Edaravone
June 2017

Background
The drug edaravone was developed by Mitsubishi Tanabe (MT) Pharma Corporation in Japan. Edaravone was originally marketed for use in stroke patients. Later, the company decided to test edaravone in people with ALS/MND. After a series of Phase 3 trials in Japan in 2015, regulatory bodies approved edaravone to treat people with ALS/MND in Japan and South Korea. Edaravone is marketed under the brand name Radicut® in Japan and South Korea.

In June of 2016, MT Pharma America submitted an application to the FDA for regulatory approval in the US. This application was approved by the FDA on 5 May 2017. Edaravone will be marketed as Radicava™ in the US and will be distributed commercially by MT Pharma America.

What is edaravone?
Edaravone is a drug with antioxidant properties. It protects nerve cells by mopping up damaging "free radicals" in the body.

Edaravone is administered at a hospital or clinic by a doctor via an intravenous infusion. It should be administered in 28-day cycles. For the initial cycle, the treatment is infused for 14 consecutive days, followed by a two-week drug-free period. All cycles after that are infused for 10 days within a 14-day period, followed by a two-week drug-free period. It takes 60 minutes to receive each 60 mg dose.

A company called Treeway is currently working to develop an oral preparation of the drug for testing.

Some adverse reactions of edaravone have been reported and include bruising, walking difficulties, headache, inflammation, eczema and dermatitis.

What does the trial data tell us to date?
The clinical trials conducted to date in Japan suggest that edaravone slows the progression of MND, potentially helping people preserve function longer. It appears to work in a **subset of people** and is most beneficial as an early treatment.

In The Lancet Neurology, Makoto Akimoto and colleagues report that the edaravone-treated group showed a significantly smaller decline in ALS Functional Rating Scale (ALSFRS-R) score compared with placebo. This suggests a beneficial effect of the drug over a period of 24 weeks in this cohort of people with ALS/MND. The group was not followed long enough to gather information on the longer-term effects and to establish impact on length of life.

A comment article by Orla Hardiman and Leonard van den Berg published in The Lancet estimated that using the stated criteria and applying them to population-based registers in Ireland and the Netherlands, less than 7% of patients with ALS/MND would have met the rules for taking part in the study. This is supported by data from the Australian MND Registry. It is estimated that around 140 people diagnosed with MND in Australia would meet the specific eligibility criteria for access to edaravone:

- Aged 20 to 75
- Forced vital capacity of 80% or more
    - i.e breathing not affected
- A score of at least 2 on all items of the ALS Functional Rating Scale – R (ALSFRS-R)
    - i.e function not affected too much
- Disease duration of 2 years or less

It remains to be determined whether edaravone might be effective in a wider population of patients with ALS/MND who do not meet the stated criteria, but at this stage, there is no clear trial data.

How can I access edaravone?
At this time, edaravone is only approved for use in Japan, South Korea and the United States. Based on current information, it is anticipated edaravone will be available in the US from August 2017.

MND Australia's position statement on the development and approval of drugs to treat MND outlines ways that people can gain access to drugs that have not been approved for use in Australia.

Until approved by the TGA, Australians who wish to access edaravone from overseas will need the cooperation of an Australian medical professional to prescribe through the Special Access Scheme or the Authorised Prescriber Scheme. This process can be challenging and expensive. The current cost of buying edaravone from Japan is around $US26,000 for a six month course of treatment. The cooperation of local medical professionals to administer the drug in a hospital and to monitor the patient is also required.

Will edaravone be available in Australia?
Mitsubishi Tanabe Japan is responsible for making an application to the Therapeutic Goods Administration (TGA) to approve edaravone for the treatment of MND in Australia. As yet no application has been made.

The TGA usually requires data over a longer period of time than the trial data available on edaravone to date and evidence on whether the drug can extend life.

MND Australia and 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. We will continue to work collaboratively 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.

As an active member of the International Alliance of ALS/MND Associations, MND Australia will continue to monitor the global response to edaravone and make this information available to the MND community in Australia as we learn more.

Edaravone News June 2017

The ALS Association: Press Release

The ALS Association: FAQ About Radicava

ALS Therapy Development Institute

ALS Hope Foundation

Les Turner ALS Foundation

MND Association of England, Wales and Northern Ireland

MND Association of England, Wales and Northern Ireland – edaravone a month on since the FDA announcement

Other Resources

Official FDA Announcement

Official MT Pharma America Press Release

Reuters News Story

Published papers

Makoto Akimoto and colleagues on behalf of the Edaravone (MCI-186) ALS 19 Study Group, 15 May 2017, The Lancet, *'Safety and efficacy of edaravone in well-defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial'.*

http://thelancet.com/journals/laneur/article/PIIS1474-4422(17)30115-1/abstract

Orla Hardiman and Leonard H ven den Berg, The Lancet, 15 May 2017, '*Edaravone: a new treatment for ALS on the horizon?'*

http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(17)30163-1/fulltext?rss=yes