Western Locality Shared care information on the prescribing of Sirolimus

April 2013

- Sirolimus
- Prophylaxis of acute rejection in renal transplant recipients

Aim of Treatment

Sirolimus is used for prophylaxis of acute rejection in renal transplant recipients in combination with other immunosuppressive agents in adults. Sirolimus may be selected as an alternative to CNI (Calcineurin inhibitor i.e. ciclosporin and tacrolimus) immunosuppression due to intolerance or to avoid graft loss associated with chronic allograph nephropathy.

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 sirolimus 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

Monitoring

Monitoring will be performed within secondary care. More attention is paid to FBC, lipids and clinical complications such as rash, mouth ulcers and pneumonitis.

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

Derriford Medicines Information: 01752 439976

Medicines Optimisation Teams

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

Supporting Information

Preparations

Sirolimus is available as 500 micrograms, 1mg and 2mg tablets and a 1mg/mL oral solution.

The 500 microgram tablet is not bioequivalent to the 1mg and 2mg tablets. Multiples of 500 microgram tablets should **not be used** as a substitute for other tablet strengths

Dose

- **Initial therapy**: According to PHNT renal transplant protocol. Sirolimus will always be initiated by secondary care.
- Sirolimus is usually avoided early post transplantation due to wound healing complications. It may be initiated at 6 months or later post-transplant if there is evidence of Calcineurin inhibitor (Tacrolimus or Ciclosporin) toxicity.
- **Maintenance therapy:** to achieve trough levels of 4-12nanograms/ml (levels currently sent for analysis at Harefield). Normal maintenance dose in the general range 2-4mg daily.
- Sirolimus should be administered as a single daily dose, the patient advised to take the dose at the same time each day. Ideally the dose should be taken on an empty stomach or at least 1 hour before or 2-3hours after a meal.
- If ciclosporin is co-prescribed then sirolimus should be taken at least 4 hours after the ciclosporin dose to avoid the drug-drug interaction.

Contraindications

- Pregnancy
- Breast feeding
- Known hypersensitivity to sirolimus or formulation excipients

Cautions

- Sirolimus therapy requires careful regular monitoring by adequately qualified and equipped personnel
- Afro Caribbean patients may require higher doses
- Hepatic impairment
- Increased susceptibility to skin cancer and infections
- Bone marrow suppression – Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection an inexplicable bruising or bleeding

Side effects

(Refer to SPCs for further information)

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

- **General:** Lymphocele, Peripheral oedema, abnormal hearing, fever, infection
- **GI disturbances:** Abdominal pain, diarrhoea, stomatosis
- **Cardiac disorders:** tachycardia

- **Vascular disorders:** venous thromboembolism
- **Blood and lymphatic system disorders:** Anaemia, thrombocytopenia, leucopenia, neutropenia, thrombotic thrombocytopenia / haemolytic uraemic syndrome
- **Metabolic and nutritional disorders:** Raised cholesterol and triglycerides, hypokalaemia, increased LDH, abnormal LFTs, hypophosphataemia and hyperglycaemia.
- **Musculoskeletal:** Arthralgia, bone necrosis
- **Respiratory, thoracic:** epistaxis, pneumonia, pneumonitis
- **Skin:** Acne, skin cancer, rash, impaired healing
- **Renal and urinary:** Proteinuria, UTI, pyelonephritis

Less commonly: pancreatitis, lymphoma, PTLPD (post-transplant lympho proliferative disorder), pancytopenia, lymphodema, hypersensitivity reactions, nephrotic syndrome.

Interactions

(Refer to the BNF for further information)

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

Sirolimus is extensively metabolised by the CYP3A4 isoenzyme.

Drugs which may increase sirolimus levels:

- Ciclosporin (via CYP3A4 substrate mechanism; give sirolimus at least 4 hours after dose)
- Ketoconazole, voriconazole, fluconazole, itraconazole, clotrimazole, miconazole
- Erythromycin, clarithromycin, telithromycin
- HIV protease inhibitors
- Danazol
- Bromocritptine
- Cimetidine, metoclopramide
- Diltiazem, verapamil, nicardipine
- Grapefruit and grapefruit juice – avoid concomitant use

Drugs which may decrease sirolimus levels:

- Rifampicin, rifabutin
- Phenytoin
- Phenobarbital
- Carbamazepine
- St John's wort

The SPC does not exclude the risk of sirolimus affecting the efficacy of the oral contraceptive pill (both POC and COC).

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.