**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 Inflammatory Bowel Disease (IBD)

APC PG 033

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 |
|---|---|---|
| BW Area Prescribing Committee | APC, Chair | May 2016 |
| RBH Drugs and Therapeutics Committee | DTC Chair | June 2016 |

## Change History

| Version | Date | Author | Reason |
|---|---|---|---|
| v.1.1 | 2014 | Surrey PCT | Shared Care from Surrey PCT |
| v.1.2 | 2016 | A Scott | Adaptation of guidance |
| v.1.3 | 2016 | A Scott | Minor changes following APC May 2016 |
| v.1.3 | October 2017 | n/a | Updated APC Categories |

***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

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|---|---|---|---|
| Author | A Scott | Date of production: | April 2016 |
| Job Title | Lead Pharmacist | Review Date | September 2019 |
| Protocol Lead | A Scott | Version | v.1.3 |

# TACROLIMUS for the treatment of INFLAMATORY BOWEL DISEASE (IBD)

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 IBD.

Tacrolimus is an immunosuppressant drug with a narrow therapeutic index that is used to induce and maintain remission in Ulcerative Colitis. Although unlicensed for this use, it is now recognised in the treatment of Inflammatory Bowel Disease (see BSG, 2011)

## 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 aiming to achieve trough levels of 10ng/ml (+/- 5ng/ml).

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 gastroenterologist.**

## 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.
- Caution is advised when using live vaccines.
- 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.
- Patients should avoid taking grapefruit juice as this can increase tacrolimus levels.

### 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
- hyperkalaemia

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 IBD nurse. This should then be reported to the Consultant and GP.

**Interactions**

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

| Interacting Drug | Effect on Tacrolimus Blood Level |
|---|---|
| Erythromycin and Claithromycin | 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 (as a minimum supply the first month of treatment or until patient is stabilised). |
| 2 | Carry out baseline and subsequent monitoring (apart from blood pressure 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 | Advise GP on review, duration or discontinuation of treatment where necessary. |
| 8 | Inform GP of patients who do not attend clinic appointments. |
| 9 | Ensure that backup advice is available at all times |

| Monitoring requirements and actions (to be undertaken by the hospital) | | |
|---|---|---|
| • Pre-treatment FBC, U&Es, LFT's, CRP, cholesterol, blood glucose, blood pressure<br>• Subsequent Monitoring<br>▪ **U&E's, LFT's & FBC** – Fortnightly for one month, monthly for three months then two monthly thereafter<br>▪ Tacrolimus trough levels as per frequency above | | |
| WBC <3.5 (x10(9)/L) or neutrophils <1.5 (x10(9)/L) | | - STOP tacrolimus<br>- Monitor WCC weekly<br>- When within normal range restart at ½ previous dose and build up to optimum dose as tolerated |
| Creatinine above 130 mmol/l | | - Reduce tacrolimus dose by 1/3<br>- Monitor Creatinine weekly<br>- If continues to rise – STOP tacrolimus<br>- Arrange clinic review to assess other causes for possible raised Creatinine |
| Tacrolimus trough levels | <5ng/ml | Increase dose by 1/3 |
| | >15ng/ml | Decrease dose by 1/3 |
| Drug related side effects | | Decrease dose by 1/3 |

| | |
|---|---|
| Blood pressure Systolic >150mmHg (to be monitored by the GP) | Decrease dose by 1/3 |

| 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. |
| 7 **Monitor blood pressure as per blood test monitoring frequency as above and inform hospital as necessary** |

| Patient's / Carer's role |
|---|
| 1 Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment. |
| 2 Tell the specialist or GP 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: |
|---|---|---|---|
| **IBD Nurses:** | Rebecca Merrick/Charlotte King/Jessica Aparo/Tiago Almeida | (0118) 322 8914 | Ibd.nurses@royalberkshire.nhs.uk |