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MS Research Australia is writing to support the inclusion of ozanimod (Zeposia) on the Pharmaceutical Benefits Scheme (PBS) for people with relapsing remitting MS.

As the largest national not-for-profit organisation dedicated to funding MS discoveries and coordinating MS research in Australia, we are proud to advocate on behalf of people affected by this disease. One area of particular importance to MS Research Australia and the MS community is the affordable availability of treatments that have been shown to be effective in clinical trials to reduce the impact of MS.

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.

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[1]. 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[1].

Ozanimod is a sphingosine 1-phosphate receptor modulator that acts by targeting lymphocytes and retaining them in lymphoid tissues[2]. This retention prevents potentially auto-aggressive lymphocytes from moving into the central nervous system, the site of inflammation in MS, and contributing to the ongoing damage to myelin and nerves that can lead to progressive disability. Ozanimod is an oral tablet that is taken once daily. Therefore, this treatment regime provides a potentially convenient option for people with relapsing remitting MS, particularly to those whom are located rurally and face a geographical barrier.

Two international phase III clinical trials have shown ozanimod to be an effective and safe treatment to significantly reduce disease progression in people with relapsing remitting MS compared to interferon beta-1a, a treatment option currently available for people with relapsing remitting MS. The SUNBEAM trial recruited 1,346 people across 20 countries and tracked them for at least 12 months[3], and the RADIANCE trial recruited 1,320 people across 21 countries and tracked them over a 24 month period[4].

Participants were split into three different treatment arms – one that took a lower dose of ozanimod (0.46mg) daily, one that took a higher dose of ozanimod (0.92mg) daily, and one that had weekly interferon beta-1a injections. To mitigate cardiac effects common with sphingosine 1-phosphate receptor modulators, there was a 7 day dose escalation of ozanimod. Markers of disease progression, including annualised relapse rate, the number of new and active lesions, changes in brain volume and time to confirmed disability progression based on the expanded disability status scale (EDSS), were tracked.

The trials showed that the annualised relapse rates were significantly lower in the ozanimod treatment groups compared to the interferon beta-1a groups. In the SUNBEAM trial, the annualised relapse rate ratio compared to interferon beta-1a after treatment for at least 12 months was 0.69 (CI = 95%, 0.55-0.86; p = 0.0013) for lower dose of ozanimod and 0.52 (CI = 95%, 0.41-0.66; p < 0.0001) for higher dose of ozanimod[3]. For the RADIANCE trial, the annualised relapse rate ratio compared to interferon beta-1a after treatment for 24 months was 0.79 (CI = 95%, 0.65-0.96; p = 0.0167) for lower dose of ozanimod and 0.62 (CI = 95%, 0.51-0.77; p < 0.0001) for higher dose of ozanimod[4].

In both studies, the number of new or enlarging T2 lesions as seen by magnetic resonance imaging (MRI) was significantly lower after treatment with ozanimod compared to the interferon beta-1a group. In the SUNBEAM trial, there was a 25% reduction (p = 0.0032) in the lower dose ozanimod group and a 48% reduction (p < 0.0001) in the higher ozanimod group of new or enlarging T2 lesions compared to the interferon beta-1a group. In the RADIANCE trial, there was a 34% reduction in the lower dose ozanimod group (p = 0.0001) and a 42% reduction in the higher ozanimod group (p < 0.0001) of new or enlarging T2 lesions compared to interferon beta-1a. Likewise, the number of gadolinium-enhancing lesions was significantly lower after treatment with ozanimod compared to interferon beta-1a. The SUNBEAM trial showed a 34% reduction (p = 0.0182) in the lower ozanimod group and 63% reduction (p < 0.0001) in the higher ozanimod group of gadolinium-enhancing lesions compared to interferon beta-1a. The RADIANCE trial showed a 47% reduction (p = 0.003) in the lower ozanimod group and 53% reduction (p = 0.006) in the higher ozanimod group of gadolinium-enhancing lesions compared to interferon beta-1a. The effects of ozanimod on reducing brain atrophy compared to interferon beta-1a was also robust in both trials.

Ozanimod was well-tolerated in both studies, with minimal cardiac effects[3,4]. The most common side effects were nasopharyngitis, headache, and upper respiratory tract infection. Overall, side effects were similar across all treatment groups.

MS Research Australia supports affordable access to all proven treatment options to increase the opportunity for people with MS and their doctors to find effective therapies suited to their individual circumstances. Reducing disease progression will improve quality for people with MS and their loved ones, enabling their full participation in social and family life, and employment.

MS Research Australia appreciates the opportunity to make this submission and applauds the Committee for seeking the views of people with MS and the wider community as part of the process of considering new MS treatments for inclusion on the PBS.

1) Health Economic Impact of MS in Australia in 2017. https://msra.org.au/wp-content/uploads/2018/08/health-economic-impact-of-ms-in-australia-in-2017_ms-research-australia_web.pdf
2) Ozanimod (RPC1063) is a potent sphingosine-1-phosphate receptor-1 ($S1P_1$) and receptor-5 ($S1P_5$) agonist with autoimmune disease-modifying activity. Scott FL, Clemons B, Brooks J, Brahmachary E, Powell R, Dedman H, Desale HG, Timony GA, Martinborough E, Rosen H, Roberts E, Boehm MF, Peach RJ. Br J Pharmacol. 2016 Jun; 173(11): 1778–1792. doi: 10.1111/bph.13476
3) Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 12-month, phase 3 trial. Comi G, Kappos L, Selmaj KW, Bar-Or A, Arnold DL, Steinman L, Hartung HP, Montalban X, Kubala Havrdová E, Cree BAC, Sheffield JK, Minton N, Raghupathi K, Ding N, Cohen JA; SUNBEAM Study Investigators. Lancet Neurol. 2019 Nov; 18(11):1009-1020. doi: 10.1016/S1474-4422(19)30239-X.
4) Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (RADIANCE): a multicentre, randomised, 24-month, phase 3 trial. Cohen JA, Comi G, Selmaj KW, Bar-Or A, Arnold DL, Steinman L, Hartung HP, Montalban X, Kubala Havrdová E, Cree BAC, Sheffield JK, Minton N, Raghupathi K, Huang V, Kappos L; RADIANCE Trial Investigators. Lancet Neurol. 2019 Nov; 18(11):1021-1033. doi: 10.1016/S1474-4422(19)30238-8.