HSC Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Ciclosporin (Neoral®)

Post Transplant Shared Care Guideline

Specialist Details	Patient Identifier
Name: ______________________	
Location: ______________________	
Tel: ______________________	Date: ______________________

Introduction

Licensed indication: prevention of graft rejection following transplantation.
Ciclosporin is no longer first line therapy post solid organ transplant. Transplant patients previously established on ciclosporin will usually remain on this drug. Ciclosporin is never prescribed concurrently with tacrolimus.

Adult Dosage and Administration

- **Post renal transplant**: ciclosporin may be prescribed alone or in combination with other immunosuppressants. Doses of ciclosporin are titrated to a desired trough ciclosporin blood level and may vary between patients, but are usually in the range of 100mg to 250mg twice daily. Doses may be reduced as the time elapsed from transplant increases.
- **Post liver transplant**: ciclosporin may be prescribed alone or in combination with prednisolone. Doses of ciclosporin are titrated to achieve the lowest effective dose and are adjusted according to liver function tests. Initially the levels are usually above 100 micrograms/L but later on can be lower.
- **Bone marrow transplant:** ciclosporin may be prescribed alone or in combination with prednisolone and on occasion other immunosuppressants. Doses of ciclosporin are titrated to a desired trough ciclosporin blood level usually 100-250 micrograms/L. Doses required to achieve this vary between patients, but are usually in the range of 50mg to 200mg twice daily. Treatment is usually only for 3-6 months with gradual dose reductions as the time elapsed from transplant increases. Some patients who develop graft verse host disease may require to continue on treatment for years or even lifelong.

Available as: ciclosporin (Neoral®) 10mg, 25mg, 50mg and 100mg capsules, and 100mg/ml solution (note small volumes required for dosing). (A minority of patients are prescribed the original brand of ciclosporin, Sandimmun® which remains available on a named-patient basis). **Other brands of ciclosporin may be available but due to differences in bioavailability between brands, ciclosporin should be prescribed by brand name).**

Neoral® should be taken every twelve hours. The 100mg capsule is large and often patients will prefer to take the 50mg strength.

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	• Lipids
• U&E	• Blood glucose	• Blood pressure
• Urinalysis	• Trough ciclosporin level	

- Drug monitoring and ciclosporin 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.

GP Responsibilities

- Prescribe ciclosporin as Neoral®.
- Monitor patient's overall health and well-being.
- 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.
- Identify and report any adverse drug reactions to the initiating specialist and usual bodies (e.g. MHRA/CHM)
- Ensure no drug interactions with other medicines.
- Administer inactivated influenza vaccine annually unless otherwise advised by the initiating specialist.
- 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/Green Book
- Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in non-immune patients exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals for advice if exposure is suspected.
- 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.
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)
Infection: immunosuppressants can increase susceptibility to infection.
Blood disorders: Leucopenia, thrombocytopenia and anaemia 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
Hypertension is common. If treatment is required, follow guidelines but do not use diltiazem, nicardipine, lercandipine or verapamil as they may increase plasma ciclosporin levels. Nifedipine levels may be increased by ciclosporin. Refer if hypertension remains uncontrolled.
Benign gingival hyperplasia is relatively common. Patients should be advised on good oral hygiene. (Increased risk with concomitant use of nifedipine)
Hypertrichosis Facial hair bleaches and depilatory creams are safe and often effective.
Headache, tremor and paraesthesia are frequently seen. If persistent or severe they may reflect toxic levels of ciclosporin - refer to the initiating specialist.
Hepatic dysfunction and **hyperlipidaemia** are screened for at outpatient appointments. Statin therapy is recommended for hyperlipidaemic patients.
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.
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.
Breastfeeding. Patients should not breastfeed whilst receiving ciclosporin.
Vaccines. Live vaccines should be avoided, except on the advice of initiating specialist.

Common Drug Interactions

The interactions listed below relate to ciclosporin. Consideration should be given to the other agents used as part of a regime.
Ciclosporin is metabolised by cytochrome P450 and interacts with many drugs that are metabolised by this group of liver enzymes.
The following drugs should not be initiated by a GP unless discussed with the specialist:
Antibiotics: erythromycin, clarithromycin and azithromycin increase ciclosporin levels; rifampicin decreases ciclosporin levels.
Antifungals: fluconazole, itraconazole, posaconazole and voriconazole increase ciclosporin levels.
Calcium channel blockers: diltiazem; nicardipine, verapamil and lercanidipine increase ciclosporin levels. Nifedipine levels may be increased by ciclosporin.
Anti-epileptics: carbamazepine; phenobarbital and phenytoin decrease ciclosporin levels.
Anti-obesity drugs: orlistat decreases ciclosporin levels.
Dabigitran: concomitant use should be avoided.
Patients should avoid taking **grapefruit juice or eating grapefruit** as this can cause an increase in ciclosporin levels. Patients may also counselled to be cautious with Seville orange, pomelo, pomegranate.
Potassium-sparing diuretics, Potassium salts, Aldosterone antagonists e.g. spironolactone and eplerenone may exacerbate ciclosporin-induced hyperkalaemia and should only be initiated with regular monitoring of U&Es.
St John's Wort is known to decrease ciclosporin levels. Herbal medicines may have an effect on drug levels. Avoid concomitant use.
Statins. Lower doses of statins should be used to reduce the risk of muscular toxicity.
Other interacting drugs of significance: aliskerin, ambrisentan, amiodarone, antiretrovirals, bosentan, carvedilol, colchicine, digoxin, methotrexate, octreotide.

Communication

Renal Units

- 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
- Omagh hospital and primary care complex (OHPCC): 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

- Royal Victoria Hospital 028 9615 6222

Bone Marrow Transplant

- Belfast City Hospital: Haematology Helpline 028 9504 0666

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

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