Health and Social Care Board

Interface Pharmacist Network
Specialist Medicines

# Sirolimus

## Post Solid Organ Transplant Shared Care Guideline

Using a printed guideline? Always check you are using the most up to date version. See www.ipnsm.hscni.net

| Specialist Details | Patient Identifier |
|---|---|
| **Name:** _____ | |
| **Location:** _____ | |
| **Tel:** _____ | **Date:** _____ |

### Introduction

**Licensed indication**: immunosuppression post organ transplant.

**Post renal transplant**: sirolimus is licensed to be initially prescribed as part of a triple therapy immunosuppressive regimen, but in practice is rarely used in this way and is not prescribed in the early post-transplant period in Northern Ireland. It is used occasionally when other immunosuppressive drug combinations are not clinically suitable for the individual patient.

- **Adult dosage and administration.** The dose will be advised by the specialist. The patient will be commenced on a dose of 1- 2mg once daily; the dose will vary according to the individual patient. Maintenance doses will vary between renal transplant patients.

**Post-liver transplant:** sirolimus is rarely used post liver transplant and is indicated only when tacrolimus or ciclosporin have not been tolerated.

- **Adult dosage and administration:** The dose will be adjusted to individual requirements and will be titrated to achieve the desired trough blood level.

**Available as**: sirolimus (Rapamune® ) 500micrograms, 1mg and 2mg tablets, and oral solution 1mg/ml. The 500microgram tablet is not bioequivalent to the 1mg and 2mg tablets. Multiples of 500microgram tablets should not be used as a substitute for other tablet strengths. If changing between oral solution and tablets it is recommended that a trough concentration be taken 1 or 2 weeks after switching formulations or tablet strength to confirm that the trough concentration is within the recommended target range
Doses should be taken consistently either with food or without food.

### Hospital Specialist Responsibilities

- Agree shared care with the patient's GP.
- Send a copy of this guideline to the GP.
- Provide patient/carer with relevant information on use, side effects and the need for monitoring of medication
- Baseline tests and ongoing safety monitoring:
  - FBC
  - LFT
  - U&E
  - Urinalysis
  - Lipids
  - Blood glucose
  - Blood pressure
  - Trough sirolimus level
- Drug monitoring and any sirolimus dose adjustments.
- Review results of safety monitoring and request additional tests as necessary.
- Investigate, as appropriate, where symptoms suggest viral or fungal infections or possible tumours.
- Provide any other information or advice for the GP if required

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| **GP Responsibilities** | • Prescribe sirolimus (Rapamune®).<br>• Monitor patient's overall health and wellbeing.<br>• The Liver Unit may occasionally request levels or tests to be repeated at the GP practice but will provide specific advice on this and the process to follow.<br>• Identify and report adverse drug reactions to the initiating specialist and the usual bodies (e.g. MHRA/CHM).<br>• Ensure no drug interactions with other medicines.<br>• Administer **inactivated** influenza vaccine annually unless otherwise advised by the initiating specialist.<br>• Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia.) - see BNF or Green Book.<br>• Passive immunization using Varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals, for advice if exposure is suspected.<br>• **Suspected non-compliance** with immunosuppression is serious and can lead to loss of the graft - refer to the specialist urgently. |
| **Adverse Effects, Precautions and Contraindications** | **Nephrotoxicity:** If a significant sustained reduction in GFR occurs consider referral to specialist. The development of proteinuria should be highlighted to the specialist.<br>**Acute Kidney Injury (AKI):** Transplant patients are at increased risk of developing AKI. ACEI, ARBs, and NSAIDs should be withheld in situations of hypotension/hypovolaemia. (GAIN, 2014)<br>**Infection:** immunosuppressants can increase susceptibility to infection.<br>**Wound healing**: sirolimus may impair wound healing and should be substituted with an alternative if a patient is to have surgery, or has an ulcer etc. This should be high lighted to the specialist.<br>**Nausea, diarrhoea** can occur initially. Refer if persistent or severe.<br>**Hyperlipidaemia** and **hepatic dysfunction** are screened for at outpatient appointments. Statin therapy is recommended for hyperlipidaemic patients<br>**Blood disorders;** Leucopenia, anaemia, thrombocytopenia, thrombocytopaenic purpura, pancytpopenia and neutropenia have been reported are most likely to be discovered at outpatient appointments. GPs should be alert to any oral ulceration / sore throat, unexplained rash or abnormal bruising or bleeding.<br>**Hypertension** may be encountered. If treatment is required follow guidelines but do not use diltiazem or verapamil as they may increase plasma sirolimus levels. If hypertension remains uncontrolled refer to specialist<br>**Acne** can occur in a minority of patients.<br>**Cancer risk.** Patients receiving long-term immunosuppressive drugs are at increased risk of developing a malignancy. The most frequently occurring types are lymphoma and skin malignancy. The avoidance of excessive exposure to the sun, and the use of high factor sunscreen and protective clothing are advised. Adherence to population screening programmes is particularly important in this population.<br>**Pregnancy / Contraception.** Patients discovered or planning to become pregnant should be referred to the specialist at the earliest opportunity. Initially post-transplant, barrier contraception is the preferred method of contraception, but at a later stage the combined oral contraceptive is a suitable option for transplant recipients. Intra-uterine devices are not suitable for this group of patients.<br>**Breastfeeding.** Patients should not breastfeed while receiving sirolimus.<br>**Vaccines**. Live vaccines should be avoided, except on the advice of initiating specialist. |
| **Common Drug Interactions** | **The interactions listed below relate to sirolimus. Consideration should be given to the other agents used as part of a regimen.**<br>The degree of renal function should be taken into consideration when co-prescribing for renal transplant patients. Sirolimus is metabolised by cytochrome P450 and interacts with many drugs that are also metabolised by this group of liver enzymes.<br><br>**The following drugs should not be initiated by GP unless discussed with specialist:**<br>**Antibiotics:** erythromycin and clarithromycin increase sirolimus levels; rifabutin and rifampicin decrease sirolimus level.<br>**Anti-epileptics**: carbamazepine; phenobarbital and phenytoin decrease sirolimus levels.<br>Patients should avoid taking **grapefruit juice or grapefruit** as this can cause an increase in sirolimus levels. |

## Common Drug Interactions (continued)

**Antifungals:** fluconazole; itraconazole, posaconazole and voriconazole increase sirolimus levels
**Antriretrovirals:** some may increase sirolimus levels.
**Calcium-channel blockers**: diltiazem, and verapamil increase sirolimus levels.
**Diuretics** may exacerbate sirolimus-induced hypokalaemia and should only be initiated with regular monitoring of U&Es.
**St John's Wort** is known to decrease sirolimus levels. Herbal medicines may have an effect on drug levels. Avoid concomitant use.

## Communication

**Renal Units**

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| Altnagelvin Hospital: Renal Unit | 028 7161 1162 |
| Antrim Hospital: Renal Unit | 028 9442 4894 or 028 9442 4472 |
| Belfast City Hospital: Renal Unit | 028 9504 0719 |
| Daisy Hill Hospital: Renal Unit | 028 3083 5036 |
| Tyrone County Hospital: Renal Unit | 028 8283 3350 |
| Royal Belfast Hospital for Sick Children: Dialysis Unit | 028 9063 6621 |
| Ulster Hospital: Renal Unit | 028 9056 4839 |

**Liver Unit**

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| Royal Victoria Hospital | 028 9063 3182 |

**This information is not inclusive of all prescribing information and potential adverse effects.**
**Please refer to full prescribing data in the SPC or the BNF**