R-CVP

For use in previously untreated patients with symptomatic Stage III or IV follicular lymphoma - NICE approved Sept 2006

For all other indications, only for use after funding approved by Trust/PCT
e.g. relapsed follicular lymphoma in rituximab-naïve patients;
patients who obtained a prolonged remission after previous rituximab-based therapy;
high grade lymphoma patients not fit enough for the anthracycline component of R-CHOP

Drugs/Dosage:	**Rituximab**	375mg/m^2	IV	D1
	then			
	Cyclophosphamide	750mg/m^2	IV	D1
	Vincristine	1.4mg/m^2 (max 2mg)	IV	D1
	Prednisolone	100mg (flat dose)	po daily	D1 to D5

Age > 60 yrs and pre-existing constipation or neurological problems, consider vincristine dose of 1mg. If in doubt, check with Consultant.

Premedication:	Paracetamol 1000mg po	60 minutes pre rituximab
	Chlorphenamine 10mg IV	15 minutes pre rituximab
	Dexamethasone 8mg or Hydrocortisone 100mg IV	15 minutes pre rituximab

Other drugs: Allopurinol 300mg po daily, starting at least 24 hours before first dose – review after 3 weeks
Use of proton pump inhibitor or H_2 receptor antagonist (eg ranitidine) is recommended whilst treating with steroids

Administration: Rituximab should be given before CVP, diluted in 0.9% Sodium Chloride & administered according to following instructions:

First infusion: start at 50mg/hr; escalate in 50mg/hr increments every 30 minutes to a maximum of 400mg/hr

Subsequent infusions: if no problems with first infusion, start at 100mg/hr; escalate in 100mg/hr increments every 30 minutes to a maximum of 400mg/hr
if reactions occurred with first infusion, give second infusion as for first infusion

If reactions occur at any time, stop infusion. If symptoms improve, restart at 50% dose and accelerate as tolerated.

Vincristine via fast running infusion of 0.9% Sodium Chloride
Cyclophosphamide may be given as a bolus

Frequency: 3 weekly cycle for a maximum of 8 cycles

Reason for Update: NICE approved for given indication	Approved by Chair of Network TSSG: Dr A Laurie
Version: 1	Date: 10/11/06
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Prepared by: S Taylor	Checked by Network Pharmacist: Dermot Ball

Main Toxicities: severe cytokine release syndrome – usually occurs within 1–2 hours of the first rituximab infusion (see Comments); myelosuppression; alopecia; mucositis; peripheral neuropathy; constipation; haemorrhagic cystitis; ovarian failure; infertility; tumour lysis syndrome (ensure pre-medicated with allopurinol and good hydration)

Anti- emetics: highly emetogenic (but oral dexamethasone not needed due to prednisolone)

Extravasation: Vincristine is a vesicant

Regular Investigations:	FBC	D1
	LFTs & U&Es	D1
	LDH	D1

Comments: Omit rituximab if WBC > 25 x 10^9/l, as increased risk of severe cytokine release syndrome. If in doubt, check with Consultant.

Full resuscitation equipment must be available, with immediate access to clinical staff trained in resuscitation for the first hour of the first rituximab infusion. Blood pressure, pulse and respiration must be measured and recorded every 15 minutes for the first hour of the first infusion.

Dose Modifications

Haematological Toxicity: If neutrophils < 1.0 x 10^9/l or platelets < 100 x 10^9/l on Day 1, delay chemotherapy until FBC recovered, then continue with 20% dose reduction of cyclophosphamide

If low counts are due to marrow infiltration, discuss with Consultant.

Renal Impairment: If serum creatinine above normal range, estimate creatinine clearance using Cockcroft & Gault and dose cyclophosphamide accordingly.

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

Hepatic Impairment:

Bilirubin (µmol/l)		ALT / AST (units/l)	Vincristine Dose
26 – 51	**or**	60 – 180	Give 50%
> 51	**and**	Normal	Give 50%
> 51	**and**	> 180	Omit

Neurotoxicity: Give 50% vincristine dose if Grade 2 motor and/or Grade 3 sensory toxicity
If in doubt, discuss with Consultant.

Patient Information: CancerBACKUP leaflets for Rituximab, Cyclophosphamide and Vincristine

References: Marcus, R et al; Blood 2005; 105: 1417-1423.
Solal-Celigny, P et al; Blood 2005; 106: 106a, abstract number 350

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