Living Better for Longer: MND Australia Fact Sheet EB4

Riluzole

What you should know

Riluzole:

- is an anti-glutamate medication
- does not cure MND but may slow disease progression
- probably prolongs average survival by 6 to 19 months
- is best taken soon after diagnosis to have the greatest benefits
- has only been studied for its safety and efficacy in ALS, including progressive bulbar palsy (PBP).

About riluzole

Some neurones in the brain and spinal cord release an amino acid, called glutamate, to carry signals to other neurones. Glutamate is released at the synaptic junction where two neurones meet. If too much glutamate is released by the neurone sending a signal, it can over-stimulate the neurone receiving the signal. This is called glutamate excitotoxicity. Riluzole is an anti-glutamate medication that appears to block the release of glutamate from neurones. Riluzole may also exert some effects on MND through other mechanisms but this has yet to be firmly established.

Riluzole and MND

Motor neurone disease is a general term applying to progressive, degenerative disorders affecting the motor neurones. Motor neurones carry signals from the brain to the muscles. In people with motor neurone disease, the motor neurones deteriorate and can no longer carry these signals.

Researchers have found that glutamate excitotoxicity may accumulate to harmful levels and contribute to motor neurone deterioration (Miller et al. 2012). The effect of riluzole, an anti-glutamate medication, has been investigated on people with the following forms of motor neurone disease:

- amyotrophic lateral sclerosis (ALS) – that first affects muscles controlling the limbs
- progressive bulbar palsy (PBP) – that first affects bulbar muscles (speech and swallowing muscles) but often progresses to ALS.

Medical literature about riluzole generally uses the term amyotrophic lateral sclerosis (ALS) as an umbrella term to include progressive bulbar palsy (PBP). This is because there is:

- uncertainty about the cause and mechanism of motor neurone deterioration
- debate about the extent to which different forms are simply variations in the same disease process or whether there are several different disease mechanisms
- international difference in terms used to describe motor neurone disease.

Getting riluzole

Riluzole is manufactured under the names Rilutek™ and APO-Riluzole. In Australia riluzole is available for eligible people at a subsidised price on the Pharmaceutical Benefits Scheme (PBS) under an authority prescription. To get your first authority prescription for riluzole you must be diagnosed with the ALS form (including PBP) of MND by a neurologist, have had the disease for five years or less and meet several other criteria. Your doctor needs to provide your date of diagnosis and information about your forced vital capacity* with the first application. Subsequent prescriptions may be issued by your general practitioner.

Teglutik® (riluzole) a liquid formulation (for ease of swallowing or use via PEG tube) of riluzole, distributed by Seqirus (Australia) Pty Ltd, was listed on the PBS in April 2019 under the same prescribing conditions as Rilutek™ and APO-Riluzole.

*Forced vital capacity (FVC) is a respiratory function test. For more information about FVC see Living Better for Longer Fact Sheet Breathing and motor neurone disease: an introduction (EB5).

Evidence about riluzole

For people with MND who have ALS (including PBP)

In their analysis of the results of four double-blind randomised controlled trials, involving 1477 people with the ALS form (including PBP) of motor neurone disease, Miller et al. (2012) found that taking 100 mg of riluzole daily:

- probably prolongs median survival by two to three months - (median is the mid-point – half those taking riluzole have survival prolonged by more than two to three months).

One of the trials included in the analysis only enrolled people older than 75 years or who had the disease for more than five years. The inclusion of this trial decreased median survival time.

Several riluzole studies were not included in the analysis because they were not double-blind randomised controlled trials (the best evidence). These excluded studies reported a median survival prolongation ranging from 6 to 21 months. It is not known what other factors, such as other interventions and stage of the disease, might have influenced the results of these excluded studies (Miller et al. 2012).

More recently a review undertaken by Andrews et al. (2020) suggests that taking riluzole may be more effective than first thought. A review of 15 population studies undertaken by clinicians treating people with ALS/MND found that people who took riluzole, when compared with those who didn't, generally lived longer, anywhere between 6 to 19 months longer (Andrews et al. 2020). The review, which was of real world evidence studies, provides additional insights on the effectiveness of riluzole as an important treatment option for people living with ALS. Additionally, the review found that in several population studies the greatest benefit of riluzole occurs early in the course of disease thereby providing evidence both for early and prolonged riluzole therapy (Andrews et al. 2020).

For people with other forms of MND

All trials of riluzole published in the medical literature have only allowed people diagnosed with the ALS form (including PBP) of motor neurone disease to participate. There is strong clinical support for the use of riluzole in other forms of motor neurone disease (National Institute for Clinical Excellence 2001). However, in Australia, subsidised PBS prescriptions for riluzole are limited as a treatment for the ALS (including PBP) forms of motor neurone disease alone (Australian Government Department of Health and Ageing 2009).

Adverse effects

Adverse effects from riluzole are relatively minor and, for the most part, reversible after stopping the drug (Miller et al. 2012). The most common adverse effects are fatigue and nausea. Riluzole affects liver function and should be prescribed with care in people who have pre-existing problems with liver function.

Ongoing liver function testing

Regular blood testing to monitor liver function (every month for three months, then every three months for a further nine months and annually thereafter) is recommended for people taking riluzole (National Institute for Clinical Excellence 2001).

Getting advice about riluzole

Your neurologist can offer advice about riluzole. If you have been refused access to riluzole under the PBS and think you are eligible, talk with another neurologist or contact your MND clinic. Contact your local MND Association for more information.

References:

Andrews JA, Jackson CE, Heiman-Patterson TD, Bettica P, Brooks BR, and Pioro EP 2020, Real-world evidence of riluzole effectiveness in treating amyotrophic lateral sclerosis, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, Ahead of Print 1-10, https://doi.org/10.1080/21678421.2020.1771734

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Miller RG, Mitchell JD, Moore DH 2012, Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND), *Cochrane Database of Systematic Reviews* 2012(3). Art. No CD001447

National Institute of Clinical Excellence 2001, NICE: Guidance on the use of riluzole (Rilutek) for the treatment of motor neurone disease, http://guidance.nice.org.uk/TA20

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Pharmaceutical Benefits Scheme, Department of Health, accessed 3 April 2020, Riluzole, http://www.pbs.gov.au/medicine/item/11662T-8664B

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Breathing and motor neurone disease: medications and non-invasive ventilation (EB7)
Considering gastrostomy - PEG and RIG (EB8)