**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**
**Health Technology Evaluation**

# Tofersen for treating amyotrophic lateral sclerosis caused by SOD1 gene mutations

## Draft scope

### Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of tofersen within its marketing authorisation for treating amyotrophic lateral sclerosis caused by superoxide dismutase 1 (SOD1) gene mutations.

### 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[1]. 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)[2]. SOD1 gene mutations have been identified to cause around 15% of familial and 1% of sporadic ALS[3].

Approximately 4000 people in England and Wales have MND of which 90% have the ALS type of the disease[4,5]. It can affect adults of any age, but most people are diagnosed between the ages of 50 and 70[6]. ALS is more common in men than women[7]. Approximately 1,500 people are diagnosed with ALS per year in the UK[8] and more than half die within three years of diagnosis[9]. The rate of disease progression varies between individuals and the presence of SOD1 gene mutations could be associated with shorter survival times[10].

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 (brand name unknown, Biogen) does not currently have a marketing authorisation in the UK for treating ALS. It has been studied in clinical trials compared with placebo in adults with ALS and confirmed SOD1 mutations.

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| **Intervention(s)** | Tofersen |
| **Population(s)** | People with amyotrophic lateral sclerosis |
| **Subgroups** | If the evidence allows the following subgroups will be considered:<br>• Choice of background therapy<br>• Rate of progression |
| **Comparators** | Established clinical management without tofersen, including but not limited to:<br>• Riluzole<br>• Best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• disease progression<br>• time to first tracheotomy<br>• adverse effects of treatment<br>• health-related quality of life (for patients and carers). |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br>The availability and cost of biosimilar and generic products should be taken into account.<br>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: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation). |

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| **Other considerations** | 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. |
| **Related NICE recommendations** | **Related Technology Appraisals:**<br>'Guidance on the use of Riluzole for the treatment of Motor Neurone Disease' (2001). NICE Technology Appraisal 20. Guidance on static list.<br>**Appraisals in development (including suspended appraisals)**<br>'Masitinib for treating amyotrophic lateral sclerosis' NICE technology appraisals guidance [ID967]. Publication date to be confirmed [suspended]<br>**Related Guidelines:**<br>'Motor Neurone Disease: assessment and management' (2016). NICE guideline 42. Last updated July 2019.<br>**Related Interventional Procedures:**<br>'Intramuscular diaphragm stimulation for ventilator-dependent chronic respiratory failure caused by motor neurone disease' (2017) Interventional procedures guidance 593<br>**Related Quality Standards:**<br>'Motor Neurone Disease' (2016) NICE quality standard 126 |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 11: Adult specialist neurosciences services<br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017<br>NHS RightCare (2019) RightCare Progressive Neurological Conditions Toolkit |

**Questions for consultation**

Is the population defined appropriately?

How many people have amyotrophic lateral sclerosis (ALS) and confirmed superoxide dismutase 1 (SOD1) gene mutations in England?

Are people with ALS routinely tested for genetic mutations in the NHS?

Would tofersen be used in combination with riluzole, or after riluzole in people with ALS and confirmed SOD1 gene mutations?

Have all relevant comparators for tofersen been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for amyotrophic lateral sclerosis?

Are the outcomes listed appropriate?

Are the subgroups listed appropriate?

Would tofersen be a candidate for managed access?

Do you consider tofersen to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of tofersen can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which tofersen will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

**References**

1. Motor neurone disease association (2019) Basic facts about MND. Accessed August 2021.

2. Tang L, Ma Y, Liu X-l, Chen L, Fan D-s (2019). Better survival in female SOD1-mutant patients with ALS: a study of SOD1-related natural history. Translational Neurodegeneration. 8(1):2.
3. Zou et al. (2017). Genetic Epidemiology of Amyotrophic Lateral Sclerosis: A Systematic Review and Meta-Analysis. J Neurol Neurosurg Psychiatry. 88(7):540-549.
4. National Institute for Health and Care Excellence (2016). Motor neurone disease: assessment and management. NICE guideline NG42. Accessed August 2021.
5. Sheffield MND Care and Research Centre (2015) What is the difference between MND and ALS? Accessed September 2021.
6. Motor neurone disease association (2019) Introduction to motor neurone disease. Accessed August 2021.
7. McCombe PA, Henderson RD (2010). Effects of gender in amyotrophic lateral sclerosis. Gender Medicine. 7(6):557-70.
8. Gowland A et al. (2019). Predicting the future of ALS: the impact of demographic change and potential new treatments on the prevalence of ALS in the United Kingdom, 2020-2116. Amyotrophic Lateral Sclerosis Frontotemporal Degeneration. 20(3-4):264-274.
9. Talbot K (2009). Motor neuron disease. Practical Neurology. 9(5):303.
10. Simon NG et al. (2014) Quantifying disease progression in amyotrophic lateral sclerosis. *Ann Neurol*. 76(5):643-657.