Multiple Sclerosis Research Australia
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MS Research Australia submission to the Advisory Committee on Medicines Scheduling (ACMS #25) meeting, November 2018 regarding nabiximols

About Multiple Sclerosis Research Australia

MS Research Australia is the largest not-for-profit organisation dedicated to funding and coordinating MS research in Australia. Our Mission is to accelerate Australian MS research toward the prevention, better treatments and a cure for MS.

MS Research Australia achieves our mission by working in partnership with relevant medical research institutes and scientists around Australia, encouraging collaborations and focusing on Australian strengths in this research. MS Research Australia is ultimately working towards *freedom from MS*.

Our research strategy aims to accelerate research activity in areas where Australian scientists can have the greatest impact in worldwide MS research. We work in close partnership with and encourage collaboration between a number of Australia's top medical research centres.

MS Research Australia is guided by an informed scientific agenda to accelerate advances and focus on funding research that will increase our understanding of the triggers for MS, the biology driving MS and how we may prevent the ongoing damage caused by MS and repair existing damage that can reverse disability. We also encourage research that will lead to improvements in symptom management, rehabilitation and support services to help people with MS maintain quality of life. Together with a robust governance structure, MS Research Australia believes this approach will result in further significant breakthroughs in the knowledge and effective treatment of MS and major steps toward understanding the cause and developing the cure.

Introduction

MS Research Australia welcomes the opportunity to provide a submission to the Therapeutic Goods Administration (TGA) proposed amendments to the Poisons Standard referred to the Advisory Committee on Medicines Scheduling (ACMS #25) meeting, November 2018. The focus of the comments, suggestions and recommendations provided in this submission are specifically on key areas that will impact on people affected by MS.

MS Research Australia response to the proposed amendments

There are currently over 25,600 people living with MS across the country and this number is increasing. MS can be a particularly debilitating disease with an unpredictable disease course that affects people in different ways. For some it is a disease with periods of unpredictable relapse and remission. For others it is a progressive decline over time. For all, it is life changing.

As such, MS Research Australia supports any proven treatment that has been deemed safe by the Therapeutic Goods Administration and that helps to minimise the impact of the disease and allow people with MS to live more fulfilling lives.

The availability of medicinal cannabis-based products is a complex area and there are risks as well as potential benefits to consider. It is very important that medicinal products derived from cannabis are strictly regulated and have standardised doses of active ingredients, to ensure products are safe and effective, and can produce reliable effects with a controlled risk of adverse events.

Robust and reliable evidence is needed to determine the possible benefits and risks of cannabis-based products for managing symptoms of chronic illnesses such as MS. As part of any debate on this issue, MS Research Australia encourages the promotion of randomised controlled clinical trials to be conducted to

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determine the components, dosage and frequency of either cannabis or cannabis-based products and their efficacy and safety for managing a range of symptoms for people living with chronic conditions like MS.

A 2004 international survey of over 2,500 people with MS conducted by Australian researchers, indicated that around 10% of people with MS believed that cannabis was a factor that can help improve their MS symptoms (Simmons et al., 2004).

The most significant cannabis-derived product to have been studied for potential benefits in people with MS to date is the Sativex (nabiximols). Its principal active cannabinoid components are the cannabinoids: tetrahydrocannabinol (THC) and cannabidiol (CBD). Sativex is a mouth spray with evidence from clinical trials for benefits for muscle spasticity and motor control in people with MS. Sativex has been made available to people with MS in Australia under Schedule 8, and this submission is to support the proposed amendment to have Sativex included as part of Schedule 4.

Muscle spasticity is a significant problem for many people living with MS, affecting over 80% during the course of the disease and negatively impacting mobility and personal independence. Spasticity can cause pain, sleep disturbance and reduced mobility. These symptoms can significantly limit a person's quality of life as they have less energy, ability to complete everyday tasks and social activity. It can also lead to an increased reliance on carers and the health system if symptoms progress to a stage where mobility is significantly hampered or hospitalisation is required.

To date, available medications to treat spasticity for people with MS are not always effective and can have intolerable side effects. Sativex represents a potential new choice of symptom modifying therapy for people with MS who experience spasticity. To date, clinical trials of Sativex have indicated that it can reduce spasticity, pain and spasms and improve the quality of sleep.

Being able to better manage and limit the impact of spasticity would help give people with MS greater coordination and ability to complete everyday tasks which at times can be vital to maintaining self-esteem and a connection with family, friends and loved ones. It can also mean less time in hospital, meaning less strain on valuable medical and disability resources, which helps to reduce the economic impact of MS on society.

It is important to acknowledge that Sativex does have side effects that will vary with each case. These can include dizziness, tiredness, depression, memory loss and nausea. Sativex at established therapeutic dosage levels does not produce dependency or have a high propensity for misuse, abuse, or illicit use. Real world registry data is a robust method for tracking this type of information and a number of registries have reported the real world outcomes of Sativex. Registry data from UK, Germany and Spain showed the previously reported safety profile and no evidence of addiction, abuse or misuse (Fernández, 2016).

A registry of Italian patients using Sativex for spasticity in MS that followed the patients over six months found just over 18% of people discontinued Sativex due to side effects such as cognitive and psychiatric effects, fatigue and drowsiness and that this was in line with other reports of side effects for Sativex studies (Patti 2016a). The same group showed that at 18 months following treatment initiation 15% of patients reported adverse events but that no new safety concerns beyond the approved label were identified (Patti, 2016b). A further interim analysis of Italian patients showed that the real world use of Sativex showed a lower number of adverse events in comparison to those seen in clinical trials (Trojano 2016).

A registry of the UK, Germany and Switzerland including data totalling over 2200 patient years of exposure showed that adverse events were reported in people taking Sativex. The most common treatment-related AEs included dizziness (2.3%) and fatigue (1.7%). Other adverse events included psychiatric adverse events in 6% of the patients, falls requiring medical attention in 6% and suicidality in 2%. Driving ability was reported to have worsened in 2% of patients, but improved in 7%. There were no signals to indicate

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abuse, diversion, or dependence. The long-term risk profile from this registry was consistent with the known safety profile of THC:CBD, covered under the current labelling conditions of these countries and there was no evidence of new long-term safety concerns (Etges et al, 2016).

As a national body supporting research and the dissemination and translation of research findings as well as providing evidence-based information for people with MS in Australia, we are passionate about affordable access to proven treatments that can improve the lives of people with MS. We are guided by the most up-to-date research and evidence-based recommendations to support the application of potential new therapies for MS symptom management. MS Research Australia previously wrote to the PBAC secretariat in support of an application for inclusion of Sativex on the Pharmaceutical Benefits Scheme (PBS) and the listing of Sativex under the original schedule 8 designation. Based on the data above, MS Research Australia would strongly support the inclusion of nabiximols as Schedule 4 entries, such that Sativex can be made available in Australia under this schedule. The requirements of storage and sale of drugs under Schedule 4 provide adequate controls and protections for nabiximols and the Schedule 4 level of control mirrors that seen in other countries. Under Schedule 8, the stringent storage requirements has resulted in very few pharmacies dispensing this medication and is restricting access to Sativex for people with MS that require effective treatment for their spasticity.

Conclusion

MS Research Australia is committed to supporting the provision of proven therapies for improving the lives of people with MS. As stated earlier, our position on these issues is guided by a scientific, evidence-based approach and we would advocate for a regulatory framework that while providing access for proven indications and preparations of cannabis-based medications in MS, will also facilitate further clinical trials to determine the optimal components, dosage and frequency of cannabis-based products and their effectiveness in managing a range of symptoms for people living with chronic conditions like MS.

We advocate for access, via authorised medical professionals, to approved, proven standardised formulations that have been clinically shown to be beneficial for specific medical needs (such as spasticity in MS where other medications are not effective or are contraindicated), while providing regulation that facilitates further research.

MS Research Australia would welcome licensed products such as Sativex being made available for people with MS in Australia, through the inclusion of nabiximols as Schedule 4 entries.

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