MS Australia
ABN: 51 008 515 508
PO Box 625
North Sydney NSW 2059

1300 010 158
info@msaustralia.org.au

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PBAC Secretariat
MDP 952
Office of Health Technology Assessment Branch
Department of Health and Ageing
GPO Box 9848
Canberra ACT 2601

By email to: pbac@health.gov.au

Re: Submission of a new form of natalizumab (Tysabri®) for RRMS to PBAC meeting March 2023

MS Australia is writing to the Pharmaceutical Benefits Advisory Committee (PBAC) to support the inclusion of natalizumab (Tysabri®) via subcutaneous delivery on the Pharmaceutical Benefits Scheme (PBS) for people with multiple sclerosis (MS).

MS Australia is Australia's national MS not-for-profit organisation that empowers researchers to identify ways to treat, prevent and cure MS, seeks sustained and systemic policy change via advocacy, and acts as the champion for Australia's community of people affected by MS. MS Australia is the largest Australian not-for-profit organisation dedicated to funding, coordinating, educating and advocating for MS research as part of the worldwide effort to solve MS. MS Australia collaborates closely with our member organisations and various national and international bodies to help meet the needs of people affected by MS.

Declaration of interest

MS Australia is making this submission as we have an interest in the health and well-being of all people with MS. MS Australia is the national peak body for people living with MS in Australia. We work with governments at all levels, engaging on the issues that concern the lives of people living with MS, their families and carers, the community and the economy. We declare that we have in the past received funding support from pharmaceutical companies (2% of total revenue for FY2022), including Biogen Inc, with an interest in MS in the form of grants for projects and support of our national MS research scientific conference.

About MS

As the national peak body for people with MS, we are proud to advocate on behalf of our state member organisations and the MS community. One area we are particularly passionate about is the provision of more affordable and accessible treatments that can improve the lives of people with MS.

There are currently more than 25,600 people living with MS across the country and over 7.6 million Australians know or have a loved one with this disease. MS can be particularly debilitating and has an unpredictable disease course. No two cases of MS are the same.

MS affects everyone differently and people also respond to treatments and their potential side effects differently. Life circumstances, such as family planning, career and travel, as well as other health conditions, can also greatly affect treatment options and decisions. Even geography can affect treatment choices with close access to hospitals and health professionals for treatment, administration and monitoring being a big consideration relating to some medications for people with MS living outside of major metropolitan areas. There is no one-size fits all treatment for people living with MS and to date, there is no known cure.

Relapsing-remitting form MS (RRMS) is characterised by partial or total recovery after attacks, also called exacerbations, relapses, or flares. It is the most common form of MS with about 75% of people with MS initially diagnosed with a relapsing-remitting course.

The challenges faced by people with MS can be significant and can have a devastating impact on their families and the wider community. Relapses, as part of the course of RRMS can cause short-term or long-term disability, resulting in the need for physical and/or psychological care and support, medical investigations, treatments and hospitalisation.

About natalizumab (Tysabri®)

Natalizumab is a humanised monoclonal antibody which locks onto certain immune cells, called T cells. Once natalizumab is attached to the T cells, they cannot cross the blood brain barrier to attack the myelin or nerves of the brain and spinal cord.

Clinical trials found that natalizumab (Tysabri®) has a significant beneficial effect in people with RRMS by reducing the accumulation of permanent physical disability, relapse frequency and disease activity measured by active lesions on brain magnetic resonance images (MRI)[1,2].

Natalizumab (Tysabri®) is infused intravenously (IV) over one hour, once every 28 days, usually at a hospital or infusion clinic. This is not a convenient option for people with RRMS, particularly to those who are located rurally or remotely, and face a geographical barrier.

In 2021, the European Commission (EC) approved the subcutaneous (SC) administration of natalizumab (Tysabri®) for the treatment of RRMS. This now provides two routes of administration and enables flexibility to meet patients' needs and preferences.

Clinical trials for SC natalizumab (Tysabri®)

In the 32-week phase I DELIVER study, SC and IV administration of 300mg natalizumab (Tysabri®) every four weeks yielded similar serum trough concentrations and pharmacodynamic (PD) effects after repeated dosing, as well as similar efficacy, safety, and immunogenicity[3].

The 60-week phase II REFINE study also showed comparability of SC administration to the IV administration of 300mg natalizumab (Tysabri®) every four weeks in efficacy, pharmacokinetic and pharmacodynamic profiles[4].

Overall, the safety of natalizumab (Tysabri®) SC in both studies was consistent with the well-established benefit-risk profile of natalizumab (Tysabri®) IV in other clinical studies and post-marketing setting, with the exception of pain at the injection site which can occur with SC injections[3,4].

Impact of new MS medications

Being able to better manage and limit the frequency and impact of relapses, reduce the number of new lesions and experience less worsening of disability, can help alleviate the burden of MS on the community and the individual.

A key distinction is the SC option expands the clinical settings, beyond infusion centres, where patients can be treated. Many patients may have limited availability to attend infusion centres, where infusion of Tysabri® can take up to an hour. The SC option would allow patients to attend their local healthcare professional for administration.

In addition, the SC formulation is administered in a shorter timeframe compared to the IV formulation and allows physicians to reduce or remove the post-dose observation period for some patients after six doses as clinically appropriate.

The addition of the SC administration also offers people living with MS another option at a time when they are being encouraged to minimise the risk of COVID-19 exposure within large healthcare settings. This treatment route also provides a potentially convenient option for people with RRMS, particularly for those located in rural or remote regions, who would not have to travel long distances to infusion centres to receive their treatment.

Finding the right treatment option for every individual with MS is paramount as suboptimal treatment can lead to an increased symptom burden and irreversible accumulation of disability. This in turn leads to an increased burden on the healthcare system and a further reduction in the quality of life of patients and their families.

MS costs the Australian community over $1.75 billion per year with an average cost of MS per person of $68,382 (similar to that of someone with Parkinson's disease or the first year after a

stroke, and triple that of a person with type 2 diabetes)[5]. The impact of MS on quality of life can be equivalent to that experienced by people with terminal metastatic cancer, chronic kidney disease and severe heart disease.

Including this medication on the PBS will make a valuable addition to the repertoire of medications available to people with MS and their neurologists. It will allow for an additional appropriate treatment choice to be made according to the efficacy and possible side-effects in relation to an individual's circumstances and will help to improve the quality of life and alleviate the economic cost of MS to individuals, their families and the broader community.

We appreciate you considering this treatment for inclusion on the PBS.

1. Polman CH, O'Connor PW, Havrdova E, Hutchinson M, Kappos L, Miller DH, Phillips JT, Lublin FD, Giovannoni G, Wajgt A, Toal M, Lynn F, Panzara MA, Sandrock AW; AFFIRM Investigators. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006 Mar 2;354(9):899-910. doi: 10.1056/NEJMoa044397.

2. Butzkueven H, Licata S, Jeffery D, Arnold DL, Filippi M, Geurts JJ, Santra S, Campbell N, Ho PR; REVEAL Investigators. Natalizumab versus fingolimod for patients with active relapsing-remitting multiple sclerosis: results from REVEAL, a prospective, randomised head-to-head study. *BMJ Open*. 2020 Oct 20;10(10):e038861. doi: 10.1136/bmjopen-2020-038861.

3. Plavina T, Fox EJ, Lucas N, Muralidharan KK, Mikol D. A Randomized Trial Evaluating Various Administration Routes of Natalizumab in Multiple Sclerosis. *J Clin Pharmacol*. 2016 Oct;56(10):1254-62. doi: 10.1002/jcph.707.

4. Trojano M, Ramió-Torrentà L, Grimaldi LM, Lubetzki C, Schippling S, Evans KC, Ren Z, Muralidharan KK, Licata S, Gafson AR. A randomized study of natalizumab dosing regimens for relapsing-remitting multiple sclerosis. Mult Scler. 2021 Dec;27(14):2240-2253. doi: 10.1177/13524585211003020.

5. *Health Economic Impact of MS in Australia in 2017*. https://www.msaustralia.org.au/wp-content/uploads/2018/08/health-economic-impact-of-ms-in-australia-in-2017_ms-research-australia_web.pdf