Western Locality Shared Care information ~ Ciclosporin (other conditions)

April 2013

Specialist: Please complete the Shared Care letter sending a request to GP (see bottom of the page)

GP: Please indicate whether you wish to share patient's care by completing letter and return to specialist

Aim of treatment

Ciclosporin is used as primary immunosuppression to prevent graft rejection following a variety of organ, including liver and kidney, and tissue transplantation. Ciclosporin is used in the prevention and treatment of graft versus host disease and other autoimmune disorders such as immune thrombocytopenia and autoimmune haemolytic anaemia. Ciclosporin is also used in a number of other conditions, usually when conventional therapy is ineffective or inappropriate, including psoriasis, atopic dermatitis, rheumatoid arthritis and nephrotic syndrome.

For Rheumatology and Dermatology patients refer to the appropriate guideline

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 ciclosporin 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. Prompt verbal communication followed up in writing to GP of changes in treatment or monitoring requirements, results of monitoring, assessment of adverse events or when to stop treatment. Urgent changes to treatment should be communicated by telephone to GP
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. Check for possible drug interactions when newly prescribing or stopping concurrent medication

N.B Cardiac transplant patients remain under the care of Harefield Hospital, London.

Monitoring during treatment: general practice

Monitoring will be performed within secondary care. More attention is paid to U&E, hyperlipidaemia, hypertension, glucose intolerance and cosmetic problems (hirsuitism / gingival hypertrophy).

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

Hepatology

- Dr M Cramp 01752 792434
- Dr J Mitchell 01752 792725

Haematology

- Dr J Copplestone 01752 792393
- Dr M Hamon 01752 792876
- Dr A Prentice 01752 792394
- Dr S Rule 01752 517504
- Dr T Nokes 01752 431001
- Dr H Hunter 01752 431003
- Dr D W Thomas 01752 517615

Derriford Medicines Information: 01752 439976

Renal Pharmacist 01752 763404

Medicines Optimisation Teams

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

Supporting Information

This guideline highlights significant prescribing issues, not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Preparations

Ciclosporin is available as 10mg, 25mg, 50mg and 100mg capsules, also as a 100mg/mL oral solution and a concentrate for IV infusion 50mg in 1 mL, 250mg in 5mL.

The prescriber should specify the brand of ciclosporin to be dispensed because of differences in bioavailability. **The oral brand used in Plymouth is Neoral®**

Dose

- **Kidney and organ transplantation**: Commences at 8-10mg/kg per day in two divided doses immediately post transplantation (local guidelines), maintenance dose of generally 2 to 6 mg /kg per day. Doses are frequently lower in liver transplantation.
- **Bone marrow transplantation / prevention and treatment of graft versus host disease**: maintenance dose 12.5mg /kg per day for 3 to 6 months before tailing off to zero.
- **Nephrotic syndrome**: Maintenance dose should not exceed 5mg/kg per day for adults or 6mg/kg per day for children
- Ciclosporin should be administered as two divided doses (i.e. morning and evening). Capsules should be taken with a mouthful of water and swallowed whole.
- Oral solution should be diluted with water, orange juice or squash (not grapefruit juice) immediately before being taken.

Doses are adjusted according to response or side effects.

Post kidney transplantation, doses are adjusted by monitoring ciclosporin through levels and kidney function. Higher levels are targeted early post-transplant when the risk of rejection is highest. After renal transplantation "C2" levels (i.e. levels taken 2 hours after the dose) are monitored for the first 6 months after which trough levels are monitored. Only troughs levels are monitored after liver transplantation. Troughs: >6 months 75-150ng/ml (traditionally 0-6 months 150-300ng/ml)

C2 levels

Month post-transplant	Target C2 level ng/ml
1	1500
2	1300
3	1100
4-6	900
>6	700

Contraindications

- Breast feeding
- Known hypersensitivity to ciclosporin

- Psoriatic and atopic dermatitis patients with abnormal renal function, uncontrolled hypertension, uncontrolled infections or any other kind of malignancy other than that of the skin
- Rheumatoid arthritis (RA) patients with abnormal renal function, uncontrolled hypertension, uncontrolled infections or any other kind of malignancy
- RA patients < 18 years old
- Nephrotic syndrome patients with uncontrolled hypertension, uncontrolled infections or any other kind of malignancy
- Concomitant use with tacrolimus
- If ciclosporin is to be concomitantly administered with a statin then the prescriber should refer to the product information for the relevant statin as the dose may need to be reduced. Rosuvastatin is specifically contraindicated with ciclosporin

Cautions

- Ciclosporin can impair renal function. Close monitoring of serum creatinine and urea is required and dosage adjustment may be necessary
- Therapy requires careful regular monitoring by adequately qualified and equipped personnel

Side effects

(Refer to SPCs for further information)

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

- Haematological -anaemia, thrombocytopenia
- Metabolism and Electrolytes - hyperlipidaemia, hypercholesterolaemia, hyperuricaemia, hyperkalaemia, hypomagnesaemia
- Nervous System - tremor, headache
- Cardiovascular - hypertension
- Gastrointestinal – anorexia, nausea, vomiting, abdominal pain, diarrhoea, gingival hyperplasia
- Hepato-biliary disorders – hepatic dysfunction
- Skin – hypertrichosis
- Musculoskeletal – muscle cramps, myalgia
- Kidney – renal dysfunction
- Miscellaneous – fatigue
- Malignancies – increased risk of malignancies including lymphomas, skin and other tumors
- Infections – predisposes patients to infection with a variety of pathogens including bacteria, parasites, viruses and other opportunistic pathogens.

Interactions

(Refer to the BNF for further information)

The following drugs have a potentially serious interaction with ciclosporin and caution must be used when prescribing concurrently: Ciclosporin is known to interact with a wide range of medicines. If concomitant use of a drug known to interact with ciclosporin cannot be avoided frequent assessment of renal function and monitoring for side effects will be required and in transplant patients ciclosporin blood level and dosage adjustment may be necessary.

- Other nephrotoxic drugs e.g. Co-trimoxazole, NSAIDs, aminoglycosides
- Other neurotoxic drugs e.g. Aciclovir

- Other drugs causing hyperkalaemia e.g. ACE Inhibitors, potassium sparing diuretics and salt substitutes

For all interactions below, drugs marked * will probably necessitate cicrolimus dose alteration.

Drugs which may increase ciclosporin levels

- Macrolide antibiotics (mainly erythromycin* and clarithromycin)
- Diltiazem, niocardipine, verapamil
- Oral contraceptives
- Danazol
- Methylprednisolone (high dose)
- Allopurinol
- Ketoconazole*, fluconazole*, itraconazole*
- Metoclopramide
- Ursodeoxycholic acid
- Protease inhibitors
- Tacrolimus
- Grapefruit juice – avoid concomitant use
- Amiodarone

Drugs which may decrease ciclosporin levels:

- Barbiturates
- Carbamazepine
- Phenytoin*
- Rifampicin*
- Octreotide
- Orlistat
- St John's Wort – avoid concomitant use
- Ticlopidine

Other interactions:

- Digoxin – reduced clearance
- Prednisolone – reduced clearance
- Colchicine - increased risk of muscular toxicity
- HMG-Co reductase inhibitors – increased risk of muscular toxicity
- Nifedipine – increased risk of gingival hyperplasia
- 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.