RITUXIMAB INTRAVENOUS for low-grade lymphomas

1. NICE approved as monotherapy for patients with relapsed or refractory Stage III or IV CD20 +ve follicular NHL where there is resistance to or intolerance of chemotherapy

2. Monotherapy for first line use in asymptomatic patients with Stage III-IV follicular NHL

3. Maintenance therapy:
   a) NICE approved for maintenance therapy for previously untreated, or relapsed, Stage III or IV CD20 +ve follicular NHL which has responded to rituximab-containing induction chemotherapy
   b) Maintenance therapy for mantle cell lymphoma in patients who respond to standard 1st line chemotherapy
   c) Maintenance therapy for marginal zone lymphoma in patients who respond to standard 1st line chemotherapy

All patients should be screened for hepatitis B virus before starting treatment with rituximab

Drugs/Dosage: **Rituximab** 375mg/m^2 IV Day 1 (dose 'banded' as table below)

Frequency: *Monotherapy:* weekly cycle for 4 doses (= one course)
A second course may sometimes be given to a patient who has responded to the first course.

First-line maintenance for previously untreated follicular, mantle cell or MZ lymphoma:
one dose every **2 months** (starting 2 months after last dose of induction chemotherapy), until relapse, or for a maximum of 2 years (total of 12 doses)

Maintenance for relapsed follicular lymphoma:
one dose every **3 months** (starting 3 months after last dose of induction chemotherapy), until relapse, or for a maximum of 2 years (total of 8 doses)

Premedication:

Paracetamol 1000mg	po	60 minutes before treatment
Chlorphenamine 10mg	IV	15 minutes before treatment
Dexamethasone 8mg	IV	15 minutes before treatment

Other drugs: Allopurinol 300mg po daily, starting at least 24 hours before first dose - review after 3 weeks (not required for maintenance therapy)

Main Toxicities: severe cytokine release syndrome – usually occurs within 1–2 hours of the first rituximab infusion (see Comments) and consists of fever, headache, rigors, flushing, nausea, rash, URTI symptoms;
transient hypotension and bronchospasm are usually infusion rate related;
tumour lysis syndrome (ensure pre-medicated with allopurinol and good hydration)
increased risk of infections

Anti- emetics: mildly emetogenic (anti-emetic not routinely needed)

Extravasation: non-vesicant

Administration: Use with caution if WBC > 25 x 10^9/l, as increased risk of severe cytokine release syndrome. Consider giving with a reduced infusion rate and monitor very closely. If in doubt, check with Consultant.

Rituximab diluted in 500ml 0.9% sodium chloride & administered according to the following instructions:

First infusion for monotherapy:

start at 50mg/hr, according to infusion table below, or locally approved method of calculating infusion rates;
escalate in 50mg/hr increments every 30 minutes to a maximum of 400mg/hr.

Monitor patient's vital signs at baseline and then every 30 minutes (before each increase in infusion rate) until end of infusion.

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, temperature and O_2 saturation must be measured and recorded at regular intervals as specified above.

	Infusion Rate (mg/hour)							
	50	100	150	200	250	300	350	400
Rituximab 'banded' dose	**Infusion Rate (ml/hour) for rituximab in 500ml volume only**							
450mg	55	111	166	222	277	333	388	444
500mg	50	100	150	200	250	300	350	400
600mg	42	83	125	167	208	250	292	333
700mg	36	71	107	143	178	214	250	286
800mg	31	62	94	125	156	187	219	250
900mg	28	56	83	111	139	167	194	222
1000mg	25	50	75	100	125	150	175	200
1100mg	23	45	68	90	114	136	159	182

Subsequent infusions / first infusion for maintenance:

*** Only patients who tolerated previous infusions at the standard rate ***
Give 20% of dose (i.e. 100ml) over 30 minutes, then the remaining 80% (i.e. 400ml) over 1 hour, to give a total infusion time of 90 minutes.
Monitor patient's vital signs at baseline, then every 30 minutes until end of infusion.

* **Patients who did not tolerate their previous infusion at the standard rate ***
Administer and monitor as per first infusion, or at a slower rate if required.

If reactions occur at any time, stop the infusion. If symptoms improve, restart at half the previous infusion rate, and escalate as tolerated.

Regular Investigations:

Monotherapy:	FBC	baseline only*	* consider further repeats prior to each weekly infusion if baseline abnormal or clinical concerns
	LFTs	baseline only*	
	U&Es	baseline only*	
	LDH	baseline only*	
Maintenance (first line or relapsed):	FBC		before every dose
	LFTs & U&Es & LDH		before every dose

Dose Modifications

Haematological Toxicity: If counts become low during treatment, this may be due to marrow infiltration and should be discussed with Consultant before any further treatment is given.

Patient Information: Macmillan leaflet for Rituximab

References:

McLaughlin, P et al; JCO 1998; 16: 2825 – 2833 (monotherapy)
Van Oers et al; JCO 2010; 28 (17): 2853 - 2858 (maintenance for relapsed follicular)
Sehn et al; Blood 2007; 109 (10): 4171 – 4173 (rapid infusion)
Salles, G et al; Lancet 2011; 377 (9759): 42 – 51 (1st line maintenance for follicular)

Reason for Update: added 1st line monotherapy indication, as NICE NG52	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 9	Date: 25.7.17
Supersedes: Version 8	Review Date: August 2020
Prepared by: S Taylor	Checked by: C Tucker