Drug Prescribing Guideline

RITUXIMAB	
Title	RITUXIMAB (anti-CD20 monoclonal antibody—Mabthera®)
Areas where **Guideline applicable**	Paediatric Oncology and Immunology patients
Areas where Guideline **not applicable**	Adult wards and NICU
Keywords	JHCH, Paediatric Oncology, RITUXIMAB, anti-CD20 monoclonal antibody, Mabthera®, medication, drug, prescribing, administration
Authorised Prescribers:	Paediatric Oncology and Haematology Team, Paediatric Immunologist
Indication for use	CD20-postive B-cell non-Hodgkin lymphoma Chronic lymphocytic leukaemia Autoimmune haematological disorders such as idiopathic thrombocytopenia, autoimmune haemolytic anaemia Non-formulary indications may require an Individual Patient Use (IPU) Approval. For Rituximab Approval Guide and IPU form please follow this link: http://intranet.hne.health.nsw.gov.au/*new_john_hunter_pharmacy/pharmacy_policies_and_forms
Contra-indications	Serious or untreated infection (e.g. sepsis, abscess, hepatitis B, active tuberculosis) Known hypersensitivity to murine proteins or to any component of the product.

Precautions	Consider withholding antihypertensive medication for 24 hours to prevent hypotension. Screen for hepatitis B before starting rituximab as treatment may reactivate infection; continue to monitor for signs of infection during, and for several months after treatment. Stop rituximab if fulminant hepatitis develops. Severe gastrointestinal adverse effects including obstruction and perforation have been reported. Complaints of abdominal pain, especially early in the treatment course, should be investigated. Patients with pre-existing pulmonary disease may be at greater risk of respiratory adverse effects. Concomitant nebulised salbutamol should be considered. Cardiac monitoring may be required for patients with cardiac dysfunction as rituximab may exacerbate or induce arrhythmias or angina. Fever and chills/rigors occur in over 50% of patients. Other infusion-related symptoms include nausea, vomiting, urticaria, headache, bronchospasm, dyspnoea, angioedema and hypotension. **Cytokine-release syndrome manifests as severe dyspnoea and hypoxia. It usually is delayed in onset and occurs concurrently with tumour lysis syndrome.** These reactions are most likely to occur after the first rituximab infusion and are less severe with subsequent infusions. Anaphylaxis can occur at any time and at any stage of treatment. Emergency treatments (adrenaline (epinephrine) and corticosteroid) must be readily available. Store at 2–8°C and protect from light. This is a high-cost drug and a JHH expensive drug use approval form should filled out and approved before prescribing http://intranet.hne.health.nsw.gov.au/*new_john_hunter_pharmacy/pharmacy_policies_and_forms
Dosage and Duration of therapy	Generally, 375 mg/m^2 once weekly for 4 to 8 weeks. Dose and duration of therapy may vary depending on the indication.

Administration instructions	The occupational hazard of intermittent low-dose exposure to rituximab is not known. Wear a mask and gloves when preparing the infusion solution to minimise exposure. Rituximab is not a cytotoxic agent. Vials of 100 mg/10 mL and 500 mg/50 mL. No reconstitution required. **PREMEDICATION** Should be administered orally 30–60 minutes prior to each infusion. Typical agents include paracetamol 15 mg/kg PO (max 1 g) and an antihistamine e.g. PO loratadine. If the patient is unable to tolerate oral medications, IV promethazine 0.125 mg/kg is an appropriate alternative. A corticosteroid may also be given if required e.g. dexamethasone PO/IV 0.1 mg/kg (max 8mg) **DILUTION** Dilute in sodium chloride 0.9% or glucose 5% to result in a final concentration of 1 mg/mL to 4 mg/mL. Mix gently to avoid foaming. Diluted solution is stable refrigerated (2°C to 8°C) for up to 24 hours. **RATE OF ADMINISTRATION** **Initial rate:** 50 mg/hour for the first 30 minutes, then increase rate by 50 mg/hour every 30 minutes to a maximum of 400 mg/hour. For patients less than 50 kg, start at 0.5 mg/kg/hr for the first 30 minutes, then increase rate by 0.5 mg/kg/hour every 30 minutes to a maximum of 400 mg/hour. **Subsequent infusions:** **May be started at 100 mg/hour for the first 30 minutes, then increase rate by 100 mg/hr every 30 minutes (to a maximum of 400 mg/hour). If 100 mg/hr not tolerated, start subsequent infusions at maximum tolerated rate.** For patients less than 50 kg, subsequent infusions can be given at 1 mg/kg/hr for the first 30 minutes, then increase the rate by 1 mg/kg/hour every 30 minutes to a maximum of 400 mg/hour. Use the initial infusion rate for patients with high tumour burden. If a hypersensitivity or infusion-related event develops, the infusion should be stopped or slowed. If administration is stopped, upon improvement of symptoms the infusion can continue at one half of the previous rate. Flush with sodium chloride 0.9% or glucose 5% before and after infusion.

Monitoring requirements	Patients on rituximab require 1:1 nursing for the duration of the infusion and up to two hours after. Baseline temperature, heart rate, respiratory rate and blood pressure. <u>For the initial infusion</u> Temperature, heart rate, respiratory rate and blood pressure observations every fifteen minutes. If stable, infusion rate can be increased incrementally as above. Routine observations are to continue at thirty minute intervals for TWO hours following completion of infusion to exclude any delayed reactions. <u>For subsequent infusions</u> Temperature, heart rate, respiratory rate and blood pressure observations every thirty minutes. If stable, infusion rate can be increased incrementally as above. Routine observations are to continue at thirty minute intervals for ONE hour following completion of infusion to exclude any delayed reactions.
Management of complications	Alert a medical officer immediately and stop the infusion if any adverse effects arise. If the effects are deemed mild by medical officer, the infusion may be restarted at half the previous rate when symptoms resolve. An emergency resuscitation kit should be available to treat hypersensitivity and anaphylactic reactions. An adrenaline (epinephrine) dose should be prescribed prior to each dose to be used in case of anaphylaxis.
Important Drug Interactions	As rituximab causes myelosuppression, be aware that combinations with other drugs which also have this effect may result in additional myelosuppression. Combination with drugs which affect platelet function (aspirin, non-steroidal anti-inflammatory drugs, clopidogrel) should be avoided unless the benefit outweighs the risk. Avoid live vaccines.
Basis of Guideline: (including sources of evidence, references)	Drug Information Handbook for Oncology 9th Ed. 2011 American Pharmacists Association Lexi-comp, Inc. pp1120-1127 Australian Medicines Handbook accessed via CIAP November 2017 British Columbia Cancer agency (www.bccancer.br.ca) Rituximab monograph accessed November 2017 SHPA Injectable Drugs Handbook accessed via CIAP November 2017 eMIMs accessed via CIAP November 2017 Rituximab Drug Guideline, John Hunter Hospital 2015 Rituximab Administration Protocol, Children's Hospital Westmead 2015 Protocol: Inter-B-NHL ritux 2010 Vn3.0 03/2015. European Intergroup for Children Non-Hodgkin's Lymphoma (EICNHL) And Children Oncology Group (COG)

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