NHS
Shropshire
Clinical Commissioning Group

Effective Shared Care Agreement for oral Ciclosporin for dermatological indications

This local safety monitoring schedule supports clinicians providing shared care under the Local Enhanced Service for High Risk Drug Monitoring (formerly Near Patient Testing)

This shared care agreement outlines suggested ways in which the prescribing responsibilities can be shared between the specialist and GP. GPs are invited to participate. If the GP feels that undertaking the roles outlined in the shared care agreement is outside their area of expertise or have clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, clinical responsibility for the patient's health remains with the specialist. If a specialist asks the GP to prescribe, the GP should reply to this request as soon as practicable. Sharing of care assumes communication between specialist, GP and patient.

Consultant details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	NHS Number:
Email:	Email:	Date of birth:
Contact number:	Contact number:	Contact:

Signing indicates agreement with the responsibilities suggested in this document, and that the patient has been informed of the need to report any issues with their treatment to their doctor.

Specialist signature: **Date:**	**General Practitioner signature:** **Date:**

Introduction

Ciclosporin is a cyclic peptide immunosuppressive agent, and is thought to act specifically and reversibly on lymphocytes.

Licensed indications: severe psoriasis when conventional therapy is inappropriate or ineffective; short-term therapy for severe atopic dermatitis when system therapy is required

For rheumatological uses of ciclosporin, please consult the separate ESCA.

Adult dosage and administration

Dose adjustments are made during therapy based on clinical response and blood levels.[i], [ii]

Indication	Initial Dose	Dosing Schedule
Psoriasis	2.5mg/kg daily in two divided doses for 6 weeks	May be increased gradually after 4 weeks if no improvement but should not exceed 5mg/kg. Discontinue in patients if sufficient response cannot be achieved within 6 weeks on 5mg/kg/day or if effective dose not compatible with safety guidelines
Atopic dermatitis (usually for max. 8 weeks but can be longer under specialist)	2.5mg/kg daily in two divided doses	If 2.5mg/kg/day does not achieve satisfactory response within 2 weeks, the daily dose can be rapidly increased to a maximum of 5 mg/kg/day.

Patients should be stabilised on a **single brand** of oral ciclosporin because switching between different brands/formulations without close monitoring may lead to clinically important change in bioavailability.
Prescribing and dispensing of ciclosporin should be by brand name to avoid inadvertent switching.

Available as:

Brand	10mg capsule	25mg mg capsule	50mg capsule	100mg capsule	100mg/ml solution (note small volumes required for dosing)
Capimune®		x	x	x	
Capsorin®		x	x	x	
Deximune®		x	x	x	
Neoral®	x	x	x	x	x

Specialist responsibilities

- Discuss with the patient options for treatment and the suitability of ciclosporin, including the potential benefits and side-effects of treatment.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of medication. Check for interactions with other medicines.
- Discuss the need for adequate contraception if appropriate.
- Provide monitoring record booklet and record baseline results
- Baseline tests:
    - **FBC** (including differential white cell count)
    - **U&Es** (2 tests**,** including creatinine (twice, 2 weeks apart for mean value) and eGFR)
    - **LFTs**
    - **Blood pressure** (2 tests, ≤ 140/90 mmHg on 2 occasions, 2 weeks apart)
    - **Fasting Lipids**
- Review results of safety monitoring and request additional tests as required
- Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss this with the patient
- Perform trough drug levels and adjust dose if required
- Titrate ciclosporin to an effective dose.
- Provide GP with clear written advice on required dosage and frequency of ciclosporin, written monitoring guidelines and drug information. Check for interactions with other medicines.
- Monitor disease response to treatment and need to continue therapy
- Continue to review the patient at agreed specified intervals (at least annually), sending a written summary to the GP whenever the patient is reviewed
- Advise the GP on dosage adjustment and when and how to stop treatment
- Provide any other information for the GP including ciclosporin dose adjustments
- Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition and ensure that clear backup arrangements exist for GPs to obtain advice and support
- Report adverse events to the MHRA via Yellow Card Scheme

Primary Care responsibilities

- Prescribe ciclosporin **by brand name initiated by specialist**
- Arrange and record ongoing monitoring as agreed with specialist
    - **U&E+ creatinine:** every 2 weeks until dose stable for 3 months, then monthly thereafter
    - **Blood pressure:** every 2 weeks until dose stable for 3 months, then monthly thereafter. If diastolic blood pressure ≥ 95 mmHg, consider anti-hypertensive therapy (be aware of potential interactions and discuss with specialist team)
    - **FBC, LFTs:** monthly until dose stable for 3 months, then three monthly thereafter
    - **Fasting Lipids:** six monthly
- Frequency of monitoring may be increased if ciclosporin dose is adjusted
- Identify and report adverse drug reactions to initiating specialist and usual bodies (e.g. MHRA)
- Ensure no drug interactions with other medicines
- Administer 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 or Green Book
- Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in non-immune patients exposed to chickenpox or shingles
- Ask about oral ulceration/sore throat; unexplained rash or unusual bruising at every consultation.
- Ensure a clinician updates the patient's record following specialist review

Withhold ciclosporin and contact specialist if:[iii]

• Creatinine	Increase by >30% of baseline value
• Potassium	>5.3 mmol/L
• Platelets	<150 x10^9/L (except BMT and ITP)
• AST/ALT/ALP	>2 times the upper limit of normal
• Blood pressure	>140/90 mmHg on two consecutive readings 2 weeks apart. Treat with anti-hypertensives (note interactions). If still uncontrolled, stop ciclosporin and obtain BP control before restarting. Discuss with specialist team.
• Lipids	Significant rise in lipids
• Oral ulceration/ sore throat	
• Unexplained rash/ abnormal bruising	

Please note: a rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance. Some patients may have abnormal baseline values, specialist will advise. Results should be recorded in the patient's shared care monitoring booklet, if issued.

Adverse effects, Precautions and Contra-indications

Adverse effects

General: Tremor, hirsutism, diarrhoea, anorexia, nausea and vomiting.
Hypertension is common. Standard antihypertensive therapy can be used. Refer if hypertension remains uncontrolled.
Nephrotoxicity: can be acute. If serum creatinine consistently >30% above patients baseline, decrease ciclosporin dose by 25-50%.
Benign gingival hyperplasia is relatively common. Patients should be advised on good oral hygiene.
Hypertrichosis – discuss management with specialist.
Headache, tremor and parathesia are frequently seen. If persistent or severe they may reflect toxic levels of ciclosporin - refer to initiating specialist.
Hyperlipidaemia: Ciclosporin can induce a reversible increase in blood lipids. It is therefore advisable to perform lipid determinations before treatment and thereafter as appropriate.
Cancer risk: Patients receiving ciclosporin are at increased risk of lymphomas and malignancies of the skin: avoiding excessive exposure to the sun and use of high factor sunscreens are advised.

Cautions

Pregnancy / Contraception: Women of childbearing potential receiving ciclosporin should be advised to use effective contraception. Patients discovered or planning to become pregnant should be referred to the initiating specialist at the earliest opportunity without stopping ciclosporin.
Breastfeeding: Patients should not breastfeed whilst receiving ciclosporin.
Vaccines: Live vaccines should be avoided, except on the advice of initiating specialist (see Green Book re Zoster vaccine)

Contraindications

- Known hypersensitivity to ciclosporin
- Concomitant administration with *Hypericum perforatum* (St John's Wort)
- Uncontrolled hypertension
- Renal failure and liver failure

- Hyperkalaemia
- Suspected systemic infection or sepsis, malignancy
- Patients under 18 years of age
- Use with medicines that are substrates for the multidrug efflux transporter P-glycoprotein (P-gp) and for which elevated plasma concentrations are associated with serious and/or life-threatening events (see BNF)

Common Drug Interactions

There are numerous drug interactions with ciclosporin. Please refer to the latest BNF/SPC before starting any new drugs.

The following drugs should not be initiated by a GP unless discussed with the specialist:

Antibiotics: erythromycin and clarithromycin increase ciclosporin levels; rifampicin decreases ciclosporin level.

Antifungals: fluconazole; itraconazole and ketoconazole increase ciclosporin levels.

Calcium-channel blockers: diltiazem; nicardpine and verapamil increase ciclosporin levels.

Anti-epileptics: carbamazepine; phenobarbital and phenytoin decrease ciclosporin levels.

Anti-obesity drugs: orlistat decreases ciclosporin levels.

Colchicine: Avoid due to risk of serious muscle disorders.

Digoxin: Ciclosporin causes a large rise in digoxin levels in some patients.

NSAIDs (and other nephrotoxic drugs) should be used with caution. Close monitoring of renal function is essential. Lower doses of NSAIDs may be necessary if given concomitantly.

Statins: lower doses of statins should be used to reduce the risk of muscular toxicity (maximum simvastatin 10mg); **rosuvastatin** contra-indicated

Potassium-sparing diuretics, **ACE inhibitors and angiotensin II receptor antagonists** may exacerbate ciclosporin-induced hyperkalaemia and should only be initiated with regular monitoring of U&E.

St John's Wort is known to decrease ciclosporin levels. Herbal medicines may have an effect on drug levels. Avoid concomitant use.

Patients should avoid taking **grapefruit juice** or eating grapefruit as this can cause an increase in ciclosporin levels.

Tacrolimus is contra-indiated. Concomitant use should be avoided.

Communication

For any queries relating to this patient's treatment with oral ciclosporin, please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org)

Adapted with permission from work by MG, NHS Telford and Wrekin CCG Medicines Management

[i] British National Formulary, Edition 68, Section 1.5.3 and 13.5.3. Ciclosporin

[ii] Neoral Soft Gelatin Capsules – Summary of Product Characteristics. Available at www.medicines.org.uk/emc/medicine/1307

[iii] Suggestions for Drug Monitoring in Adults in Primary Care. NHS UKMi. February 2014, Available at www.evidence.nhs.uk