Thames Valley
Strategic Clinical Network

ORAL CYCLOPHOSPHAMIDE WITH OR WITHOUT PREDNISOLONE

INDICATION

First-line or subsequent lines of therapy treated with a palliative approach. Suitable alternative to melphalan particularly if blood counts are below the required level.

TREATMENT INTENT

Disease modification

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - CRP
   - Baseline random blood glucose level if starting on prednisolone
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   - Virology : HIV, Hepatitis B (including core antibody), and Hepatitis C
   - Calculated creatinine clearance (CrCl), urine protein/ creatinine ratio
   - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   - Serum free light chain assay (Freelite)
   - β_2 microglobulin
   - LDH
   - Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions Samples should be sent to Wessex Regional Genetics Laboratory (address below)
   - Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
   - Group and save
   - Imaging as per NICE/network guidance and clinical presentation
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury Disctrict Hospital
Salisbury
Wiltshire

Additional investigation:

1. Plasma viscosity if hyperviscosity suspected
2. Hydration - fluid intake of at least 3 litres /day should be attempted.
3. Document patient's height and weight, dose on actual body weight.
4. Document patient's performance status.
5.
6. Counselling - all patients should receive verbal and written information on oral chemotherapy. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures
7. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all the information that has been given and that patient consent has been obtained.
8. Treatment must be agreed at the relevant MDT

DRUG REGIMEN

Cyclophosphamide	50-100 mg oral daily, continuously until disease progression or 300 mg/m^2 (rounded down to nearest 50 mg) once per week orally or intravenously
WITH OR WITHOUT	
Prednisolone	20 mg daily orally for 6 weeks then tailed off over 2 subsequent weeks

NB: Cyclophosphamide tablets are 50 mg in strength.

CYCLE FREQUENCY

Continue until plateau phase (paraprotein level stable for 3 months) or clinical / biochemical progression; whichever comes first.

DOSE MODIFICATIONS

Renal		Hepatic
Clinical decision GFR > 20ml/min GFR 10 – 20ml/min GFR < 10ml/min	 100% dose 75% dose 50% dose	Exposure to active metabolites may not be increased, suggesting that dose reduction may not be necessary. Clinical decision.

Dose should be held/modified if grade 3 and 4 haematological toxicity occurs.

INVESTIGATIONS - First and subsequent cycles

- FBC.
- U&Es, creatinine, glucose (if on Prednisolone), calcium.

ADDITIONAL INVESTIGATIONS - Alternate cycles

- Serum electrophoresis with paraprotein and immunoglobulin quantification.
- Serum free light chains in light chain or non-secretory myeloma.

OTHER INVESTIGATIONS

- Consider repeat BM aspirate and trephine after 3 or 4 months in non-secretory myeloma.

CONCURRENT MEDICATIONS

- Consider Allopurinol 300 mg daily for 7 days for first cycle only.
- Prophylactic aciclovir 200 mg TDS (consider reducing to 200mg BD if CrCl)<10ml/min)
- Consider prophylactic fluconazole 50mg OD if appropriate
- Consider prophylactic co-trimoxazole 960mg OD on M/W/F if heavily pre-treated or previous autograft.
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- Proton pump inhibitor or H2 antagonist at clinician's discretion.
- Bone protection as per NSSG Bone Protection protocol MM.3

EMETIC RISK

Moderate emetic risk on weekly cyclophosphamide days, otherwise low risk.

ADVERSE EFFECTS/REGIEMN SPECIFIC COMPLICATIONS

Cyclophosphamide related toxicities include: leucopenia, haemorrhagic cystitis, hair loss, mucosal ulceration, anorexia, nausea and vomiting, pigmentation (typically affecting the palms and nails of the palms and the soles of the feet) pneumonitis and interstitial pulmonary fibrosis.

Steroid-related side effects: mood changes, restlessness, withdrawal effects, glucose intolerance

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REFERENCES

1. Smith A, Wisloff F, Samson D; UK Myeloma Forum; Nordic Myeloma Study Group; British Committee for Standards in Haematology. Guidelines on the diagnosis and management of multiple myeloma 2005. Br J Haematol. 2006 Feb;132(4):410-51.
2. Bunn & Ashley, UK Renal Pharmacy Group. The renal drug handbook 3rd Edition.

Cyclophosphamide 50 mg tablets, Baxter Healthcare eMC UK Summary of Product Characteristics. Baxter Healthcare, Last updated December 2016

REVIEW

Name	Revision	Date	Version	Review date
Nadjoua Maouche Pharmacist	Formatting, concurrent medication section, drug regimen, adverse effects	May 2016	4.3	May 2018
Manuela Sultanova Service Coordinator	Formatting, standardisation of Pre-assessment section	July 2017	4.4	May 2018
Network Protocol Review 2019	Indication, pre-assessment, cycle frequency, dose modification, other investigations, references	June 2019	4.5	June 2020