MONOGRAPH

Natalizumab

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Natalizumab is an α4-β7 integrin inhibitor used for the management of multiple sclerosis.[1]

Natalizumab is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Monotherapy for treatment of relapsing-remitting forms of Multiple Sclerosis (MS) with the aim to delay the progression of physical disability and reduce the frequency of relapse.[1, 2, 3,4]
- All indications require Individual Patient Approval (IPA) from the Drug and Therapeutics Committee.
- A consent form must be completed prior to the first infusion.
- Pre-infusion questionnaire (see Appendix 1) must be completed by the patient/guardian, and reviewed by the prescribing doctor, prior to each infusion.

CONTRAINDICATIONS

- Hypersensitivity to natalizumab or any component of the formulation.
- Current or a history of progressive multifocal leukoencephalopathy (PML). PML is an opportunistic infection caused by John Cunningham virus (JCV), which may be fatal or result in severe disability.[1,2]

- Patients with increased risk for opportunistic infections, including immunocompromised patients due to:
  - recent (within 3 months) or current treatment with antineoplastic, immunosuppressant or immunomodulatory drugs (excluding short course corticosteroids).[1,2]
  - systemic medical conditions resulting in significantly reduced immune system function (e.g. active malignancy, HIV infection, haematological cancer, rheumatic disease).[1,2]

PRECAUTIONS

- Seropositive anti-JC virus antibody status is associated with an increased risk of PML.[1,2]
- History of liver disease; natalizumab may cause liver damage.[1,2]
- Natalizumab is a category C drug in pregnancy. These are drugs which, owing to their pharmacological effects, have caused, or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. The risks of receiving natalizumab must be discussed with all female patients (or parents/guardians) before commencing therapy.[2,5]
- Administration of live vaccines during treatment with natalizumab is not recommended.[1,2]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Natalizumab 300 mg/15 mL vial
- Natalizumab 150 mg/1 mL prefilled syringe

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: **Refer to Neonatal Medication Protocols**

Hepatic impairment: – Discontinue treatment in the presence of jaundice or signs/symptoms of hepatic injury.[6]

- ≥12 years: 300 mg IV every 4 weeks.[4]
  Continued therapy must be carefully reconsidered in patients who show no evidence of therapeutic benefit beyond 6 months.[2]

RECONSTITUTION & ADMINISTRATION

- All natalizumab infusions are prepared by the Pharmacy Compounding Service.
- Treating neurologists, and nurses involved in the care of patients receiving natalizumab must undertake the Tysabri® Australian Prescribing Program.[7]

- Occupational hazard status is unknown, therefore, exercise handling precautions (wear mask and gloves to minimise exposure). [7]
- Patients with history of natalizumab infusion reaction should be given a dose of an antipyretic and/or antihistamine 30 minutes prior to the infusion.
- If stored at 2°C to 8°C, allow the solution to warm to room temperature prior to its infusion.[7]
- Do not shake. Inspect for particulate material prior to administration.[7]
- Slowly prime the IV line with prepared natalizumab solution to prevent foaming.[7]
- Infuse over 1 hour. After the infusion is complete, flush with sodium chloride 0.9%.[7]
- Management of extravasation is described in the PCH "Central Venous Access Devices (CVAD) and Midline Insertion and Management" Guideline.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids: Sodium chloride 0.9%.[7]

Compatible at Y-site: No information available.[7]

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs: No information available.[6]

MONITORING

- Monitor baseline temperature, pulse, respiratory rate, blood pressure and oxygen saturation. Frequency of monitoring to be determined by medical officer.
- Observe patient closely for 1 hour post infusion for signs of hypersensitivity (including anaphylaxis) and infusion reactions. Delayed reactions have also been reported.2
- If infusion-related reaction occurs, stop the infusion, and notify RMO/Registrar to review patient and advise on management options.
- The treating neurologist should re-evaluate the patient 3 months after the first administration, 6 months after the first administration and every 6 months thereafter.2
  This should include, but not be limited to, brain MRI and testing for anti-JCV antibody as described in the Tysabri® approved Australian Product Information.

ADVERSE EFFECTS

Common: Infection, headache, fatigue, arthralgia, muscle cramp, rigors, cough, rash, itch, dermatitis, depression, gastroenteritis, dysmenorrhoea, amenorrhoea, nausea, drowsiness, anti-natalizumab antibodies, hypersensitivity, and infusion-related reactions (headache, dizziness, fatigue, urticaria, pruritus, rigors).[1,2,6]

Infrequent or rare: Progressive multifocal leucoencephalopathy (PML), anaphylaxis, serious CNS or ocular herpes simplex or varicella zoster virus infection, hepatotoxicity, hypereosinophilia, anaemia.[1,2,6]

STORAGE

Single use vial and diluted preparation – Store between 2-8°C; do not shake or freeze. Protect from light.[2]

Complete the infusion within 24 hours of preparation, or 72 hours for solutions prepared by pharmacy under aseptic conditions. Allow to reach room temperature before infusing.[7]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **natalizumab**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Central Venous Access Devices (CVAD) and Midline Insertion and Management

Related external legislation, policies and guidelines

Tysabri® Australian Prescribing Program

References

1. Natalizumab monograph. In Australian Medicines Handbook [online] 2024. [accessed 11/4/2024].
2. Natalizumab monograph. In MIMS Australia Pty Ltd. [online] 2024 [accessed 11/4/2024].
3. Moreau A, et al. Early use of high efficacy therapies in pediatric forms of relapsing-remitting multiple sclerosis: A real-life observational study. Multiple Sclerosis and Related Disorders. 2023; 79: article 104942.
4. Ghezzi A, et al. Pharmacokinetics and pharmacodynamics of natalizumab in pediatric patients with RRMS. Neurol Neuroimmunol Neuroinflamm 2019; 6:e591.
5. Prescribing medicines in pregnancy database. Therapeutic Goods Administration [accessed 11/4/2024]. Prescribing medicines in pregnancy database | Therapeutic Goods Administration (TGA)
6. Natalizumab monograph. In UpToDate Lexidrug. [on-line] 2024. [accessed 11/4/2024].
7. Natalizumab. In Symons K, Wong E, editors. Australian Injectable Drugs Handbook. 9th ed. [on-line] The Society of Hospital Pharmacists of Australia; 2024 [accessed 11/4/2024].

Appendix 1.

PRE-INFUSION QUESTIONNAIRE

Patient's name: .....

Address: .....

..... Date: / /

Review each statement with the patient before every infusion of TYSABRI (natalizumab). Ask the patient to sign and date the form only after discussing the responses with them.

This Questionnaire is an important checklist to make sure that you are in suitable state of health to receive your infusion. Please take the time to answer all questions to the best of your ability as your safety is of utmost importance.

When did you last see your Neurologist?	Date: / /	
When was your last MRI?	Date: / /	
When is your next appointment with your Neurologist?	Date: / /	
Have you discussed with your Neurologist any new conditions (e.g. pregnancy) or worsening medical problems (such as new or sudden change in your thinking, eyesight, balance, strength or other problems) that lasted or worsened over several days before you came for this infusion?	Y	N
Have you had any medical issues after your last infusion (e.g. rash, itchiness)?	Y	N
If yes, have you discussed these with your Neurologist and/or Nursing Staff at this infusion centre?	Y	N
Have you spoken to your support person/partner/caregiver about whether they have noticed any difference in your personality, thinking abilities or behaviour that you have NOT already discussed with your Neurologist?	Y	N
Have you recently experienced, or are you currently experiencing, any unexplained fevers, severe diarrhoea, prolonged dizziness, headache or stiff neck, weight loss or listlessness worse than usual, that your neurologist doesn't know about?	Y	N
Are you currently taking antibiotics?	Y	N
Have you started taking any other new medications, herbal treatments or supplements, that you haven't told your Neurologist, MS Nurse, pharmacist or the nursing staff at this infusion centre about as yet?	Y	N
If yes, what are you now taking?		
Do you have any further questions to ask the nursing staff at this infusion centre before receiving your infusion?	Y	N
Do you have a copy of the Consumer Medicine Information (CMI) and Patient Alert Card for TYSABRI?	Y	N
Have you read the CMI within the past 24 hours?	Y	N

Patient's name: .....

Signature: ..... Date: / /

Once signed, please attach this to the patient's notes

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

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