Effective Shared Care Agreement (ESCA)

Ciclosporin

ESCA: For the treatment of rheumatoid arthritis or psoriatic arthritis

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of ciclosporin for rheumatoid arthritis or psoriatic arthritis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with rheumatoid arthritis or psoriatic arthritis are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of rheumatoid arthritis or psoriatic arthritis.
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient.
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made.
4. Do baseline monitoring prior to initiation of ciclosporin , confirm the brand.
5. Initiate treatment and stabilise dose of ciclosporin.
6. Review the patient's condition and monitor response to treatment regularly.
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay.
8. Report serious adverse events to the MHRA.
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below).

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days.						
2. Prescribe ciclosporin at the dose recommended, by the brand defined as per the consultant.						
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist.						
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment.						
6. Refer back to specialist if condition deteriorates.						
7. Report serious adverse events to specialist and MHRA.						
8. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with ciclosporin with the specialist, clinical nurse specialist or GP.
3. Report any adverse effects to the specialist or GP whilst taking ciclosporin.
4. Attend regular outpatient appointments with the specialist.

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

Based on MTRAC template
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Interface Lead Pharmacist
Birmingham CrossCity CCG

SUPPORTING INFORMATION

Indication	Rheumatoid arthritis or psoriatic arthritis	
Dosage and Administration	Starting dose: 2.5 mg/kg/day in two divided doses for 6 weeks and then may be increased at 2–4 weeks intervals by 25 mg until clinically effective or the maximum dose of 4 mg/kg/day is reached Maintenance dose: Often effective between 2.5–3.2 mg/kg/ day. Adjust to patient's tolerance and benefit. Constantly evaluate response and toxicity before increasing to the maximum dose. Maximum dose: 4 mg/kg/day Avoid taking drug with grapefruit juice. If no response at maximum dose for three months, cease treatment.	
Renal Impairment	Patients with impaired renal function should not receive ciclosporin	
Hepatic impairment	Dose reduction may be necessary in patients with severe liver impairment to maintain blood levels within the recommended target range and it is recommended that ciclosporin blood levels are monitored until stable levels are reached.	
Contra-indications / Special precautions BSR Recommendations	**Contraindications** • Uncontrolled hypertension • Renal and liver failure (in patients with RA) • Severe electrolyte imbalance i.e. hyperkalaemia • Suspected systemic infection or sepsis **Cautions** • Pregnancy and lactation • Grapefruit including grapefruit juice must be avoided for 1 h before or after taking ciclosporin tablets as bioavailability is increased • Malignancy such as lymphomas, etc	
Side Effects	Very common	Hyperlipidaemia, tremor, headache, hypertension, hirsutism, renal dysfunction
	Common	Leucopenia, hyperglycaemia, anorexia, hyperuricaemia, hyperkalaemia, hypomagnesaemia, convulsions, paraesthesia, flushing, nausea, vomiting, abdominal discomfort/pain, diarrhoea, gingival hyperplasia, peptic ulcer, hepatic function abnormal, acne, hypertrichosis, myalgia, muscle cramps, pyrexia, fatigue

Monitoring

Treatment should not be initiated unless patients can be adequately monitored for toxic effects throughout the duration of therapy.

PLEASE NOTE:- The monitoring criteria differ from the BSR guidelines

	BSR
Pre-treatment Assessment	FBC including differential white cell count, U&E, creatinine: (check twice, 2 weeks apart, to obtain a mean value for creatinine), LFT, fasting lipids, creatinine clearance prior to starting the drug. Blood pressure: to be 140/90 mmHg before treatment on two measurements 2 weeks apart [8]. If greater than this treat hypertension before starting ciclosporin. In patients with psoriatic arthritis: assess whether patient has received PUVA before commencing ciclosporin.
After commencing treatment	FBC & LFT: once a month until dose and trend stable for 3 months and then 3 monthly. Serum electrolytes including potassium and creatinine every 2 weeks until dose and trend stable for 3 months and then monthly. Watch when NSAID is added, particularly diclofenac. Check fasting lipids periodically. Blood pressure (BP): Check BP each time patient attends monitoring clinic and maintain 140/90 mmHg.
Disease monitoring	Occasional ESR/CRP helps assessment
Dose reduction	• For side effects, e.g. mouth ulcers, headache, GI upset, recurrent infection • For raised blood pressure as above • For raised creatinine 30% above baseline

Actions to be taken (BSR Recommendations)	Creatinine rises >30% from baseline	Repeat in 1 week and if still >30% above baseline withhold until discussed with the specialist team.
	Potassium rises to above the reference range	Withhold until discussed with the specialist team.
	Platelets <120.000	Withhold until discussed with the specialist team.
	'Significant' rise in fasting lipids	Withhold until discussed with the specialist team.
	High BP: ≥140/90 mmHg 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 specialist team.
	AST, ALT or alkaline phosphatase more than 2 x upper limit of reference range	Withhold until discussed with the specialist team. Check any other reason such as alcohol, drug interaction including over the counter medication.
	Abnormal bruising	Check FBC immediately and withhold until discussed with the specialist team.
Important notes	• Live vaccines should not be administered • Influenza and pneumovax vaccines are recommended • Contraception during treatment is recommended - may be continued in pregnancy under specialist guidance • Patients without immunity who are exposed to chickenpox or shingles should be administered varicella zoster immunoglobulin	

Drug Interactions

Ciclosporin has the following interaction information:

ACE Inhibitors	increased risk of hyperkalaemia when ciclosporin given with ACE inhibitors
Acetazolamide	plasma concentration of ciclosporin possibly increased by acetazolamide
Aciclovir	increased risk of nephrotoxicity when ciclosporin given with aciclovir **Note:** Interactions do not apply to topical aciclovir preparations
Afatinib	ciclosporin possibly increases the plasma concentration of afatinib —manufacturer ofafatinib advises separating administration of ciclosporin by 6 to 12 hours
Aliskiren	ciclosporin increases plasma concentration of aliskiren —avoid concomitant use
Allopurinol	plasma concentration of ciclosporin possibly increased by allopurinol (risk of nephrotoxicity)
Ambrisentan	ciclosporin increases plasma concentration of ambrisentan (see under Ambrisentan,here)
Aminoglycosides	increased risk of nephrotoxicity when ciclosporin given with aminoglycosides
Amiodarone	plasma concentration of ciclosporin possibly increased by amiodarone **Note:** Amiodarone has a long half-life; there is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped
Amphotericin	increased risk of nephrotoxicity when ciclosporin given with amphotericin **Note:** Close monitoring required with concomitant administration of nephrotoxic drugs or cytotoxics
Angiotensin-II Receptor Antagonists	increased risk of hyperkalaemia when ciclosporin given with angiotensin-II receptor antagonists
Atazanavir	plasma concentration of ciclosporin possibly increased by atazanavir
Atorvastatin	increased risk of myopathy when ciclosporingiven with atorvastatin (see under Atorvastatin, here)
Bezafibrate	increased risk of renal impairment when ciclosporin given with bezafibrate
Boceprevir	plasma concentration of ciclosporin increased by boceprevir
Bosentan	ciclosporin increases plasma concentration of bosentan (also plasma concentration ofciclosporin reduced—avoid concomitant use)
Carbamazepine	metabolism of ciclosporin accelerated by carbamazepine (reduced plasma concentration)
Carvedilol	plasma concentration of ciclosporin increased by carvedilol

Caspofungin	ciclosporin increases plasma concentration of caspofungin (manufacturer of caspofungin recommends monitoring liver enzymes)
Chloramphenicol	plasma concentration of ciclosporin possibly increased by chloramphenicol
Chloroquine	plasma concentration of ciclosporin increased by chloroquine (increased risk of toxicity)
Cimetidine	plasma concentration of ciclosporin possibly increased by cimetidine
Clarithromycin	metabolism of ciclosporin inhibited byclarithromycin (increased plasma concentration)
Colchicine	possible increased risk of nephrotoxicity and myotoxicity when ciclosporin given with colchicine —suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)
Colesevelam	absorption of ciclosporin reduced bycolesevelam **Note:** Other drugs should be taken at least 4 hours before or after colesevelam to reduce possible interference with absorption
Colestilan	manufacturer of colestilan advises give ciclosporin at least 1 hour before or 3 hours after colestilan **Note:** Other drugs should be taken at least 1 hour before or 3 hours after colestilan to reduce possible interference with absorption
Crizotinib	caution with ciclosporin advised by manufacturer of crizotinib
Dabigatran	ciclosporin possibly increases plasma concentration of dabigatran —manufacturer of dabigatran advises avoid concomitant use
Danazol	metabolism of ciclosporin inhibited by danazol (increased plasma concentration)
Daptomycin	increased risk of myopathy when ciclosporin given with daptomycin (preferably avoid concomitant use)
Darifenacin	avoidance of ciclosporin advised by manufacturer of darifenacin
Dexrazoxane	increased risk of immunosupression with ciclosporin advised by manufacturer ofdexrazoxane
Diclofenac	ciclosporin increases plasma concentration of diclofenac (halve dose of diclofenac)
Digoxin	ciclosporin increases plasma concentration of digoxin (increased risk of toxicity)
Diltiazem	plasma concentration of ciclosporin increased by diltiazem
Diuretics, Potassium-sparing and Aldosterone Antagonists	increased risk of hyperkalaemia when ciclosporin given with potassium-sparing diuretics and aldosterone antagonists
Diuretics, Thiazide and related	increased risk of nephrotoxicity and possibly hypermagnesaemia when ciclosporin given with thiazides and related diuretics
Docetaxel	*in vitro* studies suggest a possible interaction between ciclosporin and docetaxel (consultdocetaxel product literature)
Doxorubicin	increased risk of neurotoxicity when ciclosporin given with doxorubicin
Efavirenz	plasma concentration of ciclosporin possibly reduced by efavirenz
Epirubicin	ciclosporin increases plasma concentration of epirubicin
Erythromycin	metabolism of ciclosporin inhibited by erythromycin (increased plasma concentration) **Note:** Interactions do not apply to small amounts of erythromycin used topically
Etoposide	ciclosporin possibly increases plasma concentration of etoposide (increased risk of toxicity)
Everolimus	ciclosporin increases plasma concentration of everolimus (consider reducing the dose ofeverolimus — consult everolimus product literature)
Ezetimibe	plasma concentration of both drugs may increase when ciclosporin given with ezetimibe
Fenofibrate	increased risk of renal impairment when ciclosporin given with fenofibrate
Fidaxomicin	avoidance of ciclosporin advised by manufacturer of fidaxomicin

Fluconazole	metabolism of ciclosporin inhibited by fluconazole (increased plasma concentration) **Note:** In general, fluconazole interactions relate to multiple-dose treatment
Fluvastatin	increased risk of myopathy when ciclosporin given with fluvastatin
Fosamprenavir	plasma concentration of ciclosporin increased by fosamprenavir **Note:** Fosamprenavir is a prodrug of amprenavir
Fosphenytoin	metabolism of ciclosporin accelerated by fosphenytoin (reduced plasma concentration)
Grapefruit Juice	plasma concentration of ciclosporin increased by grapefruit juice (increased risk of toxicity)
Griseofulvin	plasma concentration of ciclosporin possibly reduced by griseofulvin
Hydroxychloroquine	plasma concentration of ciclosporin increased by hydroxychloroquine (increased risk of toxicity)
Idarubicin	ciclosporin increases plasma concentration of idarubicin
Imatinib	plasma concentration of ciclosporin possibly increased by imatinib
Indinavir	plasma concentration of ciclosporin increased by indinavir
Itraconazole	metabolism of ciclosporin inhibited by itraconazole (increased plasma concentration)
Ketoconazole	metabolism of ciclosporin inhibited by ketoconazole (increased plasma concentration)
Lanreotide	plasma concentration of ciclosporin reduced by lanreotide
Lenalidomide	ciclosporin possibly increases plasma concentration of lenalidomide (increased risk of toxicity)
Lercanidipine	combination of ciclosporin with lercanidipine may increase plasma concentration of either drug (or both)—avoid concomitant use
Lomitapide	separating administration from ciclosporin by 12 hours advised by manufacturer oflomitapide
Macrolides	metabolism of ciclosporin possibly inhibited by macrolides (increased plasma concentration)
Mannitol	possible increased risk of nephrotoxicity when ciclosporin given with mannitol
Melphalan	increased risk of nephrotoxicity when ciclosporin given with melphalan
Methotrexate	risk of toxicity when ciclosporin given with methotrexate
Methylprednisolone	plasma concentration of ciclosporin increased by high-dose methylprednisolone(risk of convulsions)
Metoclopramide	plasma concentration of ciclosporin increased by metoclopramide
Micafungin	plasma concentration of ciclosporin possibly increased by micafungin
Miconazole	metabolism of ciclosporin possibly inhibited by miconazole (increased plasma concentration)
Mifamurtide	avoidance of ciclosporin advised by manufacturer of mifamurtide
Mitoxantrone	ciclosporin reduces excretion of mitoxantrone (increased plasma concentration)
Modafinil	plasma concentration of ciclosporin reduced by modafinil
NSAIDs	increased risk of nephrotoxicity when ciclosporin given with NSAIDs **Note:***See also* Aspirin. Interactions do not generally apply to topical NSAIDs
Nicardipine	plasma concentration of ciclosporin increased by nicardipine
Nifedipine	ciclosporin possibly increases plasma concentration of nifedipine (increased risk of toxicity including gingival hyperplasia)
Octreotide	plasma concentration of ciclosporin reduced by octreotide
Oestrogens	plasma concentration of ciclosporin possibly increased by oestrogens
Omeprazole	plasma concentration of ciclosporin possibly affected by omeprazole

Orlistat	absorption of ciclosporin possibly reduced by orlistat
Oxcarbazepine	plasma concentration of ciclosporin possibly reduced by oxcarbazepine
Pasireotide	plasma concentration of ciclosporin possibly reduced by pasireotide
Phenobarbital	metabolism of ciclosporin accelerated by phenobarbital (reduced plasma concentration)
Phenytoin	metabolism of ciclosporin accelerated by phenytoin (reduced plasma concentration)
Polymyxins	increased risk of nephrotoxicity when ciclosporin given with polymyxins
Posaconazole	metabolism of ciclosporin inhibited by posaconazole (increased plasma concentration)
Potassium Salts	increased risk of hyperkalaemia when ciclosporin given with potassium salts **Note:** Includes salt substitutes
Pravastatin	increased risk of myopathy when ciclosporin given with pravastatin
Prednisolone	ciclosporin increases plasma concentration of prednisolone
Primidone	metabolism of ciclosporin accelerated by primidone (reduced plasma concentration)
Progestogens	plasma concentration of ciclosporin possibly increased by progestogens
Propafenone	plasma concentration of ciclosporin possibly increased by propafenone
Quinolones	increased risk of nephrotoxicity when ciclosporin given with quinolones
Ranolazine	plasma concentration of both drugs may increase when ciclosporin given with ranolazine
Repaglinide	ciclosporin possibly enhances hypoglycaemic effect of repaglinide
Rifampicin	metabolism of ciclosporin accelerated by rifampicin (reduced plasma concentration)
Ritonavir	plasma concentration of ciclosporin possibly increased by ritonavir
Rosuvastatin	increased risk of myopathy when ciclosporin given with rosuvastatin (avoid concomitant use)
Saquinavir	plasma concentration of both drugs increased when ciclosporin given with saquinavir
Sevelamer	plasma concentration of ciclosporin possibly reduced by sevelamer
Simvastatin	increased risk of myopathy when ciclosporin given with simvastatin (avoid concomitant use)
Sirolimus	ciclosporin increases plasma concentration of sirolimus
St John's Wort	plasma concentration of ciclosporin reduced by St John's wort —avoid concomitant use
Sulfadiazine	plasma concentration of ciclosporin possibly reduced by sulfadiazine
Sulfinpyrazone	plasma concentration of ciclosporin reduced by sulfinpyrazone
Sulfonamides	increased risk of nephrotoxicity when ciclosporin given with sulfonamides
Tacrolimus	plasma concentration of ciclosporin increased by tacrolimus (increased risk of nephrotoxicity)—avoid concomitant use **Note:** Interactions do not generally apply to tacrolimus used topically; risk of facial flushing and skin irritation with topical tacrolimus on consumption of alcohol
Telaprevir	plasma concentration of both drugs increased when ciclosporin given with telaprevir (reduce dose of ciclosporin)
Telithromycin	plasma concentration of ciclosporin possibly increased by telithromycin
Terbinafine	plasma concentration of ciclosporin possibly reduced by terbinafine
Ticagrelor	ciclosporin increases plasma concentration of ticagrelor
Trimethoprim	increased risk of nephrotoxicity when ciclosporin given with trimethoprim , also plasma concentration of ciclosporin reduced by *intravenous* trimethoprim

Ursodeoxycholic Acid	absorption of ciclosporin increased by ursodeoxycholic acid
Valaciclovir	increased risk of nephrotoxicity when ciclosporin given with valaciclovir
Vancomycin	increased risk of nephrotoxicity when ciclosporin given with vancomycin
Verapamil	plasma concentration of ciclosporin increased by verapamil
Vitamin E	plasma concentration of ciclosporin possibly affected by vitamin E
Voriconazole	metabolism of ciclosporin inhibited by voriconazole (increased plasma concentration)

References

- British Society for Rheumatology (BSR) guidelines
- Neoral Capsules SmPC
- Ciclosporin BNF

I agree to participate in this shared care agreement for the treatment of the below named patient with ciclosporin for rheumatoid arthritis and psoriatic arthritis

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: