

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tofersen for treating amyotrophic lateral sclerosis caused by SOD1 gene mutations [ID3767]

Final scope

**Remit/evaluation objective**

To appraise the clinical and cost effectiveness of tofersen within its marketing authorisation for treating adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

**Background**

Amyotrophic lateral sclerosis (ALS) is the most common type of motor neurone disease (MND). It is a neurodegenerative condition that affects the brain and spinal cord and is characterised by the degeneration of motor neurones, leading to muscle weakness. Initial symptoms of ALS vary and may include muscle weakness, wasting, cramps and stiffness of arms and/or legs, problems with speech and/or swallowing or, more rarely, breathing problems.<sup>1</sup> According to the literature about 5-10% of people with ALS have a family history of the disease (known as familial ALS) and about 90% do not (known as sporadic disease).<sup>2</sup> SOD1 gene mutations have been identified to cause around 15% of familial and 1% of sporadic ALS.<sup>3</sup>

Prevalence estimates are uncertain, but a maximum of 4000 people in England and Wales are thought to have MND, of whom 90% have the ALS type of the disease.<sup>4,5</sup> It can affect adults of any age, but most people are diagnosed over the age of 50.<sup>1</sup> ALS is more common in men than women<sup>6</sup>. Approximately 1,500 people are diagnosed with ALS per year in the UK<sup>7</sup>. The rate of disease progression is highly variable but half of people die within 30 months of symptom onset. In total, around 2% of all ALS cases are caused by mutations in the SOD1 gene.<sup>9</sup> The rate of disease progression varies between individuals dependant on a number of factors including the SOD1 gene mutations type.<sup>9</sup>

There is currently no cure for ALS. NICE technology appraisal 20 recommends riluzole for treating ALS. NICE guideline 42 on the assessment and management of motor neurone disease recommends care by a multidisciplinary team including, where appropriate:

- Psychological and social care support.
- Interventions to manage symptoms, for example pharmacological treatment for muscle problems.
- Equipment to aid activities of daily living and mobility.
- Support for nutrition, communication, and respiratory function including surgical interventions if necessary (for example, to enable feeding).

**The technology**

Tofersen (Qalsody, Biogen) has a marketing authorisation in the UK for the treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

<b>Intervention(s)</b>	Tofersen
<b>Population(s)</b>	Adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene
<b>Subgroups</b>	<p>If the evidence allows the following subgroups will be considered:</p> <ul style="list-style-type: none"> <li>• Choice of background therapy</li> <li>• Stage/severity of the disease</li> <li>• SOD1 mutation type</li> </ul>
<b>Comparators</b>	<p>Established clinical management without tofersen, including but not limited to:</p> <ul style="list-style-type: none"> <li>• Best supportive care (including riluzole if appropriate)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• disease progression</li> <li>• time to permanent ventilation (tracheostomy or more than 22 hours a day of non-invasive ventilation)</li> <li>• respiratory status</li> <li>• nutritional status</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>The use of tofersen is conditional on the presence of SOD1 gene mutations. The economic modelling should include the costs associated with diagnostic testing for SOD1 in people with ALS who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: <a href="https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation">https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation</a>).</p>
<p><b>Other considerations</b></p>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p><b>Related NICE recommendations</b></p>	<p><b>Related technology appraisals:</b></p> <p><a href="#">Guidance on the use of riluzole (Rilutek) for the treatment of motor neurone disease</a> (2001) NICE technology appraisal guidance TA20.</p> <p><b>Related NICE guidelines:</b></p> <p><a href="#">Motor neurone disease: assessment and management</a> (2019) NICE guideline NG42.</p> <p><b>Related HealthTech guidance:</b></p> <p><a href="#">Intramuscular diaphragm stimulation for ventilator-dependent chronic respiratory failure caused by motor neurone disease</a> (2017) NICE interventional procedures guidance HTG450.</p> <p><b>Related quality standards:</b></p> <p><a href="#">Motor neurone disease</a> (2016) NICE quality standard QS126.</p>

### References

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8. Talbot K (2009). [Motor neuron disease](#). Practical Neurology. 9(5):303.
9. Simon NG et al. (2014) [Quantifying disease progression in amyotrophic lateral sclerosis](#). Ann Neurol. 76(5):643-657.