Shared care guideline

Ciclosporin (Neoral) – in rheumatic diseases

1 Scope

Trust and general practice in adult patients.

2 Purpose

Ciclosporin is used as a disease modifying agent to induce and maintain a remission of rheumatoid arthritis (RA) where other agents have proven ineffective, or are contraindicated. It's use requires close monitoring. This shared care guideline outlines the responsibility of primary and secondary care clinicians using ciclosporin in rheumatic diseases.

3 Abbreviations

BP	blood pressure
FBC	full blood count
GP	general practitioner
LFTs	liver function tests
NSAIDs	non-steroidal anti-inflammatory drug
PUVA	psoralen Ultra-Violet A
RA	rheumatoid arthritis

4 Dosage (low, slow increase)

Specific to RA – other conditions may be prescribed higher doses

- Starting dose of 2.5 mg/ kg/ day (in twice daily divided doses).
- Increased by 25mg per day after six weeks of therapy, if required.
- May be increased by 25mg at 2-4 weekly intervals until clinically effective or maximum dose 4mg/kg/day is reached.
- Maintenance dose: often effective at 2.5 - 3.2 mg/kg. Adjust to patient's tolerance and benefit. Constantly evaluate response and toxicity before increasing to maximum dose.
- Clinical response between 8 and 14 weeks.

5 Cautions

- **Potential nephrotoxicity**: see monitoring section below
- Caution with concomitant non-steroidal anti-inflammatory drug (NSAIDs), in particular diclofenac which increases plasma concentration of ciclosporin. The dose of diclofenac should be halved, if used concomitantly. See drug interactions below.

6 Monitoring and actions to be taken

	Whose responsibility	What needs doing
Pre-treatment	the hospital rheumatology team	Baseline renal function: -- creatinine and electrolytes – check twice, two weeks apart to obtain mean value for baseline creatinine (see below) -- creatinine clearance -- urinalysis Full blood count (FBC), liver function tests (LFTs), fasting lipids, Varicella immunity status Blood pressure (BP) – to be ≤ 140/90 before treatment. If greater, treat hypertension before commencing ciclosporin. If patient has psoriasis check if they have had Psoralen Ultra-Violet A (PUVA) – if total dose exceeds 1000J discuss with dermatologists
Initiation to stabilisation	the hospital rheumatology team (or general practitioner (GP) if in agreement)	Creatinine and electrolytes including potassium every two weeks until dose and trend stable for three months, then monthly. Watch closely if NSAID added, especially diclofenac. FBC and LFT monthly until dose and trend stable for three months, then 3-monthly BP – check each time patient attends for monitoring and maintain below ≤ 140/90
Ongoing monitoring once stable	GP	Creatinine and electrolytes monthly BP monthly FBC & LFTs 3-monthly Occasional fasting lipids
All results to be recorded in patient-held results booklet		

Baseline creatinine ☐ Baseline creatinine plus 30% ☐

7 Side effects and what to do

Side effect	What to do
Common: nausea, tremor, paraesthesiae, headache and abdominal discomfort	If mild, most of these subside as treatment becomes established
Less common: hyperuricaemia, hirsutism or gum hyperplasia	If efficacy has been established, it is preferable to treat the hirsutism with depilatories and the gum hyperplasia with oral hygiene, rather than stopping ciclosporin
Rare: lymphoproliferative disorders and other malignancies are thought to occur with a similar frequency as in patients on other immunosuppressives.	
Creatinine rises more than 30% above baseline	Repeat in one week and if still >30% above baseline withold until discussed with rheumatology team
Potassium rises to above reference range	Withold ciclosporin until discussed with rheumatology team – see contact list below
Platelets <150 x 10^9 /l	
Significant rise in fasting lipids	Withold ciclosporin until discussed with rheumatology team – see contact list below
High BP: >140/90 on two consecutive readings two weeks apart	Treat BP before stopping ciclosporin (note interactions with several antihypertensives). If BP cannot be controlled, stop ciclosporin and achieve BP control before restarting ciclosporin. Discuss with rheumatology team.
Alanine transaminase (ALT), aspartate transaminase (AST) or alkaline phosphatase more than two x upper limit of normal	Withold until discussed with rheumatology team. Check any other reason such as alcohol, drug interactions, including over-the–counter medication
Abnormal bruising/ bleeding	Check FBC immediately and withold ciclosporin until discussed with rheumatology team

8 Drug interactions

- **Drug interactions with ciclosporin are common** so check BNF appendix 1 and www.medicines.org.uk for other significant interactions before prescribing ciclosporin
- **Significant interactions include -**
    - Nonsteroidal anti-inflammatory drugs: particular caution with concomitant NSAIDs, especially diclofenac, which increases plasma concentration of ciclosporin and may potentiate the effects of ciclosporin (see section 4- cautions). The dose of diclofenac should be halved, if used concomitantly.
    - Statins: increased risk of myopathy on statins. If using simvastatin the maximum dose is 10mg/day.
    - Compounds known to be nephrotoxic eg aminoglycosides, ciprofloxacin, trimethoprim
    - Colchicine – avoid
    - Digoxin
    - Potassium-sparing diuretics
    - St John's wort
    - Avoid grapefruit juice.

9 Pregnancy and breast feeding

Ciclosporin is in general contraindicated during pregnancy. In exceptional cases the decision may be taken by the specialist that the benefits of continuing treatment outweigh the risks.

Ciclosporin is contraindicated in breastfeeding.
Men and women planning pregnancy should stop the drug three months before conception.

10 Immunisations

Avoid live vaccines. Annual influenza vaccine recommended.

11 Contact numbers for advice and support

Specialist	**post**	**telephone**
Rheumatology Practitioners	Advice line	01223 217398
Dr AJ Crisp	Consultant Rheumatologist	01223 216774
Prof H Gaston	Consultant Rheumatologist	01223 596235
Dr FC Hall	Consultant Rheumatologist	01223 217316
Dr J Jenner	Consultant Rheumatologist	01223 217763
Dr M Lillicrap	Consultant Rheumatologist	01223 217316
Dr A Ostor	Consultant Rheumatologist	01223 217763
Dr K Poole	Consultant Rheumatologist	01223 216774
Dr N Shenker	Consultant Rheumatologist	01223 217316
Dr B Silverman	Consultant Rheumatologist	01223 596235

12 Monitoring compliance with and the effectiveness of the guideline

The patient held results booklet will be inspected at each outpatient attendance.
Grading of recommendations: C

Equality and diversity statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

Disclaimer

It is **your** responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

Document management

Approval:	Joint Drugs and Therapeutics Committee (JDTC)- 21 February 2012		
Owning department:	Rheumatology department		
Author(s):	Dr Silverman		
Pharmacist:	Lynn Martin		
File name:	CICLOSPORIN Shared care guideline Version 2 Feb 2012.doc		
Supersedes:	Version 1, February 2008		
Version number:	2	Review date:	
Local reference:		Media ID:	6734