University Hospital of North Staffordshire NHS
NHS Trust

NHS
Stoke on Trent

North Staffordshire Combined Healthcare NHS
NHS Trust

NHS
North Staffordshire

Effective Shared Care Agreement for the prevention and treatment of **rejection following renal transplantation and nephrotic syndrome**

Ciclosporin capsules / oral solution (Neoral®)

These forms (1 and 2) are to be completed by both the Consultant initiating the therapy and the GP who is continuing care. A copy of the completed form should be retained by the GP and a copy should be returned to the Consultant, for filing in the patient's notes.

Form 1: - Consultant Copy*

Patient Name: **NHS Number:**

Date of Birth: **Telephone Number:**

Address:

(Or attach Addressograph label)

Patients Signature: **Date:**

And / or on behalf of the patient

Carer's Name: **Telephone Number:**

Address:

Carer's Signature: **Date:**

And:

Consultant Name: **Directorate:**

Address:

Telephone Number: **Fax Number:** **Email:**

Signature: **Date:**

And:

GP Name:

Address:

Telephone Number: **Fax Number:** **Email:**

Signature: **Date:**

Approved by Area Prescribing Committee on: 02/12/2009 Version: v1
Review date: 02/12/2011

Effective Shared Care Agreement for the prevention and treatment of **rejection following renal transplantation and nephrotic syndrome**

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Form 2: - GP Copy*

Patient Name: **NHS Number:**

Date of Birth: **Telephone Number:**

Address:

(Or attach Addressograph label)

Patients Signature: **Date:**

And / or on behalf of the patient

Carer's Name: **Telephone Number:**

Address:

Carer's Signature: **Date:**

And:

Consultant Name: **Directorate:**

Address:

Telephone Number: **Fax Number:** **Email:**

Signature: **Date:**

And:

GP Name:

Address:

Telephone Number: **Fax Number:** **Email:**

Signature: **Date:**

Effective Shared Care Agreement for the prevention and treatment of: -

rejection following renal transplantation and nephrotic syndrome

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This shared care agreement outlines the ways in which the responsibilities for managing the prescribing of ciclosporin for the prevention and treatment of rejection following renal transplantation and nephrotic syndrome will be shared between the specialist and general practitioner (GP). If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition will remain 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 / carer. The intention to share care should be explained to the patient / carer by the doctor initiating treatment. It is important that patients / carers are consulted about treatment and are in agreement with it. Patients who have undergone a renal transplant are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

RESPONSIBILITIES and ROLES

Specialist responsibilities
Initiation
1 Perform initial baseline tests. These include FBC, LFT's, U&E's, creatinine clearance, lipids and BP.
2 Initiate treatment with ciclosporin.
3 Discuss the benefits, side effects of treatment and warning signs that need to be reported with the patient.
4 Check for possible drug interactions with ciclosporin and avoid prescribing interacting drugs.
5 Assess likelihood of compliance.
6 Ask the GP whether he or she is willing to participate in shared care and explain the intention to share care with the patient/ carer.
7 Record results of baseline tests and monitor in accordance with local protocol.
8 Recommend the brand of ciclosporin to be prescribed.
9 Prescribe medication until care is transferred to GP.
Follow-up assessments
9 Review immunosuppressant therapy including ciclosporin levels.
10 Titrate the dose if necessary to establish patient on a safe / effective dose.
11 Monitor patients Creatinine / eGFR at required intervals.
12 Monitor patients LFT's, U&E's, blood pressure and lipids as required.
13 Check for side effects and report adverse events to the CSM and GP where appropriate.
Support to GP
14 Provide copy of effective shared care agreement and supporting information.
15 Promptly communicate with GP, advising of blood test results if requested, any dosage adjustments required and when to refer the patient back to specialist care.
16 Advise when and how to adjust the dose/ stop treatment or consult the specialist.
17 Inform GP if patient does not attend specialist appointments.
18 Have a mechanism in place to receive rapid referral of a patient from the GP in event of deteriorating clinical condition.
19 Ensure clear backup arrangements exist for GPs to obtain advice and support.
20 Advise the GP when the patient should receive the pneumococcal vaccine.

General Practitioner responsibilities
1 Reply to the request for shared care as soon as practical.
2 Prescribe ciclosporin, as directed by the specialist.
3 Prescribe by brand in accordance with the specialist's recommendation.
4 Contact the specialist if you suspect the patient is not complying with their medication.
5 Adjust the dose as advised by the specialist.
6 Check for possible drug interactions when prescribing new medication and avoid prescribing interacting drugs.
7 Ensure the patient understands which warning symptoms to report.
8 Treat hypertension as advised by the specialist.
9 Recommend that female patients attend for a cervical smear annually.
10 Recommend the patient receives an influenza vaccine yearly and pneumococcal vaccine as required.
11 Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
12 Refer the patient to the specialist if his or her condition deteriorates.
13 Report any suspected adverse events to specialist team and any severe adverse events to CSM.
14 Stop treatment on advice of specialist.

Patient's role	
1	Consent to treatment with ciclosporin.
2	Take medication according to doctors' instructions.
3	Attend follow up and other appointments.
4	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
5	Know which brand of ciclosporin they are taking and question any differences in supply received.
6	Share any concerns in relation to treatment or their condition.
7	Inform specialist if you feel you are having problems taking your medication or have stopped taking it.
8	Inform specialist or GP of any other medication being taken, including over-the-counter products.
9	Do not take any herbal remedies without checking with the specialist.
10	Alert physician prior to any vaccine administration that you are taking ciclosporin.
11	Female patients should ensure that their GP offers them a cervical smear annually.
12	Ensure that you receive the influenza vaccine annually from your GP.
13	Take adequate precautions to avoid exposure to ultraviolet light i.e. wear sunscreen / protective clothing.
14	Avoid grapefruit or grapefruit juice.
15	Report any adverse effects or warning symptoms to the specialist or GP.

SUPPORTING INFORMATION FOR CICLOSPORIN (NEORAL®) EFFECTIVE SHARED CARE AGREEMENT

This information should be read in conjunction with the Summary of Product Characteristics for Ciclosporin (Neoral®) available from www.medicines.org.uk

Licensed indications

Prevention of graft rejection following kidney transplant; treatment of transplant rejection in patients previously receiving other immunosuppressive agents and treatment of steroid dependent or steroid resistant nephrotic syndrome.

Dosage and Administration

The usual starting dose after renal transplant is 10-15mg/kg in two divided doses; initiated 12 hours before transplantation and as a general rule continued for 1-2 weeks post-operatively. This should then be gradually reduced to a usual maintenance dose of 2-6mg/kg/day given in two divided doses. Doses should be adjusted according to blood ciclosporin concentrations and renal function. At the UHNS ciclosporin dose is adjusted according to pre-dose levels (trough levels). It is important to note that any dose adjustments of ciclosporin should based on pre-dose levels only.

When ciclosporin is given with other immunosuppressants (e.g. with corticosteroids or as part of a triple or quadruple drug therapy), lower doses (e.g. 3-6mg/kg/day in two divided doses) may be used for initial treatment.

In nephrotic syndrome, the usual dose is 2.5-5mg/kg/day in two divided doses.

Prescribing should be by **brand.** This should not differ to that recommended by the specialist, due to potential differences in bioavailability between the different oral ciclosporin formulations. Currently only one brand of oral ciclosporin (Neoral®) is commercially available, however generic preparations may become available at any point in the future- therefore it is important that ciclosporin is prescribed by brand. Other oral brands are available in the UK on a named patient basis.

Neoral capsules® should be swallowed whole with a mouthful of water.

Neoral oral solution® should be diluted with water, orange juice or squash or apple juice immediately before being taken and stirred well.

Contraindications

Patients with a known hypersensitivity to ciclosporin, concomitant use of tacrolimus or rosuvastatin. In nephrotic syndrome- patients with uncontrolled hypertension, uncontrolled infections or any kind of malignancy.

Therapeutic Use

- Refer to NICE technology appraisal guidance 85 (September 2004) – Immunosuppressive therapy for renal transplantation in adults, available from **www.nice.org.uk**
- Midland Therapeutic Review Advisory Committee (MTRAC). Verdict & Summary: - Ciclosporin (Neoral®), July 2000.

Monitoring

Regular monitoring is essential to detect adverse events at an early stage and patients should be counselled about the risk factors and to report all signs and symptoms of toxicity.
At UHNS trough levels of ciclosporin will be checked by the hospital. For the first three months post-transplant, a level of 200-250 micrograms / litre is aimed for, and this is reduced to 75-150 micrograms /litre for the maintenance phase. Levels may be individualised for patients. The frequency of blood level monitoring should be based on clinical needs.

Ciclosporin can impair renal function. Close monitoring of serum creatinine and urea is required; deterioration may necessitate dose reduction or discontinuation in favour of an alternative immunosuppressive agent. Serum potassium and magnesium should be monitored.

LFT's should be monitored, dose adjustment may be necessary based on the results of bilirubin and liver enzymes.

Monitoring of blood pressure is required, appropriate antihypertensive treatment must be initiated if necessary. Lipids should be measured before treatment and thereafter as appropriate.

Side Effects

Very common (≥1/10): hypertension, renal dysfunction, lower respiratory tract infection, bronchiolitis, urinary tract infection, cytomegalovirus infection, upper respiratory tract infection, hyperlipidaemia, hypercholesterolaemia, tremor, headache.

Common (≥1/100, <1/10): sepsis, herpes infections, candidal infection, skin papillomas, basal cell carcinoma, squamous cell carcinoma of the skin, Bowen's disease, lymphoproliferative disorders, anorexia, hyperuricaemia, hyperkalaemia, hypomagnesaemia, paraesthesia, nausea, vomiting, abdominal pain, diarrhoea, gingival hyperplasia, hepatic dysfunction, hypertrichosis, muscle cramps, myalgia, fatigue

Uncommon (≥1/1000, <1/100): seborrhoeic keratosis, melanoma, squamous cell carcinoma, anaemia, thrombocytopenia, signs of encephalopathy such as convulsions, confusion, disorientation, decreased responsiveness, agitation, insomnia, visual disturbances, cortical blindness, coma, paresis, cerebellar ataxia, allergic rashes, oedema, weight increase

Rare (≥1/10,000, <1/1000): microangiopathic haemolytic anaemia, haemolytic uraemic syndrome, hyperglycaemia, motor polyneuropathy, pancreatitis, muscle weakness, myopathy, menstrual disturbances, gynecomastia

Very rare (<1/10,000 including isolated reports) optic disc oedema including papilloedema, with possible visual impairment secondary to benign intracranial hypertension.

Patients should be advised to avoid excess ultraviolet light exposure or limit it by wearing protective clothing and using a sunscreen with a high protection factor and the use of live attenuated vaccines should be avoided.

Drug Interactions

Grapefruit juice has been reported to increase the bioavailability of ciclosporin.

Drugs may either increase or decrease plasma or whole blood ciclosporin levels usually by inhibition or induction of enzymes involved in ciclosporin metabolism, particularly CYP3A4.

Drugs that decrease ciclosporin levels:
Barbiturates, carbamazepine, oxcarbazepine, phenytoin, rifampicin, octreotide, orlistat, St John's Wort, ticlopidine, sulfinpyrazone, terbinafine, bosentan, sulfadiazine, primidone, griseofulvin lanreotide, modafinil, sevelamer.

Drugs that increase ciclosporin levels:
Macrolides, ketoconazole, fluconazole, itraconazole, voriconazole, diltiazem, nicardipine, verapamil, metoclopramide, oral contraceptives, danazol, methyprednisolone (high dose), allopurinol, amiodarone, ursodeoxycholic acid, protease inhibitors, imatinib, colchicine, propafenone, chloramphenicol, doxycycline, telithromycin, quinupristin/ dalfopristin, posaconazole, miconazole, chloroquine, hydroxychloroquine, carvedilol, lercanidipine, ezetimibe, tacrolimus, cimetidine, micafungin.

Care should be taken with other drugs that exhibit nephrotoxic synergy:
Aminoglycosides, amphotericin B, ciprofloxacin, vancomycin, trimethoprim (+ sulfamethoxazole), NSAIDs, melphalan, methotrexate, tacrolimus, allopurinol, polymixins, aciclovir, colchicine, thiazides and related diuretics, bezafibrate, fenofibrate.

Care is required for concomitant use of potassium sparing drugs:
Potassium sparing diuretics, ACE inhibitors, ARBs, potassium.

Care should be taken with doxorubicin as it may cause *neurotoxicity* when used with ciclosporin.

Care should be taken with daptomycin and statins due to the *increased risk of myopathy* when used in conjunction with ciclosporin.

Ciclosporin may increase plasma concentration of:
Digoxin, colchicine, prednisolone, statins, sirolimus, everolimus, repaglinide and etoposide, diclofenac, ezetimibe, caspofungin, bosentan, nifedipine, sitaxentan, lercanidipine, methotrexate, docetaxel (oral) and paclitaxel (oral).

NSAIDs known to undergo strong first-pass metabolism should be given at half the dose normally used when given concurrently with ciclosporin.

Concomitant use of nifedipine should be avoided in patients who develop gingival hyperplasia as a side effect of ciclosporin.

Combined use with tacrolimus is not recommended.

Primary Care Costs (emims July 2009)

Neoral® capsules
10mg £18.98 / 60 capsules
25mg £19.10 / 30 capsules
50mg £37.40 / 30 capsules
100mg £70.99 / 30 capsules

Neoral® Oral Solution
100mg/ml £106.37 / 50ml

References

Joint Formulary Committee. British National Formulary. 57th ed. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; 2009

Summary of Product Characteristics – Neoral® Soft Gelatin Capsules, Neoral® Oral Solution (Ciclosporin). Novartis. Last revised 21st May 2009. Accessed via www.medicines.org.uk

Baxter, K. Stockley's Drug Interactions. Pharmaceutical Press 2009. Accessed via www.medicinescomplete.com

BACK-UP ADVICE AND SUPPORT

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