TAYSIDE PRESCRIBER

Tayside DTC Supplement No. 53

Sept 2005

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

In this issue:

SMC Advice Issued in August & September 2005

Anastrozole (Arimidex®) – HR +ve early invasive breast cancer

SMC recommendation

Advice: following a full submission

Anastrozole (Arimidex®) is accepted for restricted use within NHS Scotland in the adjuvant treatment of postmenopausal women with hormone receptor-positive early invasive breast cancer.

Anastrozole has shown benefit over standard anti-oestrogen therapy in terms of disease-free survival in this patient group. It offers an alternative to tamoxifen and has a different adverse effects profile. Treatment with anastrozole should be initiated by an oncologist.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Until recently, the licence for anastrozole in the adjuvant setting restricted use to women unable to take tamoxifen due to high risk of thromboembolism or endometrial abnormalities. This licence extension broadens use to all postmenopausal women with hormone receptor positive (HR +ve) early invasive breast cancer.
- Efficacy data to support extended use comes from the ongoing ATAC (Anastrozole, Tamoxifen, Alone or in Combination) trial. Outcomes are reported at five and a half years follow-up and show that after five years of adjuvant treatment, 82% of women who received anastrozole remain disease free compared to 79% who received tamoxifen. This represents an absolute risk reduction of 2.5% in favour of anastrozole. Overall survival was slightly higher in the anastrozole arm, but this failed to reach statistical significance.

Continued over

Anastrozole continued

- Whilst tamoxifen is associated with an increased risk of thromboembolic events and endometrial abnormalities, the incidence of musculoskeletal disorders and fractures is greater with anastrozole. The anastrozole SPC advises that women with osteoporosis or at risk of osteoporosis should have their bone mineral density formally assessed by DEXA scanning at the start of treatment and at regular intervals thereafter. Treatment or prophylaxis for osteoporosis should be initiated as appropriate.
- Anastrozole is considerably more expensive than tamoxifen. (28 days treatment with anastrozole 1mg daily costs £69 versus £2 for generic tamoxifen 20mg daily).
- **At present, local use of anastrozole for the adjunctive treatment of postmenopausal HR +ve early invasive breast cancer is restricted to women unable to take tamoxifen due to high risk of thromboembolism or endometrial abnormalities (refer to Tayside Prescriber; DTC Supplement No. 37, March 2004 for full local advice statement). The place of anastrozole, in relation to tamoxifen, will be reviewed by the Oncology and Haematology Medicines Management Group (OHMMG) in the next update of the local breast cancer protocol.**

Brimonidine tartrate/timolol (Combigan®) – glaucoma, ocular hypertension

SMC recommendation

Advice: following an abbreviated submission

Brimonidine/timolol (Combigan®) eye drops are accepted for use in NHS Scotland for the reduction of intra-ocular pressure in patients with chronic open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers alone and for whom brimonidine is an appropriate choice of adjuvant therapy. The combination product may be associated with a modest decrease in cost compared with the individual components and allows patients to administer fewer drops.

Tayside recommendation

Non-formulary

Points for consideration:

- Combigan® is a fixed combination of brimonidine 0.2% and timolol 0.5%. Lack of flexibility in dose adjustment of individual constituents may limit use.

Capecitabine (Xeloda®) – adjuvant treatment of Dukes' C colon cancer

SMC recommendation

Advice: following a full submission

Capecitabine (Xeloda®) is accepted for use within NHS Scotland for the adjuvant treatment of patients following surgery for Stage III (Dukes' C stage) colon cancer. Oral capecitabine appears to be at least as effective as standard IV 5FU/FA chemotherapy with the convenience of oral administration. It should only be prescribed by oncologists.

It is more expensive than IV chemotherapy regimens. However, its use may allow changes to service delivery that have individual patient or organisational benefits.

Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- Capecitabine is an oral pro-drug that is converted to fluorouracil at tumour sites.
- Capecitabine is also licensed for first-line monotherapy of metastatic colorectal cancer and for second-line treatment of locally advanced or metastatic breast cancer either in combination with docetaxel or alone. The above SMC advice relates only to adjuvant treatment following resection of Dukes' C colon cancer.
- In clinical studies, the incidence of serious side-effects associated with capecitabine and 5-fluorouracil (5FU) plus folinic acid (FA) was similar. Diarrhoea, nausea/vomiting, stomatitis and alopecia were more common with 5FU/FA group, whereas, hand-foot syndrome was more common with capecitabine.
- Oral capecitabine is more expensive than the IV 5FU/FA de Gramont regimen used locally. However, use of oral capecitabine has the potential to release resources associated with IV administration and is of particular benefit in the rural setting.

Continued over

Capecitabine continued

- A local protocol for the management of colon cancer is currently under development by the OHMMG .
- **Locally, oral capecitabine may be considered as an alternative to IV 5FU/FA (de Gramont regimen) for the adjuvant treatment of patients following surgery for Dukes' C stage colon cancer.**
- Refer to SIGN 57 "Management of colorectal cancer" and NICE "Improving outcomes in colorectal cancers" for further information on adjuvant therapy.

Carbomer 974P gel (Liquivisc®) – dry eye syndrome

SMC recommendation

Advice: following an abbreviated submission

Carbomer 0.25% (Liquivisc®) gel is accepted for use in NHS Scotland for the symptomatic treatment of dry eye syndrome where a carbomer product is the treatment of choice. It differs in only minor respects from other carbomer products and is less expensive.

Tayside recommendation

Recommended within formulary

Points for consideration:

- Hypromellose is the first-line tear substitute recommended in the Tayside Area Prescribing Guide (TAPG). Carbomer ophthalmic gels are more viscous and cling to the eye surface, which may allow reduced frequency of application.
- Liquivisc® is less expensive than the most frequently prescribed carbomer gel ie carbomer 980 0.2%, Viscotears® (10g Liquivisc® costs £1.99 versus £3.12 for Viscotears®).

Duloxetine (Cymbalta®) – major depressive disorder

SMC recommendation

Advice: following a full submission

Duloxetine (Cymbalta®) is accepted for restricted use within NHS Scotland for the treatment of major depressive episodes in accordance with existing guidelines (i.e. in patients who have not responded to or are unable to tolerate initial treatment options).

On the basis of the limited comparative data available, duloxetine appears to offer similar efficacy to other antidepressants in this treatment position at a similar cost.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Duloxetine is a selective serotonin (5-HT) and noradrenaline (NA) reuptake inhibitor (SNRI). It is also licensed for the treatment of stress urinary incontinence (refer to Tayside Prescriber; DTC Supplement No. 45, October 2004).
- Duloxetine shows similar efficacy to venlafaxine in short-term (12-week) studies in patients with major depressive disorder.
- A treatment duration of at least six months is recommended for patients with moderate or severe depression. Few duloxetine studies have extended past 12 weeks and data on long-term response and remission rates are lacking.
- The main adverse events seen with duloxetine are nausea, headache, dizziness, fatigue and dry mouth. Short-term studies show no difference in QT interval between duloxetine and placebo groups. Further data are required to confirm that treatment with duloxetine is not associated with cardiac problems.
- 28-days of duloxetine treatment costs £28-£55, this is similar to the cost of venlafaxine.
- In moderate to severe major depression, SSRIs are generally used first-line as they are better tolerated than tricyclic antidepressants. Fluoxetine is the first-choice SSRI recommended in the TAPG. Mirtazapine is reserved for patients who do not respond to, or are intolerant of, SSRIs or tricyclics, and may be of particular value when sedation is required. Following recent CSM advice, venlafaxine should only be prescribed under the direction of a specialist in mental health.

Continued over

Duloxetine continued

- The licensed dose of duloxetine for the treatment of depression is 60mg one daily, doses greater than 60mg per day have not been shown to offer any greater clinical advantage.
- In order to reduce the risk of discontinuation syndrome, patients who have received more than one weeks therapy should have their dose tapered over at least a two-week period before discontinuation.
- The dose of duloxetine for stress urinary incontinence is 20-40mg twice daily, under the brand name of Yentreve®. Care should be taken to ensure that the appropriate product is prescribed and supplied.
- **Locally, the use of duloxetine (Cymbalta®) may be considered in patients with major depressive disorder who have failed to respond to, or are unable to tolerate, initial treatment options.**
- Further advice on the treatment of depression is available in the NICE 2004 Guideline: "Management of depression in primary and secondary care" and in "Using antidepressants in primary care" within the Psychiatric Notes in the TAPG.

Eflornithine cream (Vaniqa®) – facial hirsutism in women

SMC recommendation

Advice: following a resubmission

Eflornithine 11.5% cream (Vaniqa®) is accepted for restricted use within NHS Scotland for the treatment of facial hirsutism in women.

It is restricted to use in women for whom alternative drug therapy is ineffective, contra-indicated or considered inappropriate. Eflornithine 11.5% cream, as a topical treatment, may offer advantages over existing therapy for some women as it avoids the risks associated with systemic therapies.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Refer to Tayside Prescriber, DTC Supplement No. 50, May 2005 for original SMC advice.
- Eflornithine cream is associated with a successful response rate of 24%-44% versus 4%-13% for placebo. It does not provide permanent hair removal.
- Co-cyprindiol (Dianette®) is the only other product licensed for female hirsutism but due to increased risk of venous thromboembolism may be unsuitable for some women.
- Data on long-term safety of eflornithine cream are unavailable. A phase IV safety study investigating whether treatment with eflornithine is associated with any degree of skin atrophy is currently taking place.
- Eflornithine is considerably more expensive than co-cyprindiol. (28 days treatment with eflornithine cream applied twice daily costs £13-£26 versus £4 for 21 days of co-cyprindiol).
- **Eflornithine cream is recommended locally for use in women with facial hirsutism in whom co-cyprindiol is ineffective, contra-indicated or inappropriate eg women who are over 35 years of age, who are overweight or are smokers, or have other contra-indications to oestrogen therapy.**

Oxybutynin transdermal patch (Kentera®) – overactive bladder

SMC recommendation

Advice: following a full submission

Oxybutynin transdermal patch (Kentera®) is accepted for restricted use within NHS Scotland for the treatment of urge incontinence and/or increased urinary frequency and urgency in patients with unstable bladder, restricted to patients who derive clinical benefit from oral oxybutynin but who experience intolerable anticholinergic side-effects. It should be used in conjunction with non-pharmacological measures, including pelvic floor muscle exercises and bladder retraining.

Transdermal oxybutynin appears to have similar efficacy to oral antimuscarinics and a lower rate of anticholinergic adverse events. However, patients have the additional effect of application site reactions, which in some patients lead to treatment discontinuation. Transdermal oxybutynin has a lower total cost than oral tolterodine, but a higher total cost than oral oxybutynin.

Click here for SMC link

Continued over

Oxybutynin patch continued

Tayside recommendation

Recommended within formulary

Points for consideration:

- Kentera® is a transdermal formulation of oxybutynin administered twice weekly.
- Transdermal administration avoids pre-systemic gastro-intestinal and hepatic metabolism, this reduces the formation of the active metabolite associated with antimuscarinic side-effects, particularly dry mouth.
- In clinical studies, 23% of patients using transdermal oxybutynin experienced application site reactions, including pruritus and erythema. The SPC recommends application to the abdomen, hip or buttock with a new application site selected with each new patch to avoid reapplication to the same site within seven days.
- No comparative data on incidence of anticholinergic adverse events versus modified release oxybutynin are available.
- As with other antimuscarinic preparations, transdermal oxybutynin is contraindicated in patients with urinary retention, severe gastro-intestinal condition, myasthenia gravis or narrow-angle glaucoma and in patients who are at risk for these conditions.
- The transdermal patch is considerable more expensive than standard oxybutynin, slightly more expensive than modified release oxybutynin and less expensive than tolterodine. (£27 per 28 days treatment with oxybutynin patch twice weekly, versus £21 for standard oxybutynin 15mg daily, £23 for modified release oxybutynin 10mg daily, and £29 for modified release tolterodine 4mg daily.)
- Standard oxybutynin tablets are recommended first-line for the treatment of overactive bladder in the TAPG.
- **Locally, oxybutynin transdermal patches are reserved for patients who experience intolerable anticholinergic side-effects with oral oxybutynin preparations.**
- Further advice on physical therapies and pharmacotherapy used in the treatment of overactive bladder is available in SIGN 79 "Management of urinary incontinence in primary care".

Oxycodone prolonged release (OxyContin®) – severe non-malignant pain

SMC recommendation

Advice: following a full submission

Oxycodone prolonged release (OxyContin®) is accepted for restricted use within NHS Scotland for the treatment of severe non-malignant pain requiring a strong opioid analgesic.

Oxycodone prolonged release is restricted to use in patients in whom controlled release morphine sulphate is ineffective or not tolerated.

Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- OxyContin® is also licensed for the treatment of moderate to severe cancer pain and post-operative pain, these indications were approved prior to the introduction of the SMC.
- Oxycodone prolonged release has been studied in three different pain aetiologies: neuropathic pain, osteoarthritis and chronic low back pain. Reduction in pain intensity and tolerability associated with prolonged release oxycodone appear similar to that of standard release oxycodone and oxycodone in combination with paracetamol.
- Comparative data versus other opioid analgesics are unavailable.
- The adverse effect profile of oxycodone prolonged release is similar to that of other strong opioids.
- OxyContin® is a similar price to transdermal fentanyl but considerably more expensive than controlled release morphine. (30 days treatment with 40mg Oxycontin® 12 hourly costs £103 versus £27 for 80mg controlled release morphine 12 hourly).
- Oral morphine is the strong opioid of choice for the control of severe pain recommended in the TAPG.
- **Locally, oxycodone prolonged release is reserved for patients in whom controlled release morphine is ineffective or not tolerated.**

Pemetrexed (Alimta®) – malignant pleural mesothelioma (MPM)

SMC recommendation
Advice: following a full submission
Pemetrexed (Alimta®) in combination with cisplatin is accepted for restricted use within NHS Scotland for the treatment of chemotherapy-naïve patients with stage III/IV unresectable malignant pleural mesothelioma. Pemetrexed in combination with cisplatin prolonged survival compared with cisplatin alone in patients with unresectable malignant pleural mesothelioma. Pemetrexed is the first licensed agent for the treatment of malignant pleural mesothelioma.
Pemetrexed is also indicated as monotherapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after prior chemotherapy. SMC has not yet received a submission for this indication and therefore cannot currently recommend its use.
Click here for SMC link

Tayside recommendation

Not currently recommended – pending OHMMG approval of local MPM protocol

Points for consideration:

- Pemetrexed is a folic acid analogue licensed for the treatment of malignant pleural mesothelioma (MPM) – a rare cancer associated with a history of asbestos exposure.
- Pemetrexed in combination with cisplatin has been shown to increase survival by three months in patients with MPM compared to cisplatin alone (12 versus nine months). Sub-group analysis of patients with more advanced disease (stage III/IV), who also received folic acid and vitamin B_{12} supplementation, showed survival gain of five months.
- In the above study, the combination of pemetrexed and cisplatin was associated with increased incidence of grade 3 or 4 haematological toxicities.
- The comparative efficacy and safety of pemetrexed/cisplatin compared to currently used off-label regimens of cisplatin/vinorelbine or mitomycin/vinblastine/cisplatin (MVP) and to active symptom control (ASC) is unknown. A phase III trial (MS-01) is currently underway to define the role of chemotherapy in MPM. Patients are assigned to either ASC without chemotherapy, ASC with vinorelbine or ASC with MVP.
- Pemetrexed costs £1,600 per cycle. Patients in the above study completed a median of six cycles.
- NICE advice on the use of pemetrexed for the treatment of MPM is due in August 2006.

Pioglitazone (Actos®) – monotherapy for type 2 diabetes mellitus

SMC recommendation
Advice: following a resubmission
Pioglitazone (Actos®) is accepted for restricted use within NHS Scotland as monotherapy for type 2 diabetes mellitus patients in whom consideration is otherwise being given to commencing insulin therapy. It is not recommended as monotherapy for any other group of patients.
It is one of two peroxisome proliferator-activated receptor-γ agonists marketed in the UK for this indication. Its use should be restricted to patients who have already experienced severe hypoglycaemia or patients in whom metformin and sulphonylureas are contra-indicated or not tolerated.
Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No. 43, August 2004 for original SMC advice.
- Studies indicate that pioglitazone monotherapy provides similar diabetic control, in terms of HbA_{1c} levels, as sulphonylureas.
- Pioglitazone is considerably more expensive than sulphonylurea therapy.
- Pioglitazone monotherapy may be considered as an alternative to rosiglitazone monotherapy for use in type 2 diabetic patients who would otherwise commence insulin therapy eg patients in whom metformin and sulphonylureas are contraindicated or not tolerated. Treatment should be under the direction of the diabetes clinic.

Pregabalin (Lyrica®) – neuropathic pain

SMC recommendation
Advice: following a resubmission
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.
It has been agreed, at the request of the licence-holder, to refer this recommendation to an Independent Review Panel.
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.
- An open-label study suggests that pregabalin may have some effect in patients who are intolerant/refractory to other treatments. However this study was not designed or powered to investigate the efficacy of pregabalin relative to placebo or to an active control, it was open-label which may have biased subjective assessments of pain, and patients could remain on other analgesic medications which had failed to control pain after just two weeks.
- In the absence of data from robust randomised controlled trials conducted in patients that are refractory to other treatments, it is difficult to estimate the clinical benefits of pregabalin that are likely to be achieved in practice.
- Advice on the management of neuropathic pain is available in the Pain Guidance Notes within the TAPG.

Strontium ranelate (Protelos®) – postmenopausal osteoporosis

SMC recommendation
Advice: following a full submission
Strontium ranelate (Protelos®) is accepted for restricted use within NHS Scotland for the treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hip fractures when bisphosphonates are contra-indicated or not tolerated and then only in women aged over 75 with a previous fracture and T-score < -2.4 or other women at equivalent risk.
In the trial population of postmenopausal women, strontium ranelate reduced the risk of developing a vertebral fracture by 41%. In women ≥ 74 years with a femoral neck Bone Mineral Density (BMD) T-score < -2.4 the risk of hip fractures was reduced by 36%. However equivalent cost-effectiveness to bisphosponate therapy has not been demonstrated.
Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Strontium ranelate is the first of a new class of agents, the Dual Acting Bone Agents (DABAs). It acts by increasing bone formation and decreasing bone resorption. It is licensed for the treatment of postmenopausal osteoporosis only ie not steroid induced osteoporosis.
- Compared to placebo, strontium ranelate has shown significant reductions in the number of new vertebral fractures in postmenopausal women with osteoporosis and a history of vertebral fracture, and in the number of non-vertebral fractures (including hip fractures) in postmenopausal women with low femoral neck BMD.
- No comparative data versus other osteoporosis treatments eg alendronate or risedronate, are available. Indirect comparison with bisphosphonates suggests similar vertebral and non-vertebral fracture reductions, but note that populations and fracture definitions may vary between studies. Raloxifene has been shown to reduce vertebral fractures but non-vertebral fracture data are lacking.
- In clinical studies, the overall incidence of adverse events were similar in strontium ranelate and placebo groups. An increased risk of venous thromboembolism (VTE) was observed for strontium ranelate

Continued over

Strontium ranelate continued

(relative risk 1.42 95% CI 1.02-1.98). The SPC states that strontium ranelate should be used with caution in patients with increased risk of VTE. The risk is lower than has been shown with raloxifene, which is contraindicated in patients with active or past history of venous thromboembolic events (VTE).

- Note that due to the high atomic mass of strontium, BMD measured by DXA is unreliable.
- The absorption of strontium ranelate is affected by food and milk/derivatives. It should ideally be given at bedtime, at least two hours after these products.
- Strontium ranelate costs slightly more than existing treatment options of bisphosphonates and raloxifene. (£26 per 28 days treatment with strontium ranelate 2g daily versus £23 for alendronate 70mg weekly, £20 for risedronate 35mg weekly, and £20 for raloxifene 60mg daily.)
- The bisphosphonates, risedronate and alendronate are included in the TAPG and are generally considered as first-line options for the treatment of postmenopausal osteoporosis. A small proportion of women may be unable to tolerate bisphosphonates due to oesophageal side-effects.
- **Locally, 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 under the direction of the bone clinic.**
  *** until fracture risk assessment scores are available Tayside-wide, high risk of fracture is defined as a risk equivalent to that of a woman aged over 75 years with a previous fragility fracture and T-score < -2.4.**
- 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.

Tamsulosin (Flomaxtra® XL) – benign prostatic hypertrophy (BPH)

SMC recommendation

Advice: following an abbreviated submission

Tamsulosin hydrochloride film-coated extended release tablets 400 microgram (equivalent to 367 microgram tamsulosin) are accepted for use in NHS Scotland for functional symptoms of benign prostatic hypertrophy as an alternative to modified release capsules.

Tayside recommendation

Non-formulary

Points for consideration:

- The patent for Flomax® MR (tamsulosin mr capsules) is due to expire early 2006.
- Doxazosin is the first-choice alpha-blocker recommended within the TAPG, tamsulosin mr capsules are included as a second-line option.

Voriconazole (Vfend®) – candidaemia in non-neutropenic patients

SMC recommendation

Advice: following a full submission

Voriconazole (Vfend®) is accepted for restricted use within NHS Scotland for the treatment of candidaemia in non-neutropenic patients.

Voriconazole provides an additional agent for the treatment of candidaemia in non-neutropenic patients. Its use is restricted to patients with fluconazole-resistant *Candida* infection who do not respond to, or cannot tolerate amphotericin B therapy or who are at an increased risk of serious side-effects with amphotericin.

Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- Voriconazole is already licensed, and accepted by the SMC, for the treatment of serious invasive candidiasis refractory to fluconazole.
- Voriconazole (IV followed by oral administration) has been shown to be as effective as a regimen of conventional amphotericin B followed by oral fluconazole in non-neutropenic patients with candidaemia.

Continued over

Voriconazole continued

- IV voriconazole is a similar cost to caspofungin (which is also accepted for use in patients with fluconazole resistant *Candida* infection who do not respond to, or cannot tolerate amphotericin B). Voriconazole has the advantage of being available as both IV and oral formulations.
- **Voriconazole is recommended locally for the treatment of fluconazole resistant serious invasive *Candida* infections, under the direction of an ID specialist or microbiologist.**
- Refer to the Tayside Hospitals Adult Antibiotic Policy.

TAPG Update

Below are the changes to the TAPG agreed by the Medicines Advisory Group and approved by the Drug & Therapeutics Committee in September 2005. Updated sections are available on the TAPG pages of the DTC intranet site. Where possible and appropriate, first-line drug choices are clearly indicated in reviewed sections. An updated Gpass-TADF fly file for use in general practice will also be available shortly.

	TAPG section	Drug(s) / topic	Changes
3	Respiratory	Volumatic® AeroChamber Plus®	AeroChamber Plus® mentioned in place of Volumatic® due to discontinuation of the latter.
	Guidance on inhaler devices	As above	As above
	COPD guidelines	Inhaler device	Advice added on consistency of type of device and preference of MDI and spacer for administration of inhaled medicines.
5	Anti-infectives	-	Antibiotic list removed. Users referred to primary care or ASD antibiotic policies for specific advice on choice and doses of antibiotics.
7.4	Drugs for urinary frequency	Trospium Oxybutynin patches*	Trospium mentioned in prescribing notes as an alternative to first-line agents in patients who experience intolerable side-effects, especially CNS side-effects. Oxybutynin patches added as an extra presentation.
11.8	Tear substitutes	Liquivisc®* Viscotears®	Liquivisc® added in place of the more expensive Viscotears®
14	ASD antibiotic policy	-	Various, including new haematology sepsis policy, haematology antifungal policy, gynae surgery antibiotic prophylaxis guidelines, PID antibiotic protocol, MRSA protocol
15	Paediatric antibiotic policy	-	Few minor changes. BNF for Children due Sept 2005
16	Primary care anti-infectives advisory notes	-	Various minor changes.

* SMC accepted medicines

ASCOT- results of blood pressure lowering arm

The results of the blood pressure lowering arm of the ASCOT study have been published (*Lancet* 2005; 366: 895-906). This study compared use of a calcium channel blocker plus an ACE inhibitor if required (amlodipine plus perindopril) versus a beta-blocker plus a diuretic if required (atenolol plus bendroflumethiazide). The primary endpoint was a combined endpoint of either non-fatal MI or death from CHD; secondary endpoints included stroke, coronary events, cardiovascular death and heart failure. Whilst statistical analysis of secondary endpoints (except heart failure) favoured the amlodipine-based regimen, there was no statistically significant difference between the two arms of the study with respect to the primary endpoint. ASCOT also included a cholesterol lowering arm, where patients also received atorvastatin or placebo. The complete trial results have not yet been published and so we cannot yet assess any benefits of the combination of anti-hypertensive drugs with a statin.

Existing local hypertension guidance should be followed until the results of this and other trials have been fully discussed at a national level.

Forthcoming SMC Advice

Gastro-intestinal system
Esomeprazole (Nexium®)
Beclometasone Dipropionate 5mg (Clipper®)
Glyceryl trinitrate 0.4% ointment (Rectogesic®)
Mesalazine (Asacol®)
Lansoprazole (Zoton FasTab®)
Cardiovascular system
Perindopril (Coversyl®)
Cilostazol (Pletal®) – ***Re-submission***
Bemiparin (Zibor®)
Atorvastatin (Lipitor®) - ***Abbreviated***
Anagrelide (Xagrid®) - ***Re-submission***
Nebivolol (Nebilet®)
Iloprost (Ventavis®)
Olmesartan (Olmetec Plus®) - ***Abbreviated***
Respiratory
Beclometasone (Clemil Modulite)
Central nervous system
Tramadol/paracetamol (Tramacet®)
Ropinirole (Adartrel®)
Rivastigmine (Exelon®)
Pregabalin (Lyrica®) – ***IRP***
Palonosetron (Aloxi®)
Aprepitant (Emend®)
Iloprost (Ventavis®)
Zomisamide (Zonegran®)
Infections
Tipranavir (Aptivas®)
Clarithromycin (ClaroSip®)

Endocrine system
Triptorelin (Decapeptyl SR® 11.25mg) - ***Abbrev***
Alendronate/colecalciferol (Fosavance®) - ***Abbrev***
Ibandronic acid (Bonviva®)
Metformin (Glucophage MR®) – ***Re-submission***
Obstetrics, gynae and urinary-tract disorders
Solifenacin (Vesicare®) – ***Re-submission***
Drospirenone/oestradiol (Angeliq®)
Malignant disease & immunosuppression
Carmustine implant (Gliadel® Implant)
Docetaxel (Taxotere®)
Oxaliplatin (Eloxatine®)
Fludarabine (Fludara® Oral)
Erlotinib (Tarceva®)
Bevacizumab (Avastin®)
Exemestane (Aromasin®)
Cetuximab (Erbitux®) - ***IRP***
Nutrition & Blood
Darbepoetin alfa (Aranesp®)
Lanthanum carbonate (Fosrenol®)
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Diclofenac (Voltarol® Gel Patches 1%)
Infliximab (Remecade®) - ***Re-submission***
Adalimumab (Humira®)
Etanercept (Enbrel®)

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