Specialised Medication - Rituximab Guideline for ADULT patients

1. Guiding Principles

Provides guidance for the prescription and administration of Rituximab when being used for rheumatoid arthritis in adults **only**. If Rituximab is being used as an anti-neoplastic agent, please refer to the appropriate guideline for that specific indication. This guideline must be used in conjunction with the associated mandatory MR173D WACHS Specialised Medication - Rituximab Pre-Infusion Checklist.

Information in this guideline is specific to Mabthera®.

This infusion may only be administered when there is a doctor who is:

- familiar with this guideline
- aware of the patient receiving the infusion
- credentialed and appointed to the hospital site where the infusion is being administered
- willing and able to respond in the event of an emergency in the absence of a dedicated Medical Emergency Response (MER) team.

2. Guideline

In rheumatoid arthritis, Rituximab may suppress inflammatory activity by reducing B lymphocyte-induced T cell activation and subsequent cytokine production.

2.1 Presentation[1]

Vial containing 500mg/50mL of concentrated Rituximab solution for dilution prior to intravenous infusion.

Alternatively, some WACHS Pharmacy Departments may purchase infusions prepared by sterile manufacturing facilities due to handling precautions for preparation of the infusion.

2.2 Indication[2]

- **Availability of Rituximab is currently restricted to indications listed on the PBS on presentation of an approved PBS authority prescription.** Rheumatoid arthritis

2.3 Contraindications[1]

- Hypersensitivity reactions to Rituximab, any excipient contained or other murine proteins
- Previously diagnosed Progressive Multifocal Leukoencephalopathy (PML)
- Severe immunosuppression
- Serious or untreated infection

- Pregnancy. Limited data; avoid use, Australian category C. Effective contraception is recommended during and for 1 year after completion of therapy.

2.4 Precautions[1]

- Patients with a history of cardiac disease are to be monitored closely as hypotension, angina pectoris, cardiac arrhythmia (atrial flutter and fibrillation), heart failure and myocardial infarctions have occurred in patients treated with rituximab. Patients with a history of cardiac disease are to have an ECG prior to infusion. The treating doctor can then approve commencement of the infusion. If the treating doctor deems that telemetry is required due to cardiac risk the patient would require admission to a suitable facility.
- Rituximab may be associated with Progressive Multifocal Leukoencephalopathy (PML). Patients are to be monitored for any new or worsening symptoms and therapy suspended until appropriately investigated.
- Hepatitis B carriers or patients with a history of hepatitis B are to be appropriately monitored for clinical and laboratory signs, as reactivation is a well-known complication of therapy
- Patients should be monitored for severe skin reactions
- Breastfeeding. It is unknown whether Rituximab is excreted into breast milk. It is recommended that woman discontinue breastfeeding while undergoing treatment, unless otherwise advised by the referring consultant.
- Previous adverse event associated with a Rituximab infusion.
- If treated for hypertension, consideration is to be given to withholding antihypertensive medication for 12 hours before the commencement of the infusion due to increased risk of developing hypotension.

2.5 Dosage [1,3]

Condition	Usual Dose Recommendation	Frequency
Rheumatoid arthritis (adults)	1000mg	Total of 2 doses, 2 weeks apart
If patients respond to the initial course, retreatment after 6-12 months can be considered if there is deterioration.		

The prescription of a pre-medication, taken 30 minutes prior to the infusion, is often utilised to reduce the rate and severity of infusion reactions. This often includes: paracetamol, an antihistamine and intravenous corticosteroids (refer to referring consultant's instructions).

2.6 Administration[1,4]

Specific considerations for handling:

- Prepare using aseptic technique.
- Personal Protective Equipment (PPE) - A respirator mask (N95) and protective eye wear should be worn during preparation.

These PPE should also be worn during administration processes for IV formulations where the dis/connecting of administration lines may present a risk of aerosolisation, particularly with new or inexperienced staff.

- Closed system drug transfer devices are not required for the preparation of doses for administration but can be utilised by individual sites based on availability.
- All waste is to be handled as per standard procedures for parenterally administered agents.
- Avoid preparation and handling if pregnant, breastfeeding or immunosuppressed.

2.6.1 Withdraw and discard 100mL from a 500mL **sodium chloride 0.9%** or **glucose 5% bag.**
2.6.2 Withdraw 50mL (500mg) of Rituximab from the vial and add to the sodium chloride 0.9% or glucose 5% bag. Repeat to obtain the 1000mg dose.
2.6.3 To mix the infusion, gently invert to avoid foaming.
2.6.4 **Do not** use if the vials contain visible particulates or are discoloured.
2.6.5 **Do not** administer concurrently with any other IV medication
2.6.6 Follow the infusion rates outlined below (based on a 2mg/mL final concentration with a maximum rate of 400mg per hour):

Time (minutes)	Infusion rate for the FIRST infusion	Infusion rate for the SECOND infusion
0	25mL/hr	50mL/hr
30	50mL/hr	100mL/hr
60	75mL/hr	150mL/hr
90	100mL/hr	200mL/hr
120	125mL/hr	Until completed
150	150mL/hr	
180	175mL/hr	
210	200mL/hr	
240	Until completed	

2.7 Storage[1,5]

Store vials between 2 and 8°C, protected from light.
Following dilution, infuse immediately, or commence infusion within 24 hours of preparation, if stored between 2 and 8°C.

2.8 Infusion reactions[1,6]

Infusion related reactions are generally not serious and are relatively uncommon.

However, if a patient does have an infusion related reaction, **the prescriber should always be informed with details included in the patient's medical record**. In some circumstances, infusion related reactions can occur days after the infusion.

2.8.1 'Mild' infusion reactions

These reactions involve symptoms such as (but not limited to): Headache, nausea, dizziness, fever, flushing, pruritis, urticaria, muscle pain, flu-like symptoms.

Patients should be managed on an individual case basis but reduction in infusion rates and symptom management with medications such as paracetamol, antihistamines or glucocorticoids (e.g. dexamethasone) may allow the completion of the infusion.

In most circumstances, when the symptoms have completely resolved, the infusion can be recommenced at a 50% reduction in rate.[1]

2.8.2 Severe' hypersensitivity/ anaphylactic reactions

These reactions involve symptoms such as (but not limited to): Anaphylaxis, hypo/hypertension, chest pain, dyspnoea, swelling, severe pruritis

The infusion should be **stopped** immediately and the prescriber informed.

Patients should be managed on an individual case basis with therapy including (but not limited to) adrenaline, antihistamines, glucocorticoids (e.g. dexamethasone), intravenous fluids, vasopressors, oxygen, bronchodilators and paracetamol.

Patient management should be:

- escalated according to the Observation and response chart criteria
- in accordance with Adverse Drug Reaction section of the WACHS Medication Prescribing and Administration Policy.

For guidance on the management of anaphylaxis, refer to the ASCIA Guidelines – Acute management of anaphylaxis.

Where applicable, the WACHS doctor should discuss this event with the referring specialist.

2.9 Monitoring requirements[6]

Minimum physiological observations to be documented pre infusion, mid infusion, post infusion and as clinically indicated during the infusion based on patient response (e.g. light-headedness, flushing).There is a potential to develop delayed serious mucocutaneous reactions. The patient is to be informed that if they develop any rash to contact their doctor.

3. Roles and Responsibilities

The **Nurse Unit Manager / Senior Nursing Staff** is responsible for:

- receiving valid referral and documentation including a valid PBS prescription as required from the prescribing consultant or other treating doctor
- inform the prescriber, if external to the hospital, that the infusion has been administered and any related outcomes (e.g. adverse events).

The **Medical Officer** is responsible for completing all treatment and duties within scope of practice.

The **Registered Nurse** is responsible for completing all nursing duties for the patient within scope of practice including escalation of care as per the MR140A Adult Observation and Response Chart (AORC).

4. Compliance

Failure to comply with this policy document may constitute a breach of the WA Health Code of Conduct (Code). The Code is part of the Integrity Policy Framework issued pursuant to section 26 of the *Health Services Act 2016* (WA) and is binding on all WACHS staff which for this purpose includes trainees, students, volunteers, researchers, contractors for service (including all visiting health professionals and agency staff) and persons delivering training or education within WACHS.

WACHS staff are reminded that compliance with all policies is mandatory.

5. Evaluation

Adverse events and clinical incidents relating to the administration of Rituximab infusions are to be zero (0).

6. Standards

National Safety and Quality Health Service Standards
Clinical Governance Standard: 1.7, 1.10
Precenting and Controlling Healthcare Associated Infection Standard: 3.9
Medication Safety Standard: 4.3, 4.4, 4.7, 4.8, 4.11, 4.15
Comprehensive Care Standard: 5.10, 5.11
Communicating for safety Standard: 6.5
Recognising and Responding to Acute Deterioration Standard: 8.4, 8.5, 8.6.

7. Legislation

Medicines and Poisons Act 2014 (WA)
Medicines and Poisons Regulations 2016 (WA)

8. References

1. MIMS Online [Accessed: 18 March 2021]
2. Pharmaceutical Benefits Scheme (PBS) [Accessed: 18 March 2021]
3. Australian Medicines Handbook Pty Ltd [Accessed: 18 March 2021]
4. Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. (May 2013) Western and Central Melbourne Integrated Cancer Services – project working group.
5. Australian Injectable Drugs Handbook [Accessed: 18 March 2021]

6. Department Pharmacy. Day infusion information - patient monitoring, handling Mabs, management of infusion reactions. Bunbury, Western Australia: WACHS-SW; Page last updated 24/8/2016

9. Related Forms

MR173D WACHS Specialised Medication - Rituximab Pre-Infusion Checklist
MR140A Adult Observation and Response Chart

10. Related Policy Documents

WACHS Aseptic Technique Policy
WACHS High Risk Medications Procedure
WACHS Medication Handling and Accountability Policy
WACHS Medication Prescribing and Administration Policy
WACHS Safe Handling and Administration of Monoclonal Antibodies Guideline

11. Related WA Health Policies

MP 0053/17 WA Clinical Alert (Med Alert) Policy
MP 0131/20 WA High Risk Medication Policy

12. WA Health Policy Framework

Clinical Governance, Safety and Quality Policy Framework

This document can be made available in alternative formats on request for a person with a disability

Contact:	WACHS Chief Pharmacist		
Directorate:	Medical Services	**TRIM Record #**	ED-CO-13-26973
Version:	3.02	**Date Published:**	31 March 2021