TAYSIDE PRESCRIBER

Tayside DTC Supplement No. 49

Mar 2005

Produced by NHS Tayside Drug and Therapeutics Committee, Medicines Advisory Group

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NHS Tayside Drug and Therapeutics Committee Sub-Group Restructuring

The NHS Tayside Drug and Therapeutics Committee (DTC) advises NHS Tayside on all matters affecting the policy, effectiveness, safety and economy in the use of medicines. Consultant Physician, Professor Dilip Nathwani has recently been appointed as Chair of the DTC. The membership continues to represent NHS Tayside, Clinical Directorates and LHCCs.
From January 2005, all operational aspects of the Committee's work are delivered by three sub-groups, as follows:

- **Medicines Advisory Group (MAG)** – responsible for the delivery of advice to support practitioners to achieve effectiveness, safety and economy in the use of medicines, through:
  - update of the Tayside Area Prescribing Guide (core formulary and guidance notes)
  - development of a browsable web-based electronic formulary
  - facilitation of implementation of advice received from the Scottish Medicines Consortium (SMC)
  - dissemination of formulary and new medicines advice via the DTC website, prescribing bulletins and educational meetings

  The MAG replaces the previous Formulary Sub-Committee and New Medicines Implementation Panel (NMIP) and will work closely with the existing ASD Anti-Infectives Group and Mental Health Prescribing Group.

- **Quality Improvement Group (QIG)** – responsible for promoting education, audit and research on the effective, safe and efficient delivery of effective medicines, through:
  - evaluation of patterns of medicines utilisation in Tayside in relation to advice from the DTC, the medicines management strategy, the medication and patient journey initiative, and feed back information to clinical groups
  - monitoring and initiating root cause analysis of reports of adverse events arising from the use of medicines
  - promotion of audit into the use of medicines
  - promotion of rigorous evaluation of interventions to improve the use of medicines
  - promotion of an educational programme focused on the implementation of DTC advice/policy
- **Medicines Policy Group (MPG)** – responsible for the delivery of policies in relation to the management of medicines in response to either national or local demand, including:
  - the safe and secure handling of medicines
  - patient group directions
  - systems for the prescribing and recording of administration of medicines
  - reporting and monitoring of adverse drug reactions
  - prescribing systems to support multidisciplinary prescribers

Final consultation and approval of the work of all sub-groups is the responsibility of the main Committee.

Information on the membership of the DTC and its sub-groups is available on the DTC intranet site. Further detail on the new DTC structure is available in the paper "NHS Tayside Drug & Therapeutics Committee – a way forward" June 2004.

SMC Advice Issued in March 2005

The SMC Detailed Advice Document (DAD) following full submissions is now available on the SMC website under Medicines. The DAD contains summarised information relating to efficacy, safety, effectiveness and cost-effectiveness.

Atomoxetine capsules (Strattera®) – attention-deficit/hyperactivity disorder (ADHD)

SMC recommendation

Advice: following a full submission

Atomoxetine (Strattera®) is not recommended for use within NHS Scotland for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children of 6 years and older or in adolescents. This advice concerns use in children and adolescents only and does not cover use in adults.

Atomoxetine is no more effective than a stimulant preparation against which it has been assessed. Tolerability was similar, though with some differences in the individual adverse events reported. Unlike the available stimulant preparations, it is not a Controlled Drug under the Misuse of Drugs Regulations 2001 and there is evidence that it lacks abuse potential. However, the economic case has not been demonstrated. The licence holder has indicated their decision to resubmit.

Click here for SMC link.

Tayside recommendation

Not recommended

Points for consideration:

- Atomoxetine is an oral once-daily selective noradrenaline reuptake inhibitor. Unlike existing ADHD therapies, atomoxetine is non-stimulant.
- Atomoxetine shows similar improvements in ADHD rating scales as methylphenidate in short-term (10-week) comparative studies. Results indicate that atomoxetine is no more effective than methylphenidate.
- No long-term efficacy and safety data comparing atomoxetine to methylphenidate are available.
- The CSM recently issued a warning informing of the risk of hepatic disorders associated with atomoxetine. The risk is rare (fewer than 1 per 50,000 patients treated) but in a small proportion of patients the reaction has been severe and resulted in liver damage and/or liver failure.
- Atomoxetine is considerably more expensive than methylphenidate preparations. (28 days treatment

Continued over

Atomoxetine continued

with atomoxetine 10mg-60mg daily costs £55 versus £16 for methylphenidate 30mg daily and £34 for methylphenatate MR (Concerta®) 36mg daily.

- Updated NICE guidance on ADHD, to include atomoxetine and dexamfetamine, is due for issue in August 2005.
- Atomoxetine is not stocked by the hospital pharmacy.

Bivalirudin (Angiox®) – anticoagulant in percutaneous coronary intervention (PCI)

SMC recommendation

Advice: accepted for restricted use

Bivalirudin (Angiox®) is accepted for restricted use within NHS Scotland as an anticoagulant in patients undergoing percutaneous coronary intervention (PCI), including percutaneous transluminal coronary angioplasty (PTCA) procedures like angioplasty and balloon angioplasty and PTCA with stenting.

It is restricted to patients who would have been considered for treatment with unfractionated heparin in combination with a glycoprotein llb/llla antagonist. In these patients bivalirudin monotherapy may be a suitable alternative. It should not be used as an alternative to unfractionated heparin alone.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Bivalirudin is a short-acting thrombin-specific anticoagulant.
- PCI is not currently undertaken in Tayside.
- Bivalirudin is not currently stocked by the hospital pharmacy

Cetuximab (Erbitux®) – metastatic colorectal cancer in combination with irinotecan

SMC recommendation

Advice: following a full submission

Cetuximab (Erbitux®) is not recommended for use within NHS Scotland in combination with irinotecan for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing metastatic colorectal cancer after failure of irinotecan-including cytotoxic therapy.

The cost effectiveness has not been demonstrated.

The licence holder has requested that this decision is referred to an independent review panel.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Cetuximab is a human/mouse chimeric monoclonal antibody that binds selectively to EGFR. EGFR is a transmembrane receptor which is over-expressed by various tumour cells, including 25-80% of colorectal cancers and has been linked to advanced disease.
- Locally, capecitabine or fluorouracil (5FU) plus folinic acid (de Gramont regimen) are considered as fourth-line options for the treatment of metastatic colorectal cancer following failure of irinotecan therapy if it is felt there may still be 5FU sensitivity.
- Cetuximab is not stocked by the hospital pharmacy.

Gemcitabine (Gemzar®) – metastatic breast cancer in combination with paclitaxel

SMC recommendation

Advice: following a full submission

Gemcitabine (Gemzar®) in combination with paclitaxel is not recommended for use within NHS Scotland for the treatment of patients with metastatic breast cancer who have relapsed following adjuvant/ neoadjuvant chemotherapy.

Continued over

Gemcitabine continued
Gemcitabine in combination with paclitaxel has improved outcomes, compared to paclitaxel monotherapy, in those previously treated with an anthracycline. However the economic case has not been demonstrated. The licence holder has indicated their decision to resubmit.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Locally, docetaxel is recommended for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including an anthracyline) has failed or is inappropriate.

Letrozole 2.5mg tablets (Femara®) – invasive early breast cancer

SMC recommendation
Advice: following a full submission
Letrozole (Femara®) is accepted for use within NHS Scotland for the treatment of invasive early breast cancer in postmenopausal women who have received prior standard adjuvant tamoxifen therapy. Treatment should continue for 3 years or until tumour relapse, whichever occurs first.
Following 5 years of adjuvant tamoxifen therapy the risk of recurrence (in ipsilateral breast, new tumour in contralateral breast or distance metastases) occurs at an aggregate rate of 2-3% per year. The use of letrozole as extended adjuvant treatment resulted in a 43% lower risk of recurrence compared with placebo. However, a significant difference for overall survival, defined as time to death from any cause, was seen in lymph-node positive patients only. Clinicians and patients should consider the residual risk of recurrent, individual preferences and the risks and benefits of treatment.
Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of an oncologist)

Points for consideration:

- The clinical trial supporting the use of letrozole for this new indication was originally planned to follow patients up for five years, but was terminated after the first interim analysis at 2.4 years when women who were on placebo were offered letrozole.
- At the interim analysis, 2.9% women in the letrozole group and 5.1% in the placebo group had a recurrence, this means that for every 45 patients treated for 2.4 years with letrozole instead of placebo one less will have a recurrence of the primary disease (in breast, chest wall, or nodal or metastatic sites) or the development of a new primary breast cancer in the contralateral breast.
- The clinical study recruited women who discontinued tamoxifen therapy less than three months before commencing letrozole. Therefore the efficacy of letrozole in women who discontinued tamoxifen therapy more than three months earlier has not been assessed.
- In the absence of long-term efficacy data, the optimal duration of letrozole therapy has not yet been established.
- The long-term effects of letrozole on serum lipid levels and bone resorption have not been evaluated. Clinical studies report higher incidence of new onset osteoporosis and greater reduction in hip bone mineral density in patients receiving letrozole. The SPC recommends that following standard adjuvant tamoxifen therapy, 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 or prophylaxis for osteoporosis should be initiated as appropriate and carefully monitored.
- The Oncology and Medicine & Cardiovascular Groups are currently addressing the funding of bone densitometry associated with the use of letrozole. Prescribing should not take place until funding is approved.
- **Letrozole is recommended locally as extended adjuvant treatment in women at continued risk of breast cancer relapse who have received prior standard adjuvant tamoxifen therapy (discontinued within the last year). Treatment should be under the direction of an oncologist and following full consideration of the risks and benefits of treatment.**

Metformin prolonged release (Glucophage SR®) – type 2 diabetes mellitus

SMC recommendation
Advice: following a full submission
Metformin (Glucophage SR®) is not recommended for use within NHS Scotland for the treatment of type 2 diabetes mellitus in adults, particularly in overweight patients, when dietary management and exercise alone do not result in adequate glycaemic control.
Metformin (Glucophage SR®) did not demonstrate any benefits in efficacy or side effect profile over the immediate release metformin and is considerably more expensive.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Metformin prolonged release shows similar glycaemic control, as measured by HbA_{1c}, as standard (immediate release) metformin.
- Prospective comparative data show no differences in gastro-intestinal tolerability and frequency of diarrhoea between prolonged release and standard formulations.
- Statistically significant increases in triglyceride levels have been reported in patients receiving the prolonged release formulation.
- Metformin prolonged release is considerably more expensive than the standard preparation. (28 days treatment with Glucophage SR® 2g once daily costs £11 versus £3 for generic metformin 1g twice daily.)
- Metformin prolonged release (Glucophage SR®) is not stocked by the hospital pharmacy.

Pregabalin (Lyrica®) – peripheral neuropathic pain in adults

SMC recommendation
Advice: following a full submission
Pregabalin (Lyrica®) is not recommended for use within NHS Scotland for the treatment of peripheral neuropathic pain in adults.
The comparative clinical and cost effectiveness have not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Pregabalin is an $alpha_2$-delta ligand that has analgesic, anxiolytic and anticonvulsant activity. It has a similar mode of action to gabapentin.
- Short-term placebo-controlled studies (8-12 weeks duration) show reduced weekly pain scores in patients with diabetic neuropathy and postherpetic neuralgia who receive pregabalin.
- Data on long-term efficacy of pregabalin in the treatment of neuropathic pain are limited and comparative data versus other established therapies for neuropathic pain (amitriptyline, carbamazepine, gabapentin) are lacking.
- The majority of trials exclude patients who had failed to respond to previous treatment with gabapentin at daily doses above 1200mg. Efficacy of pregabalin in patients unresponsive to gabapentin is therefore unclear.
- Pregabalin has a flat pricing structure for any strength of capsule. 28 days of pregabalin 100mg or 200mg three times daily costs £97 compared to £4 for amitriptyline 150mg daily, £5 for carbamazepine 200mg three times daily and £89 for gabapentin 600mg three times daily. The cost of gabapentin may fall following recent availability as a generic.
- SIGN 2001 and NICE 2004 Guidance on the management of diabetes recommend use of tricyclic antidepressants in the treatment of painful diabetic neuropathy followed by a trial of gabapentin second-line. This approach is supported in local advice on the management of neuropathic pain within the Pain Guidance Notes in the Tayside Area Prescribing Guide (TAPG).

TAPG Update

Below are changes to the TAPG agreed by the Medicines Advisory Group and approved by the Drug and Therapeutics Committee in March 2005. Updated sections are available on the TAPG pages of the DTC intranet site – these can be printed off to replace the old sections in the hard copy ring binder. Where possible and appropriate, first-line drug choices are clearly indicated in reviewed sections. An updated GPASS-TADF fly file is also available for use in general practice.

	TAPG section	Drug(s)	Changes
3	Respiratory (intro)	-	Links to BTS/SIGN asthma guidance and NICE COPD guidance. General statement added about inhaler therapy and combination products
3.1	Bronchodilators	Salbutamol	Highlighted as first choice short-acting beta-2 agonist
		Ipratropium	Dosage clarified
		Theophylline (Uniphyllin®)	Upper dose limit made in line with BNF/SPC. Statement about blood level monitoring not being routinely needed except in specific circumstances
		Combivent®	Wording changed to reflect BNF advice. Note to avoid co-prescription with tiotropium
3.2	Inhaled steroids	-	Statement added that all single agent inhaled steroids not being licensed for COPD (readers referred to COPD guidance for use of inhaled steroids in COPD)
		Beclometasone	Indicated as first choice inhaled steroid
		Seretide® / Symbicort®	Given main entries but reference to use in COPD deleted (readers referred to COPD guidance for use of inhaled steroids in COPD)
3.3	Leukotriene receptor antagonists	Montelukast	Granules formulation added. Paediatric dose now starts from 6 months
3.4	Antihistamines	Fexofenadine	Paediatric doses included, 30mg tablets added
3.6	Oxygen	Oxygen	Prescribers advised to specify mask percentage and flow rates. 8 hours/day changed to 15 hours/day therapy for LTOT. Portable oxygen cylinder size defined
3.7	Mucolytics	-	NICE guidance statement on mucolytics in COPD added
	COPD Guidelines (p3-14)		NICE definition of frequent exacerbations for use of inhaled steroids in COPD added
			NICE guidance statement on mucolytics in COPD added
6.1	Diabetes	Avandamet®* (metformin / rosiglitazone	Added for type 2 diabetes; may be prescribed for those patients already receiving rosiglitazone and metformin separately and for whom a combination product would be preferable

* SMC accepted medicine

MAG Categorisation of SMC Advice

MAG will continue to categorise SMC accepted medicines into one of four local recommendations as follows:

Formulary
Non-formulary
Specialist Treatment Pathway*
Not recommended

*medicines recommended within a Specialist Treatment Pathway require involvement of a specialist in the decision to prescribe. This category of local recommendation includes both medicines that may be prescribed in general practice under the direction of a specialist, and medicines that should be prescribed exclusively by secondary care ie hospital only medicines. Where prescribing is restricted to hospital this will be clearly stated. A formal algorithm describing the disease management process may not necessarily be available.

TAPG Review Programme 2005

Update of the Tayside Area Prescribing Guide will take place according to a set review programme as described below. MAG will work with the Lead Clinicians of relevant Managed Clinical Networks and other specialists to ensure that advice included within the various sections of the TAPG reflects agreed local evidence-based practice. Revised advice will be issued following the DTC meeting indicated.

MAG Meeting	DTC Meeting	TAPG Section/Guidance
17 February 2005	21 March 2005	Section 3 Respiratory System Respiratory Guidance Notes
17 March 2005	16 May 2005	Section 2 Cardiovascular System I Cardiovascular Guidance Notes I
21 April 2005	16 May 2005	Section 2 Cardiovascular System II Cardiovascular Guidance Notes II
19 May 2005	18 July 2005	Section 1 Gastro-intestinal System Upper Gastro-intestinal Guidelines
23 June 2005	18 July 2005	Section 4 Central Nervous System Psychiatric Guidance Notes Pain Guidance Notes Smoking Cessation Guidance Note 3 Oxygen Therapy in Acute Management Note 4 Drug Therapy in relation to Anaesthesia
18 August 2005	19 September 2005	Section 5 Anti-infectives ASD Adult Antibiotic Policy ASD Paediatric Antibiotic Policy PCD Anti-infective Advisory Notes
22 September 2005	21 November 2005	Section 13 Skin Dermatology Guidance Notes
20 October 2005	21 November 2005	Section 11 Eye Section 12 ENT Note 1 Paediatric Prescribing Note 2 Therapeutic Drug Monitoring
17 November 2005		Section 6 Endocrine System Guidance on HRT Product Selection Section 7 Obstetrics, Gynaecology and Urinary Tract Disorders Note 5 Management of Diabetic Patients Undergoing Surgical Procedures
22 December 2005		Section 8 Malignant Disease and Immunosuppression Section 9 Nutrition and Blood Section 10 Musculoskeletal and Joint Diseases Osteoarthritis Treatment Algorithm

Development of Local New Medicine Treatment Protocols

A template and guidance has been developed by MAG to assist specialist teams in drawing up Local New Medicine Treatment Protocols to define patient selection criteria, prescriber details and monitoring requirements in relation to the prescribing of new medicines. Local Treatment Protocols are required for new medicines that are categorised as appropriate for use within Specialist Treatment Pathways (see above) and where the introduction of the new medicine is associated with high clinical or financial risk. MAG will inform specialists if a protocol is needed. The template and guidance is available under New Medicine Processes on the DTC intranet site.

Updated Teriparatide Protocol

The local protocol for the use of teriparatide has been updated following the issue of the NICE guidance "Bisphosphonates, selective oestrogen receptor modulators and parathyroid hormone for the secondary prevention of osteoporotic fragility fractures in postmenopausal women". The updated protocol is available under Local New Medicine Treatment Protocols on the DTC intranet site.

Ibandronic Acid Update

Further to a review of bisphosphonates used in metastatic bone disease associated with breast cancer, the Tayside recommendation for the use of ibandronic acid has been updated as follows:

Tayside recommendation
Recommended within specialist treatment pathway (GPs may prescribe under the direction of an oncologist)

- **Oral ibandronic acid is recommended as an alternative to existing bisphosphonates used for the prophylaxis of skeletal events in patients with breast cancer and bone metastases. Treatment should be under the direction of an oncologist who should undertake regular patient review.**

Forthcoming SMC Advice

Gastro-intestinal system
Beclometasone Dipropionate 5mg (Clipper®)
Cardiovascular system
Perindopril (Coversyl®)
Candesartan (Amias®)
Valsartan (Diovan®)
Eplerenone (Inspra®) – ***Re-submission***
TachoSil®
Ezetimibe/Simvastatin (INEGY®)
Respiratory
Ciclesonide (Alvesco®)
Montelukast (Singulair®)
Beclometasone (Clemil Modulite)
Central nervous system
Atomoxetine (Strattera®) – ***Re-submission***
Methylphenidate (Equasym XL®)
Buprenorphine patch (Transtec®)
Tramadol (Tramacet®)
Galantamine (Reminyl XL®)
Ropinirole (Adartrel®)
Modafinil (Provigil®) – ***Re-submission***
Rivastigmine (Exelon®)
Aripiprazole (Ablify®)
Infections
Tenofovir-emtricitabine (Truvada®)
Lamivudine OD (Epivir®) & Abacavir OD (Kivexa®)
Fosamprenavir (Telzir®)
Abacavir (Ziagen®)
Abacavir-lamivudine (Kivexa®)
Adefovir dipivoxil (Hepsera®) – ***Re-submission***
Endocrine system
Pegvisomant (Somavert®)
Triptorelin (Gonapeptyl® Depot)

Endocrine system cont.
Strontium ranelate (Protelos®)
Somatropin (Norditropin SimpleXx®)
Insulin detemir (Levemir®)
Rosiglitazone maleate (Avandia®)
Obstetrics, gynae and urinary-tract disorders
Tamsulosin hydrochloride (Flomaxtra®)
Malignant disease & immunosuppression
Ibritumomab (Zevalin®)
Cytarabine liposomal (DepoCyte®)
Gliadel wafer
Docetaxel (Taxotere®)
Darbepoetin alfa (Aranesp®)
Oxaliplatin (Eloxatine®)
Imiquimod 5% Cream (Aldara®)
Vinorelbine oral (Navelbine® Oral)
Fludarabine (Fludara® Oral)
Pegylated interferon alpha 2b (Pegasys®)
Erlotinib (Tarceva®)
Capecitabine (Xeloda®)
Bevacizumab (Avastatin®)
Nutrition & Blood
Aranesp (Darbepoetin alfa®)
Lanthanum carbonate (Fosrenol®)
Cinacalcet (Mimpara®)
Anagrelide hydrochloride (Xagrid®)
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Diclofenac (Voltarol® Gel Patches 1%)
Skin
Eflornithine 11.5% Cream (Vaniqa®)

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