TAYSIDE PRESCRIBER

Tayside DTC Supplement No. 54

Nov 2005

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

In this issue:

SMC Advice Issued in October & November 2005

Alendronate/colecalciferol (Fosavance®) – postmenopausal osteoporosis

SMC recommendation

Advice: following an abbreviated submission

Alendronate/colecalciferol (Fosavance®) is accepted for use within NHS Scotland for the treatment of postmenopausal osteoporosis in patients at risk of vitamin D insufficiency who require treatment with both alendronate and vitamin D and for whom once-weekly administration is appropriate. The combination preparation is cost saving compared to the two drugs administered separately.

Weekly administration of vitamin D represents a departure from routine clinical practice. In patients who also require calcium supplementation this will have to be administered separately, using a calcium preparation that does not also contain vitamin D.

Tayside recommendation

Non-formulary

Points for consideration:

- Patients prescribed bisphosphonates should receive supplemental calcium and vitamin D if dietary intake is inadequate. Most patients who require vitamin D also require calcium.
- Fosavance® is the same cost as Fosamax® (alendronate) once weekly.

Continued over

Alendronate/colecalciferol continued

- Fosavance® plus calcium (Calcichew®) is more expensive than Fosamax® once weekly plus calcium/vitamin D (Calcichew-D_3® Forte or Adcal D_3®).
- Generic alendronate is now available and will shortly be added to the drug tariff.

Anagrelide (Xagrid®) – essential thrombocythaemia

SMC recommendation

Advice: following a resubmission

Anagrelide (Xagrid®) is accepted 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.

Anagrelide reduces platelet counts in patients with essential thrombocythaemia who were intolerant of another cytoreductive therapy or whose platelet count could not be controlled by it.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No. 50, May 2005 for original SMC advice.
- Anagrelide is an orphan product that has been available for the treatment of thrombocythaemia on compassionate "off-label" use for a number of years.
- A UK Medical Research Council trial has compared anagrelide to hydroxycarbamide in adults with essential thrombocythaemia at high risk of vascular events. Patients also received low dose aspirin. Similar reductions in platelet count were shown in the two groups. However, the trial was stopped after 39 months due an excess of adverse events (arterial thrombosis and major haemorrhage) in the anagrelide group.
- **Anagrelide is recommended locally, under the direction of a haematologist, as a second-line therapy in at risk essential thrombocythaemia patients who are unable to tolerate hydroxycarbamide or whose platelet counts are not controlled by hydroxycarbamide.**

Atorvastatin (Lipitor®) – hypercholesterolaemia in children

SMC recommendation

Advice: following an abbreviated submission

Atorvastatin (Lipitor®) is accepted for restricted use in the NHS in Scotland as an adjunct to diet for the reduction of elevated total cholesterol, LDL-cholesterol, apolipoprotein B and triglycerides in children aged 10 years and older with primary hypercholesterolaemia, heterozygous familial hypercholesterolaemia or combined (mixed) hyperlipidaemia when response to diet and other non-pharmacological measures is inadequate.

It is restricted to initiation by paediatricians or physicians specialising in the management of lipid disorders.

Click here for SMC link

Tayside recommendation

Recommended within specialist treatment pathway (GPs may prescribe under the direction of the paediatric metabolic clinic or the cardiovascular risk clinic)

Points for consideration:

- Previously atorvastatin has been licensed for use in adults only, this revised indication covers use of 10mg or 20mg strength tablets in children aged ten years and above.
- Pravastatin is also licensed for use in children from eight years with heterozygous familial hypercholesterolaemia. Other statins ie simvastatin, rosuvastatin and fluvastatin are indicated for use in adults only.

Bemiparin (Zibor®) – prevention of thromboembolic disease - general surgery

SMC recommendation
Advice: following a full submission
Bemiparin (Zibor®) is not recommended for use within NHS Scotland for the prevention of thromboembolic disease in patients undergoing general surgery.
In one small study neither bemiparin nor unfractionated heparin was associated with thromboembolic complications following abdominal surgery but major bleeding and wound haematoma were more common with unfractionated heparin. Bemiparin has not been evaluated in other general surgery settings or against other low molecular weight heparins. No evidence of the cost effectiveness of bemiparin during general surgery has been presented by the manufacturer.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Bemiparin is a further low molecular weight heparin (LMWH) licensed for administration 2 hours before or 6 hours after surgery, then daily on subsequent days. It has a lower mean molecular weight and a higher Xa/IIa ratio than other LMWHs.
- The cost of bemiparin is at the upper end of the range of existing LMWHs and is more expensive than dalteparin (bemiparin 2500IU sc on the day of surgery then daily for seven days costs £27 versus £15 for dalteparin).
- **Locally, dalteparin (Fragmin®) is the low molecular weight heparin of choice for venous thromboembolic prophylaxis during surgery**.
- Bemiparin is not stocked by the hospital pharmacy.

Bemiparin (Zibor®) – prevention of thromboembolic disease - orthopaedic surgery

SMC recommendation
Advice: following a full submission
Bemiparin (Zibor®) is not recommended for use within NHS Scotland for the prevention of thromboembolic events in patients undergoing orthopaedic surgery.
Bemiparin was associated with a lower incidence of thromboembolic complications than unfractionated heparin and was non-inferior to another low molecular weight heparin. The cost effectiveness has not been convincingly addressed for the Scottish context.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- See above
- Bemiparin shows a similar incidence of thromboembolic complications as enoxaparin in patients undergoing elective knee replacement in a Spanish setting.
- No comparative data versus dalteparin are available.

Bemiparin (Zibor®) – prevention of clotting in the extracorporeal circuit during haemodialysis

SMC recommendation
Advice: following a full submission
Bemiparin (Zibor®) is not recommended for use within NHS Scotland for the prevention of clotting in the extracorporeal circuit during haemodialysis.
It showed similar efficacy to unfractionated heparin in preventing coagulation in the extracorporeal circuit but has not been compared with other low molecular weight heparins. No evidence of the cost effectiveness of bemiparin during haemodialysis has been presented by the manufacturer.
Click here for SMC link

Tayside recommendation

Not recommended

Continued over

Bemiparin - haemodialysis
Points for consideration:
- See above
- **Continuous infusion of unfractionated heparin is used locally for the prevention of clotting in the extracorporeal circuit during haemodialysis.**
- Bemiparin is not stocked by the hospital pharmacy.

Bemiparin (Zibor®) – treatment of venous thromboembolism

SMC recommendation
Advice: following a full submission
Bemiparin (Zibor®) is not recommended for use within NHS Scotland for the treatment of established deep vein thrombosis, with or without pulmonary embolism, during the acute phase.
Greater numbers of patients had a reduction in thrombus size with bemiparin than unfractionated heparin, but bemiparin has not been compared with other low molecular heparins. Cost effectiveness has not been demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:
- See above
- **Locally, dalteparin (Fragmin®) is the low molecular weight heparin of choice for treatment of venous thromboembolism.**
- Bemiparin is not stocked by the hospital pharmacy.

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

SMC recommendation
Advice: following an Independent Review Panel
Cetuximab (Erbitux®) is not recommended for use within NHS Scotland in combination with irinotecan for the treatment of patients with epidermal growth factor receptor (EGFR) – expressing metastatic colorectal cancer after failure of irinotecan-including cytotoxic therapy.
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.
- Cetuximab in combination with irinotecan shows a modest decrease in disease progression when compared to irinotecan alone in patients with stage IV metastatic colorectal cancer and EGFR expression. No difference in overall survival has been shown.
- NICE guidance on the use of bevacizumab and cetuximab in advanced colorectal cancer is expected in November 2006.
- Cetuximab is not stocked by the hospital pharmacy.

Cilostazol (Pletal®) - intermittent claudication

SMC recommendation
Advice: following a resubmission
Cilostazol (Pletal®) is not recommended for use within NHS Scotland for improvement of the maximal and pain-free walking distance in patients with intermittent claudication, who do not have rest pain and who do not have evidence of peripheral tissue necrosis.
Although in clinical trials, cilostazol improved pain-free and maximal-walking distances and had limited effects on quality of life assessments of physical function and pain, its efficacy and safety profile in Scottish patients, who are concomitantly treated with an antiplatelet drug, is unclear. The clinical effectiveness and cost-effectiveness were not demonstrated.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No. 37, March 2004 for original SMC advice.
- The majority of cilostazol studies excluded patients taking antiplatelet doses of aspirin. Therefore efficacy and safety of cilostazol in combination with aspirin are unknown.
- Antiplatelet agents may improve walking distance in claudication by a similar degree to that produced by cilostazol.
- The cilostazol SPC advises caution when co-administering drugs which inhibit platelet aggregation, such as low dose aspirin and clopidogrel. It states that if co-administration is undertaken, consideration should be given to monitoring bleeding time and recommends that the dose of aspirin should not exceed 80mg daily.
- SIGN guideline No. 27 "Drug therapy for peripheral vascular disease" recommends that all patients with intermittent claudication should receive aspirin 75mg to 300mg daily as long-term prophylaxis against cardiovascular events.
- Cilostazol is not stocked by the hospital pharmacy.

Diclofenac (Voltarol Gel Patch®) – epicondylitis and ankle sprain

SMC recommendation
Advice: following a full submission
Diclofenac 1% gel patch (Voltarol Gel Patch®) is not recommended for use within NHS Scotland for the local symptomatic treatment of pain in epicondylitis and ankle sprain.
Diclofenac gel patch provides analgesia similar to that obtained with a topical gel formulation of this drug. However, on a gram per gram basis, patches cost over 40% more than the gel formulation.
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Each diclofenac patch contains 14g of 1% gel. Patches are available in a pack of ten at a cost of £14 (ie 10p per g). A 100g tube of diclofenac gel (Voltarol Emugel®) costs £7 (ie 7p per g).
- Epicondylitis and ankle sprain are generally treated with rest and support of the affected joint. Oral analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are used on an "as required" basis, corticosteroid injections may be given for epicondylitis.
- Topical NSAIDs are not included in the Tayside Area Prescribing Guide (TAPG) as marginal benefits do not appear to outweigh costs.
- Diclofenac gel patches are not stocked by the hospital pharmacy.

Docetaxel (Taxotere®) – adjuvant treatment of operable, node-positive breast cancer

SMC recommendation
Advice: following a full submission
Docetaxel (Taxotere®) is accepted for use within NHS Scotland in combination with doxorubicin and cyclophosphamide for the adjuvant treatment of operable, node-positive breast cancer.
Docetaxel in combination with doxorubicin and cyclophosphamide was associated with a significant improvement in disease free survival at 5 years when compared with one of the standard treatment regimens. However, this benefit is associated with an increased risk of toxicity. Docetaxel has demonstrated cost effectiveness in comparison to standard treatment regimen used in NHS Scotland.
Click here for SMC link

Tayside recommendation

Pending update of local breast cancer protocol

Points for consideration:

- Docetaxel is a member of the taxane group also licensed for the treatment of locally advanced or metastatic breast cancer in combination with doxorubicin or capecitabine or as monotherapy after the failure of cytotoxic therapy. It is also used in combination with trastuzumab in patients with metastatic breast cancer overexpressing HER2.
- Docetaxel in combination with doxorubicin and cyclophosphamide is associated with increased haematological toxicity compared to a regimen of fluorouracil, doxorubicin plus cyclophosphamide (FAC). The SPC states that use of granulocyte-colony stimulating factor (G-CSF) should be considered a function of the neutropenic risk of the patient.
- At £7,200 per course, docetaxel, doxorubicin plus cyclophosphamide is around five times more expensive than the chemotherapy regimen currently used locally in the majority of patients (doxorubicin plus cyclophosphamide, AC).
- **The place of docetaxel in the adjuvant treatment of operable, node-positive breast cancer will be addressed by the Oncology & Haematology Medicines Management Group (OHMMG) in the next review of the local breast cancer protocol.**
- NICE guidance on docetaxel for early breast cancer is expected in the first wave of new, rapid Single Technology Appraisals.

Docetaxel (Taxotere®) – hormone refractory metastatic prostate cancer (mHRPC)

SMC recommendation
Advice: following a full submission
Docetaxel (Taxotere®) in combination with prednisolone is not recommended for use within NHS Scotland for the treatment of patients with metastatic hormone refractory prostate cancer (mHRPC).
Overall, docetaxel offers an improvement in median survival of 2.4 months, improved pain control, greater reduction in PSA levels and improved quality of life compared with the current standard chemotherapy regimen.
However, the cost effectiveness of docetaxel for mHRPC has not been demonstrated
Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- In the pivotal study, grade 3/4 toxicities were generally higher in patients receiving docetaxel versus the mitoxantrone comparator.
- At £9,700 per course, docetaxel is considerably more expensive than existing mitoxantrone chemotherapy.
- The cost-effectiveness of docetaxel versus existing mHRPC chemotherapy depends on the increase in cost of treatment in relation to increase in length and quality of life.
- NICE guidance on docetaxel for the treatment of mHRPC is expected in July 2006.

Etanercept (Enbrel®) – ankylosing spondylitis (AS)

SMC recommendation

Advice: following a full submission

Etanercept (Enbrel®) is accepted for restricted use within NHS Scotland for the treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy. It is restricted to use in accordance with the British Society for Rheumatology (BSR) guidelines of July 2004. Etanercept improves signs and symptoms, physical function and quality of life in patients with severe active ankylosing spondylitis. It reduces acute spinal inflammation, but there is no radiological evidence that it decreases joint damage. An economic evaluation, including an assumption that etanercept reduces disease progression, demonstrated that it is a cost-effective treatment option when used in accordance with the BSR guidelines and where clear and rigorous stopping rules are applied.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Etanercept is a recombinant human tumour necrosis factor (TNF) receptor fusion protein that inhibits the binding of TNF to its cell surface receptor. Etanercept is also licensed for the treatment of severe rheumatoid arthritis, psoriatic arthritis and plaque psoriasis. A further TNF-antagonist, infliximab, is also licensed for AS (see page 8).
- Etanercept has shown improvement according to Assessment in Ankylosing Spondylitis (ASAS) response criteria versus placebo in a 24-week study where 57% of etanercept patients achieved at least 20% improvement (ASAS20 response) compared to 22% in the placebo group.
- As yet, placebo controlled radiological data to show that etanercept prevents or reduces structural joint damage are unavailable.
- No trials have compared etanercept with infliximab in the treatment of AS.
- Treatment with etanercept costs £9,300 per patient per year and requires administration by subcutaneous injection twice weekly. Supply is normally via a Healthcare at Home package of care.
- British Society of Rheumatology (BSR) guidelines recommend treatment with TNF-antagonists in patients with active spinal disease who have failed on conventional treatment with two or more NSAIDs each taken sequentially at maximum tolerated/recommended dosage for four weeks. Treatment with TNF-antagonists should be stopped if ineffective (defined as failure to achieve 50% improvement or a fall of ≥2 units in the Bath AS Disease Activity Index and/or a reduction of ≥2 units in spinal pain assessed on a visual analogue scale) after three months of therapy.
- NICE guidance on the use of adalimumab, etanercept and infliximab for the treatment of AS is expected in February 2007.
- **Locally, etanercept is recommended as first-choice TNF-antagonist for the treatment of ankylosing spondylitis. Treatment should be under the direction of a rheumatologist and in accordance with BSR guidelines.**
- Approval should be sought from the Medicine & Cardiovascular Clinical Group Director prior to starting treatment in individual patients.

Exemestane (Aromasin®) – HR +ve early invasive breast cancer after 2-3 years of initial tamoxifen

SMC recommendation

Advice: following a full submission

Exemestane (Aromasin®) is accepted for restricted use within NHS Scotland for the adjuvant treatment of postmenopausal women with oestrogen receptor positive invasive early breast cancer, following 2-3 years of initial adjuvant tamoxifen therapy.

Exemestane has shown benefit in terms of disease-free survival when given as an alternative to tamoxifen after initial adjuvant treatment with tamoxifen for 2-3 years. It offers an alternative to tamoxifen after initial adjuvant treatment with tamoxifen for 2-3 years and has a different adverse effects profile. Treatment with exemestane is restricted to initiation by a breast cancer specialist.

Click here for SMC link

Tayside recommendation

Pending update of local breast cancer protocol

Continued over

Exemestane continued

Points for consideration:

- Exemestane is also licensed for the treatment of advanced breast cancer. The above SMC advice relates only to the indication for adjuvant use.
- The evidence to support the use of exemestane in early breast cancer comes from the Intergroup Exemestane Study comparing exemestane to tamoxifen in women who remained disease free after two-three years adjuvant tamoxifen. Patients continued therapy until they had received a total of five years adjuvant treatment. Disease free survival at three years was significantly higher in the exemestane group compared to tamoxifen (90% versus 86%). Overall survival was also higher in the exemestane group, but this failed to reach statistical significance.
- Preliminary results of endometrial and bone sub-studies indicate that exemestane reduces endometrial abnormalities associated with tamoxifen but it also reduces bone mineral density (BMD). The exemestane SPC advises that women with osteoporosis or at risk of osteoporosis should have their BMD formally assessed by bone densitometry at the start of treatment and at regular intervals thereafter.
- Exemestane is considerably more expensive than tamoxifen. (28 days treatment with exemestane 25mg daily costs £83 versus £2 for generic tamoxifen 20mg daily).
- **The place of exemestane in the adjuvant treatment of postmenopausal HR +ve early invasive breast cancer, and in relation to tamoxifen and other aromatase inhibitors, will be addressed by OHMMG in the next review of the local breast cancer protocol.**

Glyceryl trinitrate 0.4% (Rectogesic®) – relief of pain associated with chronic anal fissure

SMC recommendation

Advice: following a full submission

Glyceryl trinitrate rectal ointment (Rectogesic®) is not recommended within NHS Scotland for the relief of pain associated with chronic anal fissure. It was associated with improvements in pain scores compared with vehicle but the treatment effect was small. The economic case was not demonstrated.

Click here for SMC link

Tayside recommendation

Not recommended

Points for consideration:

- Unlicensed 0.2% glyceryl trinitrate (GTN) rectal ointment has been available for a number of years and is widely used for the treatment of chronic anal fissure.
- Unlike the unlicensed 0.2% formulation, there are no data to indicate that use of Rectogesic® rectal ointment is associated with improved healing of anal fissures.
- In practice, the incidence of headache limits the tolerability of the 0.2% formulation.
- Rectogesic® is more expensive than 0.2% GTN rectal ointment produced by Tayside Pharmaceuticals. (30g of Rectogesic® costs £33 versus £7.30 for 0.2% GTN rectal ointment).
- **Locally, 0.2% GTN rectal ointment is used to heal chronic anal fissure**.
- Rectogesic® rectal ointment is not stocked by the hospital pharmacy.

Infliximab (Remicade®) – ankylosing spondylitis (AS)

SMC recommendation

Advice: following a resubmission

Infliximab (Remicade®) is accepted for restricted use within NHS Scotland for the treatment of ankylosing spondylitis in patients who have severe axial symptoms, elevated serological markers of inflammatory activity and who have responded inadequately to conventional therapy.

Infliximab has demonstrated improvements in signs and symptoms, quality of life and physical functioning and also reductions in spinal inflammation activity. As yet the magnitude of any effect on disease prognosis is unclear the treatment provides value for money only where clear and rigorous stopping rules are followed. It is restricted to use in accordance with British Society of Rheumatology (BSR) guidelines of July 2004.

Click here for SMC link

Continued over

Infliximab continued

Tayside recommendation

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

Points for consideration:

- Infliximab is a human-murine monoclonal antibody TNF-antagonist. It also licensed for the treatment of severe rheumatoid arthritis, psoriatic arthritis and Crohn's disease. A further TNF-antagonist, etanercept, is also licensed for the treatment of AS (see page 7).
- Infliximab has shown improvement according to AS response criteria versus placebo in a 24-week study where 61% of infliximab patients achieved an ASAS20 response compared to 19% in the placebo group.
- In common with etanercept, placebo controlled radiological data to show that infliximab prevents or reduces structural joint damage are unavailable.
- Treatment with infliximab costs £11,000-£15,000 per patient per year and requires administration by IV infusion every 6 to 8 weeks.
- **Locally, infliximab is considered second-choice TNF-antagonist for the treatment of ankylosing spondylitis. Treatment should be under the direction of a rheumatologist and in accordance with BSR guidelines.**
- Approval should be sought from the Medicine & Cardiovascular Clinical Group Director prior to starting treatment in individual patients.

Oxaliplatin (Eloxatin®) – adjuvant treatment of stage III colon cancer in combination with 5FU/FA

SMC recommendation

Advice: following a full submission

Oxaliplatin (Eloxatin®) is accepted for use within NHS Scotland, in combination with fluorouracil and folinic acid, for the adjuvant treatment of stage III (Dukes' C) colon cancer after complete resection of the primary tumour.

Addition of oxaliplatin to a standard regimen of fluorouracil and folinic acid increased disease-free survival in patients who had undergone complete resection of stage III (Dukes' C) colon cancer. An economic evaluation demonstrated that this is a cost-effective treatment option for these patients. Treatment with oxaliplatin (Eloxatin®) should be under the supervision of an oncologist.

Click here for SMC link

Tayside recommendation

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

Points for consideration:

- Oxaliplatin is a platinum-based antineoplastic agent. It is also licensed, in combination with 5-fluorouracil and folinic acid (5FU/FA), for treatment of metastatic colorectal cancer. The above SMC advice relates only to the indication for adjuvant use.
- The evidence to support oxaliplatin in the adjuvant setting comes from the MOSAIC trial which showed that 34% of patients with stage III disease who received 12 cycles of 5FU/FA relapsed or died after three years compared to 27% who received oxaliplatin plus 5FU/FA. Overall survival was higher in the oxaliplatin arm, but this failed to reach statistical significance. Sub-group analysis by patient age showed greater benefit of oxaliplatin in patients less than 65 years.
- The majority of patients treated with oxaliplatin experienced peripheral neuropathy which generally resolved following completion of treatment.
- Oxaliplatin plus 5FU/FA is considerably more expensive than alternative adjuvant therapies of 5FU/FA alone or oral capecitabine (refer to Tayside Prescriber; DTC Supplement No. 53, September 2005 for SMC and local advice on the use of capecitabine).
- **Locally, oxaliplatin in combination with the de Gramont 5FU/FA regimen is considered a first-line option for adjuvant treatment of Dukes' C colon cancer. Treatment should be in accordance with the recently approved local Colorectal Clinical Management Protocol.**
- Refer to SIGN 67 "Management of colorectal cancer" and NICE "Improving outcomes in colorectal cancers" for further information on adjuvant therapy.

Palonosetron (Aloxi®) – prevention of chemotherapy induced nausea and vomiting (CINV)

SMC recommendation
Advice: following a full submission
Palonosetron (Aloxi®) is accepted for use within NHS Scotland for the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy and the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.
It is as effective as other $5HT_3$ antagonists in preventing emesis when given as a single intravenous injection following highly emetogenic chemotherapy (HEC) in the acute phase and moderately emetogenic chemotherapy (MEC) in the acute and delayed phases post-chemotherapy.
Click here for SMC link

Tayside recommendation

Pending OHMMG approval of local antiemetic policy

Points for consideration:

- Palonosetron is a second-generation $5HT_3$ antagonist. It has a long half-life of around 40 hours and is given as a single IV bolus 30 minutes prior to chemotherapy.
- Palonosetron is licensed for the prevention of both acute and delayed chemotherapy-induced nausea and vomiting (CINV) following moderately emetic chemotherapy (MEC), but only for the prevention of acute symptoms in the highly emetic chemotherapy (HEC) setting.
- Clinical trials compared single IV doses of palonosetron and ondansetron administered prior to chemotherapy. Whilst this reflects the UK licence for palonosetron, it does not reflect current UK practice for ondansetron which is given IV prior to chemotherapy then orally for up to five days thereafter.
- The incidence of adverse events associated with palonesetron appears similar to that of other $5HT_3$ antagonists.
- A single dose of IV palonesetron 250mg costs more than IV ondansetron for acute prevention of CINV following HEC, and more than IV followed by oral ondansetron for acute and delayed phases following MEC.
- The UK National Comprehensive Cancer Network 2005 "Antiemesis clinical practice guideline" recommends a $5HT_3$ antagonist combined with aprepitant, and dexamethasone for acute prevention of CINV following HEC, and dexamethasone plus palonesetron for acute prevention following MEC.
- **The place of palonesetron in the prevention of CINV following MEC and HEC, and in relation to other $5HT_3$ antagonists, will be addressed by OHMMG in a local antiemetic policy.**
- Palonesetron is not stocked by the hospital pharmacy.

Solifenacin (Vesicare®) – overactive bladder (OAB)

SMC recommendation
Advice: following a full submission
Solifenacin succinate (Vesicare®) is accepted for use within NHS Scotland for the symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome.
Solifenacin is effective in reducing symptoms associated with overactive bladder, including frequency, urgency and incontinence. It is associated with adverse events typical of antimuscarinic agents used in this condition.
There are cheaper antimuscarinics available that would normally be used as first-line agents.
Click here for SMC link

Tayside recommendation

Non-formulary

Points for consideration:

- Refer to Tayside Prescriber; DTC Supplement No. 46, November 2004 for original SMC advice.
- Solifenacin shows similar efficacy to tolterodine XL in a 12-week study in patients with overactive bladder. The incidence of antimuscarinic side-effects was slightly higher in the solifenacin group.
- Solifenacin is a similar price to tolterodine XL but more expensive than standard oxybutynin. (28 days treatment with solifenacin 5mg daily costs £28 versus £14-£21 for oxybutynin 5mg tds). *Continued over*

Solifenacin continued

- Oxybutynin and tolterodine are included within the TAPG.

Triptorelin 11.25mg (Decapeptyl SR®) – endometriosis

SMC recommendation

Advice: following an abbreviated submission

Triptorelin 11.25mg injection every 3 months (Decapeptyl SR®) is accepted for use within NHS Scotland for the treatment of endometriosis in patients for whom the use of triptorelin is appropriate and who would benefit from reduced frequency of administration compared with triptorelin 3mg injection every 4 weeks (Decapeptyl®).

Tayside recommendation

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

Points for consideration:

- The only other three-monthly gonadotropin releasing hormone (GnHR) analogue injection licensed for the treatment of endometriosis is leuprorelin (Prostap® 3). Three-monthly goserelin (Zoladex® LA) is only licensed for use in prostate cancer. Both Decapeptyl® SR 11.25mg and Prostap® 3 are administered intramuscularly.
- The price of Decapeptyl® SR 11.25mg is considerably lower than Prostap® 3 (£207 versus £376).
- The maximum duration of treatment in endometriosis is six months.
- **Locally, use of triptorelin 11.25mg (Decapeptyl SR®) may be considered as an alternative to goserelin (Zoladex®) in the treatment of endometriosis. Treatment should be under the direction of a gynaecologist.**

Forthcoming SMC Advice

Gastro-intestinal system
Rabeprazole Sodium (Pariet®)
Esomeprazole (Nexium®)
Beclometasone Dipropionate 5mg (Clipper®)
Mesalazine (Asacol®) - ***Abbreviated***
Lansoprazole (Zoton FasTab®) -***Abbreviated***
Cardiovascular system
Sildenafil Cietrate (Revatio®)
Perindopril (Coversyl®)
Nebivolol (Nebilet®)
Iloprost (Ventavis®)
Olmesartan (Olmetec Plus®) - ***Abbreviated***
Respiratory
Beclometasone (Clemil Modulite)
Central nervous system
Buprenorphine (BuTrans transdermal patches)
Escitalopram (Cipralex®)
Tramadol/paracetamol (Tramacet®)
Ropinirole (Adartrel®)
Rivastigmine (Exelon®)
Pregabalin (Lyrica®) – ***IRP***
Aprepitant (Emend®)
Zomisamide (Zonegran®)
Infections
Emtricitabine (Emtriva®)
Emtricitabine/tenofovir (Truvada®)
Tipranavir (Aptivas®)
Clarithromycin (ClaroSip®)
Endocrine system
Ibandronic acid (Bonviva®)
Metformin (Glucophage MR®) – ***Re-submission***
Obstetrics, gynae and urinary-tract disorders
Ibuprofen intravenous injection 5mg/ml (Padea®)
Drospirenone/oestradiol (Angeliq®)
Malignant disease & immunosuppression
Lanreotide (Sumatuline LA)
Milotane (Lysodren®)
Carmustine implant (Gliadel® Implant)
Fludarabine (Fludara® Oral)
Erlotinib (Tarceva®)
Bevacizumab (Avastin®)
Nutrition & Blood
Darbepoetin alfa (Aranesp®)
Lanthanum carbonate (Fosrenol®)
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Adalimumab (Humira®)
Eye
Dorzolamide hydrochloride (Trusopt®)
Olopatadine (Opatanol®) – ***Re-submission***
Skin
Calcipotriol/betamethasone (Dovobet®)

TAPG Update

Below are the main changes to the TAPG agreed by the Medicines Advisory Group and approved by the Drug & Therapeutics Committee in November 2005. Updated sections are available on the TAPG pages of the DTC internet 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
4.1	Hypnotics and anxiolytics	Lormetazepam Zolpidem Zopiclone Diazepam Lorazepam	Lormetazepam indicated as first choice hypnotic. Zolpidem and zopiclone mentioned in prescribing note as alternatives when patient intolerant to benzodiazepines. Diazepam indicated as 1st choice anxiolytic. Lorazepam added (consistent with rapid tranquillisation guidance).
4.3	Antidepressants	Fluoxetine	Fluoxetine indicated as 1st choice SSRI.
4.7	Analgesics	Dihydrocodeine Migraleve®	Dihydrocodeine added as step 2 analgesic. Migraleve® deleted from migraine treatment section.
4.8	Antiepileptics	IV phenytoin	IV phenytoin mentioned as being available for status epilepticus in secondary care.
4-20	Pain Guidance Notes	Cancer Pain	Minor changes to choice of drugs in step 2.
4-24	Pain Guidance Notes	Headache Guidelines	Reference to consider medication overuse headache in aetiology of chronic daily headache. Link to PRODIGY Guidance.
4-29	Smoking Cessation Guidance	Repeat of NRT	Repeat interval for NRT reduced from 12 to 6 months in those who fail to quit (inline with NICE).
13.5	Preparations for psoriasis	Alphosyl® cream Psoriderm® cream Cocois® scalp ointment Sebco® scalp ointment Calcitriol ointment	Psoriderm® cream replaces discontinued Alphosyl® cream. Sebco® scalp ointment replaces the more expensive Cocois® scalp ointment. Calcitriol ointment added as an alternative to calcipotriol preparations (consider calcitriol if unacceptable irritation with calcipotriol). Calcitriol licensed for use on face (unlike calcipotriol).
13.6	Preparations for acne	Dianette®	Explanatory prescribing note on Dianette® added re licensing.
13.8	Sunscreens	Sunsense® Ultra SPF 60	Sunsense® Ultra SPF 60 added as first choice sunscreen.
13.10	Anti-infective skin preparations	Head lice	BNF statement on wet combing methods for head lice added.

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