INTRAVENOUS CYCLOPHOSPHAMIDE

Used for vasculitis (e.g. granulomatosis polyangitis, polyarteritis nodosum, rheumatoid vasculitis) and systemic lupus erythematosis (SLE)
May also be used for pulmonary vasculitis and connective tissue diseases

Drug/Dosage: **Cyclophosphamide** 500 – 1500mg IV Day 1

Rheumatology use: 500mg on a 2 weekly cycle for the first 3 doses, then every 3 weeks for the next 3 doses, then re-assess.
(may be increased to a maximum of 1500mg at Consultant discretion)
Further treatment, up to a maximum of 6 months in total, will depend on initial response and may range from 2-weekly to 4-weekly dosing.

Respiratory team preferred schedule:
Cyclophosphamide 1000mg IV Day 1 every 4 weeks, usually for up to 6 doses

Administration: Cyclophosphamide given as a bolus injection.
Patient should be encouraged to increase fluid intake to 2 - 3 litres over the next 24 hours.

Other Drugs: **Mesna:**

- not routinely required with the 500mg cyclophosphamide dose.
- may be added to 1000mg dose, according to individual Consultant preference.
- recommended with 1500mg dose

Locally agreed schedule:
Mesna 400mg po pre cyclophosphamide (administered at same time as anti-emetics), then Mesna 400mg po at + 2 hours and + 6 hours after cyclophosphamide

Anti- emetics: mildly emetogenic: co- prescribe with a single dose of ondansetron 8mg po pre chemotherapy, plus domperidone 10mg po tds prn, to take home

Main Toxicities: mucositis
myelosuppression; may occur
alopecia; rarely complete, occasionally partial at this dose
haemorrhagic cystitis; occurs rarely
ovarian failure / male infertility possible

Extravasation: non-vesicant

Regular Investigations:
FBC before each dose, plus nadir count on Day 10 of every cycle (or Day 14 if 4 weekly cycle)
LFTs before each cycle
U&Es before each cycle

Comments: Do not offer scalp cooling.

Reason for Update: anti-emetic update; inclusion of preferred regimen for respiratory team	Approved by Rheumatology Consultant: Dr C Neville
Version: 4	Approved by Respiratory Consultant: Dr J Dakin
Supersedes: Version 3	Date: 14.11.16
Prepared by: S Taylor	Checked by: C Tucker

Male patients may wish to consider sperm banking.

The chemotherapy nurse needs to ensure that the next IV administration appointment is made as required – the patient will be unfamiliar with St Luke's Cancer Centre systems.

Dose Modifications

Haematological Toxicity:	WBC < 3.0 x 10^9/l or Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	General advice is to delay for 1 week. Repeat FBC - if within normal parameters, resume treatment. If Consultant wishes to proceed with treatment in presence of borderline low counts, this must be clearly indicated on the prescription.

The nadir count is used as a guide for planning future treatment doses – if nadir is uncomplicated (and generally no lower than WBC 1.0 x10^9/l and neutrophils 0.5 x 10^9/l), no infectious episode and count recovers in time for next dose, the dose will generally stay the same.
In contrast, the Consultant may choose to increase the next cyclophosphamide dose in a patient whose counts do not fall significantly.

Renal Impairment: Standard advice for cyclophosphamide dose reduction within oncology is as the table below:

CrCl (ml/min)	Cyclophosphamide Dose
> 20	Give 100%
10 – 20	Give 75%
< 10	Give 50%

However, the British Society of Rheumatology also recommends the following maximum doses for this regimen in the presence of a raised serum creatinine:
If serum creatinine 300 – 500 µmol/l:
Age < 60 years 12.5mg/kg/pulse (maximum 1500mg)
Age 61 - 69 years 10mg/kg/pulse
Age > 70 years 7.5mg/kg/pulse
(If serum creatinine < 300 µmol/l, full dose is recommended)

Reference:
Lapraik, C et al; British Society of Rheumatology guidelines for the management of adults with ANCA associated vasculitis; Rheumatology 2007; 46: 1 – 11
Hoyles, R et al; Arthritis & Rheumatism 2006; 54 (12): 3962 - 3970