Specialised Medication – Natalizumab Guideline

1. Purpose

This document provides guidance for the prescription and administration of natalizumab for adult patients for multiple sclerosis.

This guideline must be used in conjunction with the associated mandatory MR173B WACHS Specialised Medication - Natalizumab 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.

For paediatric patients, refer to the Perth Children's Hospital – Medication Management Manual – Natalizumab (accessible via HealthPoint).

2. Guideline

Natalizumab is a recombinant humanised monoclonal antibody to alpha-4 integrins which is thought to inhibit leucocyte migration from blood into the central nervous system (CNS), thus reducing inflammation and demyelination.[1]

2.1 Presentation[2]

Single use vial containing 300 mg/15 mL solution of natalizumab for infusion.

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

2.2 Indication[3]

Availability of natalizumab is currently restricted to the indication listed on the PBS on presentation of an approved PBS authority prescription.
- Prophylaxis for clinically definite relapsing remitting multiple sclerosis (MS) initiated by a neurologist.

2.3 Contraindications[1,2]

- Current or previous progressive multifocal leucoencephalopathy (PML)
- Co-administration with other immunomodulatory medicines (e.g. beta interferons or glatiramer acetate)
- Known hypersensitivity to natalizumab, any excipient or murine derived proteins
- Patients with increased risk for opportunistic infections due to:

- current or recent (within three months) treatment with immunosuppressive therapy. Examples include methotrexate, azathioprine, cyclophosphamide, mycophenolate, cladribine or mitozantrone. **This excludes short courses of oral steroids**.
- systemic medical conditions resulting in significantly compromised immune function. Examples include human immunodeficieny virus (HIV) infection, organ transplant, active malignancy or a history of haematological cancer or rheumatic disease.

2.4 Precautions[1,2]

- Natalizumab may be associated with progressive multifocal leukoencephalopathy (PML). Patients are to be monitored for any new symptoms and therapy suspended until appropriately investigated. Treatment should be used with caution in patients with increased risk factors for PML such as treatment for more than two years, immunosuppressant therapy prior to natalizumab commencement and positive anti-JC virus antibody status. Testing of anti-JC virus antibody status should be conducted before starting treatment and six monthly if seronegative.
- Caution should be taken in prescribing natalizumab for patients with a history of liver disease. Regularly monitor liver function tests in these patients to prevent liver injury.
- Pregnancy (Category C).
- Breastfeeding – not recommended by the manufacturer.
- Administration of live vaccines during treatment with natalizumab is not recommended.

2.5 Dosage[1,2]

300 mg administered by IV infusion every four weeks.

Long term safety and efficacy data is limited. Therapy continuing after two (2) years should be prescribed at the discretion of the neurologist.

2.6 Administration[2,4,5]

- Specific considerations for handling:
  - Prepare using aseptic technique.
  - Personal Protective Equipment (PPE) - A N95 respirator 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.
- Dilute before use – FOR IV INFUSION ONLY
  - Add 300 mg (15 mL, one vial) to 100 mL of sodium chloride 0.9 % and gently invert. **DO NOT SHAKE.**
- **Do NOT** use if the vial contains visible particulates or is discoloured.
- **Do NOT** administer concurrently with any other IV medication.
- The use of a filtration device has not been evaluated therefore use is discouraged.
- Administer as an intravenous solution over one hour.
- Flush IV line with 0.9 % sodium chloride.

- All patients administered natalizumab infusions are to be observed for one hour post-infusion for side effects (medications, an artificial airway and other appropriate materials must be available for the treatment of these effects). See Section 2.8 below.

2.7 Storage[2,4]

Vials are to be stored between 2 and 8 ^{O}C and protected from light. Do not shake or freeze.

Following dilution, infuse solution immediately. Prepared solution may be stored for up to eight hours between 2 and 8 ^{O}C and protected from light. However, allow to reach room temperature before infusing.

2.8 Infusion Reactions[1,2]

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 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, vomiting, dizziness, fever, flushing, pruritis, urticaria, muscle pain, flu-like symptoms, fatigue and rigors.

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.

If infusion-related reactions occur, stop the infusion and notify prescriber to review patient and advise on management options.

'Severe' hypersensitivity/anaphylactic reactions

These reactions involve symptoms such as (but not limited to) anaphylaxis, hypo/hypertension, chest pain, dyspnoea, swelling, severe pruritis, anxiety and tachycardia.

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[2]

- Minimum physiological observations to be documented pre-infusion, mid-infusion and post-infusion and as clinically indicated during the infusion on the MR140A Adult Observation and Response Chart (A-ORC) based on patient response (e.g. light headedness, flushing).
- Observe patients closely during the infusion and for **one** hour post infusion for the development of an infusion reaction. See Section 2.8 above.
- Check the IV regularly to ensure correct flow rate and cannula position.

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
- informing 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).

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.

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

6. References

1. Australian Medicines Handbook [Internet]. AMH Pty Ltd. 2022 July. Natalizumab. [cited: 29 August 2022]. Available from: https://amhonline-amh-net-au.wachslibresources.health.wa.gov.au/.
2. MIMS Online [Internet]. MIMS Australia Pty Ltd. [cited: 08 September 2022] Available from: https://www-mimsonline-com-au.wachslibresources.health.wa.gov.au/Search/Search.aspx.
3. Pharmaceutical Benefits Scheme (PBS) [Internet]. Australian Government. [cited: 08 September 2022]. Available from: https://www.pbs.gov.au/.
4. Australian Injectable Drugs Handbook [Internet]. SHPA. Natalizumab. 2022 August. [cited: 08 September 2022]. Available from: https://aidh-hcn-com-au.wachslibresources.health.wa.gov.au/browse/n/natalizumab.
5. 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. Internal Medicine Journal, 2014 Oct 09;44(10):1018-26. Available from: https://doi.org/10.1111/imj.12564.

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	WA Clinical Alert (Med Alert) Policy - MP 0053/17 High Risk Medication Policy - MP 0131/20 Clinical Governance, Safety and Quality Framework
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	MR173B WACHS Specialised Medication - Natalizumab Pre-Infusion Checklist MR140A Adult Observation and Response Chart (A-ORC)
Related Training Packages	Nil
Aboriginal Health Impact Statement Declaration (ISD)	ISD Record ID: 1782
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
5.00	20 December 2022	20 December 2022	Desktop review Precaution information updated to include live vaccines. Infusion to be stopped and prescriber contacted for any infusion related reactions.

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-13-12155

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