SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR CYCLOPHOSPHAMIDE TABLETS (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: Cyclophosphamide

Formulation: Tablets

Strength: 50mg (Oral tablets are only available in strengths of 50mg. These are sugar coated and cannot be divided).

STATUS OF MEDICINE

Licence status: Off-label (for vasculitis)

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

To treat vasculitis

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); U+E and urinalysis.
2. Copy of results to be sent to GP.
3. Exclude pregnancy before starting therapy. Advise effective contraception essential during treatment and for at least 6 months after discontinuation in women and men.
4. Initiation of therapy and recommendations for dose increments. This will be controlled by the Renal Unit.
5. Monitoring clinical response to treatment:
   - FBC and LFTs (including ALT and Alk Phos) U+E and urinalysis weekly for the first 3 months. Then FBC, LFTs, U+E and urinalysis 4 weekly thereafter.
   - Advise patients to immediately report any signs or symptoms of bone marrow suppression, e.g. sore throat, fever, infection, inexplicable bruising or bleeding, mouth ulcers or rash.

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 cyclophosphamide should:

1. Prescribe medication under the guidance of the Renal Consultant.
2. Ensure the GP is aware that the drug can cause:
   - Bone marrow suppression
   - Leucopenia
   - Amenorrhoea and azoospermia which is reversible
   - Haematuria and acute haemorrhagic cystitis may occur during or after therapy
   - Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.
3. Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
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 Consultant/Renal Unit/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 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 should be given along with the annual influenza vaccine.
9. A high fluid intake should be encouraged to reduce the risk of haemorrhagic cystitis.

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 cyclophosphamide and to any of its metabolites
- Acute infections
- Bone-marrow aplasia
- Urinary tract infection
- Acute urothelial toxicity from cytotoxic chemotherapy or radiation therapy
- Urinary outflow obstruction.

PREGNANCY

Discuss with Consultant. Pregnancy should be avoided during and for 6 to 12 months after stopping therapy. Advise the patient to contact their physician immediately should pregnancy occur.

BREAST-FEEDING

Not recommended during and for 36 hours after stopping treatment. Discuss with Aberdeen Maternity hospital.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

- Myelosuppression see table below.
- Immunosuppression see table below.
- Infection see table below.
- Urinary tract and renal toxicity, haemorrhagic cystitis, pyelitis, ureteritis and haematuria, bladder ulceration/necrosis, fibrosis/contracture may develop. Withhold until discussed with consultant.
- Cardiotoxicity – Myocarditis and myopericarditis withhold until discussed with consultant.
- Pulmonary toxicity – Pneumonitis and pulmonary fibrosis withhold until discussed with consultant.
- Veno-occlusive liver disease (VOD) withhold until discussed with consultant.

Abnormal Monitoring Results	**Action To Be Taken**
• **WBC** < 4.0 x 10^9 /L	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• **Neutrophils** < 2.0 x 10^9 /L	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• **Platelets** < 150x10^9 /L	Withhold **until discussed** 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	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• MCV>105fl	Investigate and if B12 or folate low start appropriate supplementation
• Rash, oral ulceration, unexplained fever	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• Abnormal bruising or sore throat	Withhold until FBC results available. Discuss with Renal Unit/Registrar on call or Consultant
• Dipstick haematuria	Advise increased fluid intake and discuss with consultant. Monitor closely
Abnormal Monitoring Results	**Action To Be Taken**
• Suspicion of or newly diagnosed malignancies	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• Macroscopic haematuria or haematuria with dysuria	Withhold **until discussed** 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 cyclophosphamide.
- Allopurinol (increased bone marrow depression).
- Inducers of human hepatic and extrahepatic microsomal enzymes (e.g. cytochrome P450 enzymes). The potential for hepatic and extrahepatic microsomal enzyme induction must be considered in case of prior or concomitant treatment with substances known to induce an increased activity of such enzymes such as rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort and corticosteroids.
- Protease inhibitors can be associated with higher incidence of infections and neutropenia.
- Succinylcholine (prolonged apnoea).
- Etanercept higher incidence of non-cutaneous solid malignancies.
- Metronidazole possibility of acute encephalopathy casual association is unclear.
- Tamoxifen may increase the risk of thromboembolic complications.
- Ciclosporin may increase incidence of graft versus host disease.
- Coumarins both increased and decreased warfarin effect.

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/1813/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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