



POSITION STATEMENT

Development and approval of drugs to treat motor neurone disease

Background

ALS/MND associations globally are excited and enthusiastic about the new approaches and new compounds that are being tested for people with ALS/MND and are hopeful that one or more of these will become a therapy with substantial impact on slowing down or perhaps even stopping ALS/MND in the near future.

There is an urgency to find treatments for this disease which has such a rapid progression and devastating impact. MND Australia supports and commends the many people and organisations committed to identifying effective treatments more rapidly through initiatives, funding and collaborations to improve clinical trial design and encourages rigorous scientific testing of promising compounds.

Through its research arm, the MND Research Institute of Australia (MNDRIA), MND Australia funds only the best MND research that has the greatest chance of leading to the development of effective treatments and improving the lives of people with MND.

There is one medication approved for treatment of MND in Australia – riluzole (sold as Rilutek™ or APO-Riluzole). Riluzole probably prolongs median survival by two to three months. Research indicates that people who start taking riluzole early in their disease progression are more likely to remain in the milder stages of the disease for longer than those not taking riluzole. The only other therapy that has been shown to slow progression in a subset of people with MND, [edaravone](#), has been approved for use in Japan, South Korea and the United States.

Drug development process

A drug's journey from initial development in the laboratory to routine use in treating patients is a very long one, involving many stages and taking many years.

After a promising compound is discovered, lab studies involving testing in cell and animal models of the disease are needed to provide the best possible assurance that the drug might be effective and will be safe for people to take. Patients only get involved in the last stage of testing before a drug is licensed for general use in treating a disease. This final stage of testing is known as a clinical trial.

Clinical trials

Clinical trials are research studies on people that determine whether drugs are safe, the correct dose and whether they work. They are divided into different stages, called [phases](#). Drugs must perform well enough in each phase to be allowed to progress on to the next one.

Typically, drugs must successfully complete a three-phase process before being submitted by the pharmaceutical company for approval by a country's health authority.

In Australia, following approval by the [Therapeutics Goods Administration](#) (TGA), if the drug demonstrates cost-effectiveness, it may then be listed on the Pharmaceutical Benefits Scheme (PBS). [The Pharmaceutical Benefits Scheme](#) (PBS) is an Australian Government program that subsidises medicines to make them more affordable.

Why do we need clinical trials?

[Clinical trials in ALS/MND](#) are taking place worldwide. [In Australia](#), clinical trials are governed by [national ethics guidelines and codes of conduct](#). Anyone taking part in a trial must be fully informed about the objectives of the research, what is expected of them and any risks and potential inconveniences that may be experienced during and after the trial. If you are thinking of being included in a trial, as part of the process of informed consent you should be given a participant information and consent form that contains details of the trial and your participation. See [Considerations when accessing trial drugs or therapies not yet licensed in Australia](#)

MND is a disease that can present and progress quite differently from one individual to the next. The differences in how MND progresses are particularly apparent when looking at small numbers of people for short periods of time. Therefore, properly -controlled, relatively large studies are the best way to test whether a drug works. This was illustrated in the clinical trials of [dex Pramipexole](#). Results from a phase II trial of dex Pramipexole found that the drug was safe and well tolerated in 102 people and indicated a significant benefit. Unfortunately the phase III trial of 943 people showed that dex Pramipexole was not beneficial for people living with MND.

Supplying a drug broadly without a larger trial exposes people living with MND to possible side effects that may reduce their quality of life and risks making them worse. For example, excitement about [lithium as a therapy](#) for MND was followed by no effect (or worsening of symptoms) in subsequent studies.

A multinational group of neurologists, basic scientists, statisticians, patient advocates, representatives from the pharmaceutical industry, as well as regulatory agencies and patients with ALS/MND are currently revising, updating and expanding the Guidelines for Clinical Trials in ALS/MND. See [draft guidelines](#)

Current clinical trials in Australia

The [Australian New Zealand Clinical Trials Registry](#) lists clinical trials including MND studies in Australia and New Zealand, as well as trials from across the globe that have been completed, are currently recruiting or are pending.

A number of sites in Australia are undertaking Phase 1/2 Clinical Trials to test safety and efficacy of promising compounds. The number of people able to be enrolled in these early phase clinical trials is limited. The MND Australia website includes latest information and [FAQs on current Australian clinical trials](#).

Expediting trials of drugs that treat serious and life-threatening diseases

In some countries, drug companies can apply to the health authority to request permission to speed up the development and availability of drugs that treat serious or life-threatening diseases.

In recent years, most drug development for ALS/MND has occurred in the United States.

Fast Track designation

The United States Food and Drug Administration (FDA) has granted [Fast Track](#) designation to the following drugs and therapy that are being developed to treat motor neurone disease (MND):

- tirasemtiv (Cytokinetics, Incorporated) – currently in Phase III trial
- NurOwn stem cell therapy (BrainStorm Cell Therapeutics) – preparations underway for Phase III trial
- GM604 (Genervon Biopharmaceuticals) – there is no independently verifiable data supporting the efficacy or safety of GM604. [Read a review of GM604](#) by ALSUntangled.

Once a drug receives Fast Track designation, early and frequent communication between the FDA and the drug company is encouraged throughout the entire drug development and clinical trial process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

Accelerated Approval designation

When studying a new drug, it can sometimes take many years to learn whether a drug actually provides a real effect on survival and on how a patient feels or functions. Mindful of the fact that it may take an extended period of time to measure a drug's intended clinical benefit the FDA has instituted the [Accelerated Approval](#) regulations that allow drugs for serious conditions to be approved more quickly.

The FDA granted [Accelerated Approval](#) to edaravone (Radicut) which received approval in May 2017. It is anticipated that the drug will be available in the US from August 2017

Ways to access therapies not yet licensed in Australia

The Australian Therapeutic Goods Administration (TGA) does not include fast track or accelerated approval pathways for drug development or availability.

Special Access Scheme

Individuals, following discussion with their neurologist, may be able to apply to access products that have been not yet been approved in Australia through the [Special Access Scheme](#).

Authorised Prescriber Scheme

The [Authorised Prescriber Scheme](#) allows approved medical practitioners authority to prescribe a specified unapproved medicine to patients who are identified by their medical condition. If a medical practitioner becomes an Authorised Prescriber they may prescribe the product to patients in their immediate care, with the condition specified, without seeking further approval from the TGA.

Off-label prescribing

Sometimes a medicine may be licensed for one condition, but could have the potential to be used to treat other conditions or illnesses. This is referred to as "off-label" use. An unlicensed medication may be prescribed by doctors if they think it is likely to be effective for their patient and that any benefits outweigh potential side-effects or risks. Drugs not listed on the PBS for the treatment of MND are not subsidised and the full cost of the drug will apply.

Personal importation scheme

Individuals can legally import most therapeutic goods for personal use under the [Personal Importation Scheme](#). It is important to note that such therapeutic goods may not be approved for supply in Australia; this means there are no guarantees about their safety or quality.

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Considerations when accessing therapies not yet licensed in Australia

There are many considerations related to the administration of a therapy not yet approved by the TGA. People living with MND are encouraged to discuss these therapies with their neurologist and consider:

- Unknown risks and side effects not yet identified through trials
- Delivery of the medication
 - Some therapies may require hospital admission and access to suitably trained staff – public hospitals and staff may not be able to deliver drugs not yet approved by the TGA and therefore there may be costs to be met by the patient for delivery.
- The person may render themselves ineligible for inclusion in other clinical trials of potential new therapies that open for enrolment whilst receiving the therapy
- The cost of accessing the treatment over the longer term.

MND Australia's position

It can be difficult for people living with MND and their families to endure the wait for the development and approval of an effective treatment and cure. MND Australia acknowledges the urgency to advance research to better understand MND and the desperate need for an effective treatment.

MND Australia believes any drug must have been proven to be safe and to improve health outcomes of people living with MND before it is made available for widespread use.

See also [MND Australia's Position Statement](#) on alternative therapies for people diagnosed with MND.

MND Australia together with its members, the [State MND Associations](#), spearheaded the lobbying efforts for approval of riluzole by the TGA in 2001 and subsequent listing on the Pharmaceutical Benefits Scheme in 2003.

MND Australia will continue to work collaboratively to promote access to clinical trials and to ensure that therapies that have been proven to be safe and effective are made available to people living with MND in Australia as quickly as possible.

MND Australia is an active member of the [International Alliance of ALS/MND Associations](#) and is committed to keeping the Australian MND community up to date on any and all promising new therapies.

MNDRIA has been the preeminent independent funder of MND research in Australia for 30 years providing over \$25 million to the best research across Australia. This investment has led to a thriving MND research community in Australia, significant advances in understanding MND and the development of promising compounds for clinical trials. MND Australia and its members are committed to continuing to grow and support the best MND research in Australia to move us closer to realising our shared vision of a World without MND.

On behalf of the MND Australia board and state MND Associations

Signed: David Ali (President)

Dated: 31 August 2017