HERPC

Hull & East Riding Prescribing Committee

Prescribing Framework for Sirolimus for Post Solid Organ Transplant

Patient's Name:…….. NHS Number: ……

Patient's Address:……...……(Use addressograph sticker)

GP's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:…….

Where prescriber is not a consultant:

Consultant's Name: …… GMC No ……..

Consultant's Signature ……... ……. Date:…….

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.

The patient's GP should sign and **send back to specialist**, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **unwilling** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

1. BACKGROUND

These guidelines aim to provide a framework for the prescribing of sirolimus by GPs and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements.

Currently, the preferred immunosuppressant combination for new low risk renal transplants is single agent tacrolimus (brand to be specified by specialist renal team). However sirolimus may still be used for patients who are intolerant to calcineurin inhibitors (tacrolimus, ciclosporin).

Shared care will be implemented 3 months post-transplant.

This document should be read in conjunction with the guidance "Responsibility for prescribing between Primary & Secondary/Tertiary Care" https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

2. INDICATION

Immunosuppression following solid organ transplant.

3. DOSE

Sirolimus is usually given once a day and doses are titrated according to trough blood levels. The target range for blood levels is 5 to12 micrograms/L. The dose to be taken will be advised by the hospital.

4. DURATION OF TREATMENT

Long term

5. CONTRAINDICATIONS AND CAUTIONS

Sirolimus is contra-indicated in pregnancy and breast-feeding women.

Effective contraception must be established before commencing sirolimus and continued during treatment and **for twelve weeks following discontinuation of therapy.** The combined oral contraceptive is a suitable option for this group of patients.

Patients discovered or planning to become pregnant should be started on folic acid 400micrograms daily and referred to the specialist at the earliest opportunity.

6. DRUG INTERACTIONS

Patients receiving sirolimus should be advised against immunization with live vaccines. (Influenza vaccines may be given in this group of patients).

Renal function should be taken into consideration when co-prescribing for renal transplant patients.

Sirolimus is metabolised by cytochrome P450 and therefore interacts with several drugs that are also metabolised by this group of liver enzymes. It is therefore advised that the following drugs are avoided unless discussed with a renal physician.

The following medicines may **increase** sirolimus blood levels

- Erythromycin & clarithromycin
- Diltiazem, nicardipine, verapamil

- Fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole, micafungin, miconazole,

The following drugs may **decrease** sirolimus blood levels
- Rifampicin
- Carbamazepine
- Phenobarbital

In addition grapefruit juice should be avoided as it may **increase** sirolimus levels

7. ADVERSE EFFECTS

These adverse effects will not usually require additional routine appointments unless a problem is anticipated. It is most likely that, if they are going to occur, most of these effects will be seen before the GP is asked to prescribe.

Acne: this is very common. Doxycycline 100mg daily is the preferred treatment option for acne (tetracycline and lymecycline should be avoided in patients with renal impairment). Topical corticosteroid and oral antihistamines have been used for the rash.

Angioedema and peripheral oedema: occur in 10% and generally require drug withdrawal.

GI side effects: Mouth ulceration is the most frequently seen gastro-intestinal tract effect. Swab for Herpes simplex before treating established ulcers with topical triamcinolone 0.1% (Adcortyl in Orabase). Ulceration is usually transient. Abdominal pain and diarrhoea can occur.

Arthralgias: may require dose adjustment or discontinuation of sirolimus and are an indication for referral to the renal physician.

Interstitial lung disease (including pneumonitis) is seen in between 1% and 10% and is an indication for drug withdrawal by the renal physician.

Blood dyscrasias: Anaemia and thrombocytopaenia are seen more frequently than leucopenia or neutropenia, and particularly when co-prescribed with mycophenolate. Often the dose of mycophenolate is adjusted first.

Electrolyte disturbances: Sirolimus is associated with hypokalaemia and hypophosphataemia. These usually respond to dietary advice.

Hypertension: this is a common side effect, and can be monitored and treated by the GP. Patients who are started on an ACE inhibitor or Angiotensin-2 blocker should have their U&Es checked after initiation. If creatinine rises by more than 20% then refer to specialist. Amlodipine may also be used to control blood pressure, but diltiazem, verapamil and nicardipine should be avoided as they may increase sirolimus levels (See SPC)

Nephrotoxicity: This may be due to high blood levels or acute rejection. Such patients should be referred to the specialist.

Hyperglycaemia: This may occur (more likely than with ciclosporin). Blood glucose levels should be monitored in clinic.

Hepatic dysfunction and hyperlipidaemia: Patients will be monitored via the transplant clinic and appropriate treatment initiated if required.

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

8. MONITORING

Monitor patient to ensure concordance with treatment, monitor for side effects (listed in section 7)
For details and frequency of blood tests see section 10

9. INFORMATION TO PATIENT

See above – pregnancy
Patients should be informed about benefits and risks of treatment and need for monitoring.

Patients should be told to go to their GP immediately if they experience any fever, rash, bruising, bleeding, jaundice or infection.

10. RESPONSIBILITIES OF CLINICIANS INVOLVED

Stage or treatment	**Hospital Specialist**	**General Practitioner**
Initiation of treatment	Treatment is initiated in the Leeds on transplantation	Not involved
Monitoring of treatment and maintenance	<u>0 to 3 months post-transplant</u>: Prescribe Sirolimus Monitor patient for side effects. Perform blood tests when required dependant on clinical need. (U&Es, FBC, LFTs, trough tacrolimus levels) Check Mid-Stream Urine, Blood pressure, blood glucose and lipids. Inform GP of necessary changes to treatment. Inform GP when patient is approaching 3 months post-transplant and on a stable dose requesting GP continue prescribing. Month 4 and thereafter: At each clinic visit and in between times depending on clinical need Inform GP when patient is on a stable dose and request that prescribing is transferred. Inform GP of significant findings and necessary changes to therapy. Available for advice	Take on shared care when patient is stable and requested by the specialist team. Identify to specialist problems with concordance to therapy. Identify adverse reactions and treat or refer where appropriate. (U&E and FBC will be monitored by the specialist and relevant findings communicated to the GP)

Contact Details:
During office hours: Please contact the relevant renal consultant's secretary via Hull Royal Infirmary switchboard. (01482)328541
Out of hours: Contact the on call renal consultant via switchboard
Specialist Transplant Nurses: (01482) 674110
Renal Pharmacist: (01482) 674043, or ask for bleep 140 when you contact the switchboard on 01482-875875.

APPROVAL PROCESS

Written by:	**Paul Kendrew. Reviewed by Aaron Acquaye, Renal Pharmacist**
Consultation process:	**Specialists teams in Renal Medicine,**
Approved by:	**MMIG**
Ratified by:	**HERPC Updated Mar 2019**
Review date:	**Mar 2022**