Specialised Medication – Rituximab Guideline for ADULT patients

1. Purpose

This document 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.

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 Statement

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 500 mg/50 mL 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 women discontinue breastfeeding while undergoing treatment, unless otherwise advised by the referring consultant.
- Caution with patients who have had a 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.
- Vaccination with live vaccines is not recommend.

2.5 Dosage[1,3]

Condition	Usual Dose Recommendation	Frequency
Rheumatoid arthritis (adults)	1000 mg	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 utilised to reduce the rate and severity of infusion reactions. This often includes paracetamol, an antihistamine and intravenous corticosteroids (refer to referring prescriber instructions).

2.6 Administration[1,4]

- Specific considerations for handling:
  - Prepare using aseptic technique.
  - Personal Protective Equipment (PPE) - A respirator (N95) and protective eyewear 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.
  - 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.

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

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

If a patient has an infusion related reaction, **the prescriber should always be informed with details included in the patient's healthcare record**. In some circumstances, infusion related reactions can occur days after the infusion.

'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. If an infusion related reaction occurs, stop the infusion and notify the prescriber.

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]

'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 MR140A Adult Observation and Response Chart (A-ORC) 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 or nurse 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 (A-ORC).

All staff are required to work within policies and guidelines to make sure that WACHS is a safe, equitable and positive place to be.

4. Monitoring and Evaluation

4.1 Monitoring

Managers of clinical areas, health sites and services are responsible for monitoring compliance with this guideline.

Any variance from this guideline should be under the guidance of a senior medical practitioner and reported by the nurse manager to the Regional Drugs and Therapeutics Committee. This will prompt a review of the guideline.

4.2 Evaluation

Adverse events and clinical incidents relating to the prescribing and administration of this medicine are to be reported and managed as per the WACHS Medication Prescribing and Administration Policy.

5. Compliance

Guidelines are designed to provide staff with evidence-based recommendations to support appropriate actions in specific settings and circumstances. As such, WACHS guidelines should be followed in the first instance. In the clinical context, where a patient's management should vary from an endorsed WACHS guideline, this variation and the clinical opinion as to reasons for variation must be documented in accordance with the Documentation Clinical Practice Standard.

6. References

1. MIMS Online [Internet]. MIMS Australia Pty Ltd: Data Version 2022 September. [cited: 08 September 2022]. Available from https://www-mimsonline-com-au.wachslibresources.health.wa.gov.au/Search/Search.aspx.
2. Pharmaceutical Benefits Scheme (PBS) [Internet]. Australian Government. [cited: 08 September 2022]. Available from: http://www.pbs.gov.au/.
3. Australian Medicines Handbook [Internet]. AMHS Pty Ltd. Rituximab. 2022 July [cited: 08 September 2022]. Available from: https://amhonline-amh-net-au.wachslibresources.health.wa.gov.au/.
4. Alexander M, King J, Bajel A, Doecke C, Fox P, Lingaratnam S, et al. Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. Intern. Med. J, 2014 Oct 09; 44(10):1018-26. Available from: https://doi.org/10.1111/imj.12564.
5. Australian Injectable Drugs Handbook [Internet]. SHPA. Rituximab - Antineoplastic. 2022 August [cited: 08 September 2022] Available from: https://aidh-hcn-com-au.wachslibresources.health.wa.gov.au/browse/r/rituximab_-_antineoplastic.
6. WACHS - South West Pharmacy [SharePoint]. Information On Medication Infusions (Day infusions) – Patient monitoring, handling monoclonal antibodies and management of infusion reactions. [cited 30 September 2022] Available from: https://wahealthdept.sharepoint.com/sites/wachs-south-west/SitePages/Pharmacy.aspx.

7. Document summary

Coverage	WACHS wide
Audience	Medical Officers, Nurses and Midwives, Pharmacists
Records Management	Clinical: Health Record Management Policy
Related Legislation	*Medicines and Poisons Act 2014 (WA)* Medicines and Poisons Regulations 2016 (WA)
Related Mandatory Policies / Frameworks	Clinical Governance, Safety and Quality Framework WA Clinical Alert (Med Alert) Policy - MP 0053/17 High Risk Medication Policy – MP 0131/20
Related WACHS Policy Documents	Aseptic Technique Policy High Risk Medications Procedure Medication Handling and Accountability Policy Medication Prescribing and Administration Policy Personal Protective Equipment (PPE) Procedure Safe Handling and Administration of Monoclonal Antibodies Guideline
Other Related Documents	Nil
Related Forms	MR173D WACHS Specialised Medication - Rituximab Pre-Infusion Checklist MR140A Adult Observation and Response Chart (A-ORC)
Related Training Packages	Nil
Aboriginal Health Impact Statement Declaration (ISD)	ISD Record ID: 1783
National Safety and Quality Health Service (NSQHS) Standards	1.7, 1.10, 3.9, 4.3, 4.4, 4.7, 4.8, 4.11, 4.15, 5.10, 5.11, 6.5, 8.4, 8.5, 8.6.
Aged Care Quality Agency Accreditation Standards	Nil
National Standards for Mental Health	Nil

8. Document Control

Version	Published date	Current from	Summary of changes
4.00	20 December 2022	20 December 2022	Desktop Review Update precautions to include vaccination with live vaccines. If any infusion related reaction occurs, stop infusion and notify prescriber.

9. Approval

Policy Owner	Executive Director Clinical Excellence
Co-approver	Executive Director Nursing and Midwifery Services
Contact	WACHS Chief Pharmacist
Business Unit	Pharmacy
EDRMS #	ED-CO-13-26973

This document can be made available in alternative formats on request.