Tofersen therapy for SOD1-type motor neurone disease (MND)

There has been quite a lot of discussion in the international media about Tofersen (brand name Qalsody), an investigational drug developed by the company Biogen to treat MND caused by a mutation in the *SOD1* gene.

Tofersen was granted accelerated conditional approval by the Food & Drug Administration (FDA) in the United States in April 2023. In late February 2024, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended approval be granted for marketing under exceptional circumstances.

MND NZ is encouraged by the positive opinion of the CHMP and what this means for people with *SOD1*-type MND. We are in dialogue with Pharmac and international MND associations and will monitor developments to inform the best access pathway to Tofersen in New Zealand.

What is SOD1-type MND?

SOD1-type MND is MND that is caused by an error in the *SOD1* gene. In people of European descent, *SOD1* gene mutations cause about 15-30% of familial MND cases and about 2% of sporadic MND cases. *SOD1* gene mutations are the most common genetic cause of MND in people of Asian descent.

How does Tofersen work?

Tofersen works by targeting the 'photocopy' of the SOD1 gene (called SOD1 RNA) to reduce the amount of SOD1 protein being made. It is only effective in *SOD1*-type MND and cannot be used in other types of MND. The medication is given once a month via injection into the spinal fluid.

Does Tofersen benefit people with SOD1-type MND?

The first trial of this treatment, known as the VALOR trial, included 108 adults with SOD1 MND who were treated with either Tofersen or a sham drug (placebo) for ~6 months. The trial showed that Tofersen reduced signs of the

disease in the spinal fluid; SOD1 protein levels and a marker of neuron damage (neurofilament light) were both reduced. However, the primary goal of the trial was to test if Tofersen slowed the rate of disease progression, and it did not.

The trial was then continued for another ~6 months with the same group of patients. The patients who had been treated with Tofersen for the full 12 months now showed potential benefit in function and survival. It has been suggested that earlier treatment, even before symptoms begin, may provide more benefit and there is another trial, called the ATLAS trial, underway to test that. This trial is predicted to be completed in 2027.

Who can access Tofersen and how?

Biogen has announced an early access program that eligible patients can apply to. To be eligible you must have been diagnosed with MND caused by a *SOD1* gene mutation. You can request testing for this gene by your neurologist or pay to be tested in private. However, this treatment may not be suitable for everyone, and individuals should discuss this treatment with their neurologists or physicians.

Statement published: 4 April 2024

Contributors: Dr Emma Scotter, Head of Motor Neuron Disease Research at the University of Auckland; Dr Natalie Gauld, ONZM, Research Advisor and Best Practice Advocate at Motor Neurone Disease NZ; Dr Alan Stanley, Consultant neurologist in the Hawkes Bay and Motor Neurone Disease NZ board member.