TAYSIDE PRESCRIBER

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Produced by Tayside New Medicines Implementation Panel (NMIP)

In this issue:

SMC Advice Issued in November 2004

Aprepitant (Emend®) – prevention of cisplatin-induced nausea and vomiting

SMC recommendation

Advice: following a full submission

Aprepitant is accepted for restricted use within NHS Scotland for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based chemotherapy.

The antiemetic regimen incorporating aprepitant was superior to one regimen (where dexamethasone alone was used in the delayed phase of treatment), for the prevention of cisplatin-induced nausea and vomiting in the acute and delayed phases. It should be initiated only by appropriate hospital based specialists.

Tayside recommendation

Recommended within specialist treatment pathway – HOSPITAL ONLY

Points for consideration:

- Aprepitant has a novel mode of action as a selective antagonist of substance P at neurokinin 1 (NK_1) receptors. It is given as part of an antiemetic regimen with dexamethasone and a $5HT_3$ antagonist.
- In clinical studies, 68% of patients receiving aprepitant plus a "standard" cisplatin antiemetic regimen achieved complete response (no emesis and no use of rescue medication for established nausea and vomiting) compared to 48% of patients receiving the "standard" regimen alone. The "standard" regimen contained ondansetron in a higher dose than used in the UK and did not include a $5HT_3$ antagonist or metoclopramide for delayed emesis. These differences from UK practice raise concern over the relevance of the study results.
- Aprepitant appears to be well tolerated but it may interact with a range of drugs, including dexamethasone (aprepitant doubles dexamethasone levels), common chemotherapy agents and warfarin. Refer to SPC for further details.
- The effects of aprepitant on nausea and vomiting induced by other less emetogenic chemotherapy agents (eg carboplatin) and in non-chemotherapy causes of acute vomiting (eg post-operative, in palliative care etc.) are unknown. Aprepitant is a prophylactic drug and has not been investigated as a treatment for established nausea and vomiting.
- Aprepitant costs £47 per cycle of cisplatin chemotherapy. An antiemetic regimen containing aprepitant is more expensive than a UK standard regimen (£62 per cycle for aprepitant antiemetic regimen versus £45 for standard regimen).
- **Locally, aprepitant is reserved for the prevention of cisplatin-induced nausea in patients who have previously failed to respond to other available antiemetics, or are receiving particular highly emetogenic cisplatin regimens where standard antiemetic therapy is known to be ineffective.**

Conjugated oestrogen, medroxyprogesterone (Premique Low Dose®) – HRT

SMC recommendation
Advice: following a full submission
Conjugated oestrogen 0.3mg, medroxyprogesterone 1.5mg (Premique Low Dose®) is accepted for use within NHS Scotland as hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women with an intact uterus.
It is effective in controlling vasomotor symptoms and is associated with lower rates of breast pain and endometrial bleeding compared to other products with higher oestrogen content. It is more expensive than several other HRT therapies, but less expensive than the current market leader in Scotland.

Tayside recommendation

Non-formulary

Points for consideration:

- Premique® is a continuous combined oral HRT preparation containing conjugated equine oestrogens plus medroxyprogesterone. Premique Low Dose® is the only low dose continuous combined HRT preparation that contains conjugated oestrogens rather than estradiol. It is licensed only for menopausal symptoms and not osteoporosis prophylaxis.
- Clinical studies are insufficiently powered to show significant differences between various strengths of conjugated oestrogens plus medroxyprogesterone in the control of vasomotor symptoms. In practice, it is possible that Premique Low Dose® may not control vasomotor symptoms for all women, with some requiring higher dose preparations.
- Long-term use of HRT preparations is associated with a small increase in absolute risk of breast cancer, venous thromboembolism and stroke. There is little evidence to suggest that long-term risks with specific combined HRT preparations are different.
- Premique Low Dose® is considerably more expensive than alternative low dose continuous combined products and slightly more expensive than standard Premique® (36p per day for Premique Low Dose® versus 32p per day for Premique®).
- Guidance from both the Committee for Safety of Medicines and the Royal College of Physicians advises that the lowest effective dose of HRT should be used for the shortest duration to minimise the risks associated with treatment.
- HRT preparations containing conjugated oestrogens (Premarin®, Prempak-C®, Premique® and Premique cycle®) were removed from the Tayside Area Prescribing Guide (TAPG) in August. Low dose estradiol/progestogen preparations are recommended first-line in women requiring combined HRT. Kliovance® and Femoston Conti® are low dose continuous combined preparations included in the TAPG.
- **Locally, Premique Low Dose® is recommended only in women currently receiving Premique® who are able to achieve adequate symptom control on a low dose preparation.**
- Guidance on HRT product selection is available in the TAPG.

Losartan (Cozaar®) – type 2 diabetic nephropathy

SMC recommendation
Advice: following a full submission
Losartan is accepted for restricted use within NHS Scotland to delay the progression of renal disease and to reduce proteinuria in type 2 diabetic patients with nephropathy.
Losartan, for the management of renal disease in patients with hypertension and type 2 diabetes mellitus, is effective, but has not been shown to be any more effective than ACE inhibitors, which are generally less expensive products, and for which there is a strong evidence base in diabetic renal disease and other forms of cardiovascular disease. Therefore, losartan should be considered, along with other angiotensin II antagonists licensed for diabetic renal disease, as an alternative in patients unable to tolerate an ACE inhibitor.

Tayside recommendation

Not currently recommended – pending formulary decision

Points for consideration:

- Losartan is the second angiotensin II antagonist (AIIA) to be licensed for the treatment of diabetic renal disease.

Continued over

Losartan continued

- The RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) study showed that losartan plus standard anti-hypertensive therapy is more effective than standard anti-hypertensive therapy alone in delaying the time to doubling of serum creatinine and in reducing the development of end stage renal disease in patients with type 2 diabetes and nephropathy. No effect on mortality was shown.
- There are no comparative efficacy data for losartan versus ACE inhibitors in the treatment of diabetic renal disease.
- Losartan is a similar cost to irbesartan (the other AIIA licensed for diabetic renal disease) and considerably more expensive than generic ACE inhibitors. (28 days treatment with losartan 50-100mg daily costs £17-£22 compared to £7 for generic lisinopril 10-20mg daily).
- 2002 NICE Guidance on the management of type 2 diabetes recommends initiation of an ACE inhibitor for patients with higher risk urinary albumin excretion for cardiovascular and renal protection. SIGN Guideline 55 "Management of Diabetes" recommends the use of ACE inhibitors, and the consideration of AIIAs, in patients with microalbuminuria or proteinuria.
- **The place of losartan in relation to irbesartan in the local treatment of diabetic renal disease will be addressed by the Formulary Committee. Prescribers are advised to await the outcome of the formulary decision.**

Solifenacin (Vesicare®) – urge incontinence

SMC recommendation

Advice: following a full submission

Solifenacin is not recommended 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. Comparison with other treatments is limited to one placebo-controlled trial involving tolterodine as an active control, and this trial was not designed to detect differences between active treatments. The economic case for using the product was not clearly demonstrated.

Tayside recommendation

Not recommended

Points for consideration:

- Solifenacin is a long-acting muscarinic receptor antagonist with high affinity for muscarinic receptors in the bladder.
- Solifenacin appears to have similar efficacy to tolterodine but with a higher incidence of constipation and blurred vision. Comparisons with other antimuscarinic agents (eg oxybutynin or trospium) or non-pharmacological interventions such as pelvic floor exercises and bladder training are lacking.
- Solfenacin is slightly cheaper than tolterodine but more expensive than generic oxybutynin. (28 days treatment with solifenacin 5mg daily costs £28 versus £14 for oxybutynin 5mg tds).
- Oxybutinin and tolterodine are recommended in the TAPG for the treatment of urinary frequency.
- Solifenacin is not stocked by the hospital pharmacy.

Testosterone 30mg mucoadhesive buccal tablets (Striant SR®) – hypogonadism

SMC recommendation

Advice: following a full submission

Testosterone as mucoadhesive buccal tablets 30mg (Striant SR®) is accepted for restricted use within NHS Scotland as testosterone replacement therapy in men with primary or secondary hypogonadism.

It offers an alternative to other routes, including transdermal application by patches or gel, for patients who would particularly benefit from this mode of administration where intramuscular treatment is not suitable.

Tayside recommendation

Recommended within specialist treatment pathway

Continued over

Testosterone mucoadhesive buccal tablets continued

Points for consideration:

- Striant SR is an innovative buccal testosterone delivery system and allows the slow release and absorption of testosterone through gum and cheek surfaces. The buccal tablet is placed behind the upper lip and is designed to stay in position until removed (12 hours later).
- Striant SR effectively restores testosterone levels to within the physiological range in hypogonadal men.
- In clinical trials, application site irritation was the most common adverse event reported by 4% of patients.
- Striant SR is available as a single strength buccal tablet and unlike testosterone gel, there is no need for dose titration.

Formulary Update

Sections 6 and 7 of the TAPG have been recently updated. Drug additions and removals were noted in DTC Supplement 44 Sept 2004. Along with the drug changes there are some revised and expanded prescribing notes and, where possible and appropriate, first and second line drug choices are clearly indicated. The updated sections replace the old sections and will soon be posted on the TAPG pages of the DTC website. These can be printed off to replace the sections in your ring binder if you prefer to use hard copy.

Forthcoming SMC Advice

Gastro-intestinal system
Creon micro (Creon®)
Beclometasone Dipropionate 5mg
Cardiovascular system
Candesartan (Amias®)
Eplerenone (Inspra®)
Nicotinic acid (Niaspan®) ***Resubmission***
Perindopril (Coversyl®)
Respiratory
Ciclesonide (Alvesco®)
Central nervous system
Methylphenidate (Equasym XL®)
Atomoxetine (Strattera®)
Buprenorphine (Transtec®) patch
Paracetamol infusion (Perfalgan®)
Tramadol (Tramacet®)
Galantamine (Reminyl XL®)
Pregabalin (Lyrica®)
Infections
Mycophenolate (Myfortic®)
Ertapenem (Invanz®)
Voriconazole (VFEND®)
Lamivudine OD (Epivir®) & Abacavir OD (Kivexa®)
Fosamprenavir (Telzir®)
Caspofungin acetate (Cancidas®)
Abacavir (Ziagen®)
Endocrine system
Strontium ranelate (Protelos®)
Somatropin (Norditropin SimpleXx®)
Rosiglitazone/Metformin (Avandamet®)

Pegvisomat (Somavert®)
Metformin hydrochloride (Glucophage SR®)
Levetiracetam (Kepra®) 750mg tabs
Levetiracetam (Kepra®) 100mg oral solution
Insulin detemir (Levemir®)
Obstetrics, gynae and urinary-tract disorders
Tamsulosin hydrochloride (Flomaxtra®)
Malignant disease & immunosuppression
Letrozole (Femara®)
Rituximab (MabThera®)
Ibritumomab (Zevalin®)
Cytarabine liposomal (DepoCyte®)
Gliadel wafer
Docetaxel (Taxotere®)
Cetuximab (Erbitux®)
Darbepoetin alfa (Aranesp®)
Oxaliplatin (Eloxatine®)
Gemcitabine (Gemzar®)
Ibritumomab (Zevalin ®)
Nutrition & Blood
Miglustat (Zavesca®)
Laronidase (Aldurazyme®) ***Resubmission***
Lanthanum carbonate (Fosrenol®)
Musculoskeletal & joint diseases
Lumiracoxib (Prexige®)
Skin
Eflornithine 11.5% Cream (Vaniqa®)
Efalizumab (Raptiva®)
Anaesthesia
Etomidate-lipuro (Etomidate®- Lipuro)

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