TAYSIDE PRESCRIBER

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In this issue:

Desogestrel (Cerazette®) – progestogen-only-contraceptive (POP)

- Desogestrel is a progestogen that has been used with oestrogen in combined-oral-contraceptives for several years. Cerazette is the first formulation of this drug as a POP.
- Further to a resubmission by the manufacturer, the SMC has revised its desogestrel advice issued in May 2003 (refer to D&TC Supplement Issue No. 26).

➢ **Recommendation pending formulary decision**

Points for consideration:

- Desogestrel has been shown to inhibit ovulation more than other POPs (98% of cycles inhibited with desogestrel versus 72% of cycles with levonorgestrel).
- Whilst desogestrel may have greater efficacy than other POPs, there is no evidence that this translates to greater effectiveness (less pregnancies) in practice.
- Currently, there is no difference in the administration schedules for desogestrel compared with other POPs i.e. extra contraceptive precautions should be taken if administration is delayed by >3 hours.
- Desogestrel is more expensive than other POPs (£38 per year for desogestrel versus £8 for norethisterone – the most frequently prescribed POP).
- Desogestrel is associated with a higher level of irregular bleeding than levonorgestrel, particularly during the first few months of treatment.
- Norethisterone (Noriday) and Etynodiol acetate (Femulen) are currently recommended in the Tayside Area Prescribing Guide as the oral POPs of choice locally.
- **The place of desogestrel in relation to other POPs will be addressed by the Formulary Committee. Prescribers are advised to await the outcome of the formulary decision.**

Evra® patch (norelgestromin / ethinylestradiol) – combined-transdermal-contraceptive

- Evra is the first contraceptive to be formulated as a patch. The patch is worn for seven days, it is replaced on days 8 and 15 of the cycle, the fourth week is patch-free.

➢ **Recommended for restricted use**

Points for consideration:

- The Evra patch has similar efficacy and tolerability to combined-oral-contraceptives (COCs).
- Data from clinical studies indicates a slight improvement in overall compliance for Evra versus COCs. However there is no evidence that Evra is associated with greater effectiveness (less pregnancies) in practice.
- Evra is more expensive than COCs. (£101 per year for Evra versus £11 for Microgynon 30 – the most frequently prescribed COC).
- Transdermal administration avoids problems of reduced efficacy due to gastro-intestinal upset or interactions with the antibiotic, tetracycline. However, women should take extra contraceptive precautions during concomitant administration with other broad-spectrum antibiotics.
- Contraceptive efficacy may be decreased in women weighing 90 kg or more.
- Users have a 48-hour window in which to change the Evra patch at the start of weeks two and three.
- The incidence of venous thromboembolism is as yet unknown with Evra.
- Progestogen-only depot injections/implants and intra-uterine devices are existing options that may be appropriate for women who are non-compliant with oral contraceptives.
- **Evra should be restricted to women who have demonstrated, or are deemed to be, at substantial risk of poor compliance with COCs.**

Ezetimibe (Ezetrol®) – hypercholesterolaemia

- Ezetimibe is a selective cholesterol absorption inhibitor that prevents the absorption of intestinal cholesterol derived from diet and bile. It is licensed as adjunctive treatment to diet for:
  - primary (familial heterozygous and non-familial) hypercholesterolaemia - as monotherapy in patients in whom a statin is considered inappropriate or is not tolerated, or in combination with a statin in patients who are not appropriately controlled on a statin alone
  - homozygous familial hypercholesterolaemia - in combination with a statin
  - homozygous familial sitosterolaemia - as monotherapy

➢ **Recommended for restricted use**

Points for consideration:

- Ezetimibe shows a significant LDL-C reduction of around 18% when given as monotherapy compared to placebo, and a significant additional reduction of 12-14% when co-administered with a statin compared to statin therapy alone in patients with primary hypercholesterolaemia.
- The LDL lowering effect of ezetimibe co-administered with the lowest dose of statin is similar to that obtained with the highest dose of statin as monotherapy.
- The use of statins in the primary and secondary prevention of coronary heart disease is supported by evidence of reductions in cardiovascular events and mortality. Whereas, data on long-term outcomes associated with ezetimibe is currently unavailable.
- Increases in liver enzymes have been reported in clinical studies of ezetimibe co-administered with a statin. Liver function tests should be performed when co-administration is initiated and according to the recommendations of the statin.
- Co-administration of ezetimibe with fibrates is not recommended.
- Treatment of children under ten years is not recommended.
- Ezetimibe costs £343 per patient per year. This is around the same cost as current treatment with simvastatin at a dose of 20mg, 40mg or 80mg. Furthermore, the patent for simvastatin has recently expired and a price reduction is anticipated.

- Use of the highest dose of statin as monotherapy is more cost-effective than ezetimibe co-administered with the lowest dose of statin. (Statin monotherapy costs on average £1.06 per patient per day versus the statin-ezetimibe combination at £1.58).
- SIGN Guidelines 'Lipids and the primary prevention of coronary heart disease' and 'Secondary prevention of coronary heart disease following myocardial infarction' recommend that patients with serum total cholesterol ≥5.0 mmol/l and a 10 year risk of a major coronary event of ≥30% should be treated with statins, titrated as necessary to reduce cholesterol to 5 mmol/l.
- Cholesterol targets can be achieved in the majority of patients (around 95%) if statin therapy is properly titrated. **Statins should therefore be titrated to maximum tolerated dose prior to addition of ezetimibe.**
- **Ezetimibe should be reserved for patients who have failed to reach target cholesterol levels despite treatment with titrated/optimised statins alone and for whom statins are inappropriate or poorly tolerated.**
- Prescribing should normally be initiated in primary care, excluding patients with familial hypercholesterolaemia who should be referred to the Lipid Clinic.

Olopatadine 1mg/ml eye drops (Opatanol®) – seasonal allergic conjunctivitis (SAC)

- Olopatadine is a new selective antihistamine indicated in the treatment of ocular signs and symptoms of SAC.

➢ **Not recommended**

Points for consideration:

- Olopatadine has similar efficacy to other ocular preparations used in the treatment of SAC (levocabastine and sodium cromoglicate).
- Olopatadine is more expensive than sodium cromoglicate, which is the most commonly prescribed eye-drop (£175 per ml for olopatadine versus £14.60 per ml for sodium cromoglicate).
- The manufacturer failed to adequately demonstrate the cost-effectiveness of olopatadine versus sodium cromoglicate in the Scottish setting.
- Olopatadine eye drops are not stocked by the hospital pharmacy.

Coversyl Plus® (perindopril / indapamide) – hypertension

- Coversyl Plus is an ACE inhibitor / thiazide combination product licensed for the treatment of essential hypertension when blood pressure is not adequately controlled on perindopril alone.

➢ **Recommendation pending formulary decision**

Points for consideration:

- Coversyl Plus shows a modest reduction in blood pressure in patients with essential hypertension uncontrolled by perindopril alone.
- The PROGRESS study showed that a perindopril/indapamide combination provides a reduction in major vascular events in a post-stroke population. It is probable that the benefit shown was due to blood pressure reduction rather than the specific agents used. Perindopril alone was not significantly superior to placebo in preventing further events. This is probably attributable to the smaller blood pressure reduction achieved with perindopril alone compared with combination therapy.
- The British Hypertension Society Guidelines recommend a low-dose thiazide diuretic as first-line treatment of hypertension, unless there is a contra-indication or a compelling indication for another class of drug. **Fixed-dose combinations should be reserved for second-line treatment when monotherapy is ineffective, the individual drug components are appropriate, and there are no major cost implications.**

- The SIGN Guideline 'Hypertension in older people' recommends a low-dose thiazide diuretic for first-line treatment, with an ACE inhibitor for initial treatment of those with type 1 diabetes, proteinuria or left ventricular dysfunction.
- **The place of Coversyl Plus in the treatment of hypertension will be addressed by the formulary committee. Prescribers are advised to await the outcome of the formulary decision**.
- Further advice on the treatment of hypertension is available in the Cardiovascular Guidance Notes within the Tayside Area Prescribing Guide (TAPG).

The following recommendation relates to a HOSPITAL ONLY medicine

Valganciclovir (Valcyte®) – prevention of cytomegalovirus (CMV) after organ transplantation

- Valganciclovir is an oral pro-drug of ganciclovir, its licence has been extended to cover the prevention of CMV disease in CMV-negative patients who have received a solid organ transplanted from a CMV-positive donor. Treatment starts within 10 days of transplant and continues until 100 days post-transplant.

➢ **Recommended for restricted use**

Points for consideration:

- Valganciclovir has the advantage of reduced pill burden and dose frequency (once daily valganciclovir versus three times daily ganciclovir).
- **Valganciclovir is restricted to secondary care, on the recommendation of a tertiary Transplantation Unit.**
- Refer to D&TC Supplement Issue No. 23 for information on the use of valganciclovir in the treatment of CMV retinitis in AIDS patients.

New medicines should not be prescribed in NHS Tayside until they have been evaluated by the SMC and a recommendation for local use has been made.

Details of local recommendations for new medicines are available on the Tayside D&TC web-site (www.show.scot.nhs.uk/thb/adtc).

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