Central Manchester University Hospitals NHS
NHS Foundation Trust

NHS

Greater Manchester Interface Prescribing Group Shared Care Template

Shared Care Guideline for **Ciclosporin in Rheumatological Conditions**		**Reference Number** **CMFT-SCG-002**
Author(s)/Originator(s): (please state author name and department) *Vanessa Reid Specialist Clinical Pharmacist, Pharmacy, Central Manchester Hospitals* *Professor Ian Bruce, Consultant Rheumatologist, The Kellgren Centre for Rheumatology, Central Manchester Hospitals* *Dr Rachel Gorodkin, Consultant Rheumatologist, The Kellgren Centre for Rheumatology, Central Manchester Hospitals* *Dr Pauline Ho, Consultant Rheumatologist, The Kellgren Centre for Rheumatology, Central Manchester Hospitals* *Dr Frank McKenna, Consultant Rheumatologist, Rheumatology Department, Trafford General Hospital*		**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Commissioners: **January 2013**	**Review Date:** **January 2015**	

Please complete all sections

1. Licensed Indications	*Licensed for the treatment of severe, active rheumatoid arthritis in patients in whom classical, slow-acting anti-rheumatic agents are inappropriate or ineffective.*
2. Therapeutic use & background	*Ciclosporin is a potent immunosuppressive agent. Studies in animal suggest that ciclosporin inhibits the development of cell mediated reactions. It appears to block the resting lymphocytes in the G_0 or early G_1 phase of the cell cycle, and also inhibits lymphokine production and release, including interleukin 2 (T cell growth factor, TCGF). The available evidence suggests that ciclosporin acts specifically and reversibly on lymphocytes. It does not depress haemopoiesis and has no effect on the function of phagocytic cells.*
3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	*Contraindications: Breastfeeding, uncontrolled hypertension, severe electrolyte imbalance i.e. hyperkalaemia, suspected systemic infection or sepsis, malignancy* *Cautions: renal and liver impairment, dose adjustment needed, pregnancy, avoid excessive exposure to UV light/sunlight*

<table>
<tr><td>4. Prescribing in pregnancy and lactation</td><td>This drug can be prescribed in the pregnant patient with caution. Under these circumstances prescribing should be the responsibility of Specialist.

There are no adequate and well controlled studies in pregnant women and, therefore ciclosporin should not be used during pregnancy unless the potential benefit to the mother justifies the potential risk to the foetus.
Patients can not breastfeed with ciclosporin.</td></tr>
<tr><td rowspan="8">5. Dosage regimen for continuing care</td><td>Route of administration | oral</td></tr>
<tr><td>Preparations available (include in this section any necessary information relating to availability of special preparations for children or those with swallowing difficulties)
Oral solution available for swallowing difficulties and Vegans as capsules contain gelatine. Ciclosporin should always be prescribed by brand (Neoral) and patients kept on the same brand (Neoral) unless Consultant decides to change.</td></tr>
<tr><td>Dose to be prescribed including units, frequency and duration of treatment.
Please prescribe: starting dose 2.5mg/kg in two divided doses.</td></tr>
<tr><td>Is titration required | Yes (complete the following section) Yes</td></tr>
<tr><td>Starting dose: 2.5mg/kg in two divided doses for 6 weeks and then may be increased at 2-4 week intervals by 25mg until clinically effective or the maximum dose of 4mg/kg/day is reached.
Maintenance dose: Often effective between 2.5-3.2mg/kg/day. Adjust to patient’s tolerance and benefit. Constantly evaluate response and toxicity before increasing to the maximum dose.</td></tr>
<tr><td>Adjunctive treatment regime

No adjunctive treatment</td></tr>
<tr><td>Conditions requiring dose reduction

Dose adjustment needed depending on serum creatinine
Dose adjustment may be needed in hepatic impairment</td></tr>
<tr><td>Usual response time

3 months</td></tr>
<tr><td>Duration of treatment ongoing</td></tr>
<tr><td>Treatment to be terminated by healthcare professional in consultation with Rheumatology Team.</td></tr>
<tr><td>NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.</td></tr>
<tr><td>6.Drug Interactions</td><td>The following drugs must <u>not</u> be prescribed without consultation with the specialist:</td></tr>
</table>

For a comprehensive list consult the BNF or Summary of Product Characteristics	*Aliskiren- avoid concomitant use* *St. Johns Wort- avoid concomitant use* *Tacrolimus- increased risk of nephrotoxicity, avoid concomitant use* *Calcium channel blockers- avoid lercanidipine, diltiazem, nicardipine, verapamil* *Diclofenac/NSAIDs- increased risk of nephrotoxicity (halve dose of diclofenac)* *Statins- increased risk of myopathy, avoid use with rosuvastatin, max. dose of simvastatin 10mg daily* *Grapefruit juice- avoid as increased risk of toxicity* *Colchicine- possible risk of nephrotoxicity and myotoxicity, suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)* *Bosentan- avoid concomitant use* *ACE inhibitors/Angotensin-II Receptor Antagonists/potassium sparing diuretics/aldosterone antagonists- increased risk of hyperkalaemia* *Digoxin- increased risk of toxicity*
	The following drugs may be prescribed with caution: *Antibacterials- check the BNF before prescribing as many increase/decrease plasma concentration of ciclosporin* *Antifungals- check the BNF before prescribing as many increase/decrease plasma concentration of ciclosporin* *Antimalarials- chloroquine and hydroxychloroquine increase plasma concentration of ciclosporin* *Metclopramide- increases ciclosporin plasma concentration* *Omeprazole- possibly affects plasma concentration of ciclosporin* *Alcohol- recommended government allowance*

7. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF

Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
Creatinine rises >30% from baseline	*Repeat in 1 week and if still >30% above baseline withhold until discussed with the Rheumatology Team*	*GP*
Potassium rises to above the reference range	*Withhold until discussed with the Rheumatology Team as risk of hyperkalaemia*	*GP*
Platelets <150 x 10^9/l	*Withhold until discussed with the Rheumatology Team*	*GP*
'Significant' rise in fasting lipids	*Withhold until discussed with the Rheumatology Team as risk of hyperlipidaemia*	*GP*
High BP ≥ 140/90 on two consecutive readings 2 weeks apart	*Treat blood pressure before stopping the ciclosporin (note interactions with several anti-hypertensives). If BP cannot be controlled, stop ciclosporin and obtain BP control before restarting ciclosporin. Discuss with the Rheumatology Team*	*GP*
AST, ALT or ALP more than 2 x upper limit of reference range	*Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction*	*GP*

	Abnormal bruising	*Check FBC immediately and withhold until discussed with the Rheumatology Team as risk of thrombocytopenia*	*GP*
	The patient should be advised to report any of the following signs or symptoms to their GP without delay: *Patients may experience anorexia, nausea, vomiting, abdominal pain, diarrhoea, headache, gingival hyperplasia and excessive hair growth. Patients may also experience a burning sensation of hands and feet - this may occur during 1st week of treatment but should subside.*		
	Other important co morbidities (e.g. chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case: *Live vaccine should be avoided in patients taking ciclosporin* *Annual flu vaccination is recommended. Passive immunization should be carried out using varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles. No official recommendation to administer Pneumovax but the rheumatology team suggest advisable.*		
	Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.		
8.Baseline investigations	*List of investigations / monitoring undertaken by secondary care* *FBC, U&E, creatinine (check twice, 2 weeks apart, to obtain a mean value for creatinine), LFT, fasting lipids, creatinine clearance prior to starting drug.* *Blood pressure to be ≤ 140/90 before treatment on two measurements 2 weeks apart. If greater than this treat hypertension before starting ciclosporin.* *Ciclosporin level to be carried out when clinically appropriate i.e. to measure compliance or if adverse effects occurring. Pre dose level, reference range 150-300*ng/ml.		
9. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**	**Yes or No (if yes complete following section)** *Yes*	

Monitoring	**Frequency**	**Results**	**Action**	**By whom**
FBC, U&E, LFT, BP, fasting lipids (ESR desirable but not essential)	***During dose titration**: Every 2 weeks for 3 months* ***Maintenance dose**: Every month thereafter*	*See Section 7: Adverse drug reactions above*		*GP*

10. Pharmaceutical aspects	*e.g. special storage requirements, washout periods Or where there are "no special considerations"* *Ciclosporin should always be prescribed by brand (Neoral) and patients kept on the same brand (Neoral) unless Consultant decides to change.*
11. Secondary care contact information	**If stopping medication or needing advice please contact:**
	To contact The Kellgren Centre Rheumatology Manchester Royal Infirmary: **Enquiries regarding blood monitoring and results please contact the specialist nurses below:**

	Specialist Nurse Jane Hawthorne 0161 276 4688 **Specialist Nurse Melissa Aris 0161 701 1454** **Specialist Nurse Carole Hill 0161 701 1454** **Fax number for GP blood results 0161 276 8690** **Consultant contact details below:** **Professor Ian Bruce 0161 276 4626** **Professor Ann Barton 0161 276 4626** **Dr Kimme Hyrich 0161 276 4627** **Dr Pauline Ho 0161 276 4397** **Dr Rachel Gorodkin 0161 276 4628** **To contact Rheumatology Department Trafford General Hospital:** **Trafford Rheumatology helpline number 0161 746 2162** **Consultant contact details below:** **Dr Frank McKenna 0161 746 2395** **Dr Preeti Shah 0161 746 2395**
12. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has no objection in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements
13. Responsibilities of initiating specialist	Initiate treatment and prescribe for the 1st 3 months of treatment. Undertake baseline monitoring. Dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP. Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient repeatedly does not attend appointments. Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable informed consent to therapy. Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action. Provide patient with relevant drug information to enable understanding of the role of

14. Responsibilities of the GP	monitoring. Provide patient with monitoring booklet. Provide patient with rheumatology nurse helpline contact number. --- Continue treatment as directed by the specialist. Ensure no drug interactions with concomitant medicines. To monitor and prescribe in collaboration with the specialist according to this protocol. To ensure that the monitoring and dosage record is kept up to date in shared care booklet. To ensure blood monitoring is carried out once dose stable and responsibility transferred from secondary care. To inform Rheumatology Team if patient repeatedly does not attend routine blood monitoring. To undertake vaccination as directed by the initiating consultant, the BNF or Green Book. Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. ---
15. Responsibilities of the patient	To take medication as directed by the prescriber, or to contact the GP if not taking medication To attend hospital and GP clinic appointments, bring monitoring booklet. Failure to attend will result in medication being stopped (on specialist advice). To report adverse effects to their Specialist or GP.
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet. Patient Information Leaflet EMC medicines Ciclosporin Arthritis Research UK Patient Information Leaflet Ciclosporin
18. Patient monitoring booklet	The patient must receive a monitoring booklet from the specialist upon initiation of treatment. The patient must bring this booklet to all specialist and GP appointments where it will be updated by the health professional conducting the appointment. The patient must also produce the booklet to any health professional involved in other aspects of their care e.g. pharmacists and dentists.