Medicine Guideline

Natalizumab - administration

Areas where Protocol/Guideline applicable	Ambulatory Care Unit / Outpatient Units
Authorised Prescribers:	Neurologists or their representatives e.g., Neurology Advanced Trainee, Registrars
Indication for use	Monotherapy for the treatment of relapsing remitting Multiple Sclerosis to delay the progression of physical disability and to reduce the frequency of relapses.
Clinical condition	Relapsing remitting Multiple Sclerosis. Treatment must be initiated and supervised by a neurologist. Patients are to be monitored for early signs and symptoms of Progressive Multifocal Leucoencephalopathy.
Proposed Place in Therapy	May be used first line or later in treatment sequence.
Contra-indications	• Known hypersensitivity to natalizumab or to murine derived proteins. • Contraindicated in patients who have or have had Progressive Multifocal Leucoencephalopathy. • Should not be administered to patients with increased risk of opportunistic infections including those immunocompromised due to current or recent immunosuppressive therapies (eg azathioprine, mitoxantrone) or systemic medical conditions resulting in significantly compromised immune system function (eg HIV, organ transplant, active malignancy). • Should not be used in combination with immunomodulatory agents (eg beta interferons or glatiramer acetate).
Precautions	• Use of natalizumab has been associated with an increased risk of Progressive Multifocal Leucoencephalopathy, an opportunistic infection caused by the John Cunningham Virus • (JCV), which may be fatal or result in severe disability. Early diagnosis and withdrawal of natalizumab therapy are important factors in management of Progressive Multifocal Leucoencephalopathy. • Other opportunistic infections have been reported with the use of natalizumab, and patients should be counselled to report any symptoms of significant or prolonged infection. • Hypersensitivity reactions have been associated with natalizumab including possible anaphylactic / anaphylactoid reactions which occurred at an incidence of <1%. • Safety and efficacy has not been established in patients under 18 years of age. • There is insufficient data to establish whether patients aged over 65years respond differently to natalizumab than younger patients. • No formal pharmacokinetic studies have been conducted in patients with renal or hepatic impairment; however results from population pharmacokinetics suggest that dose adjustment would not be necessary.

Precautions (cont.)	• Pregnancy category C. The risks and benefits of continuing or ceasing therapy during pregnancy must be assessed on a case-by-case basis. • Natalizumab has been detected in human breast milk. The risks and benefits of breast feeding whilst receiving natalizumab must be assessed on a case-by-case basis. • The safety of administering live vaccines to people on natalizumab therapy has not been studies and is not recommended.
Important Drug Interactions	The safety and efficacy of natalizumab in combination with antineoplastic or immunosuppressive therapies has not been established.
Dosage	- Intravenous infusion: 300mg/15ml injection vial every 4 weeks - Subcutaneous injection: 2 x subcutaneous injections of 150mg/1ml prefilled syringes every 4 weeks
Duration of therapy	Indefinite if patient remains stable
Prescribing Instructions	Natalizumab should be prescribed by neurologists or their representatives on electronic system, Medication Administration Record or paper NIMC during the downtime of electronic system.
Administration Instructions	Natalizumab can be administered subcutaneously or intravenously by appropriately trained health care staff. Natalizumab must be prepared and administered in accordance with the five rights as per - *NSW Health Policy Directive Medication Handling PD2022_032* - SESLHDPR/368 *Safe Handling and Management of Monoclonal Antibodies.* **Pre-administration** • Ensure the completion of Pre-Administration Questionnaire (Appendix 1) prior to each treatment. • Discuss with prescriber if there is any concern on Pre-Administration Questionnaire. • Ensure the availability resuscitation equipment, epinephrine, antihistamines, corticosteroids, etc. • Inform patient of the procedure and possible adverse effects.

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NATALIZUMAB IV INFUSION	**Preparation** Reconstitution should be performed using aseptic technique in a clean utility room with the door closed. A closed system transfer device may be used in accordance with a local Safe Work Procedure. Staff should refer to SESLHDPR368 Safe Handling and Management of Monoclonal Antibodies for guidance on personal protective equipment (PPE). – Wash hands – Don PPE as per above – Inspect the vial for particulate material. DO NOT use if evidence of particles are present – Remove flip-top from vial and clean rubber stopper with alcohol-wipe – Withdraw 300 mg/15 mL natalizumab concentrate solution from vial by using a 20 mL sterile syringe and drawing-up needle – Slowly inject the concentrate solution into 100 mL 0.9% Sodium Chloride solution bag – Gently invert the natalizumab solution to mix properly (do not shake) Note: – Following dilution, natalizumab should be administered immediately or within 8 hours if stored between 2-8°C – If solution stored between 2-8°C, the solution is to be placed in the treatment room and allowed it to warm to room temperature prior to infusion. **Administration** – Obtain peripheral intravenous access or access CVAD if present. – Connect natalizumab infusion with infusion line and through infusion pump – Administer the infusion over approximately one hour – Flush with 0.9% Sodium Chloride solution on the completion of administration. – Remove peripheral intravenous access post infusion. – All devices should be disposed into clinical waste as per Clinical and Related Waste Management for Health Services.

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NATALIZUMAB SUBCUTANEOUS INJECTIONS	**Preparation** – Remove Natalizumab subcutaneous syringes from refrigerator and store at room temperature for 30 minutes before administering – Do not use if stored at room temperature for longer than 24 hours – Check both the prefilled syringes to ensure the liquid is colourless-to-slightly-yellow and free of visible particles Note: It is normal to see small amounts of air bubbles in the display windows **Administration** – Choose appropriate subcutaneous injection sites in the thigh, abdomen, or the back of the upper arm, avoid scars, wounds or infected skin area – Subcutaenous injection sites must be at least 3cm apart – Prepare each injection site with an alcohol wipe – Use aseptic techniques during the injection procedure – Gently pinch the skin around the cleaned injection site – Quickly insert the needle straight into the skin fold until the needle is fully under the skin and slowly push the plunger in one smooth motion until the syringe is completely empty – Remove the syringe from the injection site – Press a cotton ball or gauze on the site if any blood – Both injections should be administered consecutively and within 30 minutes of each other. – All devices should be disposed into clinical waste as per Clinical and Related Waste Management for Health Services.
Monitoring requirements	• **For intravenous infusions** - patient must be observed for 1 hour after the administration, for signs and symptoms of reactions including hypersensitivity, for the **first 12 administrations**. Thereafter post injection observation may be according to clinical judgment. • **For subcutaneous injections** - patient must be observed for 1 hour after the administration, for signs and symptoms of reactions including hypersensitivity, for the first 6 administrations ever of natalizumab (regardless of route) and for the first subcutaneous administration (if the first 6 administrations were not subcutaneous). Thereafter post injection observation may be according to clinical judgment. • Patient must be reviewed clinically at regular intervals by their treating neurologist and undertake regular ongoing monitoring **MRI** scans to assess drug efficacy and screen for any early clinical and/or radiological signs of Progressive Multifocal Leucoencephalopathy. • Intermittent JVC antibody testing must be conducted to assist in risk assessment for Progressive Multifocal Leucoencephalopathy.
Management of Complications	• If any signs or symptoms suggestive of Progressive Multifocal Leucoencephalopathy occur, natalizumab must immediately be ceased and further investigations and appropriate management instituted. • If signs or symptoms of other significant infections occur, appropriate investigations and management should be instituted. • If signs or symptoms of a hypersensitivity reaction occurred during or post infusion, appropriate management should be instituted as per the CLINICAL EMERGENCY RESPONSE MANAGEMENT.

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Basis of Protocol/Guideline:	Australian Product Information Tysabri (Natalizumab, RMC).
Groups consulted in development of this guideline	Dr E Shiner, Dr M Ghadiri, Dr M Badve, TSH Neurology CNC, STG ACU/OPD CNC, STG ACU/OPD NUM

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GOVERNANCE	
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Appendix 1: Natalizumab Pre-administration Questionnaire

TYSABRI (natalizumab) PRE-ADMINISTRATION QUESTIONNAIRE

Patient name: .....

Address: .....

Date of birth: 01 / Jan .....

For HCP Administering the TYSABRI Treatment

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

For Patients Receiving the TYSABRI Treatment

This Questionnaire is an important checklist to make sure that you are in suitable state of health to receive your infusion. Some of the questions are related to early symptoms and signs of opportunistic infections, including Progressive Multifocal Leukoencephalopathy (PML).

TYSABRI CMI

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: 01 / Jan	
When is your next appointment with your Neurologist?	Date: 01 / Jan	
When was your last MRI?	Date: 01 / Jan	
When was your last STRATIFY JCV test performed?	Date: 01 / Jan	
Did you discuss your last MRI and STRATIFY JCV test results with your Neurologist?	Y	N
Have you discussed with your Neurologist any new conditions (e.g. pregnancy) or worsening physical or mental 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 treatment session?	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 Doctor or Nurse?	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
Have you started taking any other new medications (such as antibiotics), herbal treatments or supplements, that you haven't told your Neurologist, MS Nurse, pharmacist that you have told your Doctor or Nurse?	Y	N
If yes, what are you now taking?		
Do you have any further questions before the TYSABRI treatment is administered?	Y	N
Do you have a Patient Alert Card?	Y	N
Have you read the CMI (see QR code above) within the past 24 hours and in particular, do you understand the risks of developing PML, the need of vigilance for PML symptoms and PML management as explained in the CMI?	Y	N

Patient name: .....

Signature: ..... Date: 01 / Jan .....

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