TAYSIDE PRESCRIBER

Tayside DTC Supplement No 59

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

In this issue:

SMC Advice Issued in June 2006

Bevacizumab (Avastin®) - metastatic colorectal cancer

SMC recommendation

Advice: following a resubmission

Bevacizumab (Avastin®) is not recommended for use within NHS Scotland in combination with intravenous fluorouracil/folinic acid or intravenous fluorouracil/folinic acid/irinotecan for first-line treatment of patients with metastatic carcinoma of the colon or rectum.

Bevacizumab, in combination with standard regimens containing fluorouracil and folinic acid or fluorouracil, folinic acid and irinotecan, improved overall and disease-free survival times compared to these standard regimens. However the economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.55 February 2006 for original SMC advice.
- NICE guidance on bevacizumab and cetuximab in advanced colorectal cancer is due in Nov 2006.
- Further information on the local treatment of metastatic colorectal cancer is available in the Tayside "Colorectal cancer chemotherapy protocol".
- Bevacizumab is not stocked by the hospital pharmacy.

Ciclesonide inhaler (Alvesco®) - asthma in adolescents

SMC recommendation

Advice: following a full submission

Ciclesonide (Alvesco®) is accepted for restricted use within NHS Scotland for treatment to control persistent asthma in adolescents (aged at least 12 years and <18 years)

It is restricted to asthma patients who require once-daily administration of an inhaled corticosteroid and whose treatment is at step 2 or step 3 of the British Guideline on the Management of Asthma. Alternative inhaled steroids are available at lower cost.

Click here for SMC link

Tayside recommendation

Recommended within formulary (prescribing note)

Points for consideration:

- Advice on the use of inhaled ciclesonide in adults was issued in July 2005 (refer to Tayside Prescriber; DTC Supplement No.52, July 2005). The above SMC advice relates to a licence extension covering adolescents ie patients of 12 years of age and above. Note that ciclesonide is not licensed in children.
- The usual maximum dose of ciclesonide is 160mcg once daily (roughly equivalent to CFC beclometasone 200mcg twice daily).
- Ciclesonide costs less than alternative once daily inhaled steroids but is considerably more expensive than standard twice daily beclometasone. (28 days treatment with ciclesonide 160mcg once daily costs £8 versus £5 for CFC-free beclometasone (Qvar®) 100mcg twice daily, £10 for dry powder budesonide 400mcg once daily, £11 for mometasone 200mcg once daily.
- **Locally, ciclesonide is recommended as an alternative to existing once daily inhaled corticosteroids in adults and adolescents at steps 2 or 3 of the BTS/SIGN asthma guideline who require once daily administration. It may also be considered in patients who experience unacceptable oropharyngeal side-effects with low dose inhaled corticosteroids despite mouth rinsing and use of spacer device.**
- Advice on the management of asthma is available in the SIGN/BTS Guideline and within the Respiratory Guidance Notes in the Tayside Area Prescribing Guide (TAPG).

Dorzolamide preservative-free eye drops (Trusopt®) - ocular hypertension, glaucoma

SMC recommendation

Advice: following an abbreviated submission

Dorzolamide 2% preservative-free unit-dose eye drops (Trusopt®) are accepted for restricted use in NHS Scotland for the treatment of elevated intra-ocular pressure in ocular hypertension, open-angle glaucoma and pseudo-exfoliative glaucoma. They are licensed as adjunctive therapy to beta-blockers and as monotherapy in patients unresponsive to beta-blockers or in whom beta-blockers are contra-indicated.

This preparation is substantially more expensive than the equivalent multi-dose eye drop preparation and should be restricted to use in patients for whom dorzolamide is appropriate and who have proven sensitivity to the preservative benzalkonium chloride.

Tayside recommendation

Specialist treatment pathway (GPs may prescribe under the direction of the ophthalmology clinic)

Points for consideration:

- **Locally, preservative-free unit dose eye drops are reserved for patients with proven preservative allergy. Treatment should be under the direction of the ophthalmology clinic.**

Erlotinib (Tarceva®) - non-small cell lung cancer (NSCLC)

SMC recommendation

Advice: following a resubmission

Erlotinib (Tarceva®) is accepted for restricted use within NHS Scotland for the treatment of patients with locally advanced or metastatic non-small cell lung cancer, after failure of at least one prior chemotherapy regimen. When prescribing erlotinib, factors associated with prolonged survival should be taken into account. No survival benefit or other clinically relevant effect of the treatment have been demonstrated in patients with epidermal growth factor receptor (EGFR)-negative tumours.

Erlotinib is restricted to use in patients who would otherwise be eligible for treatment with docetaxel monotherapy. No economic case has been made for those whose performance status would make them ineligible to receive docetaxel.

Click here for SMC link

Tayside recommendation

Pending OHMMG approval of local lung cancer protocol

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.55 February 2006 for original SMC advice.
- Of note, sub-group analysis of the pivotal erlotinib study indicated no significant survival benefit amongst patients who were current or ex-smokers.
- There are no comparative data versus docetaxel monotherapy – the second-line chemotherapy option recommended in recent NICE and SIGN NSCLC guidance.
- Erlotinib is more expensive than docetaxel monotherapy. The cost of 125 days treatment with erlotinib (average treatment duration in the pivotal study) is £6,800 versus 4 cycles of docetaxel at £3,400-£4,100*. However, use of oral erlotinib may result in patient and service benefits.
- **The place of erlotinib in the treatment of advanced NSCLC, and in relation to docetaxel monotherapy, will be addressed by the lung cancer multidisciplinary team (MDT) in a local lung cancer protocol.**

*NHS list price excl. VAT

Esomeprazole (Nexium®) - healing of NSAID associated gastric ulcers

SMC recommendation

Advice: following a full submission

Esomeprazole (Nexium®) is not recommended for use within NHS Scotland for the healing of gastric ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy.

In the treatment of gastric ulcers associated with NSAID therapy, esomeprazole produced greater healing rates than a histamine-H_2 antagonist. However, there are no comparisons of esomeprazole with other proton pump inhibitors for this indication. The economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Existing formulary proton pump inhibitors omeprazole and lansoprazole are more cost-effective treatment options in the majority of patients.
- Refer to local "Upper Gastro-intestinal Guidelines" within the TAPG for further advice on the management of gastric ulcers.

Esomeprazole (Nexium®) - prevention of NSAID associated gastric/duodenal ulcers

SMC recommendation

Advice: following a full submission

Esomeprazole (Nexium®) is not recommended for use within NHS Scotland for the prevention of gastric and duodenal ulcers associated with non-steroidal anti-inflammatory (NSAID) therapy in patients at risk. When compared to placebo, esomeprazole reduces the rate of gastro-duodenal ulcers associated with NSAID therapy in at-risk patients. There are no comparisons of esomeprazole with other proton pump inhibitors for this indication. The economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- See above

Interferon alfa 2b (Viraferon® and Intron A®) - chronic hepatitis C in children/adolescents

SMC recommendation

Advice: following a full submission

Interferon alfa 2b (Viraferon® and Intron A®) in combination with ribavirin (Rebetol®) is accepted for use within NHS Scotland for the treatment of children and adolescents 3 years of age and older, who have chronic hepatitis C, not previously treated, without liver decompensation and who are positive for serum HCV-RNA.

The combination is effective in eliminating hepatitis C virus in children and adolescents. The decision to treat should be made on a case by case basis, taking into account any evidence of disease progression such as hepatic inflammation and fibrosis, as well as prognostic factors for response, HCV genotype and viral load. The expected benefit of treatment should be weighted against the safety findings observed for paediatric subjects in the clinical trials.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Draft SIGN guidance on the management of hepatitis C includes a grade D recommendation that children with evidence of moderate liver disease should be offered treatment with off-label pegylated interferon and ribavirin ideally as part of a clinical trial. Final guidance is due Winter 2006.

Omalizumab (Xolair®) - severe persistent allergic asthma

SMC recommendation

Advice: following a full submission

Omalizumab (Xolair®) is not recommended for use within NHS Scotland as add-on therapy to improve asthma control in adult and adolescent patients (12 years of age and above) with severe persistent allergic asthma.

The economic case for omalizumab has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Omalizumab is a humanised monoclonal antibody that blocks the binding of immunoglobulin E (IgE) to mast cells and basophils, thereby inhibiting the release of various inflammatory mediators responsible for symptoms in allergic asthma and rhinitis.
- The pivotal 28-week study showed that the addition of omalizumab to inhaled corticosteroids and long-acting beta$_2$-agonists significantly reduced the rate of clinically significant asthma exacerbations in patients with severe persistent allergic asthma.

Continued over

Omalizumab continued

- The BTS/SIGN asthma guideline recommends the addition of slow release theophylline or leukotriene antagonists in patients with severe persistent asthma (step 4). Comparative data for omalizumab versus these agents are unavailable.
- The most serious adverse events reported with omalizumab were malignancies and anaphylaxis. A pharmacovigilance plan includes an ongoing 5-year comparative observational prospective cohort study in which all serious adverse events (including malignancies) will be monitored and followed up.
- Omalizumab is expensive - roughly £7,500 per patient per year (based on the average dose used in the pivotal study). However, this should be offset by reductions in emergency treatment and hospital admission.
- The 2005 update of the BTS/SIGN asthma guideline notes that omalizumab may be of benefit in highly selected patients with severe persistent allergic asthma, and also states that, at present, its role in the stepwise management of asthma is unclear.
- Omalizumab is not stocked by the hospital pharmacy.

Pegvisomant (Somavert®) - treatment of patients with acromegaly

SMC recommendation

Advice: following a full resubmission

Pegvisomant (Somavert®) is not recommended for use within NHS Scotland for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise insulin-like growth factor 1 (IGF-1) concentrations or was not tolerated. Pegvisomant reduces IGF-1 levels significantly and improves some of the clinical manifestations of acromegaly. It is acknowledged that this is an orphan drug but the economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.50 February 2005 for original SMC advice.
- Pegvisomant is not stocked by the hospital pharmacy.

Posaconazole (Noxafil®) - specific invasive fungal infections

SMC recommendation

Advice: following a full submission

Posaconazole (Noxafil®) is accepted for use within NHS Scotland for the treatment of adults with specific invasive fungal infections refractory to or intolerant of specified antifungal agents.

The evidence to support the licensed use of posaconazole is limited to one open-label, non-comparative study mainly in patients refractory to treatment with amphotericin.

Click here for SMC link

Tayside recommendation

Pending Hospital Anti-infectives policy decision

Points for consideration:

- Posaconazole is a new broad-spectrum triazole antifungal. It is licensed for use in *Candida* and *Aspergillus* infections as well as in other rarer fungal infections eg fusariosis, chromoblastomycosis and coccidioidomycosis. Patients must be refractory to or intolerant of existing antifungal agents.
- Indirect comparative data indicate that posaconazole has similar response rates as voriconazole and caspofungin in the treatment of invasive aspergillosis in patients refractory to, or intolerant of, amphotericin B or itraconazole.
- Posaconazole treatment-related adverse events were reported in 38% of patients in phase I, II and III clinical studies. Posaconazole has a more limited drug-interaction profile compared to other triazole antifungals and appears to affect vision to a lesser extent than voriconazole.

Continued over

Posaconazole continued

- Posaconazole is only available as an oral suspension and is priced slightly above maintenance therapy with voriconazole tablets. (Posaconazole 400mg twice daily or 200mg four times daily costs £95 per day versus £80* for voriconazole 200mg twice daily as maintenance therapy).
- **The place of posaconazole in the local treatment of specific invasive fungal infections, and in relation to voriconazole and caspofungin, will be addressed by the Hospital Anti-infectives Sub-Committee.**
- Further advice on the management of fungal infections is available in the Hospital Anti-Infectives Policy within the TAPG.

* NHS list price excl. VAT

Somatropin (Norditropin SimpleXx®) – short children born small for gestational age (SGA)

SMC recommendation

Advice: following an abbreviated submission

Somatropin (Norditropin SimpleXx®) injection is accepted for restricted use within NHS Scotland for the treatment of growth disturbance (current height standard deviation score (SDS) <-2.5 and parental adjusted height SDS <-1 in short children born small for gestational age (SGA), with a birth weight and/or length below -2 standard deviations, who failed to show catch-up growth (height velocity SDS <0 during the last year) by 4 years of age or later.

Treatment should be initiated and monitored by a paediatrician with expertise in managing childhood growth disorders and growth hormone therapy.

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of the paediatric outpatient growth clinic)

Points for consideration:

- Treatment of SGA is a recent licence extension for Norditropin SimpleXx®.
- Guidance on initiation and monitoring of somatropin in children with growth failure are available in NICE Health Technology Appraisal No.42. The SPC provides further advice on discontinuation.
- Norditropin SimpleXx® is priced at parity with Genotropin®, an alternative brand of somatropin also licensed for treatment of SGA.
- See below for updated advice on Genotropin®.

Somatropin (Genotropin®) – Update

May 2006 local advice for the use of Genotropin® in the treatment of SGA has been revised to cover GP prescription under the direction of a specialist, see below:

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribed under the direction of the paediatric outpatient growth clinic).

Choriogonadotropin alfa (Ovitrelle®) – Update

May 2006 SMC advice for the use of choriogonadotropin alfa (Ovitrelle®) in assisted conception (superovulation prior to IVF, anovulation/oligo-ovulation) was deferred to the DTC. See below for final decision:

Tayside recommendation
Recommended within specialist treatment pathway – HOSPITAL ONLY (Assisted Conception Unit)

- Ovitrelle® is currently purchased as part of a wider cost-effective package of fertility treatments under an established local contracting agreement.

NICE Single Technology Appraisals (STAs)

NICE is developing a new process of single technology appraisals (STAs), similar to that of SMC, to provide early guidance on certain medicines to the NHS in England and Wales. SE HDL (2006) 29 states that the SMC remains the main source of advice and recommendations on the use of newly licensed medicines in Scotland.

TAPG Update

Below are the main changes to the TAPG agreed by the Medicines Advisory Group in May 2006. Updated sections in A5 format are available on the TAPG pages of the DTC website. An updated GPASS-TADF fly file for use in general practice will also be available shortly.

	TAPG section	Drug(s) / topic	Changes
1.2	Antispasmodics	Mebeverine	Liquid 50mg/5ml removed. Colofac® liquid discontinued, only a very expensive non-proprietary now listed in BNF
1.3	Ulcer healing drugs	PPIs	OTC omeprazole mentioned. Clarification on restricted use of esomeprazole and advice extended to cover laryngopharyngeal reflux disease
1	Gastro-intestinal system	-	Links added to useful GI guidelines (SIGN, NICE, PRODIGY and Br Soc Gastro)
1	Upper GI Guidelines	Helimet® PPIs	Helimet® discontinued, removed from TAPG. PPI step down/step off advice added to GORD notes. Clarification on restricted use of esomeprazole and advice extended to cover laryngopharyngeal reflux disease.
3.2	Inhaled corticosteroids	Ciclesonide*	Due to licence extension and SMC approval, adolescents now added to ciclesonide prescribing note.

* SMC approved medicine

Forthcoming SMC Advice

Gastro-intestinal system
Beclometasone dipropionate 5mg (Clipper®)
Mesalazine (Asacol®)
Cardiovascular system
Perindopril (Coversyl®)
Nebivolol (Nebilet®)
Losartan/hydrochlorothiazide (Cozaar®-Comp)
Respiratory
Beclometasone inhaler (Clenil® Modulite®)
Salmeterol (Serevent Evohaler®) - ***Abbreviated***
Budesonide (Novolizer Budesonide®)
Central nervous system
Ropinirole (Adartrel®)
Rivastigmine (Exelon®)
Pregabalin (Lyrica®) - ***IRP***
Zonisamide (Zonegran®)
Topiramate (Top Amax®)
Duloxetine (Cymbalta®)
Rotigotine (Neupro®)
Infections
Tigecyclin (Tygacyl®)
Ertapenem (Invanz®) - ***Abbreviated***
Tipranavir (Aptivus®)
Endocrine system
Pioglitazone/metformin - ***Abbreviated***
Inhaled insulin (Exubera®)
Testosterone (Testim®) - ***Abbreviated***
Rosiglitazone/metformin (Avandamet®) - ***Abbrev***

Endocrine system (contd)
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®)
Trastuzumab (Herceptin®)
Cetuximab (Erbitux®)
Bortezomib (Velcade®)
Nutrition & Blood
Lanthanum carbonate (Fosrenol®)
Paricalcitrol (Zemplar®)
Carglumic acid (Carbaglu®)
Musculoskeletal and joint diseases
Etoricoxib (Arcoxia®) - ***Abbreviated***
Etanercept (Enbrel®) - ***Abbreviated***
Adalimumab (Humira®)
Eye
Pegaptanib sodium (Macugen®)
Travoprost/timolol (Duotrav®) - ***Abbreviated***
Skin
Clobetasol propionate (Clarelux®) - ***Abbreviated***

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