DRC –Dexamethasone, Rituximab and Cyclophosphamide

Indication
First or second line treatment of symptomatic Waldenstrom's macroglobulinaemia for patients who are unable to tolerate a fludarabine containing regimen.

ICD-10 codes
Codes prefixed with D88

Regimen details

Day	Drug	Dose	Route
1	Dexamethasone	20mg STAT	PO or IV
1	Rituximab	375mg/m²	IV
1-5	Cyclophosphamide	100mg/m² BD	PO

Cycle frequency
21 days

Number of cycles
6 cycles

Administration
Dexamethasone is available as 500microgram and 2mg tablets. It is taken orally 30 minutes prior to rituximab.

Rituximab is administered in 500mL sodium chloride 0.9%. The first infusion should be initiated at 50mg/hour and if tolerated the rate can be increased at 50mg/hour every 30 minutes to a maximum of 400mg/hour. Subsequent infusions should be initiated at 100 mg/hour and if tolerated increased at 100mg/hour increments every 30minutes to a maximum of 400 mg/hour.

Cyclophosphamide is available as 50mg tablets, doses should be rounded to the nearest 50mg. Tablets should be swallowed whole on an empty stomach (unless gastric irritation occurs and in that case they may be taken with meals). Patients should be advised to maintain good hydration.

Pre-medication
Rituximab premedication:

- Paracetamol 1g PO 60 minutes prior to rituximab infusion
- Chlorphenamine 10mg IV bolus 15 minutes prior to rituximab infusion
- Dexamethasone 20mg PO or IV 30 minutes prior to rituximab (as per dosing table above)

Emetogenicity
This regimen has low emetic potential.

Additional supportive medication

Allopurinol 300mg OD (or 100mg OD if creatinine clearance <20mL/min) for the first cycle.
H_2 antagonist or proton-pump inhibitor as per local policy.
Antiemetics as per local policy.
Aciclovir and co-trimoxazole as per local policy.
Consider GCSF support for patient > 70 years or with neutropenia.

Extravasation

Rituximab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Glucose	14 days
DAT	14 days
Serum electrophoresis	14 days
Bone marrow aspirate and trephine biopsy	Within 8 weeks

Hepatitis B and C serology

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	72 hours
U+E (including creatinine)	72 hours
LFTs	72 hours
Serum electrophoresis	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.0 x10^9 /L
Platelets	≥ 100
CrCl	> 20mL/min

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L and/or platelets < 50 x 10^9/L delay by one week or until resolved.
In the case of febrile neutropenia (neutrophils < 0.5 × 10^9/L and fever > 38.5°C) during the previous cycle consider GCSF support (as per local policy) or reduce cyclophosphamide dose to 50%.

- **Renal impairment**

Creatinine Clearance (mL/min)	**Cyclophosphamide dose**
> 20	100%
10-20	75%
<10	50%

- **Hepatic impairment**

Cyclophosphamide is not recommended if bilirubin > 1.5 x ULN or AST/ALT > 3 x ULN (consultant decision)

- **Other toxicities**

IgM flare (rise in IgM levels by > 25%) - omit Rituximab if IgM level is > 30g/L at cycle 1.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

IgM flare
Myelosuppression
Myocardial toxicity
Infertility

- **Frequently occurring side effects**

Myelosuppression
Nausea, vomiting
Hypotension
Alopecia
Haemorrhagic cystitis

- **Other side effects**

Headache

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Cyclophosphamide:
Amiodarone: increased risk of pulmonary fibrosis – avoid if possible
Clozapine: increased risk of agranulocytosis – avoid concomitant use
Digoxin tablets: reduced absorption – give as liquid form
Indapamide: prolonged leucopenia is possible - avoid
Itraconazole: may increase adverse effects of cyclophosphamide
Phenytoin: reduced absorption - may need to increase dose of phenytoin
Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.

Additional comments

Patients should be advised of the need for contraception (both male and female patients) prior to commencing treatment.

References

- Dimopoulos MA, Agagnostopulos A, Kyrtsonis MC et al: Primary treatment of Waldenstrom's Macroglobulinaemia with Dexamethasone, Rituximab and Cyclophosphamide. J Clin Oncol 25:3344-3349 2007
- Summary of Product Characteristics Cyclophosphamide tablets (Pharmacia) accessed 8 Oct 2014 via www.medicines.org.uk
- Summary of Product Characteristics Rituximab (Roche) accessed 8 Oct 2014 via www.medicines.org.uk

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