Shared Care Guideline: *Ciclosporin*

County Durham and Darlington NHS
NHS Foundation Trust

NHS
County Durham and Darlington
Area Prescribing Committee

Overview	Ciclosporin is an immunosuppressant drug
Indication	**Licensed** • Rheumatoid arthritis • Ulcerative colitis **Unlicensed** • Psoriatic arthritis • Psoriasis • Eczema • Urticaria • Vasculitis • Lichen planus
Dose:	Usual starting dose: 2.5mg/kg/day in TWO divided doses for SIX weeks May then be increased at 2 to 4 week intervals by 25mg until clinically effective or maximum dose of 4mg/kg/day is reached. This starting dose can be up to 5mg/kg/day when used for acute severe ulcerative colitis when switching from IV. This dose is continued for THREE to SIX months Dose reduction is not required in Chronic Kidney Disease, however some protocols do suggest dose reductions if creatinine rises over 130micromol/L Maintenance dose: Often effective between 2.5-3.2mg/kg/day. Note doses may be higher if for ulcerative colitis (as described above) this will be clearly communicated to GP and doses will be divided. Adjust to patient's tolerance and evaluate response and toxicity before increasing the dose.
Specialist's Responsibilities	**Initial investigations:** • Serum Lipids, Full Blood Count (FBC), calculated creatinine clearance (CrCl) / estimated Glomerular Filtration Rate (eGFR), Liver Function Tests (LFTs), albumin, Erythrocyte Sedimentation Rate (ESR) /C-Reactive Protein(CRP), blood glucose) weight, height and Blood Pressure (BP) • BP to be less than 140/90 on 2 consecutive occasions (2 weeks apart) prior to commencing treatment. Hypertension should be treated and controlled prior to initiation of ciclosporin. • Patients with psoriatic arthritis - assess if patient has received PUVA before commencing ciclosporin. If the total dose exceeds 1000J, discuss with dermatologist. • Check Varicella Zoster status if there is an uncertain history and recent exposure to the virus. It is the responsibility of the specialist to arrange vaccination should the patient be found to not have immunity. • Check trough ciclosporin level as required

	Initial prescribing until stable: **Prescribing responsibility and monitoring to stay with the specialist until patient has been on a stable dose for at least 6 weeks at which point shared care is requested.** Specialist to issue a prescription for enough medication to last until shared care is accepted by GP. This will usually be a minimum of 28 days **Communication and Documentation to GP:** • **Must ensure that information relating to the brand of ciclosporin** to prescribe is communicated to the GP • Obtaining agreement of GP to participate in shared-care arrangement ciclosporin therapy. This will be by sending a completed copy of the shared care request letter (appendix 1) to the GP • The specialist must ensure that the GP is aware when the next blood monitoring is required. • Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment. • Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required.
GP's Responsibilities	**Maintenance prescription:** • Prescribe ciclosporin in accordance with the specialist's recommendations as outlined in the shared care request letter • **GP should ensure that ciclosporin is prescribed by brand** to ensure patient receives the brand they are stabilised on. If there is a problem obtaining a specific brand then an informed decision by the GP should be made when prescribing a different brand of ciclosporin **Clinical monitoring:** Continue to clinically monitor patient in line with this shared care agreement and referral letter from specialist (as described in clinical monitoring section below) **Criteria Requiring Specialist contact:** • Failure to attend for review or undertake blood tests • Intolerance of drugs • Communications failure • Patient pregnant, wishing to become pregnant or breastfeeding **Documentation to specialist:** • Accepting or rejecting request for shared care within 28 days, if rejecting please state concerns and reasons Blood results to specialist via use of patient-held record.
Clinical monitoring:	FBC, calculated CrCl/eGFR, LFTs, ESR/CRP, blood glucose and BP **Frequency:** Fortnightly until on stable dose for SIX weeks then monthly for at least ONE year Patients who have been stable for ONE year can be considered for reduced monitoring to 3 monthly on the advice of specialist Serum fasting lipids • Frequency: 6 monthly. NOTE – this guideline sets out the standard monitoring requirements, however it is essential that each patient is considered on an individual basis and monitoring frequency should reflect this. The GP should be made aware of any deviations.

Safety Monitoring:

Please refer to Summary of Product Characteristics (SPC) or BNF /eBNF for full details of adverse effects, contraindications, cautions and drug interactions.

- Monitoring for response and adverse drug reactions (ADRs) during the initiation period.
- Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP
- Ask about the following at each visit
  - sore throat
  - bruising or bleeding
  - rash
  - oral ulceration

Adverse Events

Adverse event	Action to be taken
Creatinine rises by 30% of baseline.	Repeat in one week, if still more than 30% above baseline withhold and discuss with specialist team
Platelets less than 120 x 10^9/L	Withhold and discuss with specialist team
More than a TWO fold rise in Alanine Transaminase(ALT) / Aspartate aminotransferase (AST) from upper limit of normal	Withhold and discuss with specialist team
BP over 140/90 on two consecutive readings TWO weeks apart	Treat BP in line with NICE guidance (note interactions with several antihypertensives). If BP cannot be controlled despite adequate trails with anti-hypertensives, STOP ciclosporin and discuss with specialist team
Rise in serum lipids	Withhold and discuss with specialist team or lipid specialist Also see NICE guidelines for lipid therapy
Potassium rises to above normal range.	Withhold and discuss with specialist team
Abnormal bruising or sore throat	Withhold, check FBC and discuss with specialist team

Please note: Any rapid fall or consistent downward trend for blood counts or rapid rise or consistent upward trend for liver enzymes should prompt caution. Action may be required even if values are within normal range. If in doubt please contact specialist team.

Many side effects associated with ciclosporin are dose related and respond to dose reduction. Some adverse effects include the following (note list is not exhaustive),

- Hirsutism
- Bone marrow suppression characterised by sore throat, infection, fever, malaise, cough, unexplained bruising or bleeding, fatigue, hypotension/ hypertension, myalgia, dizziness and rash
- GI side effects including Nausea, vomiting and diarrhoea
- Tremor
- Headache (including migraine)
- Fatigue
- Muscle cramps
- Gingival hyperplasia
- Renal impairment
- Hyperlipidaemia
- Allergic rashes
- Anaemia

	• Gynecomastia • Oedema • Abnormal hepatic function • Pancreatitis All suspected serious reactions should be reported to the specialist and the MHRA
Contra-indications	• Known hypersensitivity to ciclosporin. • Concomitant treatment with rosuvastatin. • Concomitant treatment with tacrolimus. • Treatment of rheumatoid arthritis in patients less than 18 years of age. • Uncontrolled hypertension. • Uncontrolled infections. • Breastfeeding. • Pregnancy
Cautions	• Renal or liver impairment • Serum cholesterol less than 3.0mmol/L (increased risk of seizures) • Serum magnesium less than 0.50mmol/L (increased risk of seizures
Drug Interactions	• Drugs that are nephrotoxic should be used with extreme caution in patients on ciclosporin e.g. NSAIDs, gentamicin, ciprofloxacin, trimethoprim, vancomycin, cimetidine and methotrexate. • Drugs that increase potassium levels should be used with caution as ciclosporin can cause hyperkalaemia e.g. ACE Inhibitors, Angiotensin II receptor antagonists and potassium sparing diuretics. • Many drugs can increase or decrease ciclosporin levels. Refer to the BNF or product data sheet for a full list of these agents. • Grapefruit, including grapefruit juice, must be avoided for 1 hour before or after taking ciclosporin as bioavailability is increased.

Other Information	**Vaccinations:**
	• "Live" vaccines (including Oral Polio, Oral Typhoid, measles, mumps and rubella (MMR), bacillus Calmette-Guérin (BCG) and yellow fever) are not recommended whist on treatment
	• Seasonal influenza vaccination is recommended annually
	• Pneumococcal vaccination is recommended in line with current guidance
	
	Contraception, Fertility, Pregnancy and Breast Feeding:
	• Some manufacturers of ciclosporin advise that ciclosporin should not be used in pregnancy unless the benefit to the mother outweighs the risk to the foetus
	  ○ The British Society for Rheumatology (BSR) support the use of Ciclosporin throughout pregnancy at the lowest effective dose. However, these patients are not suitable for shared care and should be managed by their specialist
	  ○ The British Association of Dermatologists (BAD) state that it is preferable to avoid ciclosporin during pregnancy but do advocate use in some circumstances. These patients would not be suitable for shared care and should be managed by their specialist.
	• Ciclosporin passes into breast milk and manufacturers of ciclosporin advise mothers not to breast feed.
	  ○ BSR advises that mothers should not be discouraged from breastfeeding however these patients are not suitable for shared care and should be managed by their specialist whilst they continue to breastfeed
	  ○ BAD advise that patients should not breastfeed whilst taking ciclosporin
	
	More information on use of ciclosporin in pregnancy and breastfeeding can be found on the

	BSR and BAD websites **https://www.guidelines.co.uk/BSR/RA-in-pregnancy-and-breastfeeding/252703.article** http://www.bad.org.uk **General** • The patient should be advised to report any signs of bone marrow suppression or hypersensitivity (i.e. infection, fever, chills, cough, unexplained bruising or bleeding, fatigue, hypotension, myalgia, dizziness). • If patient is taking other immunosuppressive therapy, including steroids they are at an increased risk of secondary infections • Avoid excessive exposure to UV light.
Contact Details	Thank you for sharing the care of this patient. If you have any concerns or queries, please contact the Consultant, secretary or call the appropriate helpline below. UHND Rheumatology Helpline: 0191 3332763 DMH Rheumatology Helpline: 01325 743881 UHND Gastroenterology Helpline: 0191 3332333 DMH Gastroenterology Helpline: 01325 743434 Note : there is no dedicated Dermatology Helpline

Department of ……..
County Durham and Darlington Foundation Trust

GP name
GP address

Dear Dr ……

Request for Shared Care of CICLOSPORIN **Date:**

Re: Patient's name DOB:
Address Hospital Number:

This patient has been prescribed **Ciclosporin via the ORAL route** for the management of

□ Rheumatoid arthritis □ Psoriasis (unlicensed) □ Ulcerative colitis
□ Psoriatic arthritis (unlicensed) □ Eczema (unlicensed)
□ Lichen Planus (unlicensed) □Urticaria (unlicensed) □ Vasculitis (unlicensed)

This medication is brand specific so should be prescribed the following brand…….

The patients' current dose is ……per day

The patient was commenced on this drug on ……..and has been stable on the current dose since…….

I would now like to ask you to take over the responsibility for prescribing this medication for this patient, as agreed by your CCGs and the Area Prescribing Committee.

The shared care document lists the monitoring requirements for this medication. Can I ask that any problems are reported back into secondary care.

The next blood monitoring is due on …… and should be continued in line with the shared care guideline.

In addition, the following patient specific monitoring is required for this patient

……

This is part of the shared care guideline approved by the Area Prescribing Committee, available at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/.

The patient will remain under regular clinical review by his or her usual consultant/ specialist nurse as described in the shared care agreement.

Please send back the second part of this letter, with 28 days, so we know that we have your agreement to this arrangement. If you are not happy to accept this patient or have any concerns, then please contact my secretary as soon as practically possible

Yours sincerely

Consultant name

Contact details

GP Agreement

Patient's Name:
DOB:
Hospital No:

I agree to take over the prescribing and monitoring of Ciclosporin in line with the approved shared care document as found at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/

Dose to be prescribed ……..

Dated ……/……/

Signed: ……

GP's Name:

GP contact details

Please return to Consultant's secretary. You may wish to keep a copy for your records.