Lincolnshire Primary Care Trust

LINCOLNSHIRE PRIMARY CARE TRUSTS in association with UNITED LINCOLNSHIRE HOSPITAL TRUST

SHARED CARE GUIDELINE: CICLOSPORIN in DERMATOLOGY

General Principles

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF*, 51, March 2006, p. 4)

Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the County-Wide PCT Prescribing Group and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further copies

Further copies of any guidelines in this series are available from PCT Prescribing Advisers.

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Drug Details
Approved Name: **Ciclosporin**
Brand Name: Neoral™
Form and Strength: 10mg, 25mg, 50mg and 100mg capsules
Oral solution 100mg/ml

Specialist Responsibilities
The specialist secondary/tertiary care service will:

1. Send a letter to the GP suggesting that shared care should be considered for this patient.
2. Ensure that the patient receives supplies of ciclosporin from the hospital or prescribed from the hospital on FP10HP until the GP formally agrees to share care.
3. Carry out BP x 2, FBC, LFTs, hepatitis and have assessed renal function (at least 2 X serum creatinine, GRR estimate) and lipids before commencing therapy.
4. Conduct a baseline malignancy screen.
5. Provide patient with ciclosporin patient treatment information leaflet.
6. Periodically review the patient's clinical condition.
7. Advise on dosage alterations where appropriate.

GP Responsibilities
The GP will:

1. Notify the consultant in writing, without undue delay, if they agree to share care.
2. Monitor the patients overall health and wellbeing.
3. Monitor the patient for adverse drug reactions and remain vigilant to the risk of potential drug interaction.
4. Prescribe the medication for the patient.
5. Carry out monitoring tests:
   Monthly BP, U/E,s & creatinine, and urinalysis.
   3 monthly LFTs and lipids.

Referral Criteria

1. Patients will have received at least 3 months of ciclosporin therapy on hospital prescription.
2. Patients will have been stabilized on a suitable dose of ciclosporin. During this time it may be more convenient for the patient to have blood tests conducted at the GP surgery.
3. The specialist will have carried out an assessment of efficacy.

Licensed Indications

Severe psoriasis where conventional therapy is ineffective or inappropriate
Severe atopic eczema – short term treatment (8 weeks) where conventional therapy is ineffective or inappropriate

Unlicensed indications in dermatology
Behcet's disease, chronic idiopathic urticaria, connective tissue diseases, immunobullous diseases, pyoderma gangrenosum, photodermatoses.

Recommended Dosage and Administration

Starting dose is 2.5mg/kg.day in split into two doses.
Increasing to a maximum of 5mg/kg/day.
For severe disease, treatment may be started at the maximum dose.
Treatment should be discontinued if sufficient response is not achieved within 6 weeks on the maximum daily dose of 5mg/kg

Once disease control is established the maintenance dose should be reduced to the minimum required.

Ciclosporin is used both in short courses (for 12 weeks to bring a disease flare under control) and as a maintenance treatment.
For atopic dermatitis the maximum course length is 8 weeks

Background Pharmacology

Ciclosporin is a potent immunosuppressive agent, which does not cause bone marrow suppression and is widely used in transplantation. It has specific effects on T-Lymphocytes inhibiting production of cytokines such as TNF-α and IL-2.

Preparations Available

Tablets: 10mg, 25mg, 50mg and 100mg
Oral solution 100mg/ml

Adverse Effects

Nephrotoxicity is the most important adverse effect. This is due to short-term vasoconstriction and longer-term structural changes. Close monitoring of serum creatinine is needed.

Hypertension may occur in up to 60% of patients. A persistent diastolic BP of >95mmHg is an indication for dose reduction. If hypertension persists it should be controlled with a calcium antagonist such as amlodipine

Metabolic effects include hyperkalaemia, hypomagnesaemia, hyperuricaemia and hyperlipidaemia.

Neurological effects include tremor, a burning sensation of the hands and feet, paraesthesia, peripheral neuropathy, and headache.

Gingival hyperplasia

Hypertrichosis

Increased risk of malignancy especially skin cancers, lymphoproliferative disorders, and solid tumours

Hepatotoxicity is generally mild and dose dependant.

Drug Interactions

The following drugs may interact with ciclosporin and increase its activity**:**
Marolide antibiotics (mainly erythromycin, clarithromycin), doxycycline
Azole anti-fungals e.g. fluconazole, itraconazole, ketoconazole
Some calcium channel blockers e.g. diltiazem, verapamil, nicardipine
Oral contraceptives, danazol, bromocriptine, metoclopramide, high-dose methyl-prednisolone, tacrolimus, chloroquine, colchicine, cimetidine, allopurinol, amiodarone, propafenone, retonavir

The following drugs may interact with ciclosporin and decrease its activity**:**
e.g. carbamazepine, phenytoin, barbiturates, rifampicin, ticlopidine, lanreotide, octreotide and orlistat

Care must be taken when using ciclosporin with other drugs that exhibit nephrotoxic synergy i.e aminogylcosides, amphotericin B, ciprofloxacin, vancomycin, trimethoprim, NSAIDs and melphalan.

Concurrent administration with nifedipine may result in a increased rate of gingival hperplasia

Ciclosporin may reduce the clearance of digoxin and prednisolone

Co-administration with statin and colcichine may induce muscle toxicity.

Contraindications

Ciclosporin is contra-indicated in psoriatic and atopic dermatitis patients with;

- known hypersensitivity to ciclosporin
- abnormal renal function
- uncontrolled hypertension
- uncontrolled infections of any kind
- any kind of malignancy other than that of the skin.

Concomitant use with tacrolimus is specifically contra-indicated

Precautions

Ciclosporin can impair renal and liver function – see monitoring
Avoid excessive sunlight exposure, UVB, and PUVA therapy
Porphyria (all types can be exacerbated)
.
Pregnancy and Breast Feeding:
No evidence of teratogenicity, but limited data, so avoid
Breast feeding should be discontinued.

Vaccines: Live vaccinations should not be administered whilst taking ciclosporin. Annual flu vaccination is recommended.

Monitoring

Baseline:
Physical examination to exclude infections and malignancies.
Resting BP on 2 occasions
Renal function, including serum creatinine (x2), GFR and urinalysis
LFTs. Lipids

During therapy:

Every 2 weeks: BP, renal function, and urinalysis for the first 3months

Then repeat every month

Every 3 months LFTs, & lipids

Action needed:
Creatinine rises to >30% of baseline on 2 consecutive occasions
-> Reduce Ciclosporin by 25-50% for 1 month

If creatinine remains elevated >30% - stop Ciclosporin
(if creatinine returns to within 10% of baseline Ciclosporin may be resumed).

Hypertension - a persistent diastolic BP of >95mmHg - withhold and contact the specialist.

Indication of Likely Cost of Therapy in Primary Care
200mg daily for 30 days costs £100

Information Given to the Patient

Ciclosporin patient information leaflet.
Useful websites: www.bad.org.uk
www.dermnetnz.org

Contact Details

ULHT Dermatology Team:
Dermatology Nurses
Lincoln (01522) 573712
Pilgrim (01205) 446111

Dermatology Secretaries Lincoln (01522) 573412 and 573 680
Dermatology Secretary Pilgrim (01205) 446436 and 446165
Dermatology Secretary Grantham (0476) 565232

References;

1. BNF 51 March 2006. BNF.org

2. Wakelin SH. Handbook of systemic drug treatment in dermatology. London, Manson Publishing. 2002.

3. Wolverton SE. Comprehensive dermatologic drug therapy. Philadelphia, Saunders. 2001.

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