

6.09 NATALIZUMAB

Solution concentrate for I.V. infusion 300 mg in 15 mL Tysabri[®], Biogen Australia Pty Ltd.

1 Purpose of Application

- 1.1 The minor submission sought to amend the current Section 100 – Highly Specialised Drugs Program (Public and Private Hospital) listings of natalizumab for the treatment of clinically-definite relapsing-remitting multiple sclerosis (RRMS) to remove the current age restrictions.

2 Requested listing

- 2.1 The submission requested the following changes to natalizumab listings to remove age restrictions.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
NATALIZUMAB 300 mg/15 mL injection, 15 mL vial	1	5	\$1,340.68 (Public) \$1,388.07 (Private)	Tysabri [®] Biogen Australia Pty Ltd

Category / Program:	Section 100 – Highly Specialised Drugs Program (Public Hospital)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Episodicity:	Clinically definite relapsing-remitting
Condition:	multiple sclerosis
PBS Indication:	Clinically definite relapsing-remitting multiple sclerosis
Treatment criteria:	Must be treated by a neurologist.
Clinical criteria:	The treatment must be a sole PBS-subsidised disease modifying therapy for this condition, AND Patient must be ambulatory (without assistance or support), AND Patient must have experienced at least 2 documented attacks of neurological dysfunction, believed to be due to multiple sclerosis, in the preceding 2 years of commencing a PBS-subsidised disease modifying therapy for this condition, AND The condition must be confirmed by magnetic resonance imaging of the brain and/or spinal cord; OR Patient must be deemed unsuitable for magnetic resonance imaging due to the risk of physical (not psychological) injury to the patient.
Population criteria:	Patient must be aged 18 years or older.

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Prescriber Instructions:	<p>The date of the magnetic resonance imaging scan must be included in the patient's medical notes, unless written certification is provided, in the patient's medical notes, by a radiologist that an MRI scan is contraindicated because of the risk of physical (not psychological) injury to the patient.</p> <p>Treatment with this drug must cease if there is continuing progression of disability whilst the patient is being treated with this drug.</p> <p>For continued treatment the patient must demonstrate compliance with, and an ability to tolerate, this drug.</p> <p>Neurologists prescribing natalizumab under the PBS listing must be registered with the Tysabri Australian Prescribing Program.</p>
Cautions:	Progressive multifocal leukoencephalopathy has been reported with this drug.

Category / Program:	Section 100 – Highly Specialised Drugs Program (Private Hospital)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required – In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined
Episodicity:	Clinically definite relapsing-remitting
Condition:	multiple sclerosis
PBS Indication:	Clinically definite relapsing-remitting multiple sclerosis
Treatment phase:	Initial treatment
Clinical criteria:	<p>The treatment must be a sole PBS-subsidised disease modifying therapy for this condition, AND Patient must be ambulatory (without assistance or support), AND Patient must have experienced at least 2 documented attacks of neurological dysfunction, believed to be due to multiple sclerosis, in the preceding 2 years of commencing a PBS-subsidised disease modifying therapy for this condition, AND The condition must be confirmed by magnetic resonance imaging of the brain and/or spinal cord; OR Patient must be deemed unsuitable for magnetic resonance imaging due to the risk of physical (not psychological) injury to the patient.</p>
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions:	<p>The date of the magnetic resonance imaging scan must be included in the patient's medical notes, unless written certification is provided, in the patient's medical notes, by a radiologist that an MRI scan is contraindicated because of the risk of physical (not psychological) injury to the patient.</p> <p>Neurologists prescribing natalizumab under the PBS listing must be registered with the Tysabri Australian Prescribing Program.</p>
Cautions:	Progressive multifocal leukoencephalopathy has been reported with this drug.

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Category / Program:	Section 100 – Highly Specialised Drugs Program (Private Hospital)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required – In Writing <input checked="" type="checkbox"/> Authority Required – Telephone <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined
Episodicity:	Clinically definite relapsing-remitting
Condition:	multiple sclerosis
Treatment phase:	Continuing treatment
Clinical criteria:	The treatment must be a sole PBS-subsidised disease modifying therapy for this condition, AND Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must not show continuing progression of disability while on treatment with this drug, AND Patient must have demonstrated compliance with, and an ability to tolerate, this therapy.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions:	Neurologists prescribing natalizumab under the PBS listing must be registered with the Tysabri Australian Prescribing Program.
Cautions:	Progressive multifocal leukoencephalopathy has been reported with this drug.

3 Background

- 3.1 In April 2019, the TGA approved an amendment to the registration of natalizumab to remove the contraindication for use in patients under 18 years old. The approved Product Information (PI) states ‘safety and effectiveness of natalizumab in MS patients below the age of 18 years have not been established. No recommendation on dosage can be made’.
- 3.2 The TGA Delegate did not support an explicit indication for paediatric onset multiple sclerosis due to inadequate data. However, the Delegate supported removing the contraindication in paediatric onset MS.
- 3.3 Natalizumab was recommended by the PBAC at its November 2007 meeting for the treatment of clinically-definite RRMS in patients aged 18 and over, on a cost effectiveness basis compared to interferon beta-1b (Natalizumab Public Summary Document, November 2007 PBAC meeting).
- 3.4 The submission claimed that there is a high, unmet need for disease-modifying therapies in paediatric patients with multiple sclerosis.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted the advice received from MS Australia and MS Research Australia supporting the removal of the age restriction for natalizumab in RRMS and highlighted a clinical need for safe and effective treatment options in paediatric disease. The advice noted a number of cohort and observational studies had found natalizumab to be safe and effective in the paediatric multiple sclerosis population and had reported no cases of progressive multifocal leukoencephalopathy (PML). The PBAC also noted the comment from one individual who described the experience of a family member who had significant clinical improvement on-treatment with natalizumab in paediatric RRMS and had failed prior treatment.

Clinical trials

4.3 The submission did not present any clinical trials, however the TGA clinical evaluation reports were available.

Estimated PBS usage & financial implications

4.4 The sponsor did not present formal utilisation estimates, however, provided patient numbers for natalizumab for paediatric MS from a compassionate access program, summarised in Table 1.

Table 1: Number of patients receiving compassionate access to natalizumab (2015-2018)

Year	Age range	Number of patients treated per year
2015*	14-16	4
2016	16-18	5
2017	15-18	10
2018	16-18	6

Source: Table 2 of the submission. *Data for 2015 only for the period July – December.

4.5 The number of paediatric patients accessing natalizumab via compassionate access remained at or below 10 patients per year over the data period. The submission considered that on this basis, it was unlikely that the removal of the age restriction would have a significant impact on financial implications.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC recommended removal of the age restriction from the PBS listings of natalizumab for clinically definite relapsing-remitting multiple sclerosis (RRMS). In making this recommendation, the PBAC noted the TGA Delegate was satisfied there was sufficient clinical evidence to remove the paediatric contraindication from the

registration of natalizumab.

- 5.2 Noting the advice received from the clinical organisations, the PBAC agreed there was a clinical need for a range of treatment options in paediatric RRMS and many current therapies had limited evidence in paediatric disease.
- 5.3 The PBAC noted the use of natalizumab in the sponsor's compassionate access program had been low and given the rarity of paediatric MS, considered the change to listing was unlikely to grow the market beyond patient numbers seen in that program. Therefore, the PBAC considered the likely financial implications to be minimal.
- 5.4 The PBAC advised under Section 101(3BA) of the *National Health Act 1953* that natalizumab should not be treated as interchangeable with any other drugs.
- 5.5 The PBAC noted that current arrangements for eligible prescribers and the Early Supply Rule remained appropriate.
- 5.6 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

- 6.1 Amend existing/recommended listing as follows:

Remove population criteria: 'Patient must be aged 18 years or older' from items 9505G and 9624M.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

Biogen welcomes the PBAC positive recommendation for the removal of the age restriction from the PBS listing of natalizumab for clinically definite RRMS.