Berkshire West Integrated Care System
Representing
Berkshire West Clinical Commisioning Group
Royal Berkshire NHS Foundation Trust
Berkshire Healthcare NHS Foundation Trust
Berkshire West Primary Care Alliance

Prescribing Guidelines

Prescribing arrangement for the management of patients transferring from ***Secondary Care to Primary Care***

Tacrolimus for the treatment of Nephrotic Syndrome

APC PG 024

For the latest information on interactions and adverse effects, always consult the latest version of the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Approval and Authorisation

Approved by	Job Title	Date
Renal CG, RBH	Dr B Alchi, CG Chair	July 2016
RBH Drugs and Therapeutics Committee	S Hussain, Chair	November 2016
BW GP Medicines Optimisation Committee	W Beecham, Chair	June 2017

Change History

Version	Date	Author	Reason
v.1.0	July 2016		New document

This prescribing guideline remains open to review considering any new evidence.

This guideline should only be viewed online and will no longer be valid if printed off or saved locally

Author	unknown	Date of production:	June 2016
Job Title	unknown	Review Date	August 2020
Protocol Lead	unknown	Version	v.1.0

Introduction

This guidance has been prepared to support healthcare professionals in the implementation of shared care management of patients who have been prescribed tacrolimus for nephrotic syndrome.

Tacrolimus is an immunosuppressant drug with a narrow therapeutic index that is used to induce and maintain remission in membranous glomerulonephritis (GN), focal segmental glomerulosclerosis (FSGS) and minimal change nephropathy. Although unlicensed for this use, it is now recognised in the treatment of the above diseases (see KDIGO, 2012).

Dose

There are three different formulations of tacrolimus: Adoport, Prograf and Advagraf. Adoport and Prograf are immediate release capsules that are taken twice daily, 12 hours apart. Advagraf is a prolonged release capsule that is taken once daily in the morning. Patients are most likely to be on a twice daily regimen.

The dose should be 0.025mg/kg twice a day for Adoport and Prograf.

Dose is 0.05mg/kg once a day for Advagraf.

When prescribing tacrolimus, all prescribers should state the brand name, formulation, the dose and the frequency.

Formulations and brands are NOT interchangeable. Any changes in formulation or brand should only be initiated by the consultant nephrologist.

Administration

On blood monitoring days, the morning dose should be omitted until after the blood is sampled.

Capsules should be taken on an empty stomach or at least **1 hour before or 2-3 hours after a meal.**

Cautions

- Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact to their GP or hospital specialist.
- Tacrolimus is best avoided during pregnancy; women of child bearing potential are advised to use a reliable means of contraception during and for at least three months after treatment.
- Tacrolimus passes into breast milk and therefore breastfeeding should be avoided while taking Tacrolimus.

Contraindications

- Hypersensitivity to tacrolimus, macrolides or any capsule excipients
- Concomitant use of ciclosporin

Side effects

- Hypersensitivity reactions (fever, rigors, rash, myalgia, arthralgia, hypotension, dizziness)
- Alopecia
- Hypertension
- Headache, tremor, insomnia, visual disorders
- Nephrotoxicity
- Hyperglycaemia
- Hepatic dysfunction and hyperlipidaemia
- Increased risk of lymphoma and skin cancer
- Pancreatitis

At the beginning of treatment the patient should be advised to report any signs of bone marrow suppression (i.e. infection, fever, unexplained bruising or bleeding) to the GP and consultant.

Interactions

The following drugs should not be initiated by a GP unless discussed with a consultant nephrologist:

Interacting Drug	Effect on Tacrolimus Blood Level
Erythromycin and Clarithromycin	Increased
Diltiazem, Nicardipine, Verapamil, Felodipine	Increased
Fluconazole, Itraconazole, Ketoconazole	Increased
Carbamazepine	Decreased
Phenobarbital	Decreased
Phenytoin	Decreased
Rifampicin	Decreased
Orlistat	Decreased
St Johns Wort	Decreased

Other interacting agents:

- Patients should not drink grapefruit juice or eat grapefruit, because it can increase tacrolimus levels
- Potassium-sparing medicines may exacerbate tacrolimus-induced hyperkalaemia and should only be initiated with regular monitoring of U&E's.
- Avoid the use of all live vaccines. such as oral polio, oral typhoid, MMR, BCG and yellow fever

Criteria for Use

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Initiate treatment and prescribe until the GP formally agrees to share care (a supply of two weeks or original pack as per agreement).
2	Carry out baseline and subsequent monitoring.
3	Send a letter to the GP requesting shared care for the patient.
4	Routine clinic follow-up on a regular basis.
5	Send a letter to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
6	Evaluation of any reported adverse effects by GP or patient.
7	Contact GP if results of blood monitoring are abnormal with advice for e.g. suspend treatment, decrease dose etc.
8	Advise GP on review, duration or discontinuation of treatment where necessary.
9	Inform GP of patients who do not attend clinic appointments.
10	Ensure that backup advice is available at all times

Monitoring requirements and actions (to be undertaken by the hospital)
• Pre-treatment FBC, renal profile, LFT's, fasting lipids, blood pressure • Subsequent Monitoring ▪ **Renal profile & FBC & tacrolimus trough level** – fortnightly after each dose adjustment, thereafter every three months. ▪ **Tacrolimus trough levels** - Induction of remission: 5 – 8ng/ml Maintenance: 3 – 6ng/ml

General Practitioner responsibilities	
1	Monitor patient's overall health and well being.
2	Prescribe the drug treatment as described
3	Report any adverse events to the hospital specialist, where appropriate
4	Help in monitoring the progression of disease.
5	Ensure the correct brand of tacrolimus is used.
6	Alert the hospital of any suspected non-compliance with treatment.

Patient's / Carer's role	
1	Ask the specialist for information, if he or she does not have a clear understanding of the treatment.
2	Tell the specialist of any other medication being taken, including over-the-counter products.
3	Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address:
Consultant nephrologists	Dr Bassam Alchi Dr Lindsey Barker Dr Nitin Bhandary Dr Cian Chan Dr Oliver Flossmann Dr Mobin Mohteshamzadeh Dr Emma Vaux	(0118) 322 1889	