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## Tacrolimus capsules – prescribe by brand name

Tacrolimus, the Lothian Joint Formulary (LJF) first choice calcineurin inhibitor, is licensed for immunosuppression in kidney and liver transplantation and for the treatment of resistant rejection. Two formulations of tacrolimus capsules are available: **Advagraf**<sup>®</sup>, a prolonged release formulation for once daily administration, and **Prograf**<sup>®</sup>, a shorter acting preparation taken twice daily.

In Lothian, all patients are commenced postoperatively with Prograf<sup>®</sup>, with some patients switched to Advagraf<sup>®</sup> in the early post transplant period. The dose of Prograf<sup>®</sup> or Advagraf<sup>®</sup> will be stabilised and the maintenance dose established before transfer to GP prescribing (approximately 14 to 21 days post transplant).

Care should be taken to distinguish clearly between these two preparations when prescribing and dispensing. The transplant unit have received case reports of patients receiving the wrong preparation in error with subsequent toxic tacrolimus blood levels.

The shared care protocol for tacrolimus for use in transplant patients is available on the LJF website [www.ljf.scot.nhs.uk](http://www.ljf.scot.nhs.uk) and on the NHS Lothian intranet at [http://intranet.lothian.scot.nhs.uk/nhslothian/healthcare/a\\_z/m/medicines\\_management/shared\\_care\\_protocols.aspx](http://intranet.lothian.scot.nhs.uk/nhslothian/healthcare/a_z/m/medicines_management/shared_care_protocols.aspx)

*Thanks to Katherine Davidson, Clinical Pharmacist,  
Royal Infirmary of Edinburgh.*

## Rimonabant – licence suspended

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use has recommended that the marketing authorisation for rimonabant (Acomplia<sup>®</sup>) be suspended across the European Union from 24 October 2008. Psychiatric side-effects were identified when its licence was approved in 2006, and the EMA has now concluded that the risks of treatment outweigh the benefits.

Rimonabant is already **not recommended** for use in Lothian, in line with SMC guidance. However, prescribing data shows that there are patients in Lothian currently receiving this medicine. The MHRA advises that **patients** currently taking rimonabant should consult their doctor or pharmacist to discuss their treatment, and patients who wish to stop taking rimonabant can do so at any time; **prescribers** should not issue any prescriptions for rimonabant and should review the treatment of patients currently taking the medicine. Further information is available at [www.mhra.gov.uk](http://www.mhra.gov.uk) and [www.emea.europa.eu](http://www.emea.europa.eu).

## Editorial Team – opportunity knocks

**Are you looking for a new challenge? We are seeking a GP and a secondary care pharmacist to join our enthusiastic editorial team, to contribute to the peer review and editing process, and to write articles on current prescribing issues.**

The Lothian Prescribing Bulletin provides clear guidance about current and local prescribing issues, new drugs and Scottish Medicines Consortium (SMC) recommendations, the latest LJF recommendations and developments, and new evidence from drug trials. The bulletin is published every two months, and the team meets at Stevenson House on three occasions for each issue. Funding is available to reimburse GP time for attendance at meetings.

**If you are interested and would like to discuss further, please contact Anne Gilchrist, Chair, Editorial Team at [anne.gilchrist@nhslothian.scot.nhs.uk](mailto:anne.gilchrist@nhslothian.scot.nhs.uk)**

# Domiciliary O<sub>2</sub>xygen equipment

Historically oxygen for domiciliary use was supplied in cylinders from community pharmacy to patients in response to a prescription from a GP. For some time this has not been the only route for obtaining domiciliary oxygen. Supply arrangements are different in Scotland than in England.

**Long Term Oxygen Therapy (LTOT)** is defined as the use of oxygen for at least 15 hours per day, including overnight.

- Patients must be referred to a respiratory specialist for assessment
- Following assessment, the respiratory specialist initiates the supply of a concentrator, which is supplied, fitted and maintained by a Health Facilities Scotland contractor, who also shows the patient/carer how to use it. The concentrator plugs into the electricity supply, so they also provide a back-up cylinder for use in the event of power failure. A technician visits quarterly to provide maintenance.

**Short Burst Oxygen Therapy (SBOT)** refers to oxygen prescribed for intermittent use for periods of breathlessness caused by respiratory disease, not relieved by other treatments.

- This is provided from community pharmacy contractors, following a GP's prescription. In NHS Lothian there are 36 community pharmacists who have an oxygen contract
- The cylinder listed in the Drug Tariff is size F, which contains 1360 litres oxygen. There are two types AF and DF
- DF cylinders have an integral regulator, but masks and tubing must also be prescribed
- AF cylinders require a regulator (head) to be prescribed. The 'giving set' (comprising regulator, 2 Ventimask Mk IV masks and tubing) must be prescribed
- If the prescriber does not specify the cylinder, the AF cylinder must be supplied.

The available Drug Tariff regulators allow for flow rate of 2 or 4 litres/minute.



Picture courtesy of Scottish Drug Tariff Part 10

## Ambulatory Oxygen Therapy (AOT)

Since 2004 portable oxygen cylinders have been prescribable for certain patients following specialist assessment. No more than three cylinders are permitted and the patient is required to sign a contract with the community pharmacy.

- The prescriber must specify 'portable oxygen' and the volume of the cylinder (460 litres)
- Currently the Drug Tariff specifies the DD 460 litre cylinder with integral regulator, supplied by BOC
- Supplies of this particular cylinder have been difficult over the past few months, so endorsement has been accepted for other portable cylinders, but as the supply improves towards the end of the year it will be important to revert to DD cylinders, requested and endorsed appropriately
- The pharmacy contractor must endorse the prescription with the oxygen supplier.

### Domiciliary oxygen equipment is not suitable for:

- × **Cluster headache**, which requires 100% oxygen at a rate of 7-12 litres/minute
- × **Emergency use**, which requires high concentration oxygen at flow rate of 10-15 litres/minute.

### Key messages:

- = **Prescribe accurately:** the Scottish Drug Tariff Part 10 has detailed guidance, 'Domiciliary Oxygen Therapy Guidance', available at [www.isdscotland.org/isd/2245.html](http://www.isdscotland.org/isd/2245.html)
- = **Endorse prescriptions accurately:** a useful guide to prescription endorsement is available at [www.psd.scot.nhs.uk/professionals/pharmacy/docs/oxygen.pdf](http://www.psd.scot.nhs.uk/professionals/pharmacy/docs/oxygen.pdf)

*Thanks to Deborah Zuckert, Prescribing Support Pharmacist, South Central Edinburgh Local Health Partnership.*

## eLJF-GPASS v2008.1 upgrade

The latest version of eLJF-GPASS was recently emailed to all practices. This includes all the latest changes to the LJF and is compatible with the latest drug dictionary, PPD 53.

EPASS accredited CPD packs for new users of eLJF-GPASS are available free of charge from MMT or can be downloaded from the LJF website.

# Gonadorelin analogues and prostate cancer

Prostate cancer is the most common cancer in men. Endocrine therapies are commonly used in the management of these patients. Metastatic cancer of the prostate usually responds to hormonal treatment aimed at androgen depletion. Standard treatments include bilateral subcapsular orchidectomy or use of a gonadorelin analogue. Gonadorelin analogues are also known as luteinising hormone releasing hormone (LHRH) or gonadotropin releasing hormone (GnRH) analogues.

There are three sustained release parenteral LHRH analogues licensed in the UK for monthly or 3-monthly treatment to treat a number of indications including prostate cancer. These are triptorelin, goserelin and leuprorelin. The indications differ and are detailed in Table 1.

There is no conclusive evidence to suggest one LHRH analogue is more effective or has fewer adverse events than other analogues for the treatment of metastatic prostate cancer. The assumption has been made that these agents are equally efficacious compared to each other, orchidectomy or diethylstilbestrol for prostate cancer. Comparative studies of the LHRH analogues are limited. Triptorelin is as effective as orchidectomy with regards improvement in pain, urinary symptoms and survival rate while reducing testosterone to castrate level.

## LJF Choices

**1st choice** triptorelin for advanced prostate cancer  
**2nd choice** goserelin for adjuvant and neoadjuvant indications

## Tumour Flare

Chronic administration of any LHRH causes an initial hormonal flare then within a few weeks a fall in pituitary derived luteinising hormone secretion. Antiandrogen cover to prevent flare is administered to all patients for three weeks, LJF antiandrogen is bicalutamide. There is no evidence to suggest that patients appropriately switched between LHRH analogues will experience tumour flare.

## Administration

Goserelin is supplied as a prefilled syringe and is administered subcutaneously. Triptorelin is supplied as a dry powder for reconstitution complete with diluent syringe and needles and is administered intramuscularly.

Full details including side effects can be found in the shared care protocol available on the LJF website [www.ljf.scot.nhs.uk](http://www.ljf.scot.nhs.uk) and on the NHS Lothian intranet at [http://intranet.lothian.scot.nhs.uk/nhslothian/healthcare/a\\_z/m/medicines\\_management/shared\\_care\\_protocols.aspx](http://intranet.lothian.scot.nhs.uk/nhslothian/healthcare/a_z/m/medicines_management/shared_care_protocols.aspx)

**Table 1. LHRH analogue licensed indications**

LHRH analogue	Brand	Strength	Cost £	Licensed Indications for Prostate Cancer				
				Advanced	Locally advanced	Metastatic	Neo-adjuvant	Adjuvant
triptorelin	Decapeptyl <sup>®</sup>	3mg	207.00	✓	✓	✓		
		11.25mg	207.00	✓	✓	✓		
	Gonapeptyl <sup>®</sup>	3.75mg	255.00	✓				
goserelin	Zoladex <sup>®</sup>	3.6mg	252.42	✓	✓	✓	✓	✓
		10.8mg	267.48	✓	✓	✓	✓	✓
leuprorelin	Prostap <sup>®</sup> SR	3.75mg	376.20	✓	✓	✓		✓
	Prostap <sup>®</sup> 3	11.25mg	376.20	✓	✓	✓		✓

### Key messages:

- = Triptorelin is the 1<sup>st</sup> choice in advanced prostate cancer based on patient acceptability and cost
- = Goserelin is the preferred choice for neoadjuvant and adjuvant indications
- = Triptorelin is as effective as orchidectomy

Thanks to Maureen Reid, Primary Care Pharmacist, South West Edinburgh Local Health Partnership and Dawn Owen, Primary Care Pharmacist, North West Edinburgh Local Health Partnership.

# Reduced co-proxamol prescribing saves lives

## Safety concerns

Co-proxamol (dextropropoxyphene and paracetamol combination) was widely prescribed in the UK. Concerns were raised about overdose deaths over 20 years ago.<sup>1</sup> The key issues were that deaths occurred out of hospital in patients who had taken overdoses, and were thought at the time to be more frequent in those who had co-ingested alcohol.<sup>2,3</sup> Subsequent studies identified the fact that dextropropoxyphene was not only a weak opioid but also had actions on sodium channels, as did its active metabolite, norproxyphene.<sup>4</sup> These actions were thought to contribute to the risk of sudden death. Work carried out in Edinburgh over the past four years clearly showed the magnitude of the excess mortality relating to co-proxamol, and it was found that the mortality rate when expressed per volume of prescription was 10 times higher with co-proxamol<sup>5</sup> than other opioid-paracetamol combinations. Many of these patients died outside hospital, and of course a significant proportion ingested drugs which had not been prescribed for them, but for a family member or friend. In response to this data, drug regulatory authorities in the UK re-evaluated co-proxamol, and its licence was withdrawn.

## Self-harm mortality rate has fallen

Media interest this year has indicated that some GPs did not take the opportunity to change patients' therapy in this time window, and may have also been confused about the legal situation of prescribing co-proxamol. In addition, because the price has significantly increased following restriction, many primary care organisations across the UK strongly advised their practitioners not to prescribe co-proxamol. For some patients the result has been somewhat chaotic, but the good news for patients and doctors is that the mortality rates from self-harm in Scotland relating to opioid and paracetamol analgesic combinations, and the mortality rate overall, has dropped dramatically, and it appears that somewhere between 20 and 30 lives a year are being saved in Scotland from this licensing change.<sup>6</sup>

## References:

1. Whittington RM. *Hum Toxicol*. 1984;3 (suppl):175S-85S.
2. Hawton K, *BMJ* 2003;326:1006-8.
3. Hawton K, *Br J Clin Pharmacol* 2005;59:207-12.
4. Afshari R, *Clin Toxicol* 2005;43:255-9.
5. Afshari R, *Br J Clin Pharmacol* 2005;60:444-7.
6. Sandilands EA, *Br J Clin Pharmacol* 2008;66(2):290-3.

Thanks to Dr Euan Sandilands, SpR in Clinical Pharmacology and Professor Nick Bateman, Professor in Clinical Toxicology and Director Scottish Poisons Information Bureau, for contributing this article.

## 'The Bottom Line' No. 4 – Which tetracycline for acne?

Oral tetracyclines are indicated for the treatment of acne, when topical treatment is ineffective or not preferred, and have been used successfully for many years. The LJF recommends oxytetracycline or erythromycin when a systemic treatment is chosen.

The choice of tetracycline, and the dose, has been the subject of debate between clinicians resulting in a wide variation of opinions. There has been a lack of evidence-based data on relative effectiveness and appropriate dosages. In the past, decisions have often been based on the 'latest evidence' from small

trials and information from pharmaceutical companies.

A review article in the British Journal of Dermatology<sup>1</sup> set out to investigate this question and conducted a systematic review of clinical trials (1962-2006). The Brussels-based investigators concluded that all forms of tetracycline had equal efficacy and the antibiotic dosage seems to have no impact on efficacy.

## Reference

1. Simonart T *et al*. Efficacy of tetracyclines in the treatment of acne vulgaris: a review. *Br J Derm* 2008; 158:208-16.

## The Bottom Line:

- One tetracycline is no more effective than another
- Prescribe oxytetracycline, as recommended in the LJF for adults, at the lowest dose (250mg twice daily for 6 months initially).

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View the Lothian Joint Formulary at [www.ljf.scot.nhs.uk](http://www.ljf.scot.nhs.uk)