NORTH AND EAST DEVON HEALTH COMMUNITY SHARED CARE PRESCRIBING GUIDELINE

http://www.devonpct.nhs.uk/Treatments/NE_Devon_Shared_Care_Guidelines.aspx#C
https://nww.devonpctinfo.nhs.uk/Prescribing/SCG/

ORAL IMMUNOMODULATING AGENTS FOR INFLAMMATORY BOWEL DISEASE

CICLOSPORIN

This shared care guideline sets out details for the sharing of care of patients with inflammatory bowel disease prescribed ***ciclosporin***. These guidelines provide additional limited information necessary to aid in the treatment of patients with inflammatory bowel disease. **As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and *do not* replace them.**

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

Treatment of **adults** with severe inflammatory bowel disease.

Please note that this drug should only be initiated in secondary care.

It may take up to 3 months to be effective, therefore prescribing will remain in secondary care for the first 3 months and will then transfer to primary care if dose is stable.

DOSAGE

The usual starting dose in secondary care is 5mg/kg per day, though dose adjustments are made during therapy based on clinical response and blood levels (usual range 100-200 ng/mL). Doses are given orally in two divided doses. The dose will be made clear in clinic correspondence. Ciclosporin blood level testing should reflect the trough level of the drug.

CONTRAINDICATIONS –

- Combination with tacrolimus
- Uncontrolled hypertension
- Uncontrolled infections
- Malignancy
- Under 18 years of age
- Pregnancy. This drug is contra-indicated in pregnancy as it has the potential to affect the development of the unborn child. Men and women of childbearing age should be advised to use a reliable method of contraception during treatment. When planning a pregnancy it is important that both men and women on this drug discuss medication with the Gastrointestinal Team (at least six months before conception) since all drugs can potentially affect the unborn child.
- Breastfeeding

PRECAUTIONS -

- Patient should avoid contact with infections such as chicken pox or shingles.
- Abnormal renal function. Renal function will always be checked and the decision to use the drug will depend on the severity of renal impairment.
- High dietary potassium intake – potassium intake should be reduced and potassium sparing diuretics or potassium supplements (including salt substitutes) should be avoided.
- Hyperuricaemia
- Porphyria

PRECAUTIONS -

- 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.

MONITORING

PRIOR TO STARTING THERAPY - GASTROENTEROLOGY TEAM:

- Measure baseline serum potassium levels, blood lipid levels and LFTs
- Measure **1st baseline** serum creatinine levels and blood pressure
- Results to be sent to GP.

ONGOING MONITORING - GENERAL PRACTICE:

- FBC, potassium, urea and creatinine and LFTs fortnightly for 3 months and then monthly N.B. more frequent checks are necessary when dose is changed or an interacting drug is added/dose changed.
- Monitor blood lipids at 3 months. Calculate cardiovascular risk where appropriate. Increases total cholesterol and LDL in >1 in 10 patients.
- In order to monitor disease activity a CRP for Crohn's disease or ESR / viscosity for Ulcerative Colitis at least 3-monthly would be helpful.
- Blood pressure should be monitored at each visit (monthly). A rise in blood pressure does not necessarily indicate withdrawal of therapy (unless resistant to treatment) but will require anti-hypertensive therapy – ACE-Inhibitor (first line – monitor potassium level) then amlodipine are suitable treatment choices.

STOP AND REFER TO THE GASTROENTEROLOGY TEAM IF:

- WCC falls on 3 occasions ***and/or*** WCC falls below 3.5 x 10^9, *or* if neutrophil count falls below 1.5 x 10^9
- Platelet count falls on 3 successive occasions ***and/or*** Platelet count falls below 150 x 10^9
- If the serum creatinine rises on two consecutive occasions greater than 50% of the baseline value, the dose should be reduced by 50%. If no reduction in levels in one month stop treatment.
- Hypertension resistant to antihypertensive therapy and ciclosporin dose reduction.
- Liver enzymes, especially transaminase increased x 3 upper limit of normal.

SIDE EFFECTS

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.

- 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 your gastroenterology team.
- The most important side effects, which needs monitoring, are impairment of renal function and hypertension.
- 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.

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

Very common/ Common – these include

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

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.

Very Rare

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

COMMON/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.

- Interference with the p450 system.
  - Drugs that **reduce** ciclosporin blood levels (Increased dosage required - danger of rejection) 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, oral 'conazole' antifungals
  - Nephrotoxic drugs
    e.g. Aminoglycoside antibiotics, quinolones, trimethoprim, co-trimoxazole, amphotericin, melphalan, colchicines
- 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
- Other drug interactions
  - An increased risk of myopathy occurs with statins.
  - Nifedipine - avoid in patients who develop gingival hypertrophy with ciclosporin. May also occur with other dihydropyridine calcium channel blockers.
  - Live attenuated vaccines should be avoided.

NOTES

- Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.
- Flu and Pneumococcal vaccines may be given if required.
- Live vaccines include: measles, mumps and rubella; BCG; yellow fever; typhoid – oral.

PRODUCT INFORMATION

- Neoral® 10, 25, 50 or 100mg soft gelatin capsules
- Neoral® 100mg/ml oral solution – to be diluted immediately before being taken.
- Solutions should be stored between 20°C and 30°C.

Ciclosporin should be prescribed by brand

REFERENCES

- Summary of Product Characteristics http://emc.medicines.org.uk/: January 2006.

AUTHORS

- The Gastroenterology Teams in Exeter and North Devon.
- North and East Devon Health Community Shared Care Guidelines Group

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AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients with inflammatory bowel disease who are prescribed ***oral ciclosporin*** can be shared between the specialist and the general practitioners. GPs are **invited** to participate. If the GP is not confident to undertake these roles, then they 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**. 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.

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

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 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 at least 3 months
- ❑ 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.
- ❑ Advice to GPs on when to stop treatment.
- ❑ Ensure clear arrangements for back-up advice and support.
- ❑ Reporting adverse events to the CSM.

General Practitioner:

- ❑ Reply to request for shared care as soon as practical.
- ❑ 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.
- ❑ 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 CSM.
- ❑ Stopping treatment in the case of a severe adverse event or as per shared care guideline.

Patient:

- ❑ 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
- ❑ Ensure they attend for monitoring requirements as per shared care guideline.
- ❑ Aware that treatment will be stopped if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT

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