Sussex MSK Partnership

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NHS
Brighton and Hove Clinical Commissioning Group
Crawley Clinical Commissioning Group
Horsham and Mid Sussex Clinical Commissioning Group
High Weald Lewes Havens Clinical Commissioning Group

OPT-OUT SHARED CARE GUIDELINE

It is assumed that shared care **will** be accepted unless the specialist is informed otherwise within 28 days of receipt of the request at the end of this document.

MEDICATION NAME: **Ciclosporin**

INDICATIONS COVERED: **Rheumatoid Arthritis, Psoriatic Arthritis and other inflammatory conditions in adults**

NHS Brighton and Hove CCG, Crawley CCG and Horsham and Mid-Sussex CCG
Traffic Light System Classification: Amber

NOTES to the general practitioner (GP) or primary care prescriber

For medicines which require specialist initiation and/or dose titration and specific ongoing monitoring. For initiation, dose stabilisation and prescribing (including monitoring) by a specialist until the patient is stabilised (usually for 3 months) after which the GP may be asked to work under shared care through the use of approved shared care guidelines.
The expectation is that these guidelines should provide sufficient information to enable GPs or primary care prescribers to be confident to take clinical and legal responsibility for prescribing these medicines.

The questions below will help you confirm this:

- Is the patient currently under your care (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge)?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. It is assumed that shared care will be accepted unless the specialist is informed otherwise within 28 days of receipt of this request.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should inform the consultant or specialist within 28 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust or specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your CCG medicines management pharmacist will assist you in making decisions about shared care if you are unsure.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The GP or primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant or specialist.

Reason for update: New BSR guidelines 2017	**Prepared by:** SCFT Medicines Management Team	**Updated by:** SB
Approved by (Specialist or Consultant): Dr Kelsey Jordan on behalf of SMSKP Rheumatologists		
Approved by (Chief Trust Pharmacist): Iben Altman Chief Pharmacist SCFT		
Approved by (CCG Medicines Management Pharmacist): Via APC		
Approved by Brighton and Hove and HWLH CCG on: 27/2/2018		
Approved by Crawley CCG, Horsham and Mid-Sussex CCG on:27/3/2018		

Information

This information sheet does not replace the Summary of Product Characteristics (SMPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SMPC website**: http://www.medicines.org.uk/emc/ .

2. **Background to use for the indication(s), including licence status:**

   Ciclosporin is a disease modifying anti rheumatic drug and potent immunosuppressant used in rheumatoid arthritis, psoriatic arthritis and other inflammatory conditions. Ciclosporin should only be initiated on the recommendation of a specialist. It can be used in combination with other DMARDs such as methotrexate with careful monitoring. This guideline covers the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PA) and other inflammatory conditions. Ciclosporin has a marketing authorisation that includes severe, active rheumatoid arthritis and the treatment of severe psoriasis in patients in whom conventional therapy is inappropriate or ineffective.

3. **Dose & administration:**

   Doses are initiated at 2.5 mg per kg per day in two divided doses for 6 weeks then may be increased at 2 to 4 week intervals by 25mg until clinically effective or a maximum dose of 4mg per kg per day is reached. Ciclosporin may need to be given for up to 3 months before therapeutic benefit is seen. Withdraw if no benefit after 3 months at maximum tolerated dose. Doses should be equally distributed throughout the day (i.e. 12 hours apart) and a consistent schedule should be maintained with regard to time of day and in relation to meals.

4. **Cautions:**

This list is not exhaustive; refer to the Summary of Product Characteristics (SMPC) or BNF for further guidance.

- Avoid excessive unprotected sun exposure, and advise the patient to use a high factor sun screen.
- Elderly– dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range. Renal function should be monitored with particular care.
- Patients receiving multiple immunosuppressive agents.
- Patients with hyperuricaemia.
- Varicella Zoster Virus Infection – in patients with close contact to chickenpox or shingles consider passive immunization with varicella zoster immunoglobulin (VZIG). Contact specialist and see Green Book Chapter 34 for further details.

5. **Contraindications:**

This list is not exhaustive; refer to the Summary of Product Characteristics (SmPC) or BNF for further guidance.

- Known hypersensitivity to ciclosporin or any of its excipients.
- Ciclosporin is contraindicated in patients with abnormal renal function, uncontrolled hypertension, uncontrolled infections or any kind of malignancy.

- Pregnancy. Any patient contemplating becoming pregnant must be seen by the specialist at the earliest opportunity to discuss the complex issues surrounding therapy with ciclosporin.
- Breastfeeding mothers. Any patient contemplating breast feeding must be seen by the specialist at the earliest opportunity to discuss the complex issues surrounding therapy with ciclosporin.
- Live vaccines (see drug interaction section).
- Patients on ciclosporin should not receive concomitant ultraviolet B irradiation or PUVA photochemotherapy

6. Side effects:

Side effects include:

- Very common: Increased infections, hypertension, hyperlipidaemia, hypercholesterolaemia, headache, tremor, nephrotoxicity.
- Common: GI disturbance, gum hyperplasia, anorexia, electrolyte disturbances, myalgia, paraesthesia, increased hair growth, fatigue, abnormal hepatic function.
- Uncommon: Anaemia and thrombocytopenia.

This list is not exhaustive; refer to the Summary of Product Characteristics (SMPC) or BNF for further guidance.

7. Notable Drug Interactions

Prescribers are advised to check the BNF or ask a pharmacist for advice where required. This is not a comprehensive list

Food interactions

- The concomitant intake of grapefruit juice has been reported to increase the bioavailability of Ciclosporin and patients should be advised to avoid it.

Drugs that decrease Ciclosporin levels:

- Barbiturates, carbamazepine, oxcarbazepine, phenytoin; nafcillin, sulfadimidine I.V: rifampicin, octreotide, probucol, orlistat, hypericum perforatum (St John's Wort), ticlopidine, sulfinpyrazone, terbinafine, bosentan.

Drugs that increase ciclosporin levels:

- Macrolide antibiotics(e.g. Erythromycin, azithromycin and clarithromycin); ketoconazole, fluconazole, itraconazole, voriconazole, diltiazem, nicardipine, verapamil; metoclopramide; oral contraceptives; danazol; methylprednisolone (high dose); allopurinol, amiodarone, cholic acid and derivatives; protease inhibitors; imatinib; colchicine; nefazodone.

Other relevant interactions:

- Care should be taken when using ciclosporin together with other nephrotoxic drugs.
- Combination with medicines that are substrates for the multidrug efflux transporter P-glycoprotein or the organic anion transporter proteins (OATP) and for which elevated plasma concentrations are associated with serious and/or life-threatening events, e.g. bosentan, dabigatran etexilate and aliskiren are contraindicated.
- Concomitant use with tacrolimus should be avoided due to increased potential for nephrotoxicity.
- The concurrent administration of nifedipine with ciclosporin may result in an increased rate of gingival hyperplasia compared with that observed when ciclosporin is given alone.
- Increased plasma levels of both larcanidipine and ciclosporin have been observed

following concomitant administration. Therefore caution is recommended when co-administering ciclosporin together with lercanidipine

- NSAIDs: Close monitoring of renal function is essential, doses may need to be reduced, seek specialist advice.
- Severe digitalis toxicity has been seen within days of starting ciclosporin in several patients taking digoxin.
- When statins are concurrently administered with ciclosporin, their dosage should be reduced according to the relevant SmPC. Statin therapy needs to be temporarily withheld or discontinued in patients with signs and symptoms of myopathy or those with risk factors predisposing to severe renal injury, including renal failure, secondary to rhabdomyolysis.
- Caution is required for concomitant use of potassium sparing drugs (e.g. potassium sparing diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists) or potassium containing drugs since they may lead to significant increases in serum potassium.
- Ciclosporin may increase the plasma concentrations of repaglinide and thereby increase the risk of hypoglycaemia.

Vaccines

- Severe or fatal infections may occur if a live vaccine is given concurrently. **AVOID LIVE VACCINES**
- Inactivated vaccines such as influenza vaccine are safe to use although they may elicit a lower response

Also consider appropriate washout period after stopping therapy before administering live vaccines if required.

8. Criteria for use:

Chronic inflammatory conditions as determined by the specialist according to this shared care guideline.

Specialist has initiated and dose stabilised (usually for a minimum 3 months).

GP or Primary Care Prescriber confident to take clinical and legal responsibility for prescribing this drug.

9. Any further information (e.g. supporting therapies):

Prescribing and dispensing of ciclosporin should be by brand to avoid any inadvertent switching. If it is necessary to switch brand this should be done under specialist supervision with close monitoring of ciclosporin levels and renal function.

Patient should avoid excessive exposure to UV light, including sunlight.

Oral formulations contain around 12% vol. ethanol, with a 500mg dose equivalent to 500mg ethanol (15mL beer or 5mL wine).

10. References:

1. Guidelines for the management of inflammatory bowel disease in adults. Mowat C, et al. Gut (2011).

2. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. 2017 Jo Ledingham et al.
http://www.rheumatology.org.uk/includes/documents/cm_docs/2017/f/full_guideline_dmards.pdf

(accessed 9/3/17)

3. Immunisation of individuals with underlying medical conditions https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/566853/Green_Book_Chapter7.pdf (accessed 09/10/2017)

4. Handbook of systemic drug treatment in dermatology 2nd edition (2015) S Wakelin et al British Society for Rheumatology, Immunisation against shingles in people with inflammatory rheumatic disease. Available at http://www.rheumatology.org.uk/includes/documents/cm_docs/2013/i/immunisation_with_zostavax_for_people_with_inflammatory_rheumatic_disease.pdf (accessed 1310/17).

5. Summary of Product Characteristics, Available at: http://www.medicines.org.uk/emc/ (accessed 13/10/17).

6. UKMI. *Suggestions for Drug Monitoring in Adults in Primary Care.* February 2014. Available at http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug%20monitoring%20document%20Feb%202014.pdf (accessed 13/10/17)

RESPONSIBILITIES and ROLES

Consultant or specialist responsibilities
• Confirm diagnosis and indication for treatment with Ciclosporin.. • To discuss fully the aims, benefits, risks and side effects of treatment and a treatment plan with the patient and/or carer and written information to be supplied to the patient and/or carer. • Prior to treatment ask GP whether patient has had pneumococcal vaccination and flu vaccination and, if not, immunise (unless contra-indicated). • Inform GP when initiating treatment so the GP is aware what is being prescribed and can add to GP clinical record. • Undertake baseline monitoring as required (specific to the medication). • Record other medications and address potential medicine interactions before starting therapy. • Discuss the potential implications of pregnancy and breastfeeding in women of child bearing potential and agree a strategy. • To initiate treatment by prescribing and monitoring usually for a minimum of 3 months. • Undertake monitoring if dose changed. • Monitor and prescribe according to guidelines until handover is appropriate (including when dose changes are made). • Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment. • Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to, or a copy of, the shared care guideline when requesting transfer of prescribing to GP or primary care prescribers. • Advise GP if treatment dose changes or treatment is discontinued. • Inform GP if patient does not attend planned follow-up.

GP or primary care prescriber responsibilities
• Continue prescribing at the dose recommended and the specified brand and undertake monitoring requirements. • Undertake all relevant monitoring as outlined in the monitoring requirements section below, and take appropriate action as set out in this shared care guideline. • Monitor for adverse effects throughout treatment and check for medicine interactions on initiating new treatments. • Add information about the medicine to the patient record, initially as "hospital prescribed", and highlight the importance that this medicine is only to be prescribed under a shared care guideline in primary care. • Report any adverse events to the MHRA and specialist team. • Refer patient back to the Consultant/Specialist if any concerns. • Provide patient with pneumococcal polysaccharide vaccine and flu vaccination unless contra-indicated. • Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline (e.g. ensuring the patient record is correct in the event of a patient moving surgery).

Patient and/or carer role
• Make sure that you understand the treatment and ask for more information, if needed. • Share any concerns in relation to treatment with whoever is prescribing this medicine for you. • Tell the prescriber of this medication about any other medication being taken, including over-the-counter products. • Read the patient information leaflet included with your medication and report any side effects or concerns you have to whoever is prescribing this medicine for you. • Report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding. • Attend any follow up appointments with the consultant or specialist.

Monitoring Requirements

Monitoring schedule[2]

Ciclosporin is subject to an increased monitoring schedule[2]

Test	Frequency	Duration
FBC Creatinine/ calculated GFR ALT and / or AST Albumin	Every 2 weeks	Until on stable dose for 6 weeks
	Monthly	For at least 12 months and until patient stable
	3 monthly if patient stable and suitable for reduced monitoring	To continue.

Additionally glucose and BP at each monitoring visit

- More frequent monitoring (monthly) is appropriate in patients at higher risk of toxicity.
- Following a dose increase monitoring should revert to 2 weekly until on stable dose for 6 weeks then revert back to previous schedule.

Contact specialist team urgently and consider interruption in treatment if any of the following develop:

White Cell Count <3.5x10^9/l	Mean cell volume >105 f/l
Neutrophils <1.6 x10^9/l	Creatinine increase >30% over 12 months and/or calculated GFR <60ml/min/1.73m^2
Unexplained eosinophilia >0.5 x 10^9/l	ALT and/or AST >100 U/l
Platelet count <140 x10^9/l	Unexplained reduction in albumin <30 g/l
Potassium >5.3 mmol/l	Uncontrolled hypertension ≥ 140/90mmHg

Whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance.

This list is not exhaustive; refer to the Summary of Product Characteristics (SMPC) or BNF for further guidance.

Other Warning Signs

- Abnormal bruising: Check FBC and withhold treatment until results available.
- Rapid falls or downwards trends in any of the monitored parameters: Monitor closely and discuss with specialist team.
- Gum hypertrophy: Monitor closely and discuss with specialist team.
- Parasthesia: Monitor closely and discuss with specialist team.

This list is not exhaustive; refer to the Summary of Product Characteristics (SmPC) or BNF for further guidance.

SHARED CARE GUIDELINE

MEDICATION NAME: Ciclosporin

INDICATION:

DATE OF REQUEST:

Agreement to transfer prescribing to general practice or primary care prescriber:

Patient details:

Name:
Address:
DoB:
NHS No:
Hospital No:

Medication name, form and strength:

The following tests and investigations have been carried out:

Date treatment initiated:

At the last patient review the medication appeared to be effectively controlling symptoms or providing benefit:
Yes/No

The patients has now been stabilised on a dose of:

The patient has been given written information about their medication:
Yes/No

The patient understands that this medication is being prescribed under a shared care agreement between their GP and specialist and that they have responsibilities under the agreement to ensure they attend their GP to be regularly monitored.
Yes/No

The patient has been informed that the GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient persistently does not attend for monitoring:
Yes/No

Date of next clinic appointment:

If the practice declines shared care, then the named consultant or specialist should be informed within 28 days of receipt of this request. Forms used to decline prescribing can be found here:

Brighton and Hove CCG:
http://www.gp.brightonandhoveccg.nhs.uk/prescribing/joint-formulary-supporting-information
Crawley CCG, Horsham and Mid Sussex CCG:
http://www.horshamandmidsussexccg.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=415216

BACK-UP ADVICE AND SUPPORT

	Name and position	Telephone	Email
Specialist or Consultant			
Alternative specialist (e.g. departmental contact)			
Specialist pharmacist			

Out of hours (e.g. medical team on call)			

Link to full SCG: http://