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Royal Cornwall Hospitals NHS Trust

Ciclosporin in Dermatology

Shared Care Guideline

V3.0

May 2019

1. Aim/Purpose of this Guideline

1.1 This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of ciclosporin when used in Dermatology.

1.2 The indication for the purpose of this guideline is treatment of adults with severe eczema, psoriasis and other dermatological conditions. A course of treatment is usually 3 – 6 months to minimise long-term risk, but can be repeated.

Please note that ciclosporin should only be initiated in secondary care.

1.3 This shared care guideline sets out details for the sharing of care of patients requiring ciclosporin in dermatology. These guidelines provide additional limited information necessary to aid in the treatment these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, ABPI summary of product characteristics and do not replace them.

1.4. Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the DPA18 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed and documented. We can't rely on Opt out, it must be Opt in.

DPA18 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the DPA18 please see the 'information use framework policy', or contact the Information Governance Team rch-tr.infogov@nhs.net

2. The Guidance

2.1 Preparations and Dosage

Different brands of ciclosporin are not bioequivalent therefore prescribing by brand is required. Clinically, no brand is superior to any other. Dermatology consultant will start patients on the most cost effective brand according to hospital contracts. Although brands can be switched, it is not advisable since it can cause a loss of therapeutic control, hence there should be consistency in the brand that is prescribed. The usual starting dose in secondary care is 2.5 - 5 mg/kg per day and then treated according to response. Maximum dose is 5mg/kg/ per day. The dose will be made clear in clinic correspondence. Doses are given orally in two divided doses. Generally, patients receive ciclosporin for a short course, typically 3 to 6 months.

2.2 Contraindications and Precautions

Contraindications are: - concomitant use of tacrolimus, Concomitant use of rosuvastatin, simvastatin, Abnormal renal function, Uncontrolled hypertension, Uncontrolled infections, Malignancy including skin cancers.

2.2.1. Ciclosporin should be used with caution as follows:

- Patient should avoid contact with infections such as chicken pox or shingles.
- Patients should not go into the sun without protecting their skin.
- Ciclosporin can impair renal function. Close monitoring of serum creatinine and urea is required and dosage adjustment may be necessary.
- High dietary potassium intake – potassium intake should be reduced and potassium sparing diuretics or potassium supplements should be avoided.
- Patients should avoid grapefruit (including grapefruit juice) for 1 hour before until 1 hour after taking ciclosporin.
- Hyperuricaemia.
- Porphyria.
- Taking other drugs - there are multiple drug interactions with ciclosporin, see side effects section and the BNF appendix for full list of interactions.
- Particular care should be taken with prescribing compounds known to have nephrotoxic effects.
- Pregnancy. Ciclosporin is not teratogenic in animals. However there are no adequate and well controlled studies in pregnant women, therefore ciclosporin should be used during pregnancy only if potential benefit justifies potential risk to the foetus.
- Breastfeeding

2.3 Monitoring

2.3.1 Dermatology department

- Consider checking ciclosporin levels if an interacting drug is prescribed in either primary or secondary care.
- Checking of lymph nodes every 6 months will be done by Dermatology department in those patients who infrequently receive more than 6 months treatment.

2.3.2 General Practice

- FBC & LFT – every 2 weeks for 3 months and then every 3 months when stable.
- U&Es – every 2 weeks for 3 months and then every 3 months when stable. Watch when NSAID is added, particularly diclofenac.
- Hyperlipidaemia should be routinely monitored for. In the event of increased lipids being found, restriction of dietary fat and, if appropriate,

a dose reduction, should be considered. Some statins are contra-indicated with ciclosporin or must be used at a lower dose.

- Check BP each time patient attends monitoring clinic and maintain below a target of 140/90 (130/80 for diabetics with eye, renal or cerebrovascular involvement).
- Consider checking ciclosporin levels if an interacting drug is prescribed in either primary or secondary care.

2.3.3 Stop and refer to Dermatology Team if:

- The serum creatinine rises by greater than 30% of the baseline value.
- Potassium rises to above normal range.
- WCC falls on three successive occasions and/or WCC fall below 3.5 x 10^9/l
- Platelets fall below 150x10^9/l
- AST, ALT or Alk. Phos are twice normal upper limit
- Blood pressure should be monitored at each visit. A rise in blood pressure does not necessarily indicate withdrawal of therapy (unless resistant to treatment) but will require anti-hypertensive therapy. A calcium antagonist such as nifedipine or amlodipine is suitable (diltiazem and verapamil are not recommended as they inhibit ciclosporin metabolism). ACE inhibitors may cause renal impairment and diuretics can cause electrolyte imbalances and volume depletion. Beta-blockers may be used but they can aggravate psoriasis.
- Hypertension develops that is resistant to antihypertensive therapy and ciclosporin dose reduction.
- Seek advice from dermatology team if the patient comes into contact with shingles or chickenpox.
- The patient becomes / plans to become pregnant.
- The patient is or is planning to breastfeed.

2.4 Side Effects

2.4.1. Patients must report mouth ulcers, sore throat, fever, epistaxis, rash, unexpected bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

2.4.2. Some patients feel a burning sensation in their hands and feet during the first weeks of therapy. This may disappear with continued therapy, if not discuss this with the dermatology team.

2.4.3. The most important side effects, which need monitoring, are impairment of renal function and hypertension.

2.4.4. All patients put on this medication will be warned of the theoretical but as yet unquantifiable risk of lymphoproliferative disorders and other malignancies in the future.

2.4.5. Very common/ Common – these include

Hyperlipidaemia, hyperkalaemia, hypomagnesaemia, hyperuricaemia, renal dysfunction, gout, gastrointestinal disturbances, gingival hyperplasia, hepatic dysfunction, hypertrichosis, muscle disorders, tremor, paraesthesia, headache, predisposition to infection.

2.4.6. Uncommon / Rare

Haemolytic anaemia, thrombocytopenia, haemolytic uraemic syndrome, menstrual disorders, gynaecomastia, diabetes, pancreatitis, allergic rash, muscle weakness, myopathy, oedema, weight increase, signs of encephalopathy or demyelination (e.g. convulsion, confusion etc.), motor polyneuropathy.

2.4.7. Very Rare

Optic disc oedema including papilloedema with possible visual impairment secondary to benign intracranial hypertension, colitis, cortical blindness.

2.5 Significant Drug Interactions

This list is NOT exhaustive, the data sheet and BNF should be consulted for a more comprehensive list of potential drug interactions.

2.5.1. Interference with the p450 system.

- Drugs that reduce ciclosporin blood levels (Increased dosage required – reduced effect) e.g. St. Johns Wort (Hypericum perforatum), carbamazepine.
- Drugs that increase ciclosporin blood levels (Reduced dosage required - danger of toxicity) e.g. Macrolide antibiotics, amiodarone, grapefruit or grapefruit juice (not to be ingested for 1 hour prior to dose of ciclosporin), ‘conazole’ antifungals

2.5.2. Nephrotoxic drugs

e.g. Aminoglycoside antibiotics, quinolones, trimethoprim, co-trimoxazole, amphotericin, melphalan, colchicine.

- Drugs that increase potassium levels e.g. ACE inhibitors, A2RBs.
- Drugs that increase ciclosporin nephrotoxicity e.g. non-steroidal anti-inflammatory drugs, allopurinol.
- Drugs that increased hepatotoxicity e.g. Danazol, anabolic steroids and oral contraceptives.

2.5.3. Other drug interactions

- Ciclosporin may reduce the clearance of digoxin, colchicine.
- Concomitant use of rosuvastatin, or simvastatin is contraindicated. For other statins used concurrently with ciclosporin, the dosage of the statin should be reduced.
- Lercanidipine may increase plasma concentrations of either drug (or both) – avoid concomitant use. Plasma concentration of ciclosporin increased by diltiazem, nicardipine and verapamil. Ciclosporin possibly increases plasma concentration of nifedipine (increased risk of toxicity including gingival hyperplasia).

- Live and live attenuated vaccines should be avoided (includes measles, mumps and rubella; herpes zoster; BCG; poliomyelitis – oral Sabin vaccine; yellow fever; typhoid – oral).

2.6 Notes

• Passive immunisation should be carried out using Varicella Zoster Immunoglobulin in non-immune patients if exposed to chickenpox or shingles.

• Flu and Pneumococcal vaccines can be given.

2.7. Areas of Responsibility for the Sharing of Care

2.7.1. These are suggested ways in which the responsibilities for the management of adult patients with who are prescribed **ciclosporin** can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

2.7.2. In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.7.3. Specialist:

- Decision to prescribe Ciclosporin.
- Discussion with the patient regarding the benefits and side effects of treatment. Refer patient to specialist nurse service where appropriate (e.g. new patient) for advice on taking the drug, its cautions, side effects associated with treatment, monitoring (including baseline) requirements and the timing of re-assessment and by whom.
- A booklet for recording test results may then be issued.
- Initiate oral ciclosporin and stabilise patient on a therapeutic dose of ciclosporin before referral to the GP. Prescribing will remain in secondary care for usually 3 months or until the patient is stable on the dose.
- Ask the GP whether they are willing to participate in shared care.
- Prompt communication with GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- Undertake checking of lymph nodes if appropriate.
- Advice to GPs on when to stop treatment.
- Ensure clear arrangements for back-up advice and support.
- Reporting adverse events to the MHRA.

2.7.4. General Practitioner:

- If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter.
- Prescribing of oral ciclosporin after communication with specialists regarding the need for treatment and upon confirmation that the patient's dose is stabilised.
- Monitoring as outlined in the shared care guideline (section 2.3.2).
- Prompt referral to a specialist if there is a change in the patient's status.
- Reporting to, and seeking advice from, a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Reporting adverse events to specialist and MHRA.
- Stopping treatment in the case of a severe adverse event or as per shared care guideline.

2.7.5. Patient / parent / guardian / carer:

- Sign the shared care agreement letter
- Report any adverse effects to their GP and/or specialist whilst being treated with oral ciclosporin.
- Ensure that they have a clear understanding of their treatment
- Keep monitoring booklet up to date and bring it to all GP and hospital visits.
- Ensure they attend for monitoring requirements as per shared care guideline.
- Aware that treatment will be stopped if patient does not attend for monitoring.

2.7.6. BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Inclusion & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Ciclosporin in Dermatology Shared Care Guideline V3.0		
Date Issued/Approved:	March 2019		
Date Valid From:	May 2019		
Date Valid To:	May 2022		
Directorate / Department responsible (author/owner):	Dermatology Team / Pharmacy - Head of Prescribing Support Unit		
Contact details:	01872 253548		
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists		
Suggested Keywords:	Ciclosporin		
Target Audience	RCHT	CFT	KCCG
	✓		✓
Executive Director responsible for Policy:	Medical Director		
Date revised:	March 2019		
This document replaces (exact title of previous version):	Shared Care Guideline for ciclosporin in Dermatology V2.1		
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee		
Care Group Manager confirming approval processes	Robin Jones		
Name and Post Title of additional signatories	Not required		
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}		
	Name: Kevin Wright		
Signature of Executive Director giving approval	{Original Copy Signed}		

Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only	
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards	None			
Related Documents:	British Association of Dermatologists guidelines for the safe and effective prescribing of oral ciclosporin in dermatology 2018. Summary of Product Characteristics			
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
May'13	V2.0	Minor updating	M Wilcock, Head of Prescribing Support Unit
July'16	V2.1	Renewal with minor changes	M Wilcock, Head of Prescribing Support Unit
Mar'19	V3.0	New forma and minor amendments to 2.1, 2.3.1, 2.3.2, 2.3.3	M Wilcock, Head of Prescribing Support Unit

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document

This document has been created following the Royal Cornwall Hospitals NHS Trust Policy for the Development and Management of Knowledge, Procedural and Web Documents (The Policy on Policies). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Initial Equality Impact Assessment Form

This assessment will need to be completed in stages to allow for adequate consultation with the relevant groups.

<table>
<tr><td colspan="6">Ciclosporin in Dermatology Shared Care Guideline V3.0</td></tr>
<tr><td colspan="3">Directorate and service area: Pharmacy</td><td colspan="3">Is this a new or existing Policy?
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="3">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="5">To provide information on prescribing of ciclosporin to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="5">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="5">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="5">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="5">General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td>Other</td></tr>
<tr><td>X</td><td></td><td></td><td>X</td><td></td></tr>
<tr><td colspan="5">Please record specific names of groups
Cornwall Area Prescribing Committee</td></tr>
<tr><td>What was the outcome of the consultation?</td><td colspan="5">Agreed</td></tr>
</table>

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:

Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No X**	

9. If you are **not** recommending a Full Impact assessment please explain why.

Not indicated.

Date of completion and submission	Nov 2018	Members approving screening assessment	Policy Review Group (PRG) **APPROVED**

This EIA will not be uploaded to the Trust website without the approval of the Policy Review Group.

A summary of the results will be published on the Trust's web site.

Appendix 3. Shared Care Agreement Letter – Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

I recommend treatment with the following drug: ……..

I request your agreement to continue the care of this patient according to the Shared Care Guideline for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Guideline.
The results of any baseline tests and any additional supportive information (target range, date of last blood test etc.) are below:

Patient agreement **I understand and agree to my responsibilities as described above.,** **Signed: ……** **Date: …….** **Name:**

Principles:
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are no obligation to do so**. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient, the intention should be explained to the patient and accepted by them,
Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequence of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number:**	
Email:			

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP response **I agree/do not agree *to share the care of this patient in accordance with the Shared Care Guideline.** **Signed: …… Date: ……** **Name: …….** *delete as appropriate