Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Cyclophosphamide

Dermatology / Immunology / Nephrology / Neurology / Respiratory / Rheumatology shared care guideline.

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

This shared care guideline refers to the use of cyclophosphamide in the treatment of **NON-CANCER CONDITIONS ONLY.**

Unlicensed indications: severe vasculitis and arteritis, end organ complications of connective tissue disease, pemphigus, dermatomyositis, polymyositis, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, inflammatory neuropathies.

Adult dosage and administration

Cyclophosphamide can be administered as pulse IV treatment (under which circumstance monitoring will be managed by secondary care) or as a daily oral dose, normally 2mg/kg/day. A typical dose may be 50 - 150mg orally daily as a single or divided dose. The dose is tailored according to the individual patient requirements with a maximum dosage of 200mg/day. Duration of treatment may be variable ranging from weeks to months depending on indication.
Use with caution if evidence of renal or hepatic dysfunction as dosage reduction may be required.
Available as: cyclophosphamide 50mg tablets.
In exceptional circumstances, a liquid preparation may be required. Cyclophosphamide **50mg/5ml** is the standard strength that must be used (available from special order manufacturers eg. Nova Laboratories).

Hospital specialist responsibilities

- Assess if the patient is suitable for treatment with cyclophosphamide.
- Agree shared care with the patient's GP.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of medication.
- Patients should be counselled regarding the recognised complication of infertility and cyclophosphamide treatment.
- If the liquid formulation is used, provide training on safe handling, storage, spillage and waste disposal (provide a cytotoxic spill kit and cytotoxic sharps box if necessary).
- Provide shared care monitoring record booklet if required.
- Undertake baseline tests as indicated in monitoring table.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

Monitoring table		Hospital specialist	GP			Hospital specialist
Test	**Indication**	Pre-treatment baseline	Stage of treatment			Annual review
			First 4 Weeks	Week 5 - 12	After 12 weeks	
FBC LFTs ESR / CRP (Rheumatology only) U&Es, eGFR*	Baseline assessment, disease activity scoring & dose adjustment	✓	Every week	Every 2 weeks	Every month	As part of annual review or as clinically indicated
Chest x-ray PFTs, TB screening if indicated	Baseline respiratory assessment and TB screening	✓	Not routinely required			If clinically indicated
Height, weight and blood pressure	Baseline assessment					
Urinalysis	To detect adverse effects	✓	Every month			
Smear test		Ensure up to date	Annually for the first 3 years and then as per the national screening programme			
Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding		✓	At every consultation			✓

* Report a drop of >20% in eGFR to the specialist but continue cyclophosphamide at the same dose.
If a further DMARD is added as combination therapy, or the dose is increased, the initial starting schedule should be reinstated.
There may be clinical circumstances where the frequency of monitoring may vary and this should be specified by the initiating specialist.

GP responsibilities

- Prescribe cyclophosphamide.
- Arrange and record ongoing monitoring as advised by specialist (see monitoring table), ensuring practice systems are in place to recall patients for monitoring blood tests.
- Prevent ongoing prescription if patient is not compliant with monitoring. Liaise with specialist if appropriate.
- Report any adverse drug reactions to the initiating specialist and the usual bodies (eg. MHRA/CHM).
- Ensure no drug interactions with other medicines.
- Administer inactivated influenza vaccine annually unless otherwise advised by the initiating specialist.
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly eg. asplenia), see BNF or Green Book.
- Passive immunization using varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals, duty virologist 07889 086 946 for advice if exposure is suspected. For other queries eg. those concerning exposure, infection or any recommendations relating to healthy susceptible household contacts, consult the Green Book and/or take additional advice from Regional Virus Laboratory, Royal Group of Hospitals.
- Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding at every consultation.

Withhold cyclophosphamide and contact specialist if:

- WCC < 3.5 x 10^9/L
- Neutrophils < 1.6 x 10^9/L
- Unexplained eosinophilia > 0.5 x 10^9/L
- Platelets < 140 x 10^9/L
- MCV > 105fL, (check B12 & folate & TFT)
- AST/ALT > 3 times the upper limit of normal (for results between 2 - 3 x ULN, continue cyclophosphamide, repeat bloods and seek specialist advice). Minor elevations of AST/ALT are common
- If renal impairment develops
- Unexplained fall in serum albumin
- Oral ulceration / sore throat
- Unexplained rash / abnormal bruising
- New or increasing dyspnoea or dry cough
- If haematuria develops (on dipstick urinalysis).

Normal reference range may vary slightly between labs.
Results should be recorded in the patient's shared care monitoring record booklet (where in use).
Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Contraindicated in: pregnancy, patients with known hypersensitivity to cyclophosphamide, with acute infections, with bone-marrow aplasia, urinary tract infection or with acute urothelial toxicity from cytotoxic chemotherapy or radiation therapy. Avoid in patients with cystitis from any cause until it has been treated.
Life threatening cutaneous reactions. Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of cyclophosphamide.
General: malaise, dizziness, diarrhoea, rash, myalgia, arthralgia, thrombocytopenia, hair loss and anaemia can occur infrequently. If severe or persistent, refer to the specialist.
Nausea can occur initially, addition of anti-emetic medication may help.
Blood disorders: leucopenia, anaemia, and thrombocytopenia. GPs should be alert to any oral ulceration, sore throat, unexplained rash or abnormal bruising/bleeding.
Haemorrhagic cystitis. For those on oral cyclophosphamide a high oral fluid intake (3-4 litres per day) should be maintained to decrease risk (not always appropriate for renal patients). Withhold oral cyclophosphamide and contact the initiating consultant if haematuria develops on dipstick urinalysis.
Infection. Immunosuppressants can increase susceptibility to infection. Patients should be reviewed rapidly and appropriate therapy instituted should signs of infection develop. Normally cyclophosphamide would be withheld if anti-infective intervention is required. Please contact the initiating specialist if any doubt exists as patients on treatment with cyclophosphamide can develop septic shock rapidly. Patients receiving immunosuppressive therapy are at increased risk of fungal infections, consider prophylactic antifungal treatment. Pneumocystis carinii prophylaxis may be considered for patients who require steroids in addition to cyclophosphamide.
Abnormal liver function can occur early in treatment.
Amenorrhoea and azoospermia often occur during treatment with cyclophosphamide.
Pregnancy / contraception. Women of childbearing potential and men receiving cyclophosphamide should be advised to use effective contraception during and at least 6 to 12 months after stopping cyclophosphamide therapy. Patients who become pregnant should stop taking cyclophosphamide and be referred to the initiating specialist at the earliest opportunity. Patients planning to become pregnant should be referred to the initiating specialist.
Breastfeeding. Women being treated with cyclophosphamide should not breastfeed.
Cancer risk. Patients receiving cyclophosphamide are at increased risk of lymphomas and malignancies of the skin. Avoiding excessive exposure to the sun and use of high factor sunscreens are advised. Adherence to population screening programmes is particularly important in this population.
Live vaccines. Consult the Green Book and take additional advice from initiating specialist if required.

Common drug interactions

Allopurinol increases incidence of bone marrow depression.
Antipsychotics: avoid concomitant use with clozapine.
Digoxin: cyclophosphamide decreases absorption of digoxin.
Oral hypoglycaemic agents: effects may be increased by cyclophosphamide.

Communication

For any queries relating to this patient's treatment with cyclophosphamide, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

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