TAYSIDE PRESCRIBER

Tayside DTC Supplement No 60

August 2006

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

In this issue:

SMC Advice Issued in July and August 2006

Beclometasone dipropionate (Clenil Modulite®) - asthma

SMC recommendation
Advice: following an abbreviated submission
The Clenil Modulite® range of inhalers is accepted for use in NHS Scotland for the prophylactic management of mild, moderate or severe asthma in adults or children.
They provide chlorofluorocarbon (CFC)-free inhalers with dose equivalence to CFC-containing inhalers. The cost is similar to another (CFC)-free inhaler, however doses are not equivalent to the other CFC-free inhaler product currently available.

Tayside recommendation

Recommended within formulary

Points for consideration:

- Note that 200mcg beclometasone via Clenil Modulite® is roughly equivalent to 100mcg beclometasone via Qvar® inhaler.
- Unlike Qvar®, Clenil Modulite® is licensed for use in children.
- The Clenil Modulite® inhaler may be used with the Volumatic® spacer in patients who have difficulty synchronising aerosol actuation with inspiration of breath.
- CFC-free beclometasone via Clenil Modulite® is a similar price to Qvar® and to generic CFC beclometasone. (200 doses of beclometasone 100mcg via Clenil Modulite® cost £7.72 versus £7.87 for Qvar® 50mcg and £7.59 for generic CFC-beclometasone 100mcg).
- CFC-free beclometasone inhalers should be prescribed by brand name (see recent MHRA advice).
- Under the Montreal Protocol, CFC beclometasone inhalers will eventually be withdrawn. Prescribers should therefore consider commencing a CFC-free formulation in new patients requiring a beclometasone inhaler.

Carbetocin (Pabal®) - prevention of uterine atony and excessive bleeding

SMC recommendation
Advice: In the absence of a submission from the holder of the marketing authorisation.
Carbetocin (Pabal®) 100mcg/1ml solution for injection, is not recommended for use within NHS Scotland for the prevention of uterine atony and excessive bleeding following delivery of the infant by Caesarean section under epidural or spinal anaesthesia.
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 NHS Scotland.

Tayside recommendation

Not recommended

Points for consideration:

- Carbetocin is not stocked by the hospital pharmacy.

Cetuximab (Erbitux®) - locally advanced squamous cell cancer of the head and neck (SCCHN)

SMC recommendation
Advice: Following a full submission
Cetuximab (Erbitux®) is accepted for restricted use within NHS Scotland in combination with radiation therapy for the treatment of patients with locally advanced squamous cell cancer of the head and neck.
It is restricted to patients who are not appropriate for or unable to tolerate chemo-radiotherapy and who are of good performance status with no evidence of distant metastases. It is also restricted to use by specialists in the management of head and neck cancer.
Click here for SMC link

Tayside recommendation

Pending OHMMG approval of local head and neck cancer protocol

Continued over

Cetuximab continued

Points for consideration:

- Cetuximab is an epidermal growth factor receptor (EGFR) inhibitor. EGFR is over-expressed in a wide variety of tumour cells including SCCHN.
- Cetuximab is also licensed for the treatment of metastatic colorectal cancer. Refer to Tayside Prescriber; DTC Supplement No. 49 and 54 for SMC advice in this indication.
- The pivotal study showed that the addition of cetuximab to radiotherapy significantly increased median progression free survival by five months (12 to 17 months) and median overall survival by 20 months (29 to 49 months) compared to radiotherapy alone in patients with previously untreated stage III/IV locally advanced non-metastatic SCCHN.
- Enrolled patients had good performance status, 50% had a Karnofsky score ≥ 90. Of note, no clinical benefit was shown in patients with a Karnofsky score ≤ 80 who were 65 years or older.
- Platinum-based chemoradiotherapy is the current recommended standard of care for patients with locally advanced SCCHN. There are no comparative data for cetuximab plus radiotherapy versus chemoradiotherapy.
- Rash is a common adverse effect associated with cetuximab. It is thought to be a class effect of EGFR inhibitors and appears to correlate with clinical response.
- Cetuximab costs £5,900 per patient per eight-week course of treatment.
- **The place of cetuximab in the treatment of advanced head and neck cancer will be addressed by the oncology team within a local protocol.**
- SIGN guidance on head and neck cancer is due later this summer.

Clobetasol propionate 0.05% foam (Clarelux®) – scalp dermatoses

SMC recommendation

Advice: Following an abbreviated submission

Clobetasol propionate 0.05% cutaneous foam (Clarelux®) is accepted for use within NHS Scotland for short-course treatment of steroid responsive dermatoses of the scalp such as psoriasis, which do not respond satisfactorily to less potent steroids.

It offers an alternative to other scalp applications of clobetasol propionate at a similar cost (depending on the rate of application).

Tayside recommendation

Non-formulary

Points for consideration:

- 100g Clarelux® foam is the same cost as 100ml Dermovate® scalp application.

Desmopressin (DesmoMelt®) - primary nocturnal enuresis

SMC recommendation

Advice: Following an abbreviated submission

Desmopressin 120mcg oral lyophilisate (DesmoMelt®) is accepted for use within NHS Scotland for the treatment of primary nocturnal enuresis.

At clinically equivalent doses there is no additional cost for the sublingual formulation compared with conventional tablets.

Tayside recommendation

Non-formulary

Points for consideration:

- DesmoMelt® tablets contain slightly less desmopressin freebase than conventional desmopressin acetate 200mcg tablets (120mcg versus 178mcg desmopressin freebase). Pharmacokinetic data shows that these two products are clinically equivalent.
- Patients should be referred to the Tayside Enuretic Service* prior to long-term use of desmopressin.
- Guidance on the management of nocturnal enuresis, including the use of non-pharmacological treatments, is available on the PRODIGY Knowledge website.

Enuretic Service contacts: Dundee CHP: Lochee Health Centre 01382 611283, P&K CHP: Perth Royal Infirmary 01738 623311, Angus CHP: Whitehills Hospital 01307 464551.

Dinoprostone (Propess®) - cervical ripening

SMC recommendation
Advice: Following an abbreviated submission
Dinoprostone 10mg vaginal delivery system (Propess®) is accepted for use in NHS Scotland for initiation of cervical ripening in patients at term (from 38th week of gestation).
This formulation replaces a product which released 5mg over 12 hours from a different 10mg vaginal delivery system. The new pessary formulation can remain in place for up to 24 hours where necessary and the cost per pessary is unchanged.

Tayside recommendation

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

Points for consideration:

- Dinoprostone pessary is an alternative to dinoprostone vaginal gel.
- **Locally, dinoprostone 10mg pessary (Propess®) is recommended for induction of labour in primigravida. Dinoprostone vaginal gel (Prostin E2®) remains the formulation of choice for paraous patient induction.**

Ertapenem (Invanz®) - intra-abdominal infections in children and adolescents

SMC recommendation
Advice: Following an abbreviated submission
Ertapenem is accepted for restricted use within NHS Scotland for the treatment of intra-abdominal infections in children and adolescents.
Ertapenem should only be used second line for the treatment of the community acquired intra-abdominal infections resistant to the current conventional treatments and under the advice of local microbiologists or specialists in infectious diseases.

Tayside recommendation

Pending antibiotic policy decision

Points for consideration:

- **The place of ertapenem in the local treatment of intra-abdominal infections in children and adolescents will be addressed by the Hospital Anti-Infectives Sub-Committee.**

Fondaparinux (Arixtra®) – VTE prophylaxis in high risk patients undergoing abdominal surgery

SMC recommendation
Advice: following a full submission
Fondaparinux (Arixtra®) is not recommended for use within NHS Scotland for the prevention of venous thromboembolic events (VTE) in patients undergoing abdominal surgery who are judged to be at high risk of thromboembolic complications, such as those undergoing abdominal cancer surgery.
Fondaparinux showed non-inferiority to one other low molecular weight heparin in preventing VTE in patients undergoing abdominal surgery. The economic case has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- The key study compared fondaparinux to dalteparin in patients undergoing abdominal surgery with at least one additional risk factor for thromboembolic complication.
- The incidence of major bleeding detected in the period between the first injection and two days after the last injection was higher with fondaparinux (3.4% versus 2.4% for dalteparin).
- Fondaparinux is more expensive than dalteparin. (Seven-day treatment cost of £47 versus £21).
- Dalteparin is the low molecular weight heparin of choice locally.
- Fondaparinux is not stocked by the hospital pharmacy.

Losartan 100mg/hydrochlorothiazide 25mg (Cozaar-Comp®) - hypertension

SMC recommendation

Advice: Following an abbreviated submission

Losartan 100mg/hydrochlorothiazide 25mg tablet (Cozaar-Comp 100/25®) is accepted for use within NHS Scotland for the treatment of essential hypertension in patients whose blood pressure is not adequately controlled on hydrochlorothiazide or losartan monotherapy.

No increased costs are associated with this product compared with losartan (Cozaar®) 100mg alone. Compared with a previously available combination product it reduces the tablet burden when higher doses of losartan and hydrochlorothiazide are required. This fixed dose combination is one of many options for the treatment of hypertension, including other less expensive angiotensin receptor blocker/diuretic combinations.

Tayside recommendation

Non-formulary

Points for consideration:

- Angiotensin receptor blockers (ARBs) are an alternative to angiotensin converting enzyme (ACE) inhibitors where the latter are not tolerated.
- 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 Tayside Area Prescribing Guide (TAPG).

Paricalcitol (Zemplar®) - secondary hyperparathyroidism

SMC recommendation

Advice: Following a full submission

Paricalcitol (Zemplar®) is not recommended for use within NHS Scotland for the prevention and treatment of secondary hyperparathyroidism in patients with chronic renal failure undergoing haemodialysis.

The benefits and adverse effects of paricalcitol are similar to another vitamin D analogue with which it has been compared. The economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Paricalcitol is a synthetic biologically active analogue of calcitriol (the active form of vitamin D3), which reduces serum concentrations of intact parathyroid hormone (iPTH). It is administered intravenously during haemodialysis.
- Paricalcitol shows similar efficacy to calcitriol in terms of reduction of iPTH, incidence of hypercalcaemia, and elevation of calcium phosphate product.
- There are no robust data to indicate that paricalcitol would be associated with improved survival or reductions in hospitalisations over calcitriol in practice. Data supporting use of paricalcitol in patients resistant to calcitriol are limited.
- There are no comparative data versus alfacalcidol which is the parenteral vitamin D formulation used locally in hyperparathyroidism secondary to renal disease.
- Paricalcitol is more expensive than IV alfacalcidol and calcitriol. (Treatment cost per dialysis session is around £12 for paricalcitol 5mcg versus £2 for IV alfacalcidol 1mcg and £5 for IV calcitriol 1mcg).
- Local guidelines for the management of bone metabolism and disease in chronic kidney disease are available on the Renal Service website.
- Paricalcitol is not stocked by the hospital pharmacy.

Pegaptanib (Macugen®) - neovascular (wet) age-related macular degeneration (AMD)

SMC recommendation

Advice: Following a full submission

Pegaptanib for intravitreal injection (Macugen®) is accepted for restricted use within NHS Scotland for the treatment of neovascular (wet) age-related macular degeneration (AMD).

It has been shown to reduce the rate of loss of visual acuity in patients with subfoveal neovascular AMD.

Pegaptanib should be restricted to patients with visual acuity between 6/12 to 6/60 (inclusive) and should be stopped if visual acuity falls below 6/60 during treatment of where severe visual loss is experienced.

The cost effectiveness of pegaptanib in patients who are also receiving photodynamic therapy has, however, not been demonstrated.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Pegaptanib is a selective vascular endothelial growth factor (VEGF) antagonist. VEGF is thought to contribute to the progression of the choroidal neovascular (CNV) form of AMD.
- Combined data from two randomised controlled trials in patients with subfoveal neovascular AMD (known together as the VISION study) show that one-year of treatment with pegaptanib 0.3mg was associated with significantly less loss of vision compared to control (sham injections). 70% of patients in the pegaptanib group had a loss of <15 letters on a visual acuity test versus 55% in the control group. On average, treatment benefit was maintained in patients re-randomised to continue pegaptanib for a further year. Sub-group analysis indicated that benefit was independent of angiographic subtype, lesion size or baseline visual acuity.
- There are no comparative data versus photodynamic therapy (PDT) with verteporfin which is currently recommended by NICE for use in the classic angiographic subtype of neovascular AMD.
- In the VISION study, 84% of patients in the pegaptanib 0.3mg group experienced an adverse event considered to be related to the procedure, these were serious in 3% of patients and included intra-ocular infection, traumatic cataract and retinal detachment.
- Pegaptanib is given by intravitreal injection every six weeks and costs £4,600 per patient per year.
- A local protocol for the use of pegaptanib has been developed by the Ophthalmology Clinic. **This recommends the use of pegaptanib in patients with the following subtypes of subfoveal choroidal neovascularisation (CNV) age-related macular degeneration (AMD):**
  - **occult CNV**
  - **minimally classic CNV**
  - **predominantly classic or classic CNV who have failed to respond to photodynamic therapy with verteporfin**

  Treatment is restricted to patients with visual acuity between 6/12 and 6/60.
- The Ophthalmology Team is currently addressing the funding of pegaptanib.
- A NICE multiple technology appraisal of pegaptanib, anecortave and ranizumab is expected in August 2007. Review of existing NICE guidance on PDT with verteporfin is due in September 2006.

Pregabalin (Lyrica®) - peripheral neuropathic pain

SMC recommendation

Advice: Following an Independent Review Panel Assessment

Pregabalin (Lyrica®) is not recommended for use within NHS Scotland for the treatment of peripheral neuropathic pain in adults.

Comparative clinical and cost effectiveness have not been demonstrated. Further controlled data are needed to establish its place in therapy in patients refractory to or intolerant of other pharmacological treatments.

Click here for SMC link

Tayside recommendation

Not recommended

Continued over

Pregabalin continued

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.49, March 2005 and No.53, September 2005 for previous SMC advice.
- There are no robust randomised controlled trials of pregabalin conducted in patients refractory to other treatments eg gabapentin.

Rivastigmine (Exelon®) - dementia in patients with Parkinson's disease

SMC recommendation

Advice: In the absence of a submission from the holder of the marketing authorisation Rivastigmine (Exelon®) is not recommended for use within NHS Scotland for the treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's 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 NHS Scotland.

Tayside recommendation

Not recommended

Points for consideration:

- Recent NICE guidance on the diagnosis and management of Parkinson's disease in primary and secondary care recommends further research to identify patients with PD dementia who will benefit from cholinesterase inhibitors.

Ropinirole (Adartrel®) - idiopathic restless legs syndrome (RLS)

SMC recommendation

Advice: Following a resubmission
Ropinirole (Adartrel®) is accepted for restricted use within NHS Scotland for the treatment of moderate to severe idiopathic restless legs syndrome (RLS). Its use should be restricted to patients with a baseline score of 24 points or more on the International Restless Legs Scale (IRLS).
Compared with placebo, ropinirole was associated with a 4-point improvement on the 40-point IRLS in a pooled analysis restricted to patients with IRLS score of 24 points.
Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of secondary care)

Points for consideration:

- Ropinirole is the second dopamine agonist to be licensed for the treatment of RLS. Refer to Tayside Prescriber; DTC Supplement No. 58, May 2006 for SMC and local advice on the use of pramipexole in this indication.
- Restless legs syndrome can be classified as idiopathic or may 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.
- Indirect comparative data indicate that treatment with pramipexole may be associated with greater improvement in RLS symptoms (ie a 4 to 9-point improvement in IRLS score versus placebo in patients with baseline IRLS ≥15) see Tayside Prescriber; DTC Supplement No. 58, May 2006.
- Symptom augmentation is the most serious adverse effect of dopaminergic therapy in RLS. Ropinirole 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.
- Ropinirole is a similar cost to pramipexole. (28 days treatment with ropinirole 2mg/day costs £32 versus £35 for pramipexole 0.36mg/day).

Continued over

Ropinirole continued

- Ropinirole is marketed under a different brand name for the treatment of Parkinson's disease (Requip®). Care should be taken to ensure that the correct product is prescribed and supplied.
- 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, ropinirole may be considered, under the direction of a secondary care physician, for the treatment of severe idiopathic RLS in patients with an IRLS score ≥ 24. Treatment should be used second-line to pramipexole in patients whose symptoms persist despite an adequate trial of non-pharmacological methods (see above).**

Rosiglitazone/metformin (Avandamet®) - triple therapy in type 2 diabetes

SMC recommendation

Advice: Following an abbreviated submission

Rosiglitazone/metformin tablet (Avandamet®) is accepted for restricted use within NHS Scotland in combination with a sulphonylurea as triple oral therapy in patients (particularly in overweight patients) who are unable to achieve sufficient glycaemic control despite dual oral therapy and where patients are unable or unwilling to take insulin.

Triple therapy should be initiated and monitored only by physicians experienced in the treatment of diabetes mellitus who will be able to identify and manage patients who might benefit.

The combination formulations are not associated with increased costs compared to equivalent combinations of single drug formulations.

Tayside recommendation

Recommended within formulary (prescribing note)

Points for consideration:

- Locally, rosiglitazone/metformin/sulphonylurea triple therapy should be initiated by the diabetes clinic or by GPs experienced in the treatment of diabetes.
- Local guidance on diabetes care is available in the Tayside Diabetes Handbook.

Rotigotine transdermal patch (Neupro®) - early-stage idiopathic Parkinson's disease (PD)

SMC recommendation

Advice: Following a full submission

Rotigotine (Neupro®) is not recommended for use within NHS Scotland for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease as monotherapy (i.e. without levodopa).

Rotigotine was superior to placebo in two randomised controlled trials. However, in one active comparator study non-inferiority to another non-ergolinic dopamine agonist comparator was not shown. The economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Rotigotine is a non-ergot-derived dopamine agonist that has been developed for once daily transdermal administration.
- A comparative study indicates that rotigotine is less effective at reducing PD symptoms than ropinirole. However, the dose of ropinirole used in this study was higher than usually seen in practice for the treatment of early-stage PD.
- As yet, there is no evidence to support the suggestion that 24 transdermal administration delays or minimises complications of dopamine receptor agonist treatment, including the development of motor fluctuations and dyskinesias.

Continued over

Rotigotine continued

- Unlike other dopamine agonists, rotigotine is not licensed as an adjunct to levodopa in more advanced PD.
- Refer to recent NICE guidance for further information on the diagnosis and management of PD in primary and secondary care.
- Rotigotine patches are not stocked by the hospital pharmacy.

Salmeterol 25mcg inhaler (Serevent Evohaler®) – reversible airways obstruction

SMC recommendation

Advice: Following an abbreviated submission

Salmeterol 25 micrograms inhaler (Serevent Evohaler®) is accepted for use in NHS Scotland for the regular symptomatic treatment of reversible airways obstruction in patients with asthma, including those with nocturnal asthma or chronic obstructive pulmonary disease. It may also be used for the prevention of exercise-induced asthma.

Where the use of this long-acting beta agonist by aerosol inhalation is appropriate, it offers a chlorofluorocarbon (CFC)-free option at no additional cost.

Tayside recommendation

Recommended within formulary

- Serevent® CFC inhaler has been discontinued.
- Salmeterol 50mcg (two puffs) via the Evohaler® is the same cost as 50mcg (one blister) delivered by the Accuhaler®.
- Whilst the patent for Serevent® inhaler has expired, no generic versions are available.

Testosterone injection (Nebido®) - hypogonadism

SMC recommendation

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

Testosterone (Nebido®) 1000mg/4ml solution for injection is not recommended for use within NHS Scotland for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests.

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 NHS Scotland.

Tayside recommendation

Not recommended

Points for consideration:

- Nebido® injection is not stocked by the hospital pharmacy.

Testosterone 50mg/5g gel (Testim®) - hypogonadism

SMC recommendation

Advice: Following an abbreviated submission

Testosterone gel (Testim®) is accepted for restricted use within NHS Scotland as replacement therapy for adult male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests.

It is an alternative to another formulation of testosterone gel, of the same strength and cost, and is restricted to use as an alternative to testosterone gel patches for those patients requiring a transdermal delivery system. Testosterone is at least as effective as testosterone patches and costs less.

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of the endocrine clinic)

Points for consideration:

- Testim® is an alternative to the Testogel® brand of testosterone 50mg/5g gel.

Tigecycline (Tygacil®) - complicated skin and soft-tissue infections

SMC recommendation

Advice: Following a full submission

Tigecycline (Tygacil®) is accepted for restricted use within NHS Scotland for the treatment of complicated skin and soft-tissue infections.

Tigecycline is associated with clinical cure rates in patients with complicated skin and skin structure infections non-inferior to those with a combination of a glycopeptide and a monocyclic beta-lactam antibiotic. It is restricted to use as a 2nd or 3rd line agent under the advice of local microbiologists or specialists in infectious diseases.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Tigecycline is a glycylcycline antibiotic ie a tetracycline that has been structurally modified to protect against some bacterial mechanisms of tetracycline resistance. It has a broad spectrum of activity against gram-positive and gram-negative organisms, including gram-positive resistant isolates eg methicillin-resistant *Staphylococcus aureus* (MRSA).
- The pivotal trials compared tigecycline to vancomycin followed by aztreonam in adults with complicated skin and and skin structure infections (cSSSIs). The majority of the patients received treatment first-line and many had pathogens sensitive to other antibiotics. In the small number of patients with MRSA infection, similar bacterial eradication rates were shown in both treatment groups.
- There are no data comparing tigecycline to standard early empiric treatment of cSSSI eg flucloxacillin plus benzylpenicillin.
- **Locally, tigecycline is restricted to use as a second or third-line agent in patients with complicated skin and soft-tissue infection refractory to, or intolerant of, other usual agents. Prior approval of an Infectious Diseases Physician or a Medical Microbiologist is required and treatment must be under the direction of this specialist.**
- Further advice on the management of complicated skin and soft tissue infection is available in the Hospital Anti-infectives Policy within the Tayside Area Prescribing Guide (TAPG).

Tigecycline (Tygacil®) - complicated intra-abdominal infection (cIAI)

SMC recommendation

Advice: Following a full submission

Tigecycline (Tygacil®) is accepted for restricted use within NHS Scotland for the treatment of complicated intra-abdominal infection.

Tigecycline is associated with clinical cure rates in patients with complicated intra-abdominal infections non-inferior to those with a broad-spectrum beta-lactam antibiotic. It is restricted to 2nd line use under the advice of local microbiologists or specialists in infectious disease.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- See above
- The pivotal trials compared tigecycline to imipenem/cilastatin (Primaxin®) in adults with cIAI. The majority of patients received treatment first-line and many had pathogens sensitive to other antibiotics. In the small number of patients with MRSA and extended spectrum β-lactamases (ESBL) producing bacteria, tigecycline was associated with eradication rates of 75% and 80% respectively.
- There are no data comparing tigecycline to local early empiric treatment of cIAI eg co-amoxiclav plus gentamicin.

Continued over

Tigecycline – cIAI continued

- **Locally, tigecycline may be considered for use in patients with complicated intra-abdominal infection refractory to, or intolerant of, other usual agents (ie co-amoxiclav plus gentamicin, piperacillin/tazobactam, or meropenem), or where these agents are not appropriate. Prior approval of an Infectious Diseases Physician or a Medical Microbiologist is required and treatment must be under the direction of this specialist.**
- Further advice on the management of complicated intra-abdominal infection is available in the Hospital Anti-infectives Policy within the Tayside Area Prescribing Guide (TAPG).

Trastuzumab (Herceptin®) - HER2 positive early breast cancer

SMC recommendation

Advice: following a full submission

Trastuzumab (Herceptin®) is accepted for restricted use within NHS Scotland for the treatment of patients with HER2 positive early breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy (if applicable).

In the pivotal trial, the addition of one year of 3-weekly trastuzumab after adjuvant chemotherapy significantly increased disease-free survival compared with that in the observation group. The trial excluded patients with a range of cardiovascular conditions and trastuzumab treatment for early breast cancer is not recommended in such patients. In patients treated with trastuzumab for early breast cancer, monitoring of cardiac function is required before treatment, every three months during treatment and for up to two years after treatment has stopped.

Trastuzumab in this indication is restricted to use by breast cancer specialists.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Trastuzumab is a monoclonal antibody against the human epidermal growth factor receptor 2 (HER2) antigen which is expressed on tumour cells in about 25% of patients with early breast cancer and is associated with a poorer prognosis.
- Trastuzumab is also licensed, and recommended by SIGN and NICE, for use in advanced breast cancer in HER2 positive women.
- The evidence to support the use of trastuzumab in early breast cancer is based on an interim analysis of the Herceptin Adjuvant (HERA) study at median follow-up of one year. This analysis showed that trastuzumab, given following standard adjuvant chemotherapy, halved the relative risk of breast cancer recurrence compared to adjuvant chemotherapy alone, and corresponded to significantly increased disease-free survival, from 77.4% to 85.8%, at 2 years ie an absolute benefit of 8.4%. Overall survival was higher in the trastuzumab arm, but not significantly so at the time of the analysis.
- Sub-group analysis indicated that the relative benefit of trastuzumab appeared to be independent of patient age, nodal involvement, hormone receptor status or type of adjuvant chemotherapy used.
- Cardiotoxicity is the key safety concern with trastuzumab. In the HERA study, the incidence of symptomatic congestive heart failure was low due to the relatively young age of the population (median age 49 years) and strict cardiac exclusion criteria and monitoring. If this isn't applied in practice, use of trastuzumab may result in higher incidence of heart failure. Longer-term data on safety is essential to determine the cumulative risk of cardiac side-effects. The SPC recommends baseline cardiac assessment prior to the use of trastuzumab including history and physical examination, ECG, echocardiogram, and/or MUGA scan. Cardiac function should be further monitored during treatment eg every 3 months.
- The cost of trastuzumab is around £22,400 per patient per year course. There are also additional service costs associated with administration of a three-weekly infusion and cardiac monitoring.
- **Locally, trastuzumab, for the treatment of women with HER2 positive early breast cancer, is recommended for use in accordance with Scottish Breast Cancer Network Guidance. The local breast cancer protocol will be updated shortly.**
- Refer to SIGN 84 "Management of breast cancer in women" for further guidance on the treatment of breast cancer.

Travoprost/timolol eye drops (Duotrav®) – glaucoma, ocular hypertension

SMC recommendation
Advice: Following an abbreviated submission
Travoprost/timolol (Duotrav®) eye drops are accepted for use in NHS Scotland for whom this is an appropriate combination of agents. They decrease intra-ocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues alone.
There is no significant additional cost associated with the combination product compared with the individual components and it allows patients to administer fewer drops.

Tayside recommendation

Non-formulary

Points for consideration:

- Duotrav® is a fixed combination of travoprost 0.004% and timolol 0.5%. Lack of flexibility in dose adjustment of individual constituents may limit use.

Docetaxel Update (metastatic hormone refractory prostate cancer)

NICE has recently published a multiple technology appraisal on the use of docetaxel for the treatment of metastatic hormone-refractory prostate cancer (mHRPC). This advice supersedes previous SMC advice issued in October 2005 (refer to Tayside Prescriber; DTC Supplement No. 54, Nov 2005) and recommends docetaxel as a treatment option for men with mHRPC and a Karnofsky performance-status score of 60% or more.

Tayside recommendation
Pending OHMMG approval of local prostate cancer protocol

- The place of docetaxel in the treatment of advanced prostate cancer, and in relation to mitoxantrone chemotherapy, will be addressed by the oncology team in a local prostate cancer protocol.

Posaconazole Update

The June 2006 SMC advice for the use of posaconazole in specific invasive fungal infections was deferred to the Hospital Anti-Infectives Committee. See below for final decision:

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

- Posaconazole may be considered for use in patients with specific fungal invasive fungal infections refractory to, or intolerant of, caspofungin or voriconazole, or where these agents are inappropriate. Prior approval of an Infectious Diseases Physician or a Medical Microbiologist is required and treatment must be under the direction of this specialist.

NICE/BTS Hypertension Guideline

Updated guidance on the treatment of hypertension in adults in primary care has recently been issued by NICE. Recommendations on drug treatment will be incorporated into TAPG advice on the management of hypertension in Autumn 2006.

TAPG Pocket Guide

A printed pocket guide including the names of medicines recommended within the TAPG will be distributed shortly. The pocket guide can also be downloaded from the DTC website (click here). This summary guide will be updated on an annual basis. The most up to date version of the TAPG is currently maintained in electronic pdf files and can be accessed via the NHS Tayside Intranet homepage (see page 14 of this bulletin) or via the DTC website (www.nhstaysideadtc.scot.nhs.uk).

TAPG Update

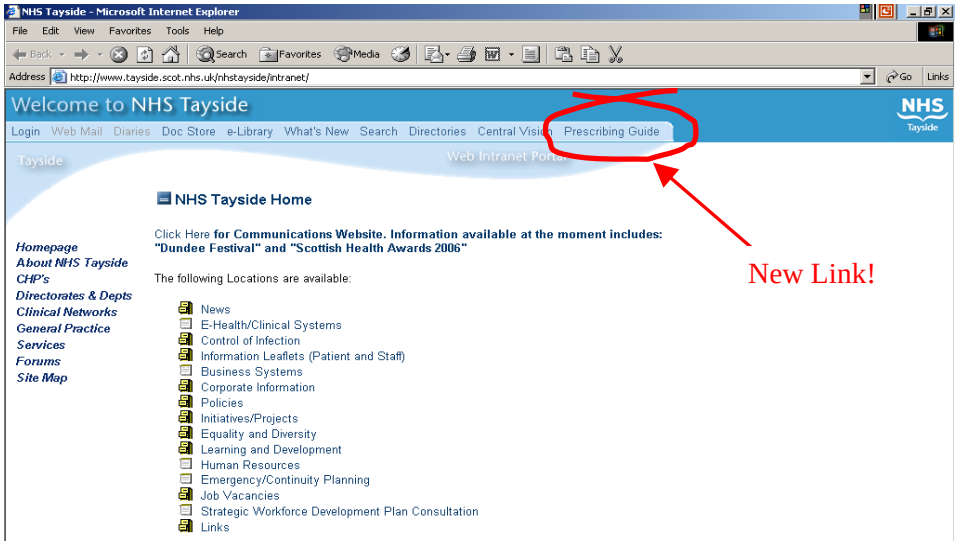
Below are the main changes to the TAPG agreed by the Medicines Advisory Group in July 2006. Updated sections in A5 format are available on the TAPG pages of the DTC intranet site. An updated GPASS-TADF fly file for use in general practice is also available.

	TAPG section	Drug(s) / topic	Changes
1.3	**Ulcer healing drugs**	PPIs	Lansoprazole now first-choice PPI. Lansoprazole also replaces omeprazole in suggested *H. Pylori* eradication regimens. Lansoprazole orodispersible tablets* and omeprazole tablets have been removed from the Formulary.
1	**Upper GI guidelines**	*H. Pylori*	Eradication regimens amended as above.
3.2	**Inhaled corticosteroids**	Beclometasone	Clenil Modulite® CFC-free inhaler* added as an option
4.3	**Antidepressant drugs**	Venlafaxine	Specialist supervision now only required for doses of 300mg or more.
5	**Adult antibiotic policy**		
	ALERT antibiotics	Meropenem Temocillin Daptomycin*	Meropenem 6 hourly local dosing recommendation removed. Revert to licensed 8 hourly dosing Temocillin and daptomycin added to ALERT antibiotics
	Bacterial, fungal and viral infections	Peritonitis and diverticulitis	Peritonitis / diverticulitis treatment changed from IV cefuroxime + metronidazole to IV co-amoxiclav
		Post-op wound infection in abdominal and female genital tract surgery	IV cefuroxime + metronidazole changed to IV co-amoxiclav
	Antibiotic prophylaxis	Endocarditis prophylaxis	Policy changed to be in-line with recently published national advice
	Antibiotic policies	Sepsis management protocol	Ceftriaxone dose changed to 2g BD, IV cefuroxime + metronidazole changed to IV co-amoxiclav in two places
		Gynae surgery prophylaxis	Policy revised to be in-line with policy on NHS Tayside intranet
		Various	New policies added on cellulitis management, penicillin hypersensitivity, oncology sepsis, IV to oral switching (IVOST), and clinical pharmacist direct referral.
	Primary Care Anti-Infective Advisory Notes		
	Skin infections	Cellulitis	Erythromycin and clarithromycin added as alternatives to clindamycin in penicillin-sensitive patients
		Shingles	Oral aciclovir added as an option (as well as valaciclovir or famciclovir)
13	**Dermatology Guidance Notes**	Psoriasis	Management of psoriasis guidance note updated to include Dovobet* ointment.

* SMC accepted medicine

Additional TAPG Access via Homepage

The TAPG can now also be accessed from the menu bar at the top of the NHS Tayside Intranet homepage as shown below:



Forthcoming SMC Advice

Gastro-intestinal system
Beclometasone dipropionate 5mg (Clipper®)
Mesalazine (Asacol®)
Cardiovascular system
Ivabradine (Procoralan®)
Nebivolol (Nebilet®)
Lercanidipine (Zanidip®)
Perindopril (Coversyl®)
Respiratory
Budesonide (Novolizer Budesonide®)
Central nervous system
Co-careldopa (Duodopa®)
Donepezil orodispersible tablets (Aricept Evess®)
Duloxetine (Cymbalta®)
Levetiracetam formulation (Keppra®)
Topiramate (Topamax®)
Zonisamide (Zonegran®)
Infections
Entecavir (Baraclude®)
Tipranavir (Aptivus®)
Tobramycin (Bramitob®)
Endocrine system
Choriogonadotropin alfa (Ovitrelle®)
Ibandronic acid (Bonviva®)
Inhaled insulin (Exubera®)

Endocrine system (contd)
Pioglitazone/metformin (Competact®) - ***Abbreviated***
Triptorelin (Decapeptyl®)
Zoledronic acid (Aclasta®)
Malignant disease & immunosuppression
Anastrozole (Armidex®)
Aranesp (Darbepoetin alfa®)
Bortezomib (Velcade®)
Clofarabine (Evoltra®)
Fludarabine (Fludara® Oral)
Lanreotide (Somatuline® LA)
Mitotane (Lysodren®)
Rituximab (Mabthera®)
Sorafenib (Nexavar®)
Sunitinib (Sutent®)
Temozolomide (Temodal®)
Nutrition & Blood
Carglumic acid (Carbaglu®)
Lanthanum carbonate (Fosrenol®)
Musculoskeletal and joint diseases
Adalimumab (Humira®)
Etoricoxib (Arcoxia®) - ***Abbreviated***
Etanercept (Enbrel®) (AS) - ***Abbreviated***
Eye
Bimatoprost 0.03% timolol (Ganfort®)
Skin
Infliximab (Remicade®)

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