro forma to assist this procedure is under development. A similar process for the various sectors of TPC is currently under discussion.

Development of SMC Website

The structure of the SMC website (www.scottishmedicines.org.uk) has been updated. Medicines reviewed by the SMC are now separate from the SMC work programme and can be searched by BNF category or alphabetically. A user subscription facility is also available to obtain monthly updates.

Details of local recommendations for new medicines are available on the Tayside D&TC website (www.show.scot.nhs.uk/thb/adtc).

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