Homerton University Hospital NHS
NHS Foundation Trust

NHS
City and Hackney

CICLOSPORIN
In Psoriasis, Atopic Dermatitis in Adults

DOCUMENT TO BE FILED IN NOTES AND SCANNED INTO ELECTRONIC RECORDS

Patient name		
Date of Birth		
Referring consultant		**Tel no:**

INTRODUCTION

Ciclosporin is licensed for use as a disease-modifying agent to induce and maintain remission of severe psoriasis and severe atopic dermatitis unresponsive to conventional therapy. Ciclosporin, a calcineurin inhibitor, is a potent immunosuppressant that is virtually non-myelotoxic but markedly nephrotoxic.

DOSE AND ADMINISTRATION

Ciclosporin use in psoriasis

Orally 2.5 mg/kg daily in 2 divided doses, increased gradually to a maximum of 5 mg/kg/day if no improvement within 1 month. Therapy discontinued if response still insufficient or effective dose not tolerated after 6 weeks. Initial treatment of 5 mg/kg/day justified if condition requires rapid improvement. Treatment is usually for up to 16 weeks, but can be continued longer at the recommendation of a specialist.

Ciclosporin use in atopic dermatitis

Orally 2.5 mg/kg daily in 2 divided doses, increased gradually to a maximum of 5 mg/kg/day if no improvement within 2 weeks. Therapy discontinued if response still insufficient after 8 weeks.
Initial treatment of 5 mg/kg/day justified if condition requires rapid improvement. Treatment is usually for up to 8 weeks but can be continued longer at the recommendation of a specialist

USUAL CARE PATHWAY AND RESPONSIBILITY ARRANGEMENTS ACROSS PRIMARY AND SECONDARY CARE

Speciality	Indication	Duration	Prescribed by	Monitored by
For initiation by a specialist and continuation by General Practitioner (GP)				
Dermatology	Severe Psoriasis	Usually up to 16 weeks, although longer course maybe recommended by the hospital specialist. Hospital to assess at 6 weeks outcome and decide if treatment appropriate to stop/continue.	Hospital Dermatologist for first 6 weeks, then GP to continue if effective + stable	Hospital. Dermatology team every 2 weeks for 6 weeks. Then every 1-3 months if stable
Dermatology	Severe Atopic dermatitis	Usually up to 8 weeks, although	Hospital Dermatologist	Hospital Dermatology team

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		longer courses maybe recommended by the hospital specialist. Hospital to assess at 8 weeks outcome and decide if treatment appropriate to stop/continue	for first 8 weeks, then GP to continue if effective + stable	every 2 weeks for 8 weeks. Then every 1-3 months if stable,

Reference: BNF September 2010

- Patient transfer to shared care will be done via a letter from the Dermatologist to the GP.
- It is unusual for a patient to require a course longer than 9 months.

ADVERSE EFFECTS

Very commonly

- **Renal toxicity** – increases in serum creatinine and urea during first few weeks of therapy dose are generally dose-dependant and reversible, usually reversible on dose reduction.
- Hyperlipidaemia
- CNS disturbances (tremor, headache)
- Hypertension

Commonly

- Electrolyte disturbances – hyperkalaemia, hyperuricaemia, hypomagnesaemia
- Hepatotoxicity – (bilirubinaemia, elevation of liver enzymes)
- Nausea, vomiting, diarrhoea, abdominal pain, pancreatitis
- Hypertrichosis, paraesthesia, muscle cramp, myalgia, fatigue.
- Lymphadenopathy- If the patient develops a single swollen lymph node that is NOT related to inflamed skin, stop the ciclosporin and refer the patient to the specialist for review.

Less commonly

- Anaemia, thrombocytopaenia
- Allergic rash
- Increased risk of Benign intracranial hypertension

See BNF Section 8.2.2 or SPC for a comprehensive list.

CAUTIONS

- In general patients should try to avoid ‘live’ vaccines such as oral polio, MMR, BCG and yellow fever.
- Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact urgently to their GP or specialist.
- Concomitant administration of other nephrotoxic drugs e.g. trimethoprim, NSAIDs, ciprofloxacin.
- Renal elimination reduced by probenecid.
- Concomitant administration of drugs potentially causing hyperkalaemia e.g. potassium sparing diuretics, angiotensin II receptor antagonists and potassium.
- Drugs increasing ciclosporin levels e.g. erythromycin, fluconazole, itraconazole, diltiazem or decreasing ciclosporin levels e.g. carbamazepine, phenytoin, rifampicin, St. John’s Wort via cytochrome p450.
- Concomitant intake of grapefruit juice increases the bioavailablity of ciclosporin and should be avoided.
- Careful assessment of risk vs. benefit to be considered before use during pregnancy and breast-feeding.
- Patients should be stabilised on a particular brand of oral ciclosporin. Prescribing and dispensing of ciclosporin should be by brand name to avoid inadvertent switching.

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CONTRAINDICATIONS

- **Moderate/severe renal or liver impairment.**
- Uncontrolled hypertension
- Uncontrolled infections
- Malignancy
- Concomitant use of tacrolimus

DRUG INTERACTIONS

COMMON/SIGNIFICANT DRUG INTERACTIONS

This list is **NOT** exhaustive, the data sheet and BNF should be consulted for a more comprehensive list of potential drug interactions.

- Food: Grapefruit or Grapefruit juice (not to be ingested for 1 hour prior to dose of ciclosporin).
- Interference with the p450 system.
- Drugs that **reduce** ciclosporin blood levels (Increased dosage required – reduced effect) e.g. St. Johns Wort (*Hypericum perforatum*), carbamazepine.
- 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.
- Nephrotoxic drugs e.g. Aminoglycoside antibiotics, quinolones, trimethoprim, co-trimoxazole, amphotericin, melphalan, colchicine.
- Drugs that increase potassium levels e.g. ACE inhibitors, A2RBs.
- Drugs that increase ciclosporin nephrotoxicity e.g. non-steroidal anti-inflammatory drugs, allopurinol.
- Drugs that increased hepatotoxicity e.g. Danazol, anabolic steroids and oral contraceptives.
- Other drug interactions
  - An increased risk of myopathy occurs with statins.
  - Nifedipine - avoid in patients who develop gingival
  - hypertrophy with ciclosporin. May also occur with other
  - dihydropyridine calcium channel blockers.
- Live and live attenuated vaccines should be avoided.

MONITORING STANDARDS FOR CICLOSPORIN

The following standards have been agreed for the monitoring of ciclosporin in dermatology patients

Pre-treatment	FBC, U&Es, LFTs, blood pressure, lipid profile	
Monitoring	FBC	Every 2 weeks for 2 months then every 1 – 3 months if stable
	U&Es	Every 2 weeks for 2 months then every 1 -3 months if stable
	LFTs	Every 2 weeks for 2 months then every 1 – 3 months if stable
	Blood Pressure	Every 1 – 3 months
	Lipid profile	6 monthly

ACTION AND ADVICE

If blood test results fall into the categories below or the patient reports one of the adverse events below, these are recommendations for considering the withdrawal or dose reduction of ciclosporin therapy. Contact the hospital for advice if identified in primary care.

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Blood Test Results

- WBC < 4.0 x 10^9 / l
- Neutrophils < 2.0 x 10^9 / l
- Platelets < 150 x 10^9 / l
- > 2-fold rise in AST, ALT (from upper limit of reference range)
- Significant increase in serum creatinine (>15%) or potassium
- Significant decrease in serum magnesium

Symptoms/signs

- Increase in blood pressure
- Paraesthesia
- Gum hypertrophy
- Hypertrichosis

The patient's further therapy should be discussed with the patient's dermatologist.

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SHARED CARE

Sharing of care assumes a partnership between the specialist, GP and the patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. **The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.** Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and co-operation in the management of patients.

SHARED CARE RESPONSIBILITIES

Consultant

1. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first 6 weeks of treatment or until patient is stabilised).
2. Monitor the treatment every 2 weeks for the first 6-8 weeks and then every 1-3 months for patients receiving continuation of the course.
3. Make an assessment at 6-8 weeks of clinical outcome and review whether appropriate to continue or stop treatment,
4. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate).
5. Send a letter to the GP requesting shared care for this patient if assessment at 6-8 weeks results in a plan to continue treatment, and ensure the patient understands they will need to make an appointment to receive a prescription.
6. Monitor the patient, and send a letter to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated
7. Evaluation of any reported adverse effects by GP or patient.
8. Advise GP on review, duration or discontinuation of treatment where necessary.
9. Inform GP of patients who do not attend clinic appointments.
10. Ensure that backup advice is available at all times.

General Practitioner

1. Prescribe the drug treatment as described
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA, where appropriate.
5. Help in monitoring the progression of disease.

PCT

1. To provide feedback to trusts via Trust Medicines Committee.
2. To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
3. To support trusts in resolving issues that may arise as a result of shared care.

Patient/Carer

1. Report any adverse effects to their GP and/or specialist
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.

COST

Ciclosporin capsules	50 mg, 30 £36.41, 100 mg, 30 £69.11 (Neoral®, BNF September 2010)

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CONTACT NUMBERS FOR ADVICE AND SUPPORT

Homerton University Hospital	
Consultant via switchboard:	0208 510 5555 (see top of guidance)
Registrar on-call out of hours	Air call Dermatology SpR via switchboard
Medicines Information (for drug information related queries)	0208 510 7000

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