SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR CICLOSPORIN (RENAL ADULT)

N.B. 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®)

Formulation: Capsule/Oral Solution

Strength: (10mg, 25mg, 50mg, 100mg Capsule), 100mg/mL Oral Solution

N.B. Prescribing should be by brand name to avoid inadvertent switching. However, NEORAL® Soft Gelatin Capsules and NEORAL® Oral Solution are bioequivalent and can be used interchangeably.

STATUS OF MEDICINE

Licence status: Licensed for prevention of kidney graft rejection following solid organ transplantation.

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

For prevention of kidney graft rejection following solid organ transplantation.

TYPICAL DOSAGE REGIME	
Licensed dose	See Renal Specialist for advice
Route of administration	Oral
Recommended starting dose	See Renal Specialist for advice
Titration dose/increment	See Renal Specialist for advice
Maximum dose	See Renal Specialist for advice
Situations requiring dose adjustment	See Renal Specialist for advice
Duration of treatment	See Renal Specialist for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

1. **Baseline:**
   Full Blood Count (FBC); liver function tests.
   (LFTs); urea, U&Es; lipids, urinalysis & blood pressure (BP).
2. Copy of results to be sent to GP.
3. Initiation of therapy and recommendations for dose increments. This will be controlled by the Renal Unit.
4. Decision on final dose required for patient.
5. The Renal Unit has primary responsibility for monitoring clinical response to treatment according to the schedule below:
   - U&Es (incl. creatinine and potassium) fortnightly until dose and results have been stable for three months, then monthly thereafter.
   - FBC and LFTs (including ALT and Alk Phos) monthly until dose and results stable for three months, then three monthly.
   - Fasting lipids should be checked every six months.
   - BP should be checked at each monitoring visit.
   - Whole blood 12 hour trough ciclosporin A level 7 days after each dosage change.

RESPONSIBILITY OF PRIMARY CARE

To preserve vital venous access, monitoring will be done by the renal service at ARI unless otherwise notified or the patient develops an intercurrent illness which would require bloods to be taken in primary care.

A Practice agreeing to prescribe Ciclosporin should:

1. Prescribe medication (**by brand name)** under the guidance of the Renal Consultant.
2. 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.
3. Ensure that the relevant monitoring requirements have been undertaken at the correct frequency above.
4. Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and make sure abnormal results are acted upon promptly.
5. Only continue to prescribe medication if it is being satisfactorily monitored.
6. Contact the Renal Unit/Consultant/On Call Registrar in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
7. Be alert for any of the known adverse reactions.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

1. Prescribe medication (**by brand name**) under guidance of consultant.
2. Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.

3. Ensure no interacting medications are prescribed in primary care.
4. Monitor for concordance with therapy.
5. Report any adverse events to consultant and the MHRA using the Yellow Card System.
6. If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient's medication.
7. If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
8. A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given.

N.B. 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.

N.B. If something unexpected occurs contact Renal Unit/On Call Registrar or Consultant. Notify the consultant if the drug is stopped.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- 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.

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

- 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

Discuss with consultant. Ciclosporin should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit.

BREAST-FEEDING

Discuss with Aberdeen Maternity Hospital. Manufacturer advises avoid.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

- Lymphomas and other malignancies
- Infection
- Renal Toxicity
- Hepatotoxicity
- Hypertension
- Blood lipids increase
- Hyperkalaemia
- Hypomagnesaemia discuss with consultant.

Abnormal Monitoring Results	Action To Be Taken
• **WBC** <4 X 10^9/L	Discuss with Renal Unit/Registrar on call or Consultant
• **Platelets** <150x10^9/L	Discuss with Renal Unit/Registrar on call or Consultant
• **>2-fold rise in ALT or Alk Phos.** (from upper limit of reference range) • Other significantly deranged LFT results	Discuss with Renal Unit/Registrar on call or Consultant
• MCV>105fl	Discuss with Renal Unit/Registrar on call or Consultant
• Abnormal bruising, sore throat, rash, oral ulceration	Check FBC. Discuss with Renal Unit/Registrar on call or Consultant
• Unexplained fever	Discuss with Renal Unit/Registrar on call or Consultant
• Suspicion of or newly diagnosed malignancies	Discuss with Renal Unit/Registrar on call or Consultant

COMMON DRUG INTERACTIONS (for a full list see SmPC)

- Live vaccines should be avoided in patients taking ciclosporin.
- Potassium sparing diuretics, ACE inhibitors, angiotensin-II receptor antagonists and potassium salts should be used with caution as co-administration may lead to hyperkalaemia.

- Colchicine, statins and digoxin levels can be increased by ciclosporin. Monitor response and use the lowest effective dose.
- Drugs that decrease ciclosporin levels include barbiturates, antiepileptics and St John's Wort, octreotide and rifampicin.
- Drugs or foods that increase ciclosporin levels include grapefruit, macrolide antibiotics (mainly erythromycin and clarithromycin) and azole antifungals (ketoconazole, fluconazole, itraconazole and voriconazole).
- Close monitoring for issues caused by any additional prescribed medication is essential. This should be carried out by the prescriber of the interacting agent.
- Concomitant administration of dabigatran etexilate is not recommended due to the P-gp inhibitory activity of ciclosporin.
- Concurrent administration of nifedipine with ciclosporin may result in an increased rate of gingival hyperplasia.

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

https://www.medicines.org.uk/emc/product/1034/smpc

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

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

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