SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR CICLOSPORIN (NEORAL®) (ADULTS ONLY – NON-RENAL PATIENTS)

Note: This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Ciclosporin (NEORAL®). Within NHS Grampian, the brand in use for solid organ transplantation is NEORAL®.

Formulation: Capsule/Oral Solution.

Strength: 10mg, 25mg, 50mg, 100mg Capsule and 100mg/mL Oral Solution.

Note: Prescribing and dispensing should be by brand name only, to minimize the risk of inadvertent switching between products, which has been associated with reports of toxicity and graft rejection – MHRA Drug Safety Update June 2012.

NEORAL® Soft Gelatin Capsules and NEORAL® Oral Solution are bioequivalent and can be used interchangeably.

STATUS OF MEDICINE

Licence status: Ciclosporin is licensed for prophylaxis of graft rejection in kidney, liver and pancreas transplantation and is used in combination with other immunosuppressants. Ciclosporin is also licensed for use in other non-transplant indications within rheumatology, gastroenterology and dermatology specialties.

Formulary status: Formulary – available for restricted use under specialist supervision

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

Ciclosporin is licensed for prophylaxis of graft rejection in kidney, liver and pancreas transplantation and is used in combination with other immunosuppressants. Ciclosporin may also be used in the treatment of rheumatoid arthritis and psoriasis.

TYPICAL DOSAGE REGIME	
Licensed dose	See Specialist service/SmPC for advice – variable according to condition being treated
Route of administration	Oral
Recommended starting dose	See Specialist service for advice – variable according to condition being treated
Titration dose/increment	See Specialist service for advice
Maximum dose	See Specialist service for advice
Situations requiring dose adjustment	See Specialist service for advice and Monitoring Schedule for DMARDs
Duration of treatment	See Specialist service for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Baseline:
  - Full Blood Count (FBC); liver function tests.
  - LFTs; urea, U&Es; lipids, urinalysis and blood pressure (BP).
- Copy of baseline results to be shared with primary care.
- Initiation of therapy and recommendations for dose increments. This should remain under the control of the specialist service.
- Decision on final dose required for patient.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given, patients should be referred to receive these vaccines in accordance with local protocol.

RESPONSIBILITY OF PRIMARY CARE

A Practice agreeing to prescribe Ciclosporin should:

- Prescribe medication **(by brand name)** under the guidance of the Consultant from the relevant specialist service.
- The General Practitioner (GP) has primary responsibility for monitoring according to the Monitoring Schedule for DMARDs.
- For transplant indications ciclosporin trough blood concentrations require to be monitored with a target range as indicated below, however, the target blood level for an individual patient will depend on the time since transplant, history of rejection and side effects and will be advised by the relevant specialist service.
- To obtain a trough level - take a morning blood sample when the patient has omitted the morning dose.
  - Liver transplant (first six months) 100-150 µg/L
  - Liver transplant (six months onwards) 70-100 µg/L
- Ensure the GP is aware that the drug can cause:
  - Nephrotoxicity

    - Increase in blood pressure
    - Infection
    - Increase risk of malignancy – lymphoma, skin and other tumours
    - Drug interactions.
- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
- Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and abnormal results are acted upon promptly.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- Contact the specialist service /On Call Registrar/Consultant in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
- Be alert for any of the known adverse reactions.
- The patient should be encouraged to ensure blood tests are undertaken at the correct intervals.
- It is responsibility of primary care to ensure that the medication is recorded on the patient's clinical medication record. This will facilitate central searches for annual vaccinations in order to ensure patients receiving DMARDs are called yearly by the HSCP teams for required vaccinations.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

- Prescribe medication (**by brand name**) under guidance of the relevant specialist service.
- Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient's medication.
- If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given, patients should be referred to receive these vaccines in accordance with local protocol.

Note: In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

Note: If something unexpected occurs contact on call registrar or Consultant for the appropriate specialty. Notify the consultant if the drug is stopped.

MONITORING

Refer to the NHSG Guidelines For The Monitoring of Disease Modifying Anti-Rheumatic Drugs (DMARDs) For Healthcare Professionals. Results should be reviewed and action taken as per monitoring guidance.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Patients are instructed to take the drug at the same times each day. This is necessary to facilitate interpretation of blood levels.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimise the risk of skin cancer, exposure to sunlight and Ultra Violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.
- The patient should ensure all blood tests are undertaken at the correct intervals.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

CONTRAINDICATIONS

- For full detail please refer to the current Summary Product Characteristic (SPC) available at www.medicines.org.uk.
- Hypersensitivity to the active substance or to any of the excipients.
- Combination with products containing Hypericum perforatum (St John's Wort).
- Combination with medicines that are substrates for the multidrug efflux transporter P-glycoprotein or the organic anion transporter proteins (OATP) and for which elevated plasma concentrations are associated with serious and/or life threatening events, e.g. bosentan, dabigatran etexilate and aliskiren.
- Do not give with tacrolimus due to increased risk of nephrotoxicity.
- Some statins are specifically contra-indicated with ciclosporin and many may require a reduced dose if concomitantly administered. Ensure the SmPC for the individual statin is checked before prescribing.

PREGNANCY

Experience with ciclosporin in pregnant women is limited. Ciclosporin should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit. Discuss with relevant specialist service.

BREAST-FEEDING

Further discussion is required with the relevant specialist service.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

Blood and lymphatic system disorders	Leucopenia
Metabolism and nutrition disorders	Hyperlipidaemia, hyperglycaemia, anorexia, hyperuricaemia, hyperkalaemia, hypomagnesaemia
Vascular disorders	Hypertension and flushing
Gastrointestinal disorders	Nausea, vomiting, abdominal discomfort/pain, diarrhoea, gingival hyperplasia, peptic ulcer
Skin and subcutaneous tissue disorders	Hirsutism, acne and hypertrichosis
Musculoskeletal and connective tissue disorders	Myalgia and muscle cramps
Other very common or common side effects	Abnormal renal and or hepatic function Pyrexia Fatigue

Action abnormal monitoring results are per NHSG Disease Modifying Anti-Rheumatic Drugs (DMARDs) Monitoring Guidance.

As with other immunosuppressive agents, exposure to UV light and sunlight should be limited by wearing protective clothing and using sunscreen with a high protection factor. This is because of the potential for malignant skin changes. Increased susceptibility to infection, especially severe chicken pox.

The specialist service should be contacted if there are any patient specific issues or concerns regarding side effects or abnormal results.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

For full detail of the numerous drug interactions with ciclosporin please refer to the current Summary of Product Characteristics (SmPC) available at www.medicines.org.uk.

Ciclosporin is extensively metabolised in the liver via the Cytochrome P450 enzyme system and may have an inducing or inhibitory effect on these enzymes. Therefore care should be taken when co-administering other drugs known to be metabolised by this system. Advice can be sought from the specialist service if required.

Interactions encountered frequently include:

- Grapefruit and grapefruit juice contain a compound which may potentially inhibit ciclosporin metabolism.
- Care should be taken when prescribing additional nephrotoxic drugs such as trimethoprim and NSAIDS.
- Caution in concomitant use of ACE inhibitors and potassium sparing diuretics due to increased risk of hyperkalemia.
- Risk of myopathy increased with concurrent administration of HMG-CoA reductase inhibitors (statins) and ciclosporin - consult SmPC for dosage adjustment information. Simvastatin and rosuvastatin are contra-indicated with ciclosporin.

ADVERSE DRUG REPORTING

If an adverse reaction should occur, inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

- Neoral Soft Gelatin Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
- Neoral Oral Solution - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of a concern being raised, the primary care practitioner should contact the referring consultant for the appropriate specialist service via the hospital switchboard, via their secretary, by email or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Registrar for the speciality may be contacted via the switchboard.

<table>
<tr><td>Publish: Public</td><td>Applies to: NHS Grampian</td><td colspan="2">Version: 3</td></tr>
<tr><td rowspan="2">Prepared by:

Consultant Rheumatologist and GI Pharmacist</td><td rowspan="2">Authorised for issue by:

Medicine Guidelines and Policies Group</td><td>Document no:
NHSG/SCA_DMARD Ciclosporin/MGPG1322</td><td rowspan="3">NHS Grampian</td></tr>
<tr><td>Effective date: October 2022</td></tr>
<tr><td rowspan="2">Signature:
Dr Lindsay Robertson/ Evelyn Finn</td><td rowspan="2">Signature:
Lesley Coyle</td><td>Review Date: October 2025</td></tr>
<tr><td>Supersedes: MGPG418</td></tr>
<tr><td colspan="4">Review/Consultation Group: This document has been reviewed by rheumatology, gastroenterology and dermatology consultants and pharmacists at ARI.</td></tr>
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