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New treatment for rare motor neurone disease recommended for approval

EMA has recommended granting a marketing authorisation in the European Union for a new therapy for the treatment of adult patients with amyotrophic lateral sclerosis (ALS), a rare and often fatal disease that causes muscles to become weak and leads to paralysis. Qalsody (tofersen) is indicated for the treatment of adults with ALS, who have a mutation in the superoxide dismutase 1 (SOD1) gene.

In patients with amyotrophic lateral sclerosis (ALS) the nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing increasing loss of muscle function and paralysis of voluntary muscles, including respiratory muscle, which ultimately leads to respiratory failure. ALS is a devastating disorder. The mean survival time with ALS is two to five years.

The exact causes of ALS are unknown but are believed to include genetic and environmental factors. In approximately 2% of people living with ALS, the condition is caused by a genetic mutation (change) that leads to the production of defective SOD1 enzymes, causing nerve cells to die.

Currently, there is only one treatment for ALS (riluzole) authorised in the EU. Patients are offered supportive treatment to relieve the symptoms of the disease, such as physical, occupational or speech therapy and breathing support. There is a large unmet medical need for effective therapies that preserve muscle function and prolong the life of patients with ALS.

Qalsody is an antisense oligonucleotide that binds to the mRNA of the SOD1 gene to reduce the production of SOD1 protein. By reducing the amount of defective SOD1 protein, this medicine is expected to improve the symptoms of ALS.

The opinion by EMA's committee for human medicines (CHMP) is based on the totality of evidence, including the targeted way the drug works, effects observed in a SOD1 animal model, biomarkers and clinical data.

Clinical data were obtained from a 28-week, randomized, double-blind, placebo-controlled clinical study in 108 patients aged 23 to 78 years with weakness attributable to ALS and a SOD-1 gene mutation confirmed by a central laboratory. The study randomly assigned 108 patients in a 2:1 ratio to receive treatment intrathecally (through a spinal injection) with either Qalsody or placebo for 24 weeks. Plasma neurofilament light chain (NfL) was measured during the study as a marker of damage and deterioration of axons (thread-like structures attached to nerve cells that send out signals away from the cell). Reductions of approximately 60% in plasma NfL concentrations were observed in patients who received Qalsody compared to the placebo group, suggesting reduced neuronal injury. There was also a numerical improvement noted in the physical abilities of patients who received Qalsody compared to the study participants who received placebo, as measured by the standard rating scale known as 'ALS Functional Ratings Scale–Revised' (ALSFRS-R)[1].

The CHMP requested the applicant to submit data post authorisation to further characterise the long-term efficacy and safety of Qalsody, on the basis of an open-label long-term extension study, collaboration with two disease registries and an observational registry-based study. In addition, it will be investigated if the use of tofersen can delay or even prevent emergence of clinically manifested ALS in presymptomatic SOD1-ALS patients.

The most commonly reported side effects were pain, fatigue, pyrexia (fever), arthralgia (joint pain), myalgia (muscle pain) and increased levels of white blood cells and proteins in the cerebrospinal (brain and spinal cord) fluid.

The CHMP consulted patient representatives during the assessment of benefits and risks of Qalsody to ensure that patients' needs and their perspective are taken into account in the regulatory decision-making process.

The recommendation made by the CHMP is for a marketing authorisation under exceptional circumstances. This route of authorisation allows patients access to medicines for which comprehensive data cannot be obtained under normal conditions of use, either because there are only very few patients with the disease, the collection of complete information on the efficacy and safety of the

medicine would be unethical, or there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.

The opinion adopted by the CHMP is an intermediary step on Qalsody's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on the EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role or use of this medicine in the context of the national health system of that country.

Notes:

1. The applicant for Qalsody is Biogen Netherlands B.V.
2. Qalsody was designated as an orphan medicinal product on 29 August 2016.
3. Following this positive CHMP opinion, the Committee for Orphan Medicinal Products (COMP) will assess whether the orphan designation should be maintained.

Biogen's QALSODY® (tofersen), the First Therapy to Treat Rare, Genetic Form of ALS, Received Positive Opinion from CHMP

Source: **EMA**