NORTH AND EAST DEVON HEALTHCARE COMMUNITY SHARED CARE PRESCRIBING GUIDELINE

http://www.devonpct.nhs.uk/Treatments/NE_Devon_Shared_Care_Guidelines.aspx#T
https://nww.devonpctinfo.nhs.uk/Prescribing/SCG/

PREVENTION OF REJECTION IN RENAL TRANSPLANTATION

TACROLIMUS

This shared care guideline sets out details for the sharing of care of adults prescribed **TACROLIMUS** for prevention of **REJECTION OF RENAL TRANSPLANTATION**. These guidelines provide additional limited information necessary to aid in the treatment of patients with **TACROLIMUS**. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and ***do not*** replace them.

INTRODUCTION/BACKGROUND INFORMATION

Immunosuppression is essential in preventing the rejection of allograft organs in hepatic and renal transplantation. However the greatest risks to life after renal transplantation are the adverse effects of long-term immunosuppression.
Tacrolimus is a macrolide immunosuppressant acting as a calcineurin inhibitor. It is similar in action to ciclosporin acting by specifically and competitively inhibiting signal transduction pathways in T-lymphocytes, preventing T-cell proliferation.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

Primary immunosuppression in kidney allograft recipients.
Kidney allograft rejection to conventional immunosuppression regimens.

NICE GUIDANCE

Tacrolimus is an alternative to ciclosporin when a calcineurin inhibitor is indicated as part of an initial or a maintenance immunosuppressive regimen in renal transplantation for adults. The initial choice of tacrolimus or ciclosporin should be based on the relative importance of their side-effect profiles for individual patients.

DOSAGE AND ADMINISTRATION

Dose can be administered by capsule either orally or by nasogastric tube. Tacrolimus should be taken on an empty stomach, at least 1hr before and 2-3hrs after eating, twice daily.

In the maintenance phase, doses are normally reduced to reflect the clinical assessment of rejection and drug tolerability in each individual patient.

CONTRAINDICATIONS

Hypersensitivity to macrolides (e.g. erythromycin, clindamycin).
Hypersensitivity to polyoxyethylated castor oil.
Pregnancy (exclude before starting—if contraception needed non-hormonal methods should be used).
Women should not breast-feed.
Avoid concurrent administration with ciclosporin (care if patient has previously received ciclosporin).

PRECAUTIONS

Cardiomyopathy has been reported and requires either dose reduction or discontinuation if detected as a consequence of therapy.

Interactions (see below)

High dietary intake of potassium (including salt substitutes and potassium supplements) and the use of potassium sparing diuretics should be avoided.
Use of sunbeds and unprotected exposure to sunlight are not recommended due to the potential risk of skin malignancy.
Porphyria.

Avoid other immunosuppressants with the exception of corticosteroids (increased risk of infection and lymphoma)
Anti-lymphocyte treatment should not be given concomitantly due to risk of developing lymphoproliferative disorders.

SIDE EFFECTS

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

Very common /common:
Anaemia, leucopenia, thrombocytopenia, haemorrhage, leucocytosis, coagulation disorders, hypertension, angina, tachycardia, cardiac arrhythmias and conduction abnormalities, thromboembolic events, ischaemic events, vascular disease, pleural and pericardial effusion, nausea/ vomiting, dyspepsia, GI ulceration, abnormal liver function tests, abdominal pain, constipation, weight and appetite change, jaundice, bile duct and gall bladder abnormalities, tremor (may be sign of high drug plasma level), headache, insomnia, visual disorders, perception disorders, hyperglycaemia, hyperkalaemia, hypomagnesaemia, hyperlipidaemia, hyperurcaemia, hypocalcaemia, acidosis, hyponatraemia, hypervolaemia, electrolyte abnormalities, dehydration, new onset of diabetes or worsening of control in Type II diabetes, paraesthesia, depression, agitation, neuropathy, convulsion, incoordination, psychosis, anxiety, nervousness, abnormal dreams, impaired consciousness, emotional ability, hallucinations, otological disturbances, thinking abnormalities, encephalopathy, increased susceptibility to infection, hair loss, pruritis, rash, sweating, acne, photosensitivity, cramps, abnormal kidney function, lesion of kidney tissue, kidney failure, localised pain, fever, peripheral oedema, asthenia, dysfunction of urination.

Uncommon /rare:

Cardiomyopathy, coagulopathies, ECG abnormalities, infarction, heart failure, shock, cardiac arrest, hypoproteinaemia, hyperphosphataemia, increased amylase, hypoglycaemia, hypertonia, atelectasis, asthma, ascites, ileus, lesion of liver tissue, pancreatitis, liver failure, eye disorders, amnesia, cataract, speech disorders, paralysis, coma, deafness, blindness, impairment of the hematopoietic system including pancytopenia, thrombotic microangiopathy, hirsutism, Lyell's syndrome, Stevens-Johnson's syndrome, joint disorders, myasthenia, proteinuria, organ oedema, disorders of female genitals.

Increased risk of malignancies including lymphoma, skin and other tumours appear to be linked to degree and duration of

immunosuppression. The incidence is similar to that of other immunosuppressive agents or therapies.

MONITORING

Secondary care

Monitoring of tacrolimus therapy is the responsibility of secondary care. Those parameters, which will normally be monitored include: blood pressure, visual status, blood trough levels of tacrolimus, electrocardiogram (ECG), blood glucose, electrolytes, creatinine & urea, full blood count and coagulation values and liver function tests.

As levels of tacrolimus in blood may significantly change during diarrhoea episodes, extra monitoring of tacrolimus concentrations is recommended.

Primary care

The monitoring of blood pressure and cholesterol level may be shared with the GP by agreement. Blood pressure should be monitored at least every 3 months or as advised by the specialist. Monitoring of cholesterol is recommended every 6 months.

REFER TO SPECIALIST TEAM IF

Side effect	Action
Increased blood pressure. The suggested treatments are made on an overall benefit assessment. The recommended monitoring of treatment diminishes risks of possible interactions.	Suggested stepwise management of hypertension using the following drug classes: 1. ACE inhibitor or Angiotensin receptor blockers (ARB) - use in glomerular disease but not with renovascular disease 2. Calcium Channel Blocker 3. Beta blocker 4. Diuretic 5. Others 6. Refer to specialist
Hypercholesterolaemia	Discuss with specialist
Cardiomyopathy	Refer to specialist
Neurological symptoms	Refer to specialist

COMMON/SIGNIFICANT DRUG INTERACTIONS

This list is **NOT** exhaustive, the data sheet and BNF must be consulted for a more comprehensive list of potential drug interactions.

Interference with the p450 system

Drugs that **decrease** blood levels (danger of rejection) e.g. St. John's Wort (*Hypericum perforatum*), carbamazepine, rifampicin, phenytoin.

Drugs that **increase** blood levels (danger of toxicity) e.g. macrolide antibiotics, amiodarone, grapefruit or grapefruit juice (not to be ingested for 1 hour prior to dose of ciclosporin), 'conazole' antifungals.

High dose prednisolone or methylprednisolone may have the potential to increase or decrease tacrolimus blood levels.

Nephrotoxic drugs e.g. Aminoglycoside antibiotics, quinolones, trimethoprim, amphotericin, melphalan, colchicine.

Drugs that increase potassium levels e.g. ACE inhibitors, potassium sparing diuretics.

Drugs that increase ciclosporin nephrotoxicity e.g. non-steroidal anti-inflammatory drugs, allopurinol

Drugs that increased hepatotoxicity e.g. Danazol, anabolic steroids, oral contraceptives.

Other drug interactions

Live vaccinations (Oral polio, measles, mumps, rubella, BCG, oral typhoid, yellow fever) should not be administered whilst taking ciclosporin. Attenuated vaccines may be less effective.

Nifedipine - avoid in patients who develop gingival hypertrophy with ciclosporin. May also occur with other dihydropyridine calcium channel blockers.

NOTES

The capsule blisters are outer wrapped in aluminum foil and include a desiccant. Once the foil is opened the capsules have a reduced shelf life of 12 months at room temperature.

- Tacrolimus (Prograf®) infusion 5mg/ml is not considered under this shared care guidance.
- Patients require counseling on the potential risk of skin malignancy from exposure to UV light, including: not using sunbeds and covering exposed skin with clothes or sunscreen with SPF of at least 25.
- Tacrolimus may affect the performance of skilled tasks e.g. driving.

PRODUCT INFORMATION:

Tacrolimus (Prograf®)

- 500 micrograms 50-cap pack = £65.69
- 1 mg 50-cap pack = £85.22
- 5 mg 50-cap pack =£314.84

Capsules should be taken in divided doses in the morning and the evening.

REFERENCES:

- Summary of Product Characteristics: accessed via **www.emc.medicines.org.uk** January 2008.

NICE Technology Appraisal 85 – Renal transplantation-immunosuppressive therapy (Adults) (review). September 2004.

http://www.nice.org.uk/nicemedia/pdf/TA085guidance.pdf

BNF 55 March 2008.

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AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients that are prescribed **TACROLIMUS** for the **PREVENTION OF RENAL TRANSPLANT REJECTION** can be shared between the specialist and the general practitioners. GPs are **invited** to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event the total clinical responsibility for the patient for the diagnosed condition remains with the specialist**. If a specialist asks the GP 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 be accepted by them.
The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Specialist responsibilities:

- ❑ Prescribing the drug is retained for 3 months or until the patient's condition/dose is stabilised and the GP agrees to take over responsibility for prescribing.
- ❑ Provide the patient or patient's parents/guardians/carers with suitable written and verbal information about the drug prior to starting medication and discuss the benefits and side effects of treatment.
- ❑ Monitoring of blood level of **tacrolimus** and other monitoring described in the Shared Care Guideline will normally be the responsibility of secondary care and will normally include creatinine levels.
- ❑ Prompt communication of test results and any treatment changes in therapy at least 3 monthly and whenever a significant change in monitoring parameters occurs or ANY change in drug therapy.
- ❑ Ensure monitoring of blood pressure at least 3 monthly and cholesterol every 6 months or as agreed with the GP.
- ❑ As appropriate, liaison with other members of the multidisciplinary team e.g. renal pharmacist, transplant nurse.
- ❑ Ask the GP whether they are willing to participate in shared care.
- ❑ Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- ❑ Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- ❑ Reporting adverse events to the CSM.

General Practitioner responsibilities:

- ❑ Reply to request for shared care as soon as practical.
- ❑ Prescribing of **tacrolimus** after communication with the specialist regarding the need for treatment.
- ❑ Undertake monitoring of blood pressure minimum of 3 monthly and cholesterol 6 monthly as agreed with the specialist and outlined in the shared care guideline (unless carried out in the renal clinic).
- ❑ Prompt referral to a specialist if there is a change in the patient's status.
- ❑ Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- ❑ Reporting adverse events to specialist and CSM.
- ❑ Immediate referral in the case of a severe adverse event or as per shared care guideline.

Patient responsibilities:

- ❑ Take **tacrolimus** as prescribed
- ❑ Report any adverse effects to their GP and/or specialist regarding their treatment.
- ❑ Ensure that they have a clear understanding of their treatment
- ❑ Ensure they attend for monitoring requirements as per shared care guideline.
- ❑ Aware of the necessity of attendance for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No:	E-mail address
Dr R D'Souza	(01392) 402587	Richard.DSouza@rdeft.nhs.uk
Dr C Bingham	(01392) 406366	Coralie.Bingham@rdeft.nhs.uk
Dr. H. Clarke	(01392) 406367	Helen.Clarke@rdeft.nhs.uk
Dr.M.Bello-Villalba	(01392) 402191	Maria.Bello@rdeft.nhs.uk
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Shared Care Agreement Letter - Consultant Request

To: Dr.....

Practice Address: .....

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Patient Name:
Hospital number:
Date of birth:
Address:

DIAGNOSED CONDITION: **.....**

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

I am requesting your agreement to sharing the care of this patient according to the Devon Primary Care Trust North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

Signed:	
Consultant name:	
Department:	
Contact telephone number:	
Date:	

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