Sussex Community Dermatology Service NHS

EFFECTIVE SHARED CARE AGREEMENT (ESCA)

DRUG NAME: **CICLOSPORIN**
INDICATION/S COVERED: **FOR RHEUMATOLOGY AND DERMATOLOGY**

Coastal West Sussex Traffic Light system classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this agreement & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the primary care prescriber

Amber drugs: Prescribing to be initiated by a consultant / specialist but with the potential to transfer to primary care. The expectation is that this agreement should provide sufficient information to enable primary care prescribers to be confident to take clinical and legal responsibility for prescribing these drugs**.**

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care agreement?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this ESCA), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of the final page to the requesting consultant / specialist. Until the requesting consultant / specialist has received a signed copy of the final page indicating that shared care has been agreed all care (including prescribing) remains with the consultant / specialist.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant / specialist within 14 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/specialist service, which 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 Medicines Management pharmacist will assist you in making decisions about shared care.

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 patient's best interests are always paramount

The 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

Information

This page should include general information relevant to the specific drug and indication/s. It should include information on the dose of the drug for the indication, cautions, contraindications, common side effects and interactions to look out for. This section should have input from a specialist consultant in the field.

This information sheet does not replace the Summary of Product Characteristics (SPC), 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 SPC website**:

http://www.medicines.org.uk/EMC/medicine/1307/SPC/Neoral+Soft+Gelatin+Capsules%2c+Neoral+Oral+Solution/

2. **Background to use for the indication/s, including licence status**

Non-transplantation indications *****INN REC (Recommended International Non-proprietary Name)

Rheumatoid arthritis: Treatment of severe, active rheumatoid arthritis in patients in whom classical DMARDs are inappropriate or ineffective.

Psoriasis: Ciclosporin (also known as cyclosporin A*) in indicated for the treatment of severe psoriasis, in whom conventional therapy is ineffective or inappropriate.

Atopic dermatitis: Short term treatment of patients with severe atopic dermatitis in which conventional therapy is ineffective or inappropriate.

Nephrotic syndrome Treatment of steroid dependent or steroid resistant nephrotic syndrome (associated with adverse prognostic features) due to minimal change glomerulonephritis, focal segmental glomerulosclerosis or membranous glomerulonephritis in both adults and children.

Unlicensed uses: inflammatory muscle disease, severe acute ulcerative colitis, severe uticaria, pyoderma gangrenosum and systemic lupus erythematosus

Transplantation indications

Organ transplantation: Prevention of graft rejection following kidney, liver, heart, combined heart-lung, lung or pancreas transplants. Treatment of transplant rejection in patients previously receiving other immunosuppressive agents.

Bone marrow transplantation Prevention of graft rejection following bone marrow transplantation and prophylaxis of graft-versus-host disease (GVHD). Treatment of established graft-versus-host disease (GVHD).

3. **Dose & administration**

Route: Oral. Capsules are swallowed whole with a glass of water. Mix solution with orange juice (or squash) or apple juice (to improve taste, but not grapefruit juice) or with water immediately before taking and stir well. (and rinse with more to ensure total dose). *Avoid grapefruit or grapefruit juice for 1 hour before dose*. Absorption is not otherwise affected by food.

Loading dose: Commence at 2.5mg/kg/day in 2 divided doses increasing after 6 weeks by 25mg increments every 2-4 weeks to a maximum of 4mg/kg/day, depending on tolerance. If after 3 months of treatment at the maximum permitted or tolerated dose the response is considered inadequate, treatment should be discontinued.

Maintenance: Rheumatology dose should be titrated according to tolerability up to a maximum of 4mg/kg/day. Dermatology maximum 5mg/kg daily in 2 divided doses if no improvement in one month (discontinue after 6 weeks)

Because of the differences in bioavailability, the prescriber should specify the brand of ciclosporin to be dispensed. Neoral® is the formulation most commonly prescribed in this Trust. Patients should be stabilised on the same brand/formulation and any change in brand/formulation should be managed by a specialist.

4. Cautions

Ciclosporin must **NOT** be given to pregnant women or those of childbearing potential not using reliable contraception throughout treatment and for at least 2 years after discontinuing treatment.

Women must not breastfeed whilst taking ciclosporin.

Patients with hyperuricaemia

Live vaccines should not be administered whilst taking ciclosporin. Pneumovax and annual influenza vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients exposed to chicken pox or shingles.

5. Contraindications

In patients with:

- Hypersensitivity to ciclosporin
- Abnormal renal function
- Abnormal liver function
- Severe electrolyte imbalance (e.g.hyperkalaemia)
- Severe herpes simplex
- Uncontrolled hypertension
- Uncontrolled infections or any kind of malignancy
- In patients under the age of 18 years (safety & efficacy not studied)
- Concomitant use of tacrolimus is specifically contra-indicated
- Concomitant use of simvastatin and rosuvastatin is specifically contra-indicated.

6. Side effects

Very common: Hyperlipidaemia, hypercholesterolaemia, hypertension, renal dysfunction, tremor, headache, lower respiratory tract infection, urinary tract infection, cytomegalovirus infection, upper respiratory tract infection.

Common: Hyperuricaemia, hyperkalaemia, hypomagnesaemia, parasthesia, anorexia, nausea, vomiting, abdominal pain, diarrhoea, gingival hyperplasia, hepatic dysfunction, hypertrichosis, muscle cramps, myalgia, fatigue, sepsis, herpes infections, candidal infection, skin papillomas, basal cell carcinoma, squamous cell carcinoma of skin, Bowen's disease, lymphoproliferative disorders.

Also see SPC or BNF for further details of side effects.

7. Interactions

Drugs that decrease ciclosporin levels: Barbiturates, carbamazepine, phenytoin; rifampicin; octreotide; orlistat; hypericum perforatum (St John's Wort), oxcarbazepine, nafcillin, sulfadimidine i.v., probucol, ticlopidine, sulfinpyrazone, terbinafine, bosentan.

Drugs that increase ciclosporin levels: Macrolide antibiotics (mainly erythromycin, azithromycin and clarithromycin); ketoconazole, fluconazole, itraconazole, posaconazole, voriconazole; diltiazem, nicardipine, verapamil; metoclopramide; oral contraceptives; danazol; methylprednisolone (high dose); allopurinol; amiodarone; chloroquine; hydorxychloroquine; cimetidine, cholic acid and derivatives; protease inhibitors, imatinib; colchicine; nefazodone.

Other relevant drug interactions: Care should be taken when using ciclosporin together with other drugs that exhibit nephrotoxic synergy: aminoglycosides (including gentamicin, tobramycin), amphotericin B, ciprofloxacin, vancomycin, trimethoprim (+ sulfamethoxazole); non-steroidal anti-inflammatory drugs (including diclofenac, naproxen, sulindac); melphalan, histamine H2-receptor antagonists (e.g. cimetidine, ranitidine); methotrexate, fibrates. Dose of diclofenac should be reduced by approximately half; aciclovir; colchicine. Concomitant use with tacrolimus should be avoided due to increased potential for nephrotoxicity.

- During treatment with ciclosporin, vaccination may be less effective; the use of live-attenuated vaccines should be avoided.
- 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.
- Caution is recommended when co-administering ciclosporin together with aliskiren due to Pgp inhibition.

- Ciclosporin may also reduce the clearance of digoxin (thereby causing digoxin toxicity), colchicine, prednisolone, HMG-CoA reductase inhibitors (statins) and etoposide.
- Administration of ciclosporin may enhance the potential of HMG-CoA reductase inhibitors to induce muscular toxicity e.g. muscle pain and weakness, myositis and occasionally rhabdomyolysis especially simvastatin and rosuvastatin (concomitant use of both with ciclosporin contraindicated). May also increase plasma concentrations of ezetimibe.
- Ciclosporin should not be used in conjunction with other DMARDs in routine clinical practice
- Caution is required when ciclosporin is co-administered with potassium sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists and potassium containing drugs as well as in patients on a potassium rich diet.
- Caution is recommended when co-administering ciclosporin together with lercanidipine.
- Elevations in serum creatinine were observed in the studies using everolimus or sirolimus in combination with full-dose ciclosporin. This effect is often reversible with ciclosporin dose reduction.
- Grapefruit and grapefruit juice should not be ingested for 1 hour prior to and after dose administration, and grapefruit juice should not be used as a diluent for the oral solution.
- Ciclosporin may increase the plasma concentrations of repaglinide and thereby increase the risk of hypoglycaemia.

8. Criteria for use

Ciclosporin (cyclosporin A) decreases the autoimmune response in rheumatoid arthritis. Therapeutic effects can take up to 3 months.

Licensed indications (see above): Treatment of adult patients with severe, active rheumatoid arthritis in whom classical disease modifying drugs have been ineffective or inappropriate. Psoriasis/psoriatic arthritis. Prevention of transplant rejection and graft versus host disease.

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

None

10. References

1. Summary of Product Characteristics – NEORAL® soft gelatin capsules and oral solution; Novartis (last updated August 2011) Available to access at: http://www.medicines.org.uk/EMC/medicine/1307/SPC/Neoral+Soft+Gelatin+Capsules%2c+Neoral+Oral+Solution/

2. Chakravarty K *et al*. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatology. *Rheumatology* 2008; 47: 924-5. Available to access at: http://rheumatology.oxfordjournals.org/content/suppl/2008/05/31/kel216a.DC1/kel216b.pdf

RESPONSIBILITIES and ROLES

Consultant / Specialist responsibilities	
1	Confirmation of diagnosis and identification of suitable patients
2	Request agreement of shared care with primary care prescriber
3	Initiation of appropriate therapy
4	Discussion of risks and benefits with patients, outline possible side effects
5	Monitoring requirements and appropriate dose adjustments (if relevant to specific drug)

Before Treatment
FBC (including differential white cell count & platelets)
Electrolytes & Creatinine (check twice, two weeks apart)
24 hr Creatinine Clearance
Liver function tests (LFT's)
Fasting lipids
Blood Pressure (BP) should be ≤140/90 on 2 separate occasions 2 weeks apart prior to treatment.
Hypertension should be treated and controlled before starting treatment.
Urine testing for protein and blood
Dermatology indications require a skin examination

During treatment (first three months)
Every TWO weeks: U&E's, Serum creatinine &, if possible, BP

Every FOUR weeks: FBC (as above) & LFT's
During treatment (after three months)
Serum creatinine, U&E monthly
FBC and LFT's 3 monthly
BP at each clinic or primary care prescriber visit
Blood lipids 6 monthly

Patients should be re-evaluated at 6 months and treatment continued only if benefits outweigh risks.

The consultant will stop, or advise to stop, ciclosporin treatment if any of the following occur:

- WBC<4.0x10^9/l OR Neutrophils<2.0x10^9/l OR Platelets<150X10^9/l - withhold until FBC normal
- Abnormal bruising or sore throat - withhold until FBC normal
- Significant rise in lipids - specialist should advise
- Rise in ALT, AST or ALK PHOS 2x upper limit of reference range - withhold until LFT's normal
- If serum creatinine levels rise 30% above patients own baseline - repeat in 1 week. If still raised >30% - withhold and seek specialist advice. A dose reduction may suffice.
- Rise in K^+ above upper limit of normal - withhold and seek specialist advice.
- Ciclosporin should be stopped if treated hypertension remains uncontrolled (>140/90, on 2 occasions, two weeks apart).
- Dermatology - Severe herpes simplex

Monitoring will be undertaken by the specialist who will act on the results appropriately and communicate these results to the primary care prescriber.

The rheumatology/dermatology team will provide patients with blood forms to present to their primary care prescriber /Phlebotomist for all monitoring blood tests. The rheumatology/dermatology team will ensure that the consultants name is on the form and that a copy of the result is sent to the patient's primary care prescriber.

6	Issuing initial prescription(s) until the patient is stabilised (minimum of one month) and until ESCA is in place.
7	Ensure that all newly treated patients (and/or their carers) receive appropriate education and advice regarding their drug therapy and shared care arrangements. This should include written information where appropriate..
8	Providing primary care prescriber with clinic letter stating planned introduction and reviews.
9	Provide outpatient reviews, monitor effectiveness/side effects.
10	Give a copy of the information sheet to the patient / carer and explain their roles.
11	Notify the primary care prescriber of the patient's failure to attend for clinical review or drug monitoring.
12	Provision of the WSHT DMARD monitoring card if appropriate.

Primary care prescriber responsibilities	
1	Initial referral to secondary care.
2	To inform the consultant if unwilling to enter into shared-care arrangements.
3	To provide repeat prescriptions once ESCA is agreed and in place and the patient is stabilised (not before initial minimum one month stabilisation period). A demonstrable system should be in place to ensure that prescribing is reviewed by the primary care prescriber if there is no record of the fact that monitoring has taken place within the agreed time scales.
4	To record any changes in therapy in the prescribing record on receipt of such communication from secondary care.
5	To monitor patients overall health and well-being and to report any adverse drug reactions or interactions to secondary care.
6	Liaise with rheumatology/dermatology if any cause for concern or drug discontinued.
7	To provide a copy of this ESCA to the patient to ensure that they are familiar with all roles and responsibilities

Patient's / Carer's role	
1	Ask the rheumatology/dermatology team or primary care prescriber for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with ciclosporin.
3	Tell the rheumatology/dermatology team or primary care prescriber of any other medication being taken, including over-the-counter products.
4	Read the patient information leaflet included with the medication and report any side effects or concerns to the rheumatology/dermatology team or primary care prescriber.
5	Arrange blood tests as per rheumatology/dermatology team's request

6	Report to their rheumatology/dermatology consultant any such symptoms such as fever, sore throat, cough, skin rash or mouth ulcers.

BACK-UP ADVICE AND SUPPORT

	Name / position	Telephone	Email
Medicine Management Lead:	Dr Andrew Morris Consultant Dermatologist	For further information & advice, please contact Grace Hancock (Assistant Service Manager): 01903 703281	grace.hancock@nhs.net
Hospital Pharmacy:	Worthing Hospital St Richards Hospital	01903 205 111, ext 5698 01243 788 122, ext 3347	pharmacy@wsht.nhs.uk
Out of hours (e.g. medical team on call):	On call physicians On call	Bleep 118 or 119 01903 205 111	

Version History			
Document Name:		CICLOSPORIN	
Document Type:		Effective Shared Care Agreement	
Relevant to:		All primary care prescribers working within Coastal West Sussex and all relevant clinicians at Sussex Community Dermatology Service.	
Version No.	Date	Author of original development or review	Details of document development
1	June 2008	Julie Sadler - Prescribing Support Pharmacist	Original development
2	04/10/12	Sarah Clarke - Prescribing Support Pharmacist	Full review and re-draft
3	30/11/12	Sarah Clarke - Prescribing Support Pharmacist	Re-draft to include dermatological indications
4	01/08/14	Chris Emerson	Modified for use within Sussex Community Dermatology Service

Approval for organisational use	
ESCA authorised for use in Coastal West Sussex by	**Medicine Management Lead:** Dr Andrew Morris

EFFECTIVE SHARED CARE AGREEMENT (ESCA)

DRUG NAME: CICLOSPORIN
INDICATION: FOR RHEUMATOLOGY AND DERMATOLOGY

Agreement for transfer of prescribing to PRIMARY CARE PRESCRIBER

Patient details:

Name:

Address:

DoB:

NHS No:

Hospital No:

Drug name and dose:

The following tests and investigations have been carried out:
Details of tests:

Date treatment initiated:

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

The patients has now been stabilised on a dose of:

I will arrange to review this patient regularly. Date of next clinic appointment:

Title of specialist:
Name:
Department:
Hospital Address:

Contact Number:

Primary care prescriber:
Address:

Contact Number:

Main Carer:
Contact Number:

Key worker if appropriate:
Contact Number:

Agreement to shared care, to be signed by primary care prescriber and Medicine Management Lead:

Medicine Management Lead signature:

Date:

Primary care prescriber signature:

Date:

If shared care is agreed and the primary care prescriber has signed above please return a copy of this page to the requesting consultant or alternatively fax to: 01903 340849