TAYSIDE PRESCRIBER

Tayside DTC Supplement No 55

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

In this issue:

SMC Advice Issued December 2005 - February 2006

Adalimumab (Humira®) – psoriatic arthritis (PsA)

SMC recommendation

Advice: following a full submission

Adalimumab 40mg pre-filled syringe (Humira®) is accepted for use within NHS Scotland for the treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate.

Adalimumab improves symptoms of arthritis and psoriasis and may slow the progression of joint damage in patients with active psoriatic arthritis.

Click here for SMC link

Continued over

Adalimumab continued

Tayside recommendation

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

Points for consideration:

- Adalimumab is the third TNF-antagonist to be licensed for the treatment of PsA. Etanercept received SMC unique status for use in this indication in July 2004 (refer to Tayside Prescriber; DTC Supplement No. 42, July 2004).
- A phase III clinical study in PsA shows significantly more patients achieving 20% improvement in American College of Rheumatology score (ACR_{20}) with adalimumab versus placebo (58% vs 15%) at three months.
- There are no trials directly comparing adalimumab with other TNF-antagonists in PsA therefore relative efficacy is unclear.
- Adalimumab is priced at parity with etanercept (both costing £9,300 per patient per year). Both are administered by sc injection – adalimumab every two weeks and etanercept twice weekly.
- British Society for Rheumatology (BSR) and local guidelines for anti-TNF therapy in PsA recommend the use of TNF-antagonists for patients with peripheral PsA who have failed to respond to adequate therapeutic trials of at least two standard DMARDs (leflunomide, sulfasalazine, methotrexate or ciclosporin) and have active disease, defined as three or more swollen joints and three or more tender joints on two separate occasions one month apart. Response to TNF-antagonist therapy is defined as achieving Psoriatic Arthritis Response Criteria (PsARC) at 3 months for joint disease and ≥75% improvement in the Psoriasis Area and Severity Index (PASI75) for skin disease. Patients who do not achieve a PsARC response should discontinue treatment, but can be considered for treatment with a different TNF-antagonist.
- **Locally, adalimumab may be considered as an alternative to etanercept for the treatment of patients with active PsA. Treatment should be under the direction of the Rheumatology Clinic and in accordance with BSR and local guidelines.**

Bevacizumab (Avastin®) - metastatic colorectal cancer

SMC recommendation

Advice: following a full submission

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

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

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Bevacizumab is the first of a new class of antineoplastic drugs that inhibit the formation of new blood vessels. It is licensed in combination with 5-fluorouracil and folinic acid (5-FU/FA) or irinotecan plus 5-FU/FA (IFL) for the first-line treatment of metastatic colorectal cancer.
- The pivotal study showed that the addition of bevacizumab to IFL significantly increased median survival by 4.7 months (from 15.6 to 20.3 months) and median progression-free survival by 4.4 months (from 6.2 to 10.6 months) in patients with metastatic colorectal cancer.
- In the above study, bevacizumab was associated with a significant increase in all grade 3 (severe) and grade 4 (life-threatening) adverse events, mainly due to an increased incidence of grade 3 hypertension. Pooled data from five clinical studies showed an increased risk of arterial thromboembolic events in patients receiving bevacizumab – particularly in those over 65 years.
- There are no data comparing bevacizumab regimens with oral capecitabine (the existing local first-line option for the treatment of metastatic colorectal cancer).
- Ten months treatment with bevacizumab (as used in the pivotal study) costs £15k-£18k per patient and is considerably more expensive than alternative treatment options.

Continued over

Bevacizumab continued

- NICE guidance on bevacizumab and cetuximab in advanced colorectal cancer is due in Nov 2006.
- Refer to the Tayside "Colorectal clinical management protocol" for further information on the local treatment of metastatic colorectal cancer.
- Bevacizumab is not stocked by the hospital pharmacy.

Buprenorphine patch (BuTrans®) - severe pain unresponsive to non-opioid analgesics

SMC recommendation

Advice: following a full submission

Buprenorphine transdermal patch (BuTrans®) is not recommended for use within NHS Scotland for the treatment of severe opioid responsive pain conditions which are not adequately responding to non-opioid analgesics.

There was a lack of evidence of comparative efficacy with a clinically relevant treatment for chronic pain available in the UK. The economic case has not been demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- BuTrans® is available as 5, 10 and 20mcg per hour patches releasing buprenorphine over a seven-day period. Transtec® is an alternative transdermal patch releasing 35 and 52.5mcg buprenorphine per hour over 72 hours. Transtec® received a negative opinion from the SMC in September 2004 (refer to DTC Supplement No.44).
- Advice on the treatment of pain is available within the Tayside Area Prescribing Guide (TAPG). **Paracetamol plus a full-dose of an oral weak opioid eg co-codamol 30/500 is recommended for the treatment of patients with moderate pain (step 2 of the WHO analgesic pain ladder).**
- Buprenorphine transdermal patches are not stocked by the hospital pharmacy.

Calcipotriol/betamethasone dipropionate (Dovobet®) – psoriasis

SMC recommendation

Advice: following a resubmission

Calcipotriol/betamethasone dipropionate ointment (Dovobet®) is accepted for restricted use within NHS Scotland for the initial topical treatment of stable plaque psoriasis. Short-term comparisons have shown that the combination is more effective than either component as monotherapy and that it is cost-effective compared to alternative therapies.

Its use is restricted to physicians experienced in treating inflammatory skin disease. Dovobet contains a potent steroid, the use of which carries risks of destabilising psoriasis and side-effects from prolonged use. The duration of treatment should not exceed four weeks.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Dovobet® is a combination ointment containing calcipotriol and a potent steroid – betamethasone dipropionate.
- Whilst short-term studies have shown that Dovobet® is more effective than either of the individual components given alone, comparative data versus both calcipotriol and steroid applied once daily at different times of the day or on alternate days are unavailable.
- The fixed Dovobet® combination prevents flexibility in potency and dosing of corticosteroid.
- Dovobet® should be applied once daily for a **maximum of four weeks**. There is no experience of repeated use and there is no experience of use in children.
- The SPC states that not more than 15g Dovobet® should be used a day and no more than 100g each week.

Continued over

Calcipotriol/betamethasone continued

- Dovobet® is considerably more expensive than calcipotriol - £35 for 60g of Dovobet® versus £12 for 60g calcipotriol (Dovonex®).
- **Locally, the use of a four-week course of Dovobet® may be considered in patients with stable plaque psoriasis of less than 10% body surface who are unresponsive to, or unable to comply with, an alternating regimen of calcipotriol and steroid.**
- In view of the fact that Dovobet® contains a potent steroid, clinical review should be undertaken after the maximum four-week treatment duration. **Dovobet® should not be prescribed on a repeat basis**.
- Local advice on the management of psoriasis is included in the Dermatology Guidance Notes within the Tayside Area Prescribing Guide (TAPG). These recommend the use of emollients and calcipotriol in the first instance. Topical steroid may be added for patients intolerant or unresponsive to calcipotriol alone. Calcipotriol and steroid should be given in an alternating am/pm or am/am regimen. Patients who fail to respond to treatment of have more extensive psoriasis (eg >20% skin involved) should be referred to consider phototherapy or systemic treatment. Further patient referral details are available in the NHS Tayside Psoriasis patient pathway.

Carmustine implant (Gliadel®) – high-grade malignant glioma

SMC recommendation

Advice: following a full submission

Carmustine implant (Gliadel®) is accepted for use within NHS Scotland for the treatment of newly diagnosed high-grade malignant glioma patients as an adjunct to surgery and radiation.

In the pivotal study, the use of carmustine implants was associated with a 29% relative decrease in the risk of death, which equates to an increase in median survival time of 2.3 months.

Click here for SMC link

Tayside recommendation

Pending OHMMG approval of brain tumour protocol

Points for consideration:

- Gliadel® implants are biodegradable polymer discs containing the antineoplastic agent carmustine. Implants are inserted in the cavity created by partial or complete resection of a brain tumour.
- The key study was placebo-controlled, all patients received tumour resection and started radiotherapy 14 days after surgery. Recruited patients had favourable Medical Research Council prognostic indices and it is unlikely that those with multifocal disease, poorer performance status or disease involving midline structures would benefit significantly from carmustine implantation.
- The incidence of adverse events associated with the use of carmustine implants appears similar to placebo. In the above study, cerebro-spinal fluid (CSF) leakage was more common with the carmustine implant, although CSF infection rates were similar in both carmustine and placebo groups.
- Temozolomide has recently received a licence for first-line treatment of glioblastoma multiforme (SMC advice is due shortly). Intraoperative radiotherapy (IORT) is a further technique used locally. Data comparing carmustine implants with these alternative treatments are unavailable.
- The cost of carmustine implants is around £4,250 per patient.
- NICE guidance on "Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma" is due for issue in August 2006.
- Carmustine implants are not stocked by the hospital pharmacy.

Clarithromycin granules (ClaroSip®) – respiratory tract, skin infections, Hp eradication

SMC recommendation
Advice: following an abbreviated submission
Clarithromycin as ClaroSip® granules for oral suspension is not recommended for use within NHS Scotland for the treatment of acute and chronic infections caused by clarithromycin susceptible organisms.
It uses sip technology, where the granules are contained within a drinking straw. ClaroSip® incurs a cost premium of up to 20% compared to alternative oral liquid clarithromycin, with no proven advantage in terms of compliance.

Tayside recommendation

Not recommended

Points for consideration:

- ClaroSip® is not stocked by the hospital pharmacy

Emtricitabine (Emtriva®) – HIV infection

SMC recommendation
Advice: following a resubmission
Emtricitabine (Emtriva®) is accepted for use within NHS Scotland for the treatment of HIV-1 infected adults in combination with other antiretroviral agents. It should be prescribed only by HIV specialists.
This indication is based on studies in treatment-naïve patients and treatment-experienced patients with stable virological control in whom, as part of antiretroviral therapy (ART) regimens, it has shown virological responses comparable with other ART. There is no experience of use in patients who are failing their current regimen or who have failed multiple regimens. *Click here for SMC link*

Tayside recommendation

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

Points for consideration:

- Emtricitabine is a nucleoside reverse transcriptase inhibitor (NRTI) licensed for use as part of an antiretroviral therapy (ART) regimen.
- Refer to Tayside Prescriber; DTC Supplement No. 42, July 2004 for original SMC advice.
- Emtricitabine is similar to lamivudine in terms of cost, resistance characteristics and dosing schedules.
- **Locally, use of emtricitabine is recommended in combination with tenofovir (Truvada®), see below.**

Emtricitabine/tenofovir (Truvada®) – HIV infection

SMC recommendation
Advice: following an abbreviated submission
Emtricitabine/tenofovir disoproxil 200mg/245mg tablet (Truvada®) is accepted for use in NHS Scotland for the treatment of Human Immunodeficiency Virus (HIV-1) infected adults in combination with other antiretroviral medicinal products. Both constituents are nucleoside reverse transcriptase inhibitors. The demonstration of the benefit of the combination emtricitabine and tenofovir disoproxil fumarate in antiretroviral therapy is based solely on studies performed in treatment-naïve patients.

Tayside recommendation

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

Points for consideration:

- Truvada® contains two NRTIs - emtricitabine and tenofovir.
- Current British HIV Association (BHIVA) guidelines recommend that treatment-naïve patients receive a dual NRTI backbone with either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a boosted protease inhibitor (PI).
- Alternative combination NRTIs include Combivir® (zidovudine plus lamivudine) and Kivexa® (abacavir plus lamivudine).
- Truvada® is more expensive than Combivir® (£5,000 vs £3,900 per patient per year).
- **Locally, Truvada® is recommended as part of an ART regimen in patients in whom Combivir® is unsuitable (eg due to anaemia or resistance to zidovudine). Use is restricted to the HIV Clinic.**

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

SMC recommendation
Advice: following a full submission
Erlotinib (Tarceva®) is not recommended for use within NHS Scotland for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen.
The economic case has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Erlotinib is an orally active Epidermal Growth Factor Receptor (EGFR) antagonist.
- In the pivotal study, erlotinib was associated with an additional 4.4 months progression free survival and 9 months overall survival compared to placebo in patients with stage IIIB/IV NSCLC. (All patients received active supportive care). Sub-group analysis indicated no significant survival benefit amongst patients who were current or ex-smokers.
- There are no comparative data versus docetaxel – the second-line chemotherapy option recommended in recent NICE and SIGN NSCLC guidance.
- Rash is a common adverse effect associated with erlotinib. It is thought to be a class effect of EGFR antagonists and it is suggested that the severity of rash is predictive of response.
- Erlotinib is not stocked by the hospital pharmacy.

Estradiol/drospirenone (Angeliq®) - prevention of menopausal symptoms

SMC recommendation
Advice: following a full submission
1mg estradiol/2mg drospirenone (Angeliq®) is not recommended for use within NHS Scotland as hormone replacement therapy for oestrogen deficiency symptoms in postmenopausal women more than 1 year post-menopause.
It is effective in reducing the frequency of hot flushes and other symptoms of the menopause but comparative data versus other low dose continuous combined treatment are lacking. The cost-effectiveness has not been demonstrated and there are cheaper alternatives.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Angeliq® is a low-dose continuous-combined hormone replacement therapy (HRT) containing oestradiol and the progestogen drospirenone.
- A two-year open-label comparative study versus the high-dose continuous-combined preparation Premique® showed a decrease in frequency and intensity of menopausal symptoms in both groups. Decrease in symptoms was numerically greater in women receiving Premique®. There are no data comparing Angeliq® with other low-dose continuous-combined HRT products.
- Angeliq® is more expensive than other available low-dose continuous-combined preparations. (Annual treatment with Angeliq® costs £112 versus £88 for Femoston-Conti® and £64 for Kliovance®).
- Refer to local guidance on HRT product selection. Femoston-Conti® and Kliovance® are low-dose continuous-combined HRT preparations included in the TAPG.
- Angeliq® is not stocked by the hospital pharmacy.

Estradiol/drospirenone (Angeliq®) - prevention of postmenopausal osteoporosis

SMC recommendation
Advice: following a full submission
1mg estradiol/2mg drospirenone (Angeliq®) is not recommended for use within NHS Scotland for prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or have contra-indications to, other medicinal products approved for the prevention of osteoporosis.
It maintains bone mineral density, relative to placebo, in post-menopausal women. However, no evidence of cost-effectiveness has been presented.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- See above.
- The CSM advises that HRT should not be considered first-line therapy for the long-term prevention of osteoporosis. HRT remains an option where other therapies are contra-indicated, cannot be tolerated, or there is lack of response.
- No fracture data are available to support the use of Angeliq® in this indication.
- The alternative low-dose continuous-combined HRT preparations; Femoston-Conti® and Kliovance® are also licensed for prevention of postmenopausal osteoporosis and are included within the TAPG.
- Angeliq® is not stocked by the hospital pharmacy

Formoterol inhaler (Atimos® Modulite®) - asthma

SMC recommendation
Advice: following an abbreviated submission
Formoterol 12 micrograms metered inhaler (Atimos® Modulite®) is accepted for use in NHS Scotland for the long-term symptomatic treatment of persistent, moderate to severe asthma in patients requiring regular bronchodilator therapy in combination with long-term anti-inflammatory therapy (inhaled and/or oral glucocorticoids).
It should be used in patients for whom formoterol is an appropriate choice of long-acting $beta_2$-agonist and for whom a metered-dose inhaler is an appropriate delivery device.

Tayside recommendation

Recommended within formulary

Points for consideration:

- Atimos® Modulite® is the only formoterol CFC-free metered-dose inhaler (MDI) available. The dose of formoterol via MDI appears to be therapeutically equivalent to dry powder formulations (Oxis® and Foradil®). Unlike other formoterol inhalers, Atimos® Modulite® is not licensed for use in children under 12 years, treatment of COPD, or prevention of exercise-induced bronchospasm.
- The SPC recommends that Atimos® Modulite® should be stored in a refrigerator prior to dispensing and that patients should not use the inhaler beyond three months from the date of dispensing. No clinical data are available for Atimos® Modulite® with spacers.
- Atimos® Modulite® is priced slightly below Oxis®, Foradil®, and Serevent® (28 days treatment with formoterol 12mcg twice daily costs £18 via Atimos® Modulite®, £23 via Oxis® Turbohaler®, and £25 via Foradil®. Salmeterol 50mcg twice daily costs £27 via MDI or Accuhaler®).

Ibandronic Acid (Bonviva®) - postmenopausal osteoporosis

SMC recommendation

Advice: following a full submission

Ibandronic acid (Bonviva®) is accepted for use within NHS Scotland for the treatment of osteoporosis in postmenopausal women in order to reduce the risk of vertebral factures. Ibandronic acid 150mg monthly is superior to daily ibandronic acid in terms of lumbar spine bone mineral density at 1 year. Compared with placebo, daily administration of ibandronic acid results in a relative risk reduction for vertebral fractures of 62%. Unlike some other bisphosphonates, efficacy in reducing femoral neck fractures (and other non-vertebral fractures) has not been established.

Although its cost is similar to that of other bisphosphonates, ibandronic acid demonstrates more limited efficacy, and therefore may not provide such good value for money.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Ibandronic acid is a third generation nitrogen containing bisphosphonate. Its licensed indication is limited to the reduction of vertebral fractures in the treatment of postmenopausal osteoporosis, ie it does not cover reduction of non-vertebral fractures, treatment of osteoporosis in men, prevention of postmenopausal osteoporosis, or prevention and treatment of corticosteroid induced osteoporosis.
- In the UK, ibandronic acid (Bonviva®) is only available as a once monthly oral preparation. The tablet should preferably be taken on the same date each month.
- The pivotal study was conducted in women who had a relatively low fracture risk and failed to show a significant difference between ibandronic acid and placebo groups in the incidence of non-vertebral fractures.
- At present there are no comparative data versus other postmenopausal osteoporosis treatments. A meta-analysis of 32 randomised clinical trials suggests that ibandronic acid is broadly equivalent to other bisphosphonates in terms of vertebral fracture reduction. However, it has not demonstrated equivalence in terms of hip fracture reduction. (The SPC states that efficacy on femoral neck fractures has not been established).
- Oral bioavailability of ibandronate is reduced in the presence of food, particularly products containing calcium and multivalent cations (such as aluminium, magnesium, or iron). Patients should be advised to fast overnight (for at least 6 hours) before taking ibandronic acid and for one hour after.
- Calcium and vitamin D supplements should be co-prescribed with bisphosphonates if dietary intake is inadequate.
- Whilst studies have shown that changing from daily to weekly dosing improves both compliance and efficacy with bisphosphonates, the evidence in terms of monthly dosing is less clear. A free telephone helpline service is available to encourage long-term adherence to therapy.
- At £260 per year, ibandronic acid is a similar cost to alternative bisphosphonates, alendronate and risedronate.
- **Locally, once monthly ibandronic acid may be considered for the treatment of postmenopausal osteoporosis in women in whom the weekly occurrence of oesophageal side-effects associated with alendronate or risedronate administered once a week is unacceptable.**
- Refer to SIGN 71 "Management of osteoporosis" and NICE appraisal "Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women" for further guidance on the treatment of osteoporosis.

Ibuprofen intravenous injection (Pedea®) – patent ductus arteriosus (PDA)

SMC recommendation
Advice: following an abbreviated submission
Ibuprofen intravenous injection 5mg/ml (Pedea®) is accepted for use within NHS Scotland for the treatment of haemodynamically significant patent ductus arteriosus in pre-term newborn infants of less than 34 weeks gestational age. Safety and efficacy compared to existing alternative treatments has not been formally assessed.

Tayside recommendation

Not recommended

Points for consideration:

- The use of IV indometacin is well established in the treatment of haemodynamically significant PDA and favoured locally.
- Ibuprofen IV is not stocked by the hospital pharmacy

Iloprost (Ventavis®) – primary pulmonary hypertension

SMC recommendation
Advice: following a full submission
Iloprost trometamol nebuliser solution (Ventavis®) is accepted for restricted use within NHS Scotland for the treatment of patients with New York Heart Association Class III primary pulmonary hypertension as a second-line treatment where bosentan is ineffective or is not tolerated. It is an orphan product and efficacy data are very limited.
Iloprost should also be restricted to use only as an alternative in patients receiving other forms of prostacyclin treatment. It is not recommended for patients who would not otherwise have received prostacyclin treatment because it is not cost effective in this situation.
It is further restricted only to use by Specialists working in the Scottish Pulmonary Vascular Unit.
Click here for SMC link

Tayside recommendation

Restricted to the Scottish Pulmonary Vascular Unit

Points for consideration:

- Iloprost is a stable analogue of prostacyclin with a pharmokinetic profile allowing nebulised administration.
- Clinical trial data on iloprost are limited. Epoprostenol infusion is the only treatment for primary pulmonary hypertension to show survival benefit in clinical studies.
- Iloprost offers an alternative to IV epoprostenol, which has problems with central venous access and associated infections.
- Nebulised iloprost is not stocked by the hospital pharmacy.

Lansoprazole oro-dispersible (Zoton FasTab®) - *Helicobacter pylori* eradication

SMC recommendation
Advice: following an abbreviated submission
Lansoprazole oro-dispersible tablet (Zoton FasTab®) is accepted for use in NHS Scotland, in combination with appropriate antibiotics, for the eradication of *Helicobacter pylori* from the upper gastrointestinal tract in patients with ulcer-like dyspepsia in whom *Helicobacter pylori* infection has been demonstrated.
The standard formulation of lansoprazole also has this indication.

Tayside recommendation

Recommended within formulary

Points for consideration:

- SIGN guideline No. 68 "Dyspepsia" and local "Upper Gastro-Intestinal Guidelines" recommend *H.pylori* eradication for *H.pylori*-positive patients in whom uncomplicated dyspepsia persists despite attention to lifestyle and antacid/H_2 antagonist therapy. Referral for assessment should be considered for patients over 55 years whose symptoms persist after initial management with the *H.pylori* test and treat strategy.

Continued over

Lansoprazole oro-dispersible tablets

- Lansoprazole (Zoton®) 30mg twice daily is more expensive than omeprazole 20mg twice daily. (7 days treatment with omeprazole costs £6 versus £10-£12 for lansoprazole).
- Omeprazole is the first choice proton-pump-inhibitor (PPI) recommended in the TAPG.
- Refer to the Upper Gastro-Intestinal Guidelines in the TAPG for details of locally recommended *H.pylori* regimens.

Metformin prolonged release (Glucophage SR®) - type-2 diabetes

SMC recommendation
Advice: following a resubmission
Metformin hydrochloride prolonged-release (Glucophage SR®) is not recommended for use within NHS Scotland for the treatment of adults with type-2 diabetes.
This new formulation appears to have similar short-term efficacy to immediate-release metformin. Evidence of improved gastrointestinal tolerability is not convincing and the prolonged-release formulation is more expensive than the immediate-release formulation.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.49, March 2005 for original SMC advice.
- 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.

Nicotinic acid modified release (Niaspan®) - dyslipidaemia

SMC recommendation
Advice: following a resubmission
Nicotinic acid modified release tablet (Niaspan®) is not recommended for use within NHS Scotland for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia, characterised by elevated levels of low-density-lipoprotein (LDL)-cholesterol and triglycerides and low high-density-lipoprotein (HDL)-cholesterol, and in patients with primary hypercholesterolaemia, either in combination with a HMG-CoA reductase inhibitor (statin), when the cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate or an monotherapy in patients who do not tolerate HMG-CoA reductase inhibitors.
Niaspan® increases HDL cholesterol, reduces triglycerides and to a lesser extent reduces LDL cholesterol. There is no clinical trial evidence that Niaspan® reduces the occurrence of long-term cardiovascular events in patients who have acceptable LDL cholesterol and triglycerides and low HDL (isolated low HDL). The economic case has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No.38 April 2004 and No.48 January 2005 for previous SMC advice.
- This resubmission focused on the HDL-raising effects of Niaspan®.
- Fibrates (eg gemfibrozil) are an alternative option to raise HDL.
- The Joint British Societies' guidelines on "Prevention of cardiovascular disease in clinical practice" (Dec 2005) recommend that the primary treatment in patients with mixed dyslipidaemia, with elevated triglycerides and low HDL, should be lowering of LDL to target using a statin. There is no treatment target for HDL cholesterol as in clinical trials it is altered only modestly and not independently of changes in other lipid parameters.
- Niaspan® is not stocked by the hospital pharmacy.

Olopatadine (Opatanol®) eye drops – seasonal allergic conjunctivitis

SMC recommendation
Advice: following a re-submission
Olopatadine eye drops (Opatanol®) are accepted for use within NHS Scotland for the treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.
Olopatadine is a new, locally applied, antihistamine and anti-allergen. It appears to have similar efficacy to other ocular preparations for seasonal allergic conjunctivitis and a lower price than some competitors, suggesting that it is cost-effective compared to these higher-priced products.
Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No. 31, Sept 2003 for original SMC advice.
- Opatanol® is priced below other antihistamine eye drops but above generic sodium cromoglicate. (Four months treatment with olopatadine costs £16 versus £10 for sodium cromoglicate).
- Sodium cromoglicate eye drops are recommended in the TAPG.

Rabeprazole (Pariet®) - Zollinger-Ellison syndrome

SMC recommendation
Advice: following an abbreviated submission
Rabeprazole 10mg and 20mg tablet (Pariet®) is accepted for use within NHS Scotland for the treatment of Zollinger-Ellison syndrome.
Other proton pump inhibitors are available for this indication at a lower cost per treatment period.

Tayside recommendation

Not recommended

Points for consideration:

- Existing formulary PPIs omeprazole and lansoprazole are more cost-effective treatment options.

Tipranavir (Aptivus®) – HIV infection

SMC recommendation
Advice: following a full submission
Tipranavir (Aptivus ®) in combination with low dose ritonavir is not recommended for use within NHS Scotland for the treatment of HIV-1 infection in highly pre-treated adult patients with virus resistant to multiple protease inhibitors.
At 48 weeks, tipranavir, in combination with low dose ritonavir, showed a significant improvement in the reduction of viral load compared with other protease inhibitor plus ritonavir regimens. Although the overall rate and type of adverse events were similar, tipranavir had a higher incidence of hepatotoxicity, hyperlipidaemia, bleeding events and rash.
Tipranavir is more expensive than other protease inhibitors and the economic case for its use has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Tipranavir is the first non-peptidic protease inhibitor for the treatment of HIV infection. It is used with ritonavir as a boosted regimen (TPV/r).
- Information on the treatment of HIV-infected adults with antiretroviral therapy is available in the British HIV Association (BHIVA) guidelines (2005).
- Tipranavir is not stocked by the hospital pharmacy.

Tramadol 37.5mg/paracetamol 325mg (Tramacet®) - moderate to severe pain

SMC recommendation
Advice: following a full submission
Tramadol 37.5mg/paracetamol 325mg tablet (Tramacet®) is not recommended for use within NHS Scotland for the symptomatic treatment of moderate to severe pain.
Tramacet® had similar efficacy to another combination analgesic in clinical studies, though the dose of paracetamol in the other analgesic preparation was lower than that usually used in the UK. Tramacet® costs significantly more than its individual components prescribed separately.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Tramacet® contains the weak opioid tramadol in combination with a sub-therapeutic dose of paracetamol.
- Comparative studies show that Tramacet® has similar efficacy to US strength co-codamol 30/300 in patients with chronic non-malignant pain. Comparative data versus UK strength co-codamol 30/500 or other opioid/paracetamol combinations used in the treatment of moderate pain are unavailable.
- Tramacet® costs twice as much as co-codamol 30/500 (28 days treatment with two tablets of Tramacet® four times daily costs £40 versus £16 for co-codamol 30/500). Tramacet® is also considerably more expensive than the individual constituents taken separately.
- Compound analgesic preparations reduce the scope for effective titration of the individual components in the management of pain of varying intensity. Paracetamol should be titrated to the maximum dose dose, ie 4g daily, prior to adding a weak opioid. The maximum dose of Tramacet® contains just 2.6g paracetamol daily.
- The CSM has highlighted a number of concerns about adverse effects associated with tramadol including the occurrence of withdrawal reactions, and the potential to cause dependence and convulsions.
- Tramacet® is not stocked by the hospital pharmacy.

Zonisamide (Zonegran®) – epilepsy

SMC recommendation
Advice: following a full submission
Zonisamide (Zonegran®) is accepted for restricted use within NHS Scotland as adjunctive therapy in adult patients with partial seizures, with or without secondary generalisation.
It should be initiated only by physicians who have appropriate experience in the treatment of epilepsy and should be used principally in patients who have not benefited from treatment with an older anti-convulsant drug such as carbamazepine or sodium valproate, or for whom these drugs are unsuitable because of contra-indications, interaction or poor tolerance.
Click here for SMC link

Tayside recommendation

Recommended within specialist pathway (GPs may prescribe under the direction of the Epilepsy Clinic)

Points for consideration:

- Zonisamide is a benzisoxazole derivative, chemically unrelated to other antiepileptic drugs (AEDs). It has been available in Japan and the US for a number of years.
- An 18-week study showed reduced seizure frequency in patients receiving adjunctive zonisamide versus placebo. Zonisamide 500mg daily significantly reduced both complex partial seizures and all partial seizures. The lower dose of 300mg per day significantly reduced the frequency of all partial seizures, but not complex partial seizures.
- No long-term efficacy data comparing zonisamide to other AEDs are available.
- Common side-effects include somnolence, dizziness and headache. Zonisamide has been associated with the development of renal calculi. Postmarketing data from the US and Japan suggest an incidence of renal calculi of between 1 in 1000 and 1 in 100.
- The cost of zonisamide therapy falls within the range of other newer AEDs.

Continued over

Zonisamide continued

- NICE guidance recommends the use of newer AEDs for the management of epilepsy in patients who have not benefited from treatment with the older AEDs such as carbamazepine or sodium valproate, or for whom the older AEDs are unsuitable because of contra-indications, interaction or poor tolerance.
- **Locally, zonisamide may be considered as an alternative to existing newer adjunctive antiepileptic drugs. Treatment should be under the direction of the Epilepsy Clinic and in accordance with NICE guidance on newer drugs for epilepsy in adults.**

Triptorelin for prostate cancer – Update

Further to a review of the cost-effectiveness of gonadotropin releasing hormone (GnRH) analogues used in prostate cancer, the Tayside recommendation for the use of triptorelin 11.25mg (Decapeptyl® SR) has been updated as follows:

Tayside recommendation
Recommended within specialist treatment pathway (GPs may prescribe under the direction of the Urology Clinic to commence treatment with a GnRH analogue)

- **Triptorelin (Decapeptyl® SR) is recommended as the first-line GnRH analogue for the treatment of advanced prostate cancer in new patients**.

Strontium ranelate – Update

Local advice on the use of strontium ranelate was issued in Tayside Prescriber; DTC Supplement No.53 September 2005. This has been updated to allow treatment following assessment by Care of the Elderly physicians. Local advice will be reviewed again following issue of the updated NICE HTA No. 87 expected in April 2006.

Tayside recommendation
Recommended within specialist treatment pathway (GPs may prescribe following assessment by the Bone Clinic or a Care of the Elderly physician).

- **Strontium ranelate may be considered as an alternative to raloxifene for the treatment of postmenopausal osteoporosis in women at high risk* of fracture in whom bisphosphonates are contraindicated or not tolerated. Treatment should be following assessment by the bone clinic or a care of the elderly physician.**
  *** until fracture risk assessment scores are available Tayside-wide, high risk of fracture is defined as a risk equivalent to that of a women aged over 75 years with a previous fragility fracture and T-score < -2.4.**

Gliclazide MR – Update

Gliclazide MR was evaluated by the Tayside Drug Evaluation Panel (DEP) in 2001.
Further to a resubmission by local diabetologists, the original DEP recommendation has been updated as follows:

Tayside recommendation
Non-formulary

- **Gliclazide MR is restricted to patients with type 2 diabetes requiring high dose gliclazide (greater than 160mg standard release gliclazide daily) who are unable to comply with twice daily dosing eg due to unusual eating patterns, unacceptable pill burden, or in whom supervised drug administration is required.**

(Note that 30mg gliclazide MR is considered equivalent to 80mg standard release gliclazide).

Temocillin

Temocillin is an injectable beta-lactam antibiotic shortly to be re-marketed in the UK under the brand name Negaban® for the treatment of gram negative infections. The place of temocillin in the local treatment of extended spectrum beta-lactamase infections (ESBLs) will be addressed by the ASD Anti-Infectives Committee.

New Medicines Search Facility on DTC Website

A search facility will shortly be available on the New Medicine Recommendations page of the DTC website. This will allows user to select medicines from an alphabetical index and then link directly to relevant DTC Supplements and local advice.

TAPG Update

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

	TAPG section	Drug(s) / topic	Changes
4.5	Anti-obesity drugs	-	New Tayside Prescriber issued to update 2002 advice on anti-obesity drugs. BMIs amended to be in line with NICE advice and product licences
6.1	Drugs used in diabetes	Blood glucose meter test strips Gliclazide "Glitazones" Hypostop®	Prescribable test strips indicated for use with 1st line meters for adult type 1 and type 2 diabetics. Link to full Tayside guidance. Gliclazide indicated as 1st choice sulphonylurea. Changes to glitazone prescribing notes to reflect current licences. Hypostop® renamed as GlucoGel®
6.2	Thyroid and antithyroid drugs	Nadolol	Nadolol indicated as 1st choice beta-blocker for relief of thyrotoxic symptoms
6.4	Sex hormones	FemTab®	Deleted from formulary (Elleste-Solo® tabs have same dose of estradiol in them)
	HRT algorithm	FemTab®	Deleted from algorithm (as above)
7.3	Oral contraceptives	Femodette®	Femodette® added as an alternative COC
		Levonelle®-2	Replaced with Levonelle® One Step
7.4	Drugs for GU disorders	Oxybutynin Propiverine Solifenacin* Desmopressin	Oxybutynin m/r tablets indicated as preparation to be used for initial titration. Propiverine and solifenacin added to prescribing notes. Desmopressin preparations for nocturnal enuresis removed as considered to be more specialist use and not first-line management.
8.3	Hormone antagonists	Cyproterone	Cyproterone indicated as short-term anti-androgen of choice for tumour flare when GnRH analogues initiated
		Triptorelin*	Triptorelin m/r IM inj indicated as long-acting GnRH analogue of choice for prostate cancer. Goserelin LA SC implant indicated in prescribing note as an alternative.
9.1	Anaemias and other blood disorders	Folic acid	5mg daily now advocated for women with diabetes to prevent first occurrence of neural tube defects as they are at increased risk.
10.1	Drugs used in rheumatic diseases and gout	NSAIDs Colchicine	NSAIDs cautions and warnings strengthened. Colchicine dosage frequency for acute gout changed to reflect BNF advice.
10	Osteoarthritis algorithm	Cox-2 inhibitors	Slight changes to wording of Cox-2 inhibitor advice to reflect BNF advice.
17	Paediatric Prescribing	-	Section removed due to general availability of BNF for Children. BNF-C is now the national recommended resource for paed prescribing and drug doses in children.
19	Oxygen Therapy in Acute Management	-	Updated with minor revisions
20	Drug Therapy in relation to Anaesthesia	-	Updated with minor revisions
21	Guidelines for the Perioperative Management of Patients with Diabetes	-	Renamed and completely revised

*SMC accepted medicine

Forthcoming SMC Advice

Gastro-intestinal system
Esomeprazole (Nexium®)
Beclometasone Dipropionate 5mg (Clipper®)
Mesalazine (Asacol®) - ***Abbreviated***
Glyceryl trinitratre (Rectogesic®) – ***Resubmission***
Cardiovascular system
Sildenafil (Revatio®)
Perindopril (Coversyl®)
Nebivolol (Nebilet®)
Olmesartan (Olmetec Plus®) - ***Abbreviated***
Respiratory
Beclometasone inhaler (Clenil® Modulite®)
Ciclesonide (Alvesco®) paed
Budesonide (Budesonide EasyHaler®)
Central nervous system
Escitalopram (Cipralex®)
Ropinirole (Adartrel®) **- *Resubmission***
Rivastigmine (Exelon®)
Pregabalin (Lyrica®) – ***IRP***
Aprepitant (Emend®)
Sodium oxybate (Xyrem®)
Pramipexole (Mirexapin®)
Zonisamide (Zonegran®)
Fentanyl patch (Durogesic® D Trans)
Rasagiline (Azilect®)
Modafinil (Provigil®) - ***Resubmission***

Infections
Daptomycin (Cubicin®)
Endocrine system
Somatropin (Genotropin®) **- *Abbreviated***
Somatropin (Norditropin® Simplex)
Pioglitazone/metformin - ***Abbreviated***
Inhaled insulin (Exubera®)
Malignant disease & immunosuppression
Lanreotide (Sumatuline® LA)
Mitotane (Lysodren®)
Letrozole (Femara®)
Fludarabine (Fludara® Oral)
Temozolomide (Temodal®)
Nutrition & Blood
Darbepoetin alfa (Aranesp®)
Lanthanum carbonate (Fosrenol®)
Cinacalcet (Mimpara®) – ***Re-Submission***
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Eye
Dorzolamide (Trusopt®)

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