Frimley Park Hospital NHS
NHS Foundation Trust

Shared Care Guidelines for the use of *Ciclosporin (Neoral)* in *Psoriasis* and *Rheumatoid Arthritis*

Section 1: Agreement for transfer of prescribing to GP
Please sign this form and return it to the named consultant if you are willing to share care for the patient. Please also keep a signed copy for your records.

Patient details/addressograph

Name……

Address……
……..
……..
……..

DOB…… Hospital no…….

Drug name and dose:……

Desired clinical outcome as agreed with the patient/carer

……

Consultant Address:…… ……... ……... ……... Contact no:……	**Agreement to shared care, to be signed by GP and Consultant before transfer of care to GP** Consultant signature: …… Date:……
GP Address:…… …….. …….. Contact no:……	GP signature: …….. Date:……..

In case of emergency contact *Name:*……

Contact number:……

Prepared by: Jacqueline Kew in conjunction with Dr Mark Lloyd and Dr Fiona Anthony, May 2007
Approved by: Prescribing Forum, Frimley Park Hospital
Date: July 2007 Review date: July 2009

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Responsibilities of the Consultant

- Identify suitable patients and initiate therapy
- Stabilise the patient on the appropriate dose
- Assess the efficacy of the therapy
- Provide written information to the patient on signs and symptoms of bone marrow depression
- Once the patient is stabilised seek agreement from the patient's GP to share the care of the patient in accordance with these guidelines
- Provide the GP with a full summary/ discharge letter at least 2 weeks before the intended implementation of the shared care scheme
- Provide the opportunity for the GP and consultant to discuss the case and the shared care guideline
- Keep the GP informed of the patient's progress after each OP clinic visit
- Inform the GP of any changes to drug therapy and dosage
- Advise on appropriate action if blood results are abnormal
- Arrange routine follow up of the patient at appropriate intervals

Responsibilities of the GP

- Provide the prescription for ciclosporin (Neoral) once the patient is stabilised
- Monitor blood results as per guideline and liaise with the consultant
- Monitor the patient's overall health and refer back to the consultant as necessary
- Report adverse events suffered by the patient to the consultant and MHRA

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Section 2: Information

Ciclosporin exerts its immunosuppressive action directly through T-lymphocytes. Ciclosporin is actively biotransformed to approximately 15 different metabolites. There is no single major metabolic pathway.

Licensed indications

Dermatology

- The treatment of severe psoriasis, in patients in whom conventional therapy is ineffective or inappropriate.
- The short-term treatment (8 weeks) of patients with severe atopic dermatitis in whom conventional therapy is ineffective or inappropriate.

Rheumatoid arthritis

- The treatment of severe, active rheumatoid arthritis in patients in whom classical, slow acting anti-rheumatic agents are inappropriate or ineffective.

Dose

Dermatology

To *induce remission*, the recommended initial dose is 2.5mg/kg a day given orally in two divided doses (5mg/kg per day may be used in patients whose condition requires rapid improvement). If there is no improvement after 1 month, the daily dose may be gradually increased to a maximum of 5mg/kg per day in 2 divided doses. Treatment should be discontinued if sufficient response is not achieved within 6 weeks on a dose of 5mg/kg per day.
For *maintenance treatment* - The dosage must be individually titrated to the lowest effective level and should not exceed 5mg/kg per day, given orally in two divided doses.
Duration of treatment - once satisfactory response is achieved ciclosporin may be discontinued and subsequent relapse managed with re-introduction at the previous effective dose. In some patients continuous maintenance therapy may be necessary.

Rheumatoid arthritis

To *induce remission*, the usual starting dose at Frimley Park Hospital is 1mg/kg per day, given orally in two divided doses, for the first 6 weeks of treatment. If the clinical effect is insufficient, the daily dose may be increased gradually as tolerability permits, but should not exceed 4mg/kg per day.
For *maintenance treatment* - the dose has to be titrated individually according to tolerability.
Duration of treatment - If, after 3 months of treatment at the maximum permitted or tolerable dose the response is inadequate, treatment should be discontinued.

Patients should be maintained on the same oral form of ciclosporin – prescribe by brand name

Cautions

- Patient should avoid contact with infections such as chickenpox and shingles
- Renal impairment

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• High dietary potassium intake – potassium intake should be reduced and potassium sparing diuretics or supplements should be avoided
• Hypomagnesaemia
• Hyperuricaemia
• Porphyria
• May increase risk of benign intracranial hypertension
• Taking other drugs – there are **multiple drug interactions with ciclosporin, see side effects section and the BNF appendix for full list of interactions**. Particular care should be taken with prescribing drugs known to have nephrotoxic effects

Contra-indications

• Combination with tacrolimus
• Uncontrolled hypertension
• Uncontrolled infections
• Malignancy
• Pregnancy – this drug is contra-indicated in pregnancy as it has the potential to affect the development of the unborn child. Men and women of childbearing age should be advised to use a reliable form of contraception during treatment. When planning a pregnancy it is important that both men and women on this drug discuss medication with the team (at least six months before conception) since all drugs can potentially affect the unborn child
• Breastfeeding

Monitoring

INDICATION	Initial monitoring	Continuous monitoring	Comments
Psoriasis **&** **Rheumatoid arthritis**	**Baseline** U&Es, creatinine & Blood Pressure on 2 occasions prior to initiation Fasting lipid levels, FBC, LFTs **Initial therapy** FBC, U&Es, creatinine, LFTs & Blood Pressure every 2 weeks, continued until 2 months after a stable dose is reached	**FBC, U&Es, creatinine & LFTs** monthly once dose is stabilised **NB** - More frequent checks are required if the dose is changed or an interacting drug is added **Blood Pressure** – at each visit (minimum monthly) **Fasting lipids** – 3 monthly	For Rheumatoid arthritis patients, ESR should also be measured at the same intervals as FBC etc

Creatinine:
• **Dermatology**: If serum creatinine rises on 2 consecutive occasions or by > 30% of the baseline level, the ciclosporin dose should be reduced by 25-50% and renal function repeated at intervals not exceeding 1 month. **If creatinine increases by 50% above baseline, ciclosporin dose must be decreased by 50%**
• **Rheumatology:** If serum creatinine rises on 2 consecutive occasions or by > 30% of the baseline level, stop ciclosporin and refer patient back to the consultant.

Lipids – Treat any hypercholesteraemia with appropriate statin therapy (see BNF for interactions)

BP – Inform the consultant if hypertension develops during ciclosporin therapy. A rise in blood pressure will not necessarily indicate withdrawal of therapy (unless resistant to treatment) but will require antihypertensive therapy – nifedipine or amlodipine are suitable (but not diltiazem, nicardipine and verapamil – inhibit ciclosporin metabolism). ACE inhibitors may cause renal impairment and diuretics can cause electrolyte disturbances and volume depletion. Beta blockers may be used but can aggravate psoriasis.

Stop therapy and refer to consultant team if:

- Hypertension develops that is resistant to antihypertensive therapy and ciclosporin dose reduction
- WCC falls on three successive occasions and/or falls below 3.5x 10^{9}/L
- The serum creatinine remains greater than 30% of the baseline value one month after a dose reduction of 25-50%
- Potassium greater than 5.5mmol/L
- Liver enzymes elevated especially transaminases increased to 3 times the upper limit of normal
- Refer to the microbiology team if the patient comes into contact with shingles or chicken pox

Side effects

Very common ≥ [10%]	**Common ≥ [1% to <10%]**
Uncommon ≥ [0.1 to <1%]	**Rare ≥ [0.01 to <0.1%]**
Very Rare < 0.01%	

- Patients must report mouth ulcers, sore throat, fever, epistaxis, rash, unexpected bruising or bleeding and any unexplained illness/infection should be seen urgently for full blood count and liver function tests
- Some patients feel a burning sensation in their hands and feet during the first weeks of therapy. This may disappear with continued therapy, if not discuss this with the team.
- The most important side effects, which need monitoring, are impairment of renal function and hypertension.
- All patients put on this medication will be warned of the theoretical but as yet unquantifiable risk of lymphoproliferative disorders and other malignancies in the future.

Very common/common
Hyperlipidaemia, hyperkalaemia, hypomagnesaemia, hyperuricaemia, renal dysfunction, hypertension, gout, anorexia, gastro intestinal disturbances, gingival hyperplasia, hepatic dysfunction, hypertrichosis, muscle disorders, tremor, paraesthesia, headache, predisposition to infection

Uncommon/Rare
Haemolytic anaemia, thrombocytopaenia, haemolytic uraemic syndrome, menstrual disturbances, gynaecomastia, hyperglycaemia, pancreatitis, allergic rash, muscle weakness, myopathy, oedema, weight increase, signs of encephalopathy or demyelination (e.g. convulsion, confusion, visual disturbances etc), motor polyneuropathy.

Very Rare
Optic disc oedema including papilloedema with possible visual impairment secondary to benign intracranial hypertension, colitis, cortical blindness

Interactions

This list is not exhaustive, the data sheet and BNF should be consulted for a more comprehensive list of potential drug interactions
Interference with the P450 system

- Drugs that **reduce** ciclosporin blood levels (increased dosage required – reduced effect) e.g. St John's Wort (Hypericum perforatum), carbamazepine, phenytoin, phenobarbitone, reboxetine
- Drugs that **increase** ciclosporin blood levels (Reduced dosage required – danger of toxicity) e.g. macrolide antibiotics, amiodarone, grapefruit or grapefruit juice (not to be

ingested for 1 hour prior to dose of ciclosporin), 'conazole' antifungals, doxycycline, diltiazem, verapamil, chloroquine, metoclopramide

Nephrotoxic drugs

- e.g. Aminoglycoside antibiotics, quinolones, trimethoprim, co-trimoxazole, amphotericin, melphalan,

Drugs that increase potassium levels

- e.g. ACE inhibitors, Angiotensin II inhibitors

Drugs that increase ciclosporin nephrotoxicity

- e.g. NSAIDs (halve dose of diclofenac if co-prescribed), allopurinol

Drugs that increase hepatotoxicity

- e.g. Danazol, anabolic steroids and oral contraceptives

Other drug interactions

- An increased risk of myopathy occurs with statins & colchicine
- Nifedipine – avoid in patients who develop gingival hypertrophy with ciclosporin. May also occur with other dihydropyridine calcium channel blockers
- Live and attenuated vaccines should be avoided

Notes

- Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles
- Flu and pneumococcal vaccines can be given
- Live and attenuated vaccines include: measles, mumps and rubella; BCG; poliomyelitis – oral Sabin vaccine; yellow fever; typhoid – oral

References

'Neoral' SPC, *www.medicines.org.uk* - accessed May 2007
BAD clinical guidelines – Psoriasis *www.bad.org.uk/healthcare/guidelines/psorcyclo.asp* - accessed May 2007
BSR National Guidelines for the monitoring of Second Line Drugs, July 2000
BNF 52 September 2006
North East Devon Health Community Shared Care Prescribing Guideline – Systemic immunosuppressive drugs in dermatology – Ciclosporin, July 2006

Shared care guidelines produced by Jacqueline Kew (Liaison Pharmacist) in conjunction with Dr Mark Lloyd and Dr Fiona Anthony.

Contact Details

Rheumatology

- **Dr Mark Lloyd – Consultant Rheumatologist – Tel: 01276 604 348**
- **Sara Burton – Rheumatology Specialist Nurse – Tel: 01276 526131**

Dermatology

- **Dr Fiona Anthony – Consultant Dermatologist - Tel: 01276 604 011**
- **Colonel Boxer – Consultant Dermatologist – Tel: 01276 604 076**

This does not replace the SPCs, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF