TAYSIDE PRESCRIBER

Tayside DTC Supplement No. 50

May 2005

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

In this issue:

SMC Advice Issued in May 2005

Abacavir (Ziagen®) – HIV

SMC recommendation

Advice: following an abbreviated submission

Abacavir tablets 300mg are accepted for use in a once-daily dosing regimen in NHS Scotland for the treatment of Human Immunodeficiency Virus Type 1 (HIV-1) infected adults and adolescents over 12 years, in combination with other antiretroviral medicinal products.

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- The recommended dose of abacavir is 600mg daily. To date, this has been administered as one 300mg tablet twice daily. The administration of two 300mg tablets once daily has the benefit of increased convenience.
- **Locally, abacavir is restricted to the HIV clinic.**

Abacavir/lamivudine (Kivexa®) – HIV

SMC recommendation

Advice: following an abbreviated submission

Tablets delivering a fixed dose combination of abacavir 600mg and lamivudine 300mg are accepted for use in NHS Scotland for the treatment of Human Immunodeficiency Virus Type 1 (HIV-1) infected adults and adolescents over 12 years, in combination with other antiretroviral medicinal products. Both products are nucleoside reverse transcriptase inhibitors.

In patients for whom this combination is appropriate, it offers a single tablet at a lower cost per dose compared with the individual components.

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- Kivexa® offers the advantage of reduced pill burden and increased convenience at a slightly reduced cost per dose compared with the individual components.
- **Locally, Kivexa® is restricted to the HIV clinic.**

Adefovir (Hepsera®) – chronic hepatitis B

SMC recommendation

Advice: following a full resubmission

Adefovir dipivoxil (Hepsera®) is accepted for restricted use within NHS Scotland for the treatment of chronic hepatitis B in adults with either compensated liver disease with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active liver inflammation and fibrosis, or decompensated liver disease.

Its use is restricted to patients who demonstrate lamivudine resistance.

Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- Refer to DTC Supplement No.29, August 2003.
- Clinical studies in patients with lamivudine resistant chronic hepatitis B and compensated liver disease show that adefovir, alone or in combination with lamivudine, is significantly more effective in reducing viral load than lamivudine alone.
- Adefovir appears to be well tolerated at the licensed dose of 10mg daily. Higher doses of 30mg daily have been associated with reversible nephrotoxicity. The SPC advises of the potential risk, particularly for patients with underlying renal dysfunction or those receiving drugs which may affect renal function. Patients with normal renal function should be monitored for changes in serum creatinine every three months.
- Adefovir is considerably more expensive than lamivudine. (28 days treatment with adefovir 10mg daily costs £294 versus £78 for lamivudine 100mg daily).
- The optimum duration of treatment with adefovir and the risk of delayed resistance remain to be determined.
- NICE guidance on the use of adefovir and pegylated interferon alpha-2a in the treatment of chronic hepatitis B is expected in February 2006.
- **Adefovir is recommended locally, under the direction of a specialist in hepatitis B, for the treatment of chronic hepatitis B infection in lamivudine resistant patients in whom interferon has failed, is contra-indicated or not tolerated.**

Anagrelide (Xagrid®) – thrombocythaemia

SMC recommendation
Advice: following a full submission
Anagrelide (Xagrid®) is not recommended for use within NHS Scotland for the reduction of elevated platelet counts in 'at risk' patients with essential thrombocythaemia who are intolerant of their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy. The cost effectiveness of anagrelide has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Anagrelide is an orphan product that has been available for the treatment of thrombocythaemia on compassionate "off-label" use for a number of years.

Candesartan (Amias®) – heart failure

SMC recommendation
Advice: following a full submission
Candesartan (Amias®) is accepted for use within NHS Scotland for the treatment of patients with heart failure and left ventricular systolic dysfunction (left ventricular ejection fraction ≤ 40%) as add-on therapy to ACE inhibitors or in patients who are unable to tolerate ACE inhibitors. Treatment with candesartan reduces mortality and hospitalisation due to heart failure.
Candesartan may be used as a second-line agent in patients with chronic heart failure and LVEF ≤ 40% following treatment with an ACE inhibitor and diuretic and with or without a beta-blocker.
Click here for SMC link

Tayside recommendation

Recommended within formulary

Points for consideration:

- Candesartan is the first angiotensin II antagonist to be licensed for the treatment of heart failure.
- The CHARM (Candesartan in Heart failure Assessment of Reduction in Mortality and Morbidity) study programme studied candesartan in three populations with chronic heart failure:
  - patients with LVEF ≤ 40% who were not receiving ACE inhibitors because of previous intolerance (CHARM-Alternative)
  - patients with LVEF ≤ 40% who were taking an ACE inhibitor (CHARM-Added)
  - patients with LVEF ≥ 40% (CHARM Preserved)
- Candesartan was associated with absolute risk reductions of 7% and 4% for cardiovascular mortality or hospitalisation due to heart failure in CHARM-Alternative and CHARM-Added sub-studies respectively. This equates to a number-needed-to-treat (NNT) of 14 over almost three years to prevent one additional cardiovascular-related death or heart failure-related hospitalisation in patients unable to tolerate ACE inhibitors, and a NNT of 23 over almost three and a half years in patients already receiving ACE inhibitors.
- The CHARM-Added sub-study also showed a 3.6% absolute risk reduction in cardiovascular death in patients who were already receiving maximum tolerated doses of ACE inhibitors, many of whom were also receiving beta-blockers. This is in contrast to the ValHeFT (Valsartan Heart Failure Trial) which reported increased mortality and cardiovascular events with the triple combination of ACE inhibitor plus beta-blocker plus valsartan.
- In the CHARM-Added sub-study, significantly more patients discontinued study medication in the candesartan group due to an adverse event or an abnormal laboratory value (24% versus 19% in the placebo group). Discontinuation for renal dysfunction and hyperkalaemia was significantly more likely among candesartan treated patients. Treatment with an ACE inhibitor, angiotensin II inhibitor and a beta-blocker should therefore be used with caution. Patients should be monitored regularly and carefully in relation to serum creatinine and potassium levels.
- Candesartan costs £210 per patient per year at a dose of 32mg daily.

Continued over

Candesartan continued

- ACE inhibitors continue to be recommended as first-line agents for the treatment of confirmed heart failure.
- **Locally, candesartan is recommended for the treatment of patients with confirmed heart failure who are unable to tolerate ACE inhibitors (eg due to troublesome cough). It may also be considered, under the direction of a heart failure specialist, as add-on therapy to ACE inhibitors in patents with confirmed heart failure whose LVEF remains ≤ 40%.**
- Advice on the treatment of confirmed heart failure is available within the Cardiovascular Guidance Notes in the Tayside Area Prescriber Guide (TAPG).

Cinacalcet (Mimpara®) – secondary hyperparathyroidism in end-stage renal disease

SMC recommendation
Advice: following a full submission
Cinacalcet (Mimpara®) is not recommended for use within NHS Scotland for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy.
Addition of cinacalcet to standard treatment with phosphate binders and/or vitamin D sterols reduced serum concentrations of parathyroid hormone and was associated with a reduced risk of fractures compared to standard treatment. However the economic case was not demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Cinacalcet is the first of a new class of agents called calcimimetics. It increases the sensitivity of calcium receptors in the parathyroid gland to activation by extracellular calcium. This leads to a decrease in parathyroid hormone (PTH) levels and a subsequent reduction in serum calcium.
- Cinacalcet is also licensed for the reduction of hypercalcaemia in patients with parathyroid carcinoma. The SMC is awaiting a submission from the manufacturer for use in this indication.
- Elevated PTH levels are associated with increased risk of mortality and cardiovascular disease. Whilst there are data to suggest that cinacalcet is associated with reduced parathyroidectomy, fracture, hospitalisation and mortality, this is based on a post-hoc analysis of pooled studies that were neither designed nor powered for assessment of clinical outcomes.
- In clinical studies, the incidence of adverse effects associated with cinacalcet was similar to standard treatment ie phosphate binders and vitamin D sterols. Nausea, vomiting and hypocalcaemia were more frequent amongst those taking cinacalcet.
- Cinacalcet is considerably more expensive than standard treatment ie phosphate binders (eg calcium, aluminium salts, and sevelamer) and vitamin D analogues (eg calcitriol and alfacalcidol). The annual cost of cinacalcet ranges from £1,600 for 30mg daily to £9,100 for 180mg daily and is in addition to standard treatment.
- Standards in the treatment of renal failure are available from the Renal Association, and guidelines for bone metabolism and disease in chronic kidney disease have been produced by the US National Kidney Foundation.

Cytarabine liposomal suspension (Depocyte®) – lymphomatous meningitis

SMC recommendation
Advice: following a full submission
Cytarabine liposomal suspension for injection (Depocyte®) is not recommended for use within NHS Scotland for the intrathecal treatment of lymphomatous meningitis.
Intrathecally administered cytarabine liposomal suspension cleared malignant cells from the cerebrospinal fluid, however effects on symptom improvement were not well defined and the cost-effectiveness compared to cytarabine solution has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Continued over

Liposomal cytarabine continued

Points for consideration:

- The Depocyte® licence does not cover the prophylaxis of lymphomatous meningitis.
- Locally, high dose methotrexate and standard cytarabine are recommended for the intrathecal treatment of lymphomatous meningitis.
- Liposomal cytarabine is not stocked by the hospital pharmacy.

Eflornithine cream (Vaniqa®) – facial hirsutism in women

SMC recommendation

Advice: following a full submission

Eflornithine 11.5% cream (Vaniqa®) is not recommended for use within NHS Scotland for the treatment of facial hirsutism in women. There is no evidence of its efficacy in comparison to existing treatments and it is substantially more expensive.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Eflornithine is an irreversible inhibitor of L-ornithine decarboxylase, an enzyme thought to be important in controlling hair growth and proliferation.
- Short-term vehicle controlled studies show that use of topical eflornithine reduces hair growth and improves appearance of remaining hairs in women with hirsutism within eight weeks. Following 24 weeks treatment, 24%-44% of women using eflornithine cream were clear/almost clear of hirsutism or showed marked improvement compared to 4%-13% in the vehicle group. Sub-group analysis showed lower success rates in black women and in obese women.
- Eflornithine does not provide permanent hair removal. Hair growth at pre-treatment levels returns within eight weeks following treatment cessation.
- Acne was the most frequent adverse reaction reported in the above studies, followed by pseudofolliculitis barbae. Long-term safety data in relation to skin atrophy are currently unavailable.
- There are no comparative efficacy or safety data for eflornithine versus other treatments used for hirsutism. Co-cyprindiol (Dianette®) is the only other product licensed for this indication but due to increased risk of venous thromboembolism may be unsuitable for some women. Other medicines used off-label include combined oral contraceptives, metformin, and spironolactone. Women also use mechanical methods of hair removal eg shaving, electrolysis and laser treatment without seeking medical help.
- Eflornithine is considerably more expensive than co-cyprindiol. (28 days treatment with eflornithine cream applied twice daily costs roughly £13 versus £9 for 21 tablets of co-cyprindiol).
- Eflornithine cream is not stocked by the hospital pharmacy.

Eplerenone (Inspra®) – heart failure post-MI

SMC recommendation

Advice: following a resubmission

Eplerenone (Inspra®) is accepted for use within NHS Scotland in addition to standard therapy including beta-blockers, to reduce the risk of cardiovascular mortality and morbidity between 3-14 days after myocardial infarction (MI) in stable patients with left ventricular dysfunction (left ventricular ejection fraction ≤40%) and clinical evidence of heart failure.

Eplerenone is the second aldosterone antagonist marketed in the UK. It reduces all-cause mortality and cardiovascular-related mortality and hospitalisation in patients with left ventricular dysfunction and clinical evidence of heart failure after an MI. There are no data on its clinical and cost-effectiveness in patients with chronic heart failure compared to the other aldosterone antagonist marketed in the UK, which reduces mortality and morbidity in patients with chronic heart failure and is considerably cheaper.

Click here for SMC link

Tayside recommendation

Recommended within formulary (prescribing note) *Continued over*

Eplerenone continued

Points for consideration:

- Refer to DTC Supplement, no. 47, Dec 2004
- There are no studies directly comparing eplerenone and spironolactone in patients with heart failure post-MI, therefore relative efficacy in this population is uncertain.
- Eplerenone appears to have a similar adverse effect profile to spironolactone including incidence of hyperkalaemia.
- Eplerenone is considerably more expensive than generic spironolactone. (28 days treatment with eplerenone 50mg daily costs £43 versus £2 for spironolactone 25mg daily.)
- The 2001 NICE guideline on prophylaxis for patients who have experienced a MI recommends that patients who have had a MI and have moderate to severe heart failure, NYHA classes III or IV, should receive spironolactone.
- **Locally, eplerenone is recommended for the treatment of moderate to severe heart failure (NYHA grades III and IV) post-MI in patients who are unable to tolerate spironolactone due to sex-hormone mediated adverse effects (eg gynaecomastia or breast pain in men). It may also be considered, under the direction of a cardiologist, for use in patients with left ventricular dysfunction and clinical evidence of less severe heart failure post-MI.**
- Advice on secondary prevention of CHD following MI is available within the Cardiovascular Guidance Notes in the TAPG.

Ibritumomab (Zevalin®) – follicular non-Hodgkin's lymphoma

SMC recommendation

Advice: following a full submission

Ibritumomab tiuxetan (Zevalin®) is not recommended for use within NHS Scotland for the preparation of a radiopharmaceutical incorporating Yttrium 90 (^{90}Y) for the treatment of adult patients with rituximab-relapsed or refractory CD20+ follicular B-cell non-Hodgkin's lymphoma.

No economic information was submitted to allow an assessment of its cost-effectiveness.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- ^{90}Y-ibritumomab is the first radioimmunotherapy product to be licensed in the UK. It combines antibody-based and radiation mechanisms of cell killing and requires pre-treatment with rituximab to improve tumour targeting.
- Ibritumomab is not stocked by the hospital pharmacy.

Imiquimod 5% cream (Aldara®) – basal cell carcinoma (BCC)

SMC recommendation

Advice: following a full submission

Imiquimod 5% (Aldara®) is accepted for restricted use within NHS Scotland for the topical treatment of small superficial Basal Cell Carcinoma in adult patients in whom standard treatment with surgery or cryotherapy is contraindicated. Its use should be supervised by specialists in dermatology.

At 12 weeks post treatment the composite clearance rates in the randomised controlled trials were between 73-77% and initial clearance rates in the open label studies were between 90-94%. There is only limited follow-up date beyond 12 months.

Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of a dermatologist)

Points for consideration:

- Imiquimod cream is a topical immune response modifier and acts as an antitumour agent through the production of interferon-alpha and other cytokines.

Continued over

Imiquimod cream continued

- Imiquimod cream is also licensed for the treatment of external genital warts. The above SMC advice relates only to the BCC indication.
- In clinical studies, 4% of patients receiving imiquimod cream in-line with the UK licence discontinued treatment due to an adverse event or local skin reaction. Local skin reactions such as severe erythema, severe erosions, and severe scabbing and crusting were all common. Although imiquimod is minimally absorbed through the skin, systemic side-effects including headache, influenza-like symptoms and myalgia have been reported.
- No comparative efficacy or safety data versus alternative therapies currently used in the treatment of superficial BCC (surgery, cryotherapy, photodynamic therapy, and 5-fluorouracil cream) are available.
- Imiquimod cream, at £128 per treatment course, is more expensive than 5-fluorouracil cream and 5-aminolevulinic acid cream (used locally with photodynamic therapy).
- Late recurrence of BCC after treatment is well recognised. The Aldara® SPC notes that long-term clearance rates beyond 12 months post-treatment are not currently available and advises that other appropriate therapeutic modalities should be considered for superficial BCC. It also notes that there is no clinical experience for the use of imiquimod cream in patients with recurrent and previously treated BCCs, therefore use for previously treated tumours is not recommended.
- A local protocol to support the prescribing of imiquimod cream in general practice is available.
- **Imiquimod cream may be considered locally, under the direction of a dermatologist, for use in adult patients with small superficial BCC unsuitable for surgery, cryotherapy or photodynamic therapy eg elderly patients, multiple tumours.**
- National general practice referral recommendations for non-melanoma skin cancer are available within a patient pathway produced by the Centre for Change and Innovation (CCI).

Methylphenidate (Equasym XL®) – attention deficit/hyperactivity disorder (ADHD)

SMC recommendation

Advice: following a full submission

Methylphenidate modified release (Equasym XL®) is accepted for restricted use within NHS Scotland for the treatment of attention deficit/hyperactivity disorder (ADHD) as part of a comprehensive treatment programme, when remedial measures alone prove insufficient.

Like other modified release methylphenidate formulations, it should be considered second line and used only in exceptional circumstances where the supervising clinician has clear evidence that administration of a midday dose is problematic or inappropriate. As for other methylphenidate preparations, initiation of treatment should be by a specialist in childhood behaviour disorders. The pharmacokinetic profile of Equasym XL® differs from that of other modified release formulations of methylphenidate. Equasym XL® would be suitable for patients who do not require therapy in the evening or could have been managed on morning and lunchtime immediate release methylphenidate.

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of a specialist in childhood behavioural disorders)

Points for consideration:

- Equasym XL® is a new modified release formulation of methylphenidate with two phases of drug release: (immediate and extended). It has a shorter duration of action than Concerta XL®, the alternative modified release formulation of methylphenidate.
- Equasym XL® shows similar improvements in ADHD rating scores within the school day as immediate release methylphenidate in children with ADHD who had previously responded to methylphenidate. Studies were short-term and were conducted in the US where the diagnosis of ADHD is based on less stringent criteria than used in the UK.
- Comparative data show that Equasym XL® is more effective than Concerta XL® during the morning, equivalent in the afternoon and less effective twelve hours after dosing. The SPC highlights the fact that if the effect of Equasym XL wears off too early in the evening, resulting in disturbed behaviour and/or inability to go to sleep, a small evening dose of immediate release methylphenidate may be needed.
- Equasym XL® is a similar price to Concerta XL® and considerably more expensive than immediate release methylphenidate.

Continued over

Equasym XL® continued

- The range of capsule strengths available (10mg, 20mg, and 30mg) allows more flexible dosing with Equasym XL® compared to Concerta XL® which is currently available as 18mg and 36mg tablets.
- **Locally, Equasym XL® may be considered as an alternative to Concerta XL® in patients demonstrating evidence of compliance problems* with midday dosing of immediate release methylphenidate, but who do not require therapy in the evening. Treatment should be under the direction of a specialist in childhood behaviour disorders.**
  * evidence of compliance problems is defined as a situation where the clinician has reports from the patient, their parent/carer, or the school that poor compliance with the standard formulation of methylphenidate is leading to increased levels of impairment in academic or social functioning on a regular basis. Evidence of compliance problems should be communicated from specialist to prescribing general practitioner.
- NICE ADHD guidance is scheduled for review in June 2005.
- A local shared care protocol for the treatment of ADHD has recently been approved by the DTC.

Paracetamol infusion (Perfalgan®) – short-term treatment of pain and fever in children

SMC recommendation
Advice: following an abbreviated submission
Paracetamol 500mg/50ml intravenous infusion (Perfalgan®) is accepted for use in children weighing less than 33kg but more than 10kg for the short-term treatment of moderate pain following surgery, and short-term treatment of fever, when administration by the intravenous route is clinically justified.
This updates SMC advice No. 137/04 which covered other patient groups.

Tayside recommendation

Recommended within specialist protocol – HOSPITAL ONLY

Points for consideration:

- Refer to DTC Supplement No. 47, Dec 2004 for information on paracetamol 1g/100ml infusion (restricted to adults, adolescents and children weighing more than 33kg).
- Clinical studies concentrate on the morphine-sparing effects of propacetamol (a pro-drug of paracetamol) for post-operative pain.
- A dose of 15mg/kg (1.5ml per kg) should be administered as a 15-minute intravenous infusion up to four times daily. The minimum interval between each administration must be 4 hours and the maximum daily dose must not exceed 60mg/kg (without exceeding 2g).
- **Paracetamol IV infusion is recommended locally for the relief of post-operative pain in children who require paracetamol but are unable to take oral medication. It may also be considered for the emergency treatment of childhood pyrexia within the High Dependency Unit (HDU).**

Pegvisomant (Somavert®) – acromegaly

SMC recommendation
Advice: following a full submission
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 IGF-1 concentrations or was not tolerated. Pegvisomant reduces IGF-1 levels significantly, as well as improving some of the clinical manifestations of acromegaly. Although it is acknowledged that this is an orphan drug the cost-effectiveness is poor.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Pegvisomant is not stocked by the hospital pharmacy

TachoSil® – liver surgery

SMC recommendation
Advice: following a full submission
TachoSil® is accepted for use within NHS Scotland for the improvement of haemostasis in liver surgery where standard techniques are insufficient.
Click here for SMC link

Tayside recommendation

Recommended within specialist protocol – HOSPITAL ONLY

Points for consideration:

- TachoSil® is a surgical supportive treatment used to control wound bleeding and support tissue integrity when standard surgical techniques such as suturing, stapling and ligation are ineffective. It consists of a collagen sponge coated with human fibrinogen and thrombin.
- **Locally, TachoSil® may be considered for use in selected cases of liver resectional surgery where troublesome bleeding is encountered.**

Triptorelin (Gonapeptyl Depot®) – central precocious puberty (CPP)

SMC recommendation
Advice: following a full submission
Triptorelin (Gonapeptyl Depot®) is accepted for use within NHS Scotland for the treatment of confirmed central precocious puberty in girls under nine years and boys under ten years.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Triptorelin (Gonapeptyl Depot®) is the only medicine licensed in the UK for CPP. Other gonadotrophin-releasing hormone (GnRH) analogues such as goserelin and leuprorelin are currently used for this indication on an "off-label" basis.
- Triptorelin shows suppression of pubertal development in uncontrolled trials in children with CPP.
- Data to show reduction in psychological problems and improved auxological outcomes associated with triptorelin are limited.
- Triptorelin (Gonapeptyl Depot®) is less expensive than other "off-label" GnRH analogues.
- No comparative efficacy or safety data versus other GnRH analogues are available.
- **Goserelin 12-weekly injection is used locally for the treatment of confirmed central precocious puberty.**

Valsartan (Diovan®) – heart failure post-MI

SMC recommendation
Advice: following a full submission
Valsartan (Diovan®) is accepted for restricted use within NHS Scotland to improve survival following myocardial infarction (MI) in clinically stable patients with signs, symptoms or radiological evidence of left ventricular failure and/or with left ventricular systolic dysfunction.
Valsartan has been shown to be as effective as the ACE inhibitor, captopril, in this patient population and should be considered a second-line alternative in patients who cannot tolerate an ACE inhibitor. The economic evaluation demonstrates that valsartan is only cost-effective in the patient population that is intolerant of ACE inhibitors.
Click here for SMC link

Tayside recommendation

Recommended within formulary (prescribing note)

Points for consideration:

- Valsartan is the first angiotensin II antagonist to be licensed for use in patients post-MI.

Continued over

Valsartan continued

- The VALIANT (Valsartan in Acute Myocardial Infarction Trial) compared valsartan, captopril and valsartan plus captopril in high risk patients with acute MI and evidence of congestive heart failure and/or left ventricular systolic dysfunction. Endpoints of all-cause mortality, death from cardiovascular causes, recurrent MI or hospitalisation due to heart failure were similar in all three groups over a two-year period. The addition of valsartan to captopril did not result in any further benefit.
- Valsartan costs £565 per patient per year at the target dose of 160mg twice daily.
- A large evidence base exists to support the use of ACE inhibitors as first-line therapy post-MI. The 2000 SIGN Guideline No.41 recommends long-term ACE inhibitor therapy in patients following an MI with or without left ventricular dysfunction. In patients with left ventricular dysfunction post-MI, therapy should be started within 48 hours of the onset of symptoms.
- **Locally, valsartan is recommended for the treatment of patients with clinical evidence of heart failure and/or left ventricular dysfunction post-MI who are unable to tolerate ACE inhibitors (eg due to troublesome cough).**
- Advice on the secondary prevention of CHD following MI is available within the Cardiovascular Guidance Notes in the TAPG.

Use of New Medicines Prior to or Outwith NHS Tayside DTC Advice in Exceptional Cases

The local exceptional case process has been extended to include situations where clinicians wish to prescribe a new medicine that is not supported by NHS Tayside DTC advice. A request form should be completed in the following situations:

1) medicines licensed since Jan 2002 that have not been evaluated by the SMC
2) medicines that have been evaluated by the SMC but NHS Tayside DTC advice is awaited
3) medicines not recommended by NHS Tayside DTC

Request forms and guidance notes are available on the DTC website www.show.scot.nhs.uk/nhstaysideadtc/ under New Medicines/Processes/Use of new medicines prior to or outwith NHS Tayside advice.

Topiramate Update

The Tayside recommendation for the use of topiramate as monotherapy for the treatment of epilepsy has been updated as follows:

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of a neurologist)

- Topiramate monotherapy is recommended locally, under the direction of a neurologist, for use in accordance with NICE guidance on newer drugs for epilepsy in adults, and newer drugs for epilepsy in children.

Application for the Introduction of a Medicine into the Formulary

The core formulary of the TAPG includes first and second-line medicine choices for the treatment of the majority of common conditions. Medicines are selected based on key criteria of safety, efficacy and cost-effectiveness. MAG has developed a form to assist GPs or consultants in making a case for the addition of a medicine to the core formulary. Note that new medicines that are potential formulary medicines are automatically considered by MAG as part of the local processing of SMC advice. The application form should be used for older, established medicines is available under Formulary Processes on the DTC intranet site.

TAPG Update

Below are changes to the TAPG agreed by the Medicines Advisory Group and approved by the Drug and Therapeutics Committee in May 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) / topic	Changes
2.2	Diuretics	Eplerenone*	Prescribing note added on the place of eplerenone in post-MI heart failure
2.5	Drugs affecting renin-angiotensin system	Lisinopril Ramipril	Lisinopril 1st choice in hypertension Lisinopril or ramipril first choices in heart failure or post-MI prophylaxis
		ACE inhibitors	Expanded prescribing notes
		Candesartan*	Candesartan added as 1st choice sartan in hypertension if ACE inhibitor not tolerated (losartan remains as other formulary choice sartan)
		Valsartan*	Main entry removed but note added indicating it as an alternative post-MI if ACE inhibitor not tolerated
		Irbesartan*	Prescribing note added indicating it as an alternative for diabetic renal disease if ACE inhibitor not tolerated
		Sartans	Expanded prescribing notes
2.6	Nitrates, CCBs etc	Diltiazem Amlodipine	Diltiazem 1st choice rate-limiting CCB and amlodipine 1st choice dihydropyridine CCB
		CCBs	Expanded prescribing note
2.9	Antiplatelet drugs	Aspirin / clopidogrel	Aspirin 1st choice antiplatelet drug at dose of 75mg daily. Prescribing note on clopidogrel/aspirin combination therapy modified
2.12	Lipid regulating drugs	Simvastatin	Simvastatin first choice statin
		Bezafibrate	Bezafibrate 1st choice fibrate
	CV Guidance Notes (p2-7 et seq)	(General)	Guidance notes changes to reflect core formulary changes and 1st choice drugs as above
		Hypertension	New BHS IV optimal and "audit standard" bp targets now indicated. Reference to using new Joint Societies CV risk charts in BNF which replace old CHD risk charts
		Heart Failure	Slight expansion to notes in algorithm
		Anticoagulant advisory notes	Patient groups identified where lowering warfarin induction dose recommended. Minor changes to doses in anticoagulant reversal table
		Prophylactic warfarin (AF) slow initiation	New schedule added on slow initiation of prophylactic warfarin
4.3	Antidepressant drugs	SSRIs	CSM advice Dec 2004 re SSRIs and venlafaxine added
		Venlafaxine	Venlafaxine removed as specialist initiation – no longer an appropriate formulary choice
4.7	Analgesics	Co-proxamol	Removed due to impending withdrawal from the market

* SMC accepted medicines

Forthcoming SMC Advice

Gastro-intestinal system
Esomeprazole (Nexium®)
Beclometasone Dipropionate 5mg (Clipper®)
Cardiovascular system
Perindopril (Coversyl®)
Ezetimibe/simvastatin (INEGY®)
Cilostazol (Pletal®) – ***Re-submission***
Respiratory
Ciclesonide (Alvesco®)
Montelukast (Singulair®)
Beclometasone (Clemil Modulite)
Central nervous system
Pregabalin (Lyrica®) – ***Re-submission***
Atomoxetine (Strattera®) – ***Re-submission***
Buprenorphine patch (Transtec®)
Tramadol/paracetamol (Tramacet®)
Galantamine (Reminyl XL®)
Ropinirole (Adartrel®)
Modafinil (Provigil®) – ***Re-submission***
Rivastigmine (Exelon®)
Aripiprazole (Abilify®)
Infections
Viread/emtriva combination (Truvada®)
Voriconazole (Vfend®)
Tenofovir/emtricitabine (Truvada®)
Lamivudine OD (Epivir®) & Abacavir OD (Kivexa®)
Fosamprenavir (Telzir®)

Endocrine system
Strontium ranelate (Protelos®)
Somatropin (Norditropin SimpleXx®)
Insulin detemir (Levemir®)
Rosiglitazone (Avandia®)
Obstetrics, gynae and urinary-tract disorders
Oxybutynin transdermal patch (Kentera®)
Tamsulosin (Flomaxtra®)
Malignant disease & immunosuppression
Permetrexed (Alimtra®)
Gliadel wafer
Docetaxel (Taxotere®)
Oxaliplatin (Eloxatine®)
Vinorelbine oral (Navelbine® Oral)
Fludarabine (Fludara® Oral)
Pegylated interferon alpha 2b (Pegasys®)
Erlotinib (Tarceva®)
Capecitabine (Xeloda®)
Bevacizumab (Avastatin®)
Nutrition & Blood
Darbepoetin alfa (Aranesp®)
Lanthanum carbonate (Fosrenol®)
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Diclofenac epolamine (Voltarol® Gel Patches 1%)

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