MULTIPLE SCLEROSIS AUSTRALIA
MULTIPLE SCLEROSIS RESEARCH AUSTRALIA

Submission to the Inquiry into approval processes for new drugs and novel medical technologies in Australia

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About Multiple Sclerosis Australia

MS Australia (MSA) is the national peak body for people living with multiple sclerosis (MS) in Australia. Our role is to work on behalf of all state and territory-based member organisations to provide a voice for people living with multiple sclerosis across the country to support the development of:

- Research
- Advocacy and Awareness
- Communication and Information
- Services provided by our member organisations
- International Collaboration

MSA advocates across all stakeholders, governments and communities, on behalf of our members, to represent people who are diagnosed with the disease, their carers and the broader MS community.

Our Vision

Is consistent with the vision of the Multiple Sclerosis International Federation – **'A world without MS'**

Our Mission

MSA will support our members and work towards meeting the needs of people with MS, their families and carers. We will facilitate a national comprehensive representation of the Member organisations through advocacy and communication.

Our Purpose

On behalf of our members and people with MS, our purpose is to develop:

- **Research:**
  Supporting ongoing research to pursue further knowledge in targeting prevention, improving treatment, enhancing quality of life and ultimately, to find a cure.
- **Advocacy and Awareness:**
  Although MS impacts people differently, there are common, fundamental issues for people affected by the disease. We are steadfastly committed to giving these people a voice and remain willing and able to work with government and the Australian society to champion issues in a dynamic policy environment to bring about change to the lives of people living with this disease.
- **Communication and Information:**
  Utilising traditional, contemporary and innovative channels to source information and share it with people with MS, our member organisations and our key stakeholders.
- **Support for our member organisations:**
  As MS specialists providing and facilitating high quality services that span the life-time needs of people affected by MS and other degenerative neurological conditions, their families and carers – from the point of early symptoms and pre-diagnosis, that addresses their changing needs.
- **International Collaboration:**
  Representing the MS cause and promoting collaboration with our domestic and international partners.

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.

As a member of the MS Australia network, 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. We currently fund over 50 investigator-led projects and 7 national collaborative platform projects to advance our understanding of MS.

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 Australia (MSA) and MS Research Australia welcome the opportunity to provide a submission to this inquiry into the approval processes for new drugs and novel medical technologies in Australia, with a particular focus on those for the treatment of rare diseases and conditions where there is high and unmet clinical need.

There are currently 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.

Around 85% of people diagnosed with MS are diagnosed with the relapsing-remitting form of MS (RRMS). Around 12% are diagnosed with Primary Progressive MS, characterized by worsening neurologic function (accumulation of disability) from the onset of symptoms, without early relapses or remissions.

While a range of medications are available for people with relapsing forms of MS and one single medication has recently been approved by the Australian Therapeutic Goods Administration (TGA) for primary progressive MS, these medications are not effective for all people with MS and can come with a host of risks and side effects. There remains an urgent need to increase treatment options for people with MS, especially for progressive MS, which could be considered a rare disease where there is critical unmet clinical need. This urgent international health priority has been recognised in the establishment of a global research and development collaborative, the International Progressive MS Alliance, of which MS Research Australia is a managing member.

The focus of the comments, suggestions and recommendations provided in this submission are specifically on key areas that will impact on people affected by multiple sclerosis (MS).

Terms of Reference

This inquiry will consider the following topics so that Australia continues to be well positioned to access new drugs and novel medical technologies in a timely manner and respond to emerging global trends:

1. The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies;
2. Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions;
3. Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies; and
4. Without compromising the assessment of safety, quality, efficacy or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of

international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

This submission is divided into sections corresponding to each of the terms of reference.

Much of the material in this submission is drawn from A Roadmap to Defeat Multiple Sclerosis in Australia – a joint publication of MS Research Australia and MS Australia, launched by the Hon Greg Hunt MP, Minister for Health, on World MS Day 2018. This Roadmap sets out what is needed within the next 10 years to ensure that we can prevent and ultimately defeat MS and remains an integral part of our policy platform. It formed a major component of our 2019 Election Commitments suite, launched by the Prime Minister in November 2018, ahead of the Federal Election in May 2019. To read the Roadmap in full, please visit: https://www.msaustralia.org.au/about-msa/2019-election-commitments-make-our-stories-matter

Term of Reference 1

The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies

As stated in the introduction, there is an urgent need to increase treatment options for people with MS, especially for progressive MS. Work is underway worldwide to address this and there is gathering national and international momentum towards clinical trials in a number of innovative areas for MS.

Funding is needed to ensure that Australians living with MS can fully participate and gain access to these clinical trials. In particular, there is intense activity in the development and testing of repurposed medications and other interventions with low commercial interest but potentially high impact for people living with MS. Not least, the significant momentum being driven by the International Progressive MS Alliance, of which MS Research Australia is a managing member will soon see numerous progressive MS clinical trials coming down the pipeline. This includes a range of emerging cell and gene-based therapies for MS.

Concerted funding is needed to support innovative clinical trials in Australia and Australian participation in international trials of these up and coming agents for the treatment of MS.

Some specific activities are proposed to underpin these developments:

Goal: Develop national data and registry infrastructure, including cross-disease approaches, to coordinate the collection and analysis of data on individual diagnostic, prognostic, and preventative factors to personalise treatment and target prevention of MS.

Proposed activity	Details
Enable at-risk individuals to be identified and also identify diagnostic, prognostic and treatment response biomarkers	Prevention strategies will be most successful if combined with methods to definitively identify the most at-risk individuals. Develop and coordinate

through the establishment of a national registry and data research platform.	a national collaborative research platform to utilise existing and emerging evidence to develop integrated genetic, clinical, imaging and fluid biomarker signatures and algorithms to enable screening and stratification of populations with, and at risk of MS to feed into trial designs and treatment strategies.

Goal: Prevention of MS

The 2016 Focussed Workshop of the European Committee for Treatment and Research in MS (ECTRIMS)[1] concluded that:

- 60% of MS cases could be prevented if smoking, vitamin D deficiency, obesity and glandular fever were addressed;
- 90% of MS could be prevented if an Epstein Barr Virus (EBV) vaccine was also developed.

Proposed activity	Details
Develop international collaborative links to address glandular fever and an EBV vaccine.	Work nationally and internationally to drive a focussed international effort to develop and test an EBV vaccine. This is likely to include identifying the most promising vaccine candidate(s), developing a feasible multinational trial design to evaluate efficacy for MS prevention and identifying funding sources to conduct the necessary large, population-based MS prevention study.

Term of Reference 2

Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions

Australian collaboration and funding towards new drugs and technologies for MS

There is significant evidence that there has been more progress in MS than in any other neurological disease in the world. However, MS remains the most commonly acquired neurological disease in younger adults around the world, with over 2.8 million people affected. The serious burden for people with MS and the community, in terms of both quality of life and economic impact, there is still a great need for urgent action.

Australian MS research has a rich and successful history with significant research strengths in many different Universities and medical research institutes. Many of our

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[1] Amato MP, Derfuss T, Hemmer B, Liblau R, Montalban X, Soelberg Sørensen P, Miller DH; 2016 ECTRIMS Focused Workshop Group. Environmental modifiable risk factors for multiple sclerosis: Report from the 2016 ECTRIMS focused workshop. Mult Scler. 2017 Jan 6:1352458516686847. doi: 10.1177/1352458516686847.

talented MS researchers are amongst the world's best and global leaders in their fields of MS research. Australia has been involved with, or led, many of the world's most successful MS research collaborations over the last two decades, with the majority of national collaborations having been funded and facilitated by MS Research Australia, whose track record in leading and coordinating major collaborative efforts in MS research is second to none.

MS Research Australia has also worked closely with the National Health and Medical Research Council (NHMRC) over the last decade, often co-funding MS research projects via an established memorandum of understanding.

MS Research Australia is a category 1 funder of research, the only national MS not-for-profit organisation in Australia to be able to provide prestigious grant funding of this nature. Moreover, this funding model has allowed MS researchers to leverage funding from other competitive sources. On average, researchers receiving our category 1 funding are able to leverage further competitive and philanthropic funds by a factor of 5 times the original investment. This is increased to 27:1 for successful incubator grant applicants.

Examples of our many funded research projects in novel drugs and devices for treating MS include:

- pre-clinical and clinical studies of non-invasive transcranial magnetic stimulation to promote repair of damaged brain tissue in MS and laboratory models[2]
- Copper delivery as a novel therapy for MS[3]

International collaborations towards new drugs and technologies for MS

MS Research Australia, MS Australia and Australian MS researchers play an integral role in the global efforts to solve MS. MS Research Australia and MS Australia are active participants of the international federated body called the Multiple Sclerosis International Federation (MSIF), and the only Australian member of this body. Over 40 MS organisations throughout the world are, or have been, involved with the global federation. It has given people affected by MS, MS societies, organisations and researchers from all over the world a chance to successfully collaborate together on items of global importance to people with MS, including research, treatment access, support, services and quality of life.

MS Research Australia and Australian MS researchers have been involved in numerous global initiatives that are making huge strides in improving our understanding of MS and the treatment of MS.

Examples of this include:

- The International MS Genetics Consortium in which Australian MS researchers played a pivotal role[4]

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[2] https://msra.org.au/project/protecting-brain-overcoming-major-hurdle-successful-ms-treatment/; https://mstrials.org.au/magnetic-brain-stimulation-for-multiple-sclerosis-trial/

[3] https://msra.org.au/project/therapy-treat-progressive-ms/

[4] https://imsgc.net/; http://www.imsgenetics.org/

- The world-first International Progressive MS Alliance, which MS Research Australia joined as a managing member – a global success story in accelerating treatments for progressive forms of MS[5].
- MSBase, the largest clinical MS database in the world, is founded and managed by a Melbourne-based team[6].
- A wealth of individual collaborations between Australian MS researchers and their global counterparts.
- MSIF global research team collaborations including the International Patient Reported Outcomes (PROs) initiative seeking to harmonise and collaborate on the collection and use of PROs for research, clinical trials, drug approvals and clinical management of MS[7].

Proposed activity	**Details**
New and innovative pre-clinical and clinical studies on myelin repair and nerve protection for MS.	Establish a fund for a targeted call for applications for innovative pre-clinical and clinical studies of novel myelin repair and neuroprotection interventions and the biomarkers and assays required to monitor drug efficacy in trials. The grant program will fund a portfolio of projects with clinical and commercial potential and bring them to proof-of-concept stage ready for further commercial investment.
Further research and development of the most promising preclinical and clinical outcomes from the above activity.	Establish a fund to provide follow-on funding to support further research and development of the most promising outcomes of the above projects.
Expansion of the successful competitive paired fellowship program (clinician and researcher working together as a pair), dedicated to translational research to better treat, prevent and find a cure for MS.	Establish a fund to continue to support new competitive paired fellowships. MS Research Australia's unique Paired Fellowship program was established in 2017 to facilitate cutting edge clinical research by funding a Senior Research Fellow and dedicated research time for a Clinical Practitioner Fellow to collaborate on a shared program of research that will accelerate translation of research outcomes into clinical practice.
Investment in longer-term competitive and prestigious senior research fellowships and senior clinical practitioner fellowships to allow their promising research programs the time to come to fruition.	Expand MS Research Australia's signature senior research fellowship (for laboratory researchers and clinicians) program to enable them to focus on long-term research programs.
Expansion of the existing one-year incubator grants designed to stimulate innovative research.	Expansion of the incredibly successful MS Research Australia Incubator grant program to fund a larger number of small pilot grants of $25,000 each which allow

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[5] https://www.progressivemsalliance.org/

[6] https://www.msbase.org/

[7] https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(19)30357-6/fulltext

	researchers to get innovative new ‘out of the box’ ideas and discoveries off the ground. These grants on average leverage 27 times the original investment through follow on grants.

Term of Reference 3
Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies

Clinical trials are the only way to answer the question of whether MS can be prevented in those at risk. Australian research in this area is strong and it is paramount that we complete ongoing clinical trials on whether vitamin D or UV could be used to prevent conversion to MS. Analysis of these trials alongside other international evidence will underpin the development of guidelines for clinical practice for at risk populations.
In addition, support for infrastructure and collaboration is needed to enhance access to Autologous Haematopoietic Stem Cell Transplant (AHSCT) as a treatment for MS. This therapy is currently offered at three centres in Australia as part of clinical observational trials and access needs to be greatly improved for those for whom it is appropriate.

Some specific activities are proposed to underpin these developments:

Proposed activity	Details
Enabling platforms for clinical trials.	Develop a shared national coordination and infrastructure platform for MS clinical trials in Australia to maximise access, efficiency, comparability and data use from clinical trials for MS – to be integrated with the shared data and registry infrastructure in the above activity and articulated with international MS clinical trials platforms and consortia.
Expansion of the Australian Immunological Alliance model to collaborate on common areas of research to identify triggers and prevention strategies for autoimmune, immunological and neurological diseases.	Support the ongoing work of the Australian Immunological Alliance with support costs and a common fund to ensure momentum and progress on common research priorities. Develop a similar approach on common research priorities with other neurological diseases.
Grant program for innovative clinical trials for progressive and/or relapsing MS relating to promising drug targets or interventions.	Establish a competitive fund for collaborative investigator-led, clinical trials for relapsing and progressive MS including both national trials and Australian arms of international trials. Consideration will be given to pharmaceutical and non-pharmaceutical interventions, and should include the development and validation of assays,

	biomarkers and tools for monitoring treatment outcomes in clinical trials, stratifying patients and optimising a personalised approach to treatment.
Expand Australian research-driven, clinical trial activity relating to innovative cell and gene-based therapies for MS.	Establish a competitive fund to support Australian clinical research centres to participate in international collaborations for the development and trialling of innovative, emerging cell- and gene-based therapies for MS, with initial priorities to include AHSCT, mesenchymal stem cells, and cell-based therapies targeting established risk factors and disease mechanisms in progressive MS.

Term of Reference 4

Without compromising the assessment of safety, quality, efficacy or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

Current issues and possible solutions:

Improve consumer engagement

Consumers are not provided with support, education, or updates throughout the process by either the sponsors or Government. This includes a lack of clarity in the overall process and in the timing of information for consumers including an impenetrable government website leading to an inability to manage consumer expectations.

The establishment of the Medicine Status Web-site was a good attempt at providing consumers with a vehicle to “search for and monitor the status of medicines as they progress through the Pharmaceutical Benefits Scheme (PBS) listing process” but there is still much more to be done to improve consumer engagement with the entire process.

We acknowledge that peak consumer organisations such as MS Australia have a role to play in informing our community about TGA and PBAC developments and encouraging people with MS to make submissions. This work is made difficult at present because the process remains “mysterious” to most consumers and, if they were to consider making a submission, have to “imagine” what the impact of a new drug might have on their life.

We think it is essential to provide those directly affected – patients and clinicians – with appropriate, clear, accessible publicly available information on HTA processes plus updates and feedback throughout the process.

Speeding up the process

There is inadequacy of speed to market in Australia when drugs are already available overseas. Also, the current process has no set time limits for commercial (i.e. pricing) negotiations which can lead to a protracted process delaying cost effective access to treatment.

Improved, open collaboration with international regulatory authorities such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) together with pharmaceutical companies regarding international approval and reimbursement contract negotiations would improve this process.

The setting of a time limit on pricing negotiations between the government and the sponsor would provide some certainty regarding access to treatment and managing consumer’s and clinician’s expectations.

Lack of patient-specific measures

There are few patient specific measures included in the evaluation of a new drug. Measure such as: Patient Reported Outcome Measures (PROMs); Patient Reported Experience Measures (PREMs); and Quality of Life scores, are not routinely collected during research and clinical trials or included in the HTA process.

A solution is to ensure the inclusion of patient measures and real-world evidence in the HTA process including clinical trials. This should include encouraging pharmaceutical companies to inform and include consumers in their TGA and PBAC submissions and to document patient reported outcomes.

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Key MS facts & figures

- MS causes significant disruption and can cause chronic disability to people in the prime of their lives and therefore has a substantive health burden and economic cost to the Australian health system.
- The prevalence of MS in Australia has increased by over 20% since 2010 – yet experts predict that 90% of MS cases could be preventable.
- 10 people on average are diagnosed with MS every week.
- The average age of diagnosis is between 30-40 and around 75% of those affected with MS in Australia are female.
- There is overwhelming evidence that MS is caused by an autoimmune process with both genetic and environmental contributors.
- The direct and indirect costs to the Australian community are increasing and now exceed $1.75 billion every year. Nearly 32% of this figure is through the lost wages for Australians living with MS and their carers.
- 12 therapies are available for relapsing MS but treatment response varies enormously and methods to target and personalise treatment to optimise management and prevent disability accumulation are urgently needed.
- Only one therapy has been approved by the Australian Therapeutic Goods Administration (TGA) for progressive forms of MS, but is yet to be PBS-listed. Solutions to stop and reverse the progress of MS for people with progressive forms of MS are urgently needed.
- Australia has a mid to high incidence of MS compared with other countries, with 105 Australian people in every 100,000 having a diagnosis of MS. As with the global prevalence of MS, there is a significant latitudinal gradient in MS prevalence in Australia, where the prevalence of MS in Tasmania is double that of Queensland[8].

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[8] *The Health Economic Impact of Multiple Sclerosis in Australia 2017 report,* commissioned by MS Research Australia and prepared by the Menzies Institute for Medical Research, University of Tasmania https://msra.org.au/wp-content/uploads/2018/08/health-economic-impact-of-ms-in-australia-in-2017_msresearch-australia_web.pdf