Appendix 1 - Expanded Information Document

Multiple Sclerosis New Zealand

What is the current situation?

Multiple Sclerosis (MS) is the most common acquired chronic neurological disease affecting young adults, often diagnosed between the ages of 20 to 50, with the average age being 38. In New Zealand, women are three times more likely to be diagnosed with MS. Latest estimates based on prevalence, incidence and mortality data indicate there to be around 4130 people currently diagnosed with MS in NZ. It is also understood that for every 1 person with MS (PwMS), a further 7 are impacted by the condition, be they whānau, friends, employers, carers, colleagues.

There is no known single cause of MS, but many genetic and environmental factors have been shown to contribute to its development. While the cause or cure are not currently known, ground-breaking research is constantly uncovering new information.

In MS, the body's own immune system mistakenly attacks and damages the fatty material – called myelin – around the nerves. Myelin is important for protecting and insulating nerves so that the electrical messages that the brain sends to the rest of the body, travel quickly and efficiently.

As the myelin breaks down during an MS attack – a process called demyelination – patches of nerves become exposed and then scarred. This renders the nerves to be unable to communicate messages properly and leave them at risk for subsequent degeneration. The damaged caused by MS mean that the brain cannot talk to other parts of the body. This results in a range of symptoms that can include a loss of motor function (e.g. walking and hand and arm function, loss of sensation, pain, vision changes and changes to thinking and memory).

Eight Disease Modifying Therapies (DMTs) are currently funded by Pharmac for those with relapsing forms of MS. There are currently only 1900 patients on DMTs, 50% of those diagnosed with MS. Two of the most commonly used treatments, Natalizumab (Tysabri) and Fingolimod (Gilenya), have an average yearly costs per patient of $19,915 and $31,790, respectively. Patients have the potential to remain on treatment over their lifetime perhaps for another 25 – 35 years.

Tysabri is widely accepted as one of the best first-line treatment options available in NZ. 70-90% of the wider population are expected to carry the John Cunningham Virus (JC Virus). While in most cases this is of no threat to them, for those with MS and on Tysabri, prolonged use can increase viral loading and trigger Progressive multifocal leukoencephalopathy (PML). PML is a rare demyelinating disease most common in immunodeficient patients. It occurs due to reactivation of the John Cunningham Virus (JCV) and carries a poor prognosis, with a median life expectancy of 6 months. Patients on Tysabri are regularly tested and are recommended to stop treatment should they be JCV positive or their viral loading increase to high risk levels. With Tysabri being one of the highest efficacy MS DMTs, discontinuation or contraindications reduce treatment options for patients.

aHSCT is an intense chemotherapy treatment which aims to wipe out harmful immune cells and rebuild the immune system. Already widely used in NZ as a treatment for blood cancer, aHSCT doesn't reverse MS damage but can restart the immune response and halt further disease progression. aHSCT can deliver solid and often remarkable results for selected patients with active relapsing MS, even some with quite advanced disease. A person receiving aHSCT potentially needs NO further treatment for MS.

aHSCT is readily available in Australia and the UK through observational trials for selected patients exhibiting early and aggressive disease.

Due to its unavailability here, over 100 New Zealanders have self-funded their own aHSCT in private clinics overseas, most commonly Russia, Mexico, Singapore, and India. This has created a sense of desperation for some Kiwi MS patients, having to find or fundraise around $70-$120,000 to pay for overseas treatment while the clock is ticking and their disease threatening to progress beyond the stage where aHSCT could potentially help them. Added to that has been the added stress and fear of such medically vulnerable patients having to take on international travel during COVID-19. The cost of aHSCT in NZ has been calculated to be $50,000 per patient.

Despite the clinical evidence and high-level clinical support for its use, patients in NZ with active relapsing MS are still being denied access to this proven, cost-effective treatment.

Supporting Evidence

Clinical Trial Evidence

MSNZ began advocating for the introduction of aHSCT in 2017, including commissioning an independent report which it presented to the Ministry of Health (attached), and bringing overseas expert, Dr Riccardo Saccardi here to discuss the positive role aHSCT treatment can play.

Dr Saccardi presented on the data collated by the European Society for Blood and Bone Marrow Transplant (ESBBMT). By 2017 across Europe 2358 cases of aHSCT for various conditions had been successfully completed and recorded. 1014 of these were for patients for MS, the highest subgroup.

In the 2017 multi-study review paper "Autologous haematopoietic stem cell transplantation for treatment of multiple sclerosis," Muraro et al summarise the results of multiple successful studies. Overall it was reviewed that:

- aHSCT can entirely suppress MS disease activity for 4–5 years in 70–80% of patients, a rate that is higher compared to DMTs.

- The safety has increased exponentially due to improvements in understanding optimal patient profiles and treatment protocol. Pre 2005, treatment-related mortality, was 3.6% in studies before 2005. Since 2005 this has decreased to 0.3% in studies.

- The proportion of patients for whom No Evidence of Disease Activity (NEDA) was achieved at 2 years with disease-modifying therapies and aHSCT (table 1)[1]. Red dots are the mean, bars represent 95% confidence intervals. The bottom 5 results represent outcomes from key aHSCT studies.

- Higher rates of no evidence of disease activity (NEDA) were achieved with aHSCT than with any other DMT, including those that are considered to have high efficacy. The findings suggest that aHSCT has a more profound effect on disease activity than current DMTs.

[1] Muraro et Al. Autologous haematopoietic stem cell transplantation for treatment of multiple sclerosis. *Nat. Rev. Neurol, 2017,*

I

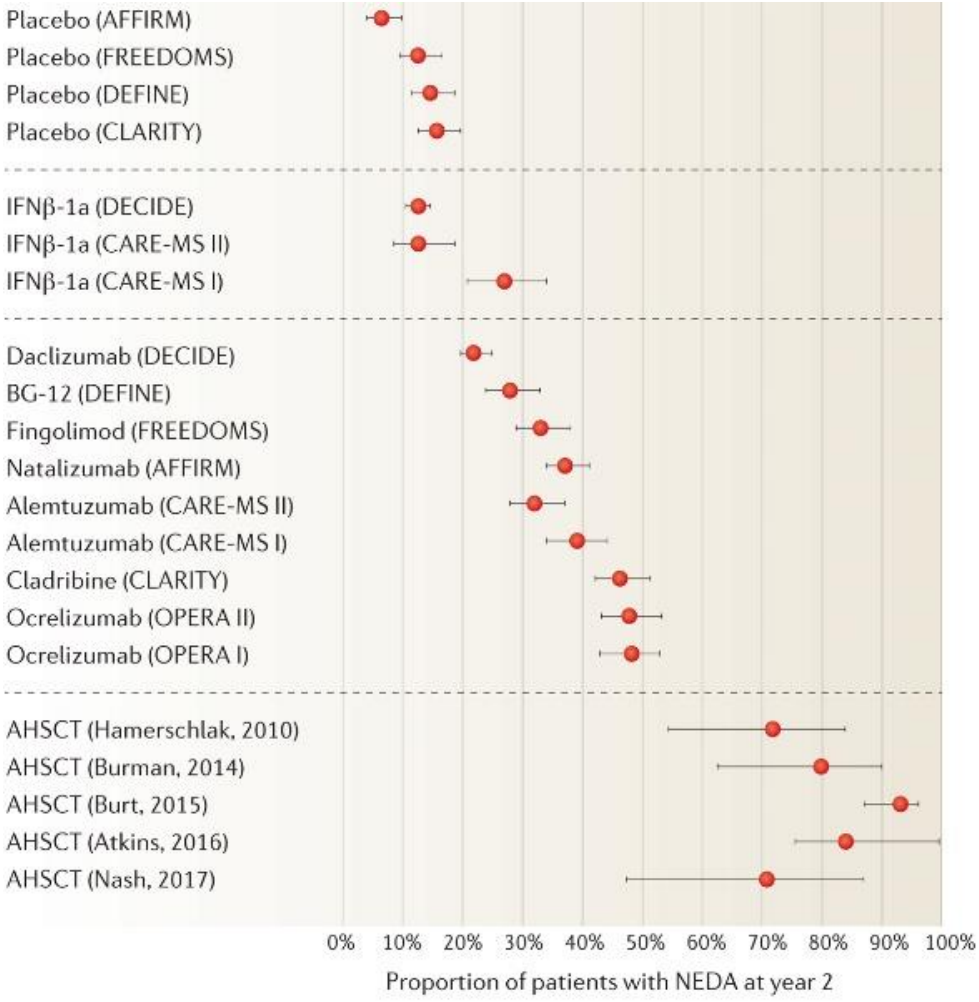

Table 1. Muraro et Al. Rev.Neurol, 2017

Initiated out of Chicago, the MIST Trial (results published in the *Journal of the American Medical Association (JAMA)*)[2] enrolled 110 patients between 2005 and 2016 from the USA, UK and Europe. Of these, the results of 103 participants were analysed. Participants had very active relapsing remitting MS with at least 2 relapses in the year prior, despite treatment. Participants ranged in age from 18 to 54, with an average of 35 years. Disability ranged from 2 to 6 on the Expanded Disability Status Scale (EDSS).

In the blind trial, patients were split into two groups, one receiving aHSCT with the cyclophosphamide chemotherapy regime which removes the circulating immune cells but leaves the bone marrow relatively unscathed (known as non-myeloablative). The other half of the participants were treated with approved MS medications which included mitoxantrone, glatiramer acetate, interferon-beta, fingolimod, dimethyl fumarate and natalizumab. These treatments are all available in NZ apart from mitoxantrone.

[2] Burt et Al. Effect of Nonmyeloablative Hematopoietic Stem Cell Transplantation vs Continued Disease-Modifying Therapy on Disease Progression in Patients With Relapsing-Remitting Multiple Sclerosis. A Randomized Clinical Trial. *Jama, 2019,*

Participants were followed for 1 to 5 years after the AHSCT treatment. The outcome of the treatment was primarily measured by progression of disease, which was defined as a worsening of one point or more on the EDSS scale after at least one year. Results published in 2019 showed:

- As a group, the participants treated with AHSCT had an average improvement in disability of 1.02 points on the EDSS scale, whereas those receiving standard medications had an average worsening in EDSS disability of 0.67 points.

- The researchers also looked at the occurrence of relapses and MRI lesions in the two groups. At one year of follow-up, 1.92% of AHSCT-treated participants had experienced relapses compared to 64.3% of participants receiving standard therapies.

- After five years of follow up 15.4% of the AHSCT-treated participants had experienced relapses compared to 85.2% in the standard therapy arm.

- There was a reduction in the total volume of existing MRI brain lesions in the aHSCT group, compared to an increase in the volume of lesions in the standard therapy group.

- Measurements of quality of life also showed improvements in the aHSCT group compared to the standard therapy group.

- The research team reported no deaths and there were no life-threatening adverse events as a result of the aHSCT treatment.

If those in the standard MS therapy group experienced progression after at least one year of treatment, they 'crossed over' and were then treated with aHSCT. 30 of the 50 participants in standard medication group met this criterion and received aHSCT. In contrast, only 3 of 52 participants treated with aHSCT from the outset experienced progression.

These results, which are in keeping with the international data that has been accumulating on this treatment for MS, indicating that aHSCT is an important treatment option for people with aggressive relapsing MS who fail to respond to other MS therapies.

NZ Clinician Support

From an OIA response from the Ministry of Health MSNZ understands that in 2018/9 a Haematology and Neurology Special Interests Group, compromising the country's leading experts, undertook its own investigative work. In 2019 the results of their review were presented to the Ministry of Health and Auckland DHB. They expressed support for the use of aHSCT for those with highly active MS who are not responding to existing drug treatments.[3]

An MSNZ-initiated OIA request to Auckland DHB in 2021 produced paperwork from meetings held by expert clinicians from the Northern Region Clinical Practice Committee[4]. They showed overwhelming support for the use of aHSCT in selected patients with relapsing remitting MS, with acknowledgment NZ has the capability to deliver the treatment but not the capacity.

[3] Relevant page (P146) from an OIA Response from MOH provided to MSNZ regarding aHSCT, received 31 August 2021, Appendix 4

[4] OIA Response from ADHB Provided to MSNZ regarding aHSCT, 1 July 2021, Appendix 3, Page 2

The Minister of Health advised MSNZ last year[5] that while the Ministry's Haematology Work Group had considered the aHSCT issue, there were still factors to be resolved, including estimating the volumes of treatment required, and commissioning and implementing the treatment amongst DHBs. The response also noted the Health and Disability System Review would be focussing on the introduction of new technologies and treatments.

Economic Benefits

AHSCT has the potential of saving the health system overall hundreds of thousands of dollars annually. AHSCT is a one-off cost. The Cost Benefit analysis (see Table 2) undertaken by health economists for the Northern Region Clinical Practice Committee[6] shows that the cost is less than the cost of MS drugs for two years. Two of the most commonly used treatments have an average yearly costs per patient of $19,915 and $31,790, respectively. The cost of aHSCT as calculated in the cost benefit analysis is $50,000 per patient. A person receiving aHSCT potentially needs NO further treatment for MS ever as compared with needing expensive drugs over their lifetime perhaps for another 25 – 35 years.

The resultant costs and QALYs accrued for ASCT and Disease Modifying Therapy (DMT) are summarised below, with and without the inclusion of disease modifying drug costs:

With drug costs included (per patient)

Years	ASCT QALYs	ASCT Cost	DMT QALYs	DMT Costs	Cost per QALY or Saving
5	3.66	$67,874	2.57	$153,763	Saving with ASCT + more QALYs (dominates)
10	6.30	$97,635	4.31	$279,151	Saving
15	8.50	$124,219	5.76	$387,365	Saving
20	10.34	$148,047	6.97	$481,577	Saving
25	11.85	$168,039	7.97	$558,970	Saving
50	15.83	$251,926	10.58	$773,569	Saving

Without drug costs included (per patient)

Years	ASCT QALYs	ASCT Cost	DMT QALYs	DMT Cost	Cost per QALY or Saving
5	3.66	$63,387	2.57	$44,144	$17,710
10	6.30	$78,446	4.31	$94,393	Saving
15	8.50	$92,752	5.76	$139,857	Saving
20	10.34	$106,375	6.97	$181,908	Saving
25	11.85	$117,936	7.97	$216,215	Saving
50	15.83	$179,713	10.58	$317,811	Saving

Table 2. Extract from OIA received by MSNZ from the Auckland DHB 1 July 2021

In June 2022 the New Zealand Institute of Economic Research (NZIER) released the Economic Burden of MS Report 2021[7], commissioned by MSNZ. We have attached this report for your reference. The report combines 2 accepted modelling tools to measure and express the research findings.
The Expanded Disability Status Scale (EDSS) to quantify impairment in multiple sclerosis and

[5] Letter from Minister of Health to MSNZ, received 5 July 2021
[6] OIA Response from ADHB Provided to MSNZ regarding aHSCT, 1 July 2021, Appendix 3, Page 8
[7] Economic Burden of MS Report 2021, New Zealand Institute of Economic Research, Appendix 2

monitoring changes in the level of impairment over time, and Quality-adjusted life years (QALYs) to measure the loss in health quality for individuals. The estimated total cost of lost QALYs associated with the prevalence of MS in NZ was $26.3 million in 2021. The health system cost for mild, moderate and severe cases of MS was estimated to be $14.9 million, $42.5 million and $73.1 million, respectively. In 2021, the total health system cost of MS was $130.5 million. This represents an average cost of $31,607 per case of MS per year.

The report shows early and aggressive intervention of MS will not only save NZs health system millions of dollars per year, but it will also contribute millions back into the economy through individual income related earnings. Understanding the total costs and benefits of a health challenge is good health economics which matters for society because a person's health has implications for families, society, and the economy.

The NZIER report provides evidence that earlier intervention and medicines funding access are key to positive outcomes for both people with MS and the NZ economy. The report describes how the progression of the disease to the severe disability level can be delayed by between 6 to 10 years with early intervention and the present value of such a delay could be between $500,000 and $1 million per case over the delay period.

The average age of diagnosis in NZ is between 25 to 50 years old. By treating people early in their condition we can keep them working. The financial consequences of lost employment and lost potential to earn due to the onset of MS are likely to be significant and increases as disability and disease progression increases. Slowing the progression of the MS will generate private and social costs savings beyond avoided pain and suffering. Delaying the disease progression will support people to be more independent, lessen the need for informal care and improve the probability of staying at work.

The population of NZ is projected to increase and age in the future, which could contribute to an increase in the number of cases and a greater burden from MS. In the context of an ageing population and MS being a disease of people aged between 25 to 50, it may become more visible in health rankings in NZ over the next 30 years.

Slowing the progression of the MS will generate private and social costs savings beyond avoided pain and suffering. Delaying the disease will support people to be more independent, lessen the need for informal care and improve the probability of staying at work.

We strongly urge consideration of the cost savings to the wider health (Health NZ and Pharmac) as well as social benefits system when reviewing the overall cost benefit. By funding treatments, early and aggressively, for those with progressive forms of MS, we can aim to delay the financial burden on the wider system, individuals and their whānau.