Western locality shared care information on the prescribing of Tacrolimus

April 2013

- Tacrolimus
- Treatment: resistant rejection in transplant recipients

Aim of Treatment

Tacrolimus is used as primary immunosuppression in liver, kidney or heart transplant recipients and for the treatment of resistant rejection.

Specialist responsibilities

1. To initiate treatment. Patients will have received at least 3 months of treatment, and have been stabilised on a suitable dose.
2. To monitor blood pressure, weight, ECG, blood glucose, U&Es, haematological parameters, lipids, liver and renal function and to communicate these results to the GP.
3. To monitor blood levels of tacrolimus and adjust the dose as necessary. If a dose change is necessary, to communicate to the patient in person or by telephone with additional written information. The letter informing of the dose change will also be sent to the GP.
4. To send a letter to the GP requesting Shared care for a particular patient. This letter will contain the following information:
    a. Diagnosis
    b. Results of blood tests
    c. Dose and name of treatment
    d. Results of any other appropriate investigations
    e. Advice on dose alterations where appropriate
5. To periodically review the patient

General practitioner responsibilities

If GP has agreed to share care:

1. To contact the referring consultant without delay if they do not wish to enter into a Shared care agreement
2. To monitor the patient's overall health and well being
3. To prescribe treatment according to the dose directed by the secondary care physician
4. To monitor side effects of treatment, and seek urgent advice as necessary
5. To contact the appropriate secondary care physician as appropriate
6. To check for possible drug interactions when newly prescribing or stopping concurrent medication
7. Cardiac transplant patients remain under the care of Harefield Hospital, London.

Monitoring

Monitoring will be performed within secondary care. More attention is paid to U&E, hyperlipidaemia and glucose intolerance.

Back-up advice and support

Renal

- Dr P Rowe 01752 792463
- Dr R McGonigle 01752 792462
- Dr W Tse 01752 517580
- Dr I Saif 01752 792467
- Dr H Cramp 01752 245119

Hepatology

- Dr M Cramp 01752 792434
- Dr J Mitchell 01752 792725

Derriford Medicines Information: 01752 439976

Renal Pharmacist 01752 763404

Medicines Optimisation Teams

- NEW Devon CCG, Western Locality 01752 398800
- Kernow CCG 01726 627953

Supporting Information

Preparations

Prograf® is an immediate release formulation of tacrolimus that must be taken twice a day, morning and evening.

Adoport® is a bioequivalent aleternative to Prograf®, is an immediate release formulation of tacrolimus that must be taken twice a day, morning and evening.

Both Advagraf® and Modigraf® are non-formulary

- Advagraf® is a prolonged release formulation that is taken once daily in the morning and is not bioequivalent to Prograf

All are available as 0.5mg, 1mg and 5mg capsules

- Modigraf® are granules for oral suspension administered twice daily as animmediate release formulation. It is available as 0.2mg and 1mg sachets. The preparation is not bioequivalent to Prograf® and has approximately 18% increased bioavailability when compared to Prograf®.

Brand name prescribing is essential to avoid confusion as brands are not interchangeable without careful therapeutic monitoring. Substitution should be made under the close supervision of a transplant specialist.

Dose

Kidney Transplantation: 0.15-0.30mg/kg/day (0.1-0.15mg/kg/day used locally as initial treatment - PHNT renal transplant protocol).

Liver Transplantation: 0.10-0.20mg/kg/day.

Prograf® and Adoprot® should be administered as two divided doses (i.e. morning and evening) on an empty stomach or at least 1 hour before or 2-3hours after a meal.

Doses are altered according to whole blood concentration levels. Higher levels (8-12 micrograms/l) are targeted early post-transplant when the risk of rejection is highest. Later post-transplant levels of 4-8 micrograms/l are targeted.

Contraindications

- Breast feeding
- Known hypersensitivity to tacrolimus or other macrolides

Cautions

Tacrolimus therapy requires careful regular monitoring by adequately qualified and equipped personnel

Side effects

(Refer to SPCs for further information)

Tacrolimus is associated with a wide range of potential adverse effects. The following is a brief overview:

- **Haematological:** anaemia, leukopenia, thrombocytopenia, haemorrhage, leukocytosis, coagulation disorders
- **Metabolism and Electrolytes**: hyperglycaemia, hyperkalaemia, diabetes mellitus, hyperlipidaemia, other electrolyte abnormalities
- **Nervous System**: tremor, headache, insomnia, paraesthesia, anxiety, depression, hallucinations
- **Cardiovascular**: hypertension, hypotension, tachycardia, arrhythmias
- **Respiratory:** dyspnoea, pleural effusion
- **Gastrointestinal**: diarrhoea, nausea, vomiting, dyspepsia, abnormal LFTs, abdominal pain, constipation, ulceration
- **Skin**: pruritis, alopecia, rash, sweating, acne, photosensitivity
- **Musculoskeletal:** cramps
- **Kidney:** abnormal kidney function, kidney failure
- **Miscellaneous:** arthralgia, fever, peripheral oedema, asthenia, dysfunction of urination
- **Malignancies:** benign and malignant neoplasms
- **Hypersensitivity reactions:** allergic and anaphylactoid reactions
- **Infections:** viral, bacterial, fungal or protozoal

Interactions

(Refer to the BNF for further information)

The following drugs have a potentially serious interaction with Tacrolimus and caution must be used when prescribing concurrently:

- Other nephrotoxic drugs e.g. Co-trimoxazole, NSAIDs, aminogylcosides
- Other neurotoxic drugs e.g. Aciclovir
- Other drugs causing hyperkalaemia e.g. ACE Inhibitors, potassium sparing diuretics and salt substitutes

For all interactions below, drugs marked * will probably necessitate tacrolimus dose alteration.

Drugs which may increase tacrolimus levels:

- Ketoconazole*, fluconazole*, itraconazole*, clotrimazole, voriconazole*
- Nifedipine, nicardipine, felodipine, diltiazem
- Erythromycin*, clarithromycin
- HIV protease inhibitors
- Danazol, ethinylestradiol
- Omeprazole
- Nefazodone
- Methylprednisolone
- Grapefruit and grapefruit juice – avoid concomitant use

Drugs which may decrease tacrolimus levels:

- Rifampicin*
- Phenytoin*
- Phenobarbitone
- Carbamazepine
- Methylprednisolone
- St John's Wort– avoid concomitant use

- Drugs whose metabolism may be inhibited by tacrolimus:
- Ciclosporin
- Cortisone
- Phenytoin
- Steroid- based contraceptives

Vaccines may be less effective in immunocompromised patients. Live vaccines should be avoided

Shared Care Agreement Letter – Consultant Request

To: Dr.....

Practice Address.....

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Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: .....

I recommend treatment with the following drug: .....

At the following dosage: .....

I request your agreement to sharing the care of this patient according to the Western Locality Shared Care Information guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Shared Care Information.

Principles of shared care:

GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:			Date:
Consultant name:			
Telephone number:		Fax number	
Email address			

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned shared care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: ..... Date: .....

GP name: ..... *Delete as appropriate.