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Newcastle University

Health Technology Briefing
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Riluzole oral film formulation for amyotrophic lateral sclerosis

Company/Developer	Zambon Company SpA

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 25454	NICE TSID: 11779	UKPS ID: 663649

Licensing and Market Availability Plans

Completed phase I clinical trial.

Summary

Riluzole oral film formulation is in clinical development for the treatment of patients with amyotrophic lateral sclerosis (ALS), a form of motor neurone disease (MND). ALS is a progressive disease where the nerve cells responsible for sending instructions to the muscles gradually deteriorate, leading to weakness, muscle wasting and paralysis. ALS is a debilitating and life-threatening disease. The gradual loss of neurons leads to a paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure. Many patients with ALS have swallowing difficulties which can make taking standard care tablets difficult.

Riluzole acts on the nervous system although the exact way in which it works in ALS is not known. It is thought that the destruction of nerve cells in motor neuron disease may be caused by too much of the neurotransmitter glutamate. Neurotransmitters are substances that nerve cells use to communicate with neighbouring cells. Riluzole stops the release of glutamate and this may help in preventing the nerve cells being damaged. Riluzole is currently available in tablet and oral suspension forms and is indicated to extend life or the time to mechanical ventilation for patients with ALS. If licenced, the new formulation of riluzole as an oral film will provide an additional treatment option for ALS patients, particularly those with difficulty in swallowing.

Proposed Indication

Riluzole is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).[1]

Technology

Description

Riluzole oral film is a new film formulation containing riluzole which is a glutamate antagonist used to prolong the survival of patients with ALS.[2,3] Riluzole is thought to protect motor neurons in the brain and spinal cord from glutamate damage by inhibiting presynaptic glutamate release and enhancing glial and neuronal glutamate uptake, thereby reducing extracellular glutamate concentrations and blocking persistent sodium currents. However, the exact mechanism in patients with ALS is unknown.[4]

Riluzole oral film is currently in clinical development for the treatment of ALS.[5,6] In the phase I clinical trial (NCT04819438), participants were given one orodispersible film containing 50mg of riluzole and reference film-coated tablets under fasting conditions, in each of 4 subsequent periods separated by wash-out intervals of at least 7 days between consecutive administrations, according to a 2-treatment, 4-period, replicate cross-over design.[7]

Key Innovation

ALS is characterised by the degeneration and death of motor neurons that control voluntary muscle movements. This leads to severe disability including difficulty in swallowing, which complicates the ingestion of oral tablets and suspensions.[8]

Riluzole oral film is a new formulation which contains a 50 mg riluzole dose that is taken twice a day by placing it on the tongue. It dissolves automatically and requires no water.[8]

If licenced, riluzole oral film will provide a new treatment formulation option for patients with ALS.

Regulatory & Development Status

Riluzole oral film does not currently have Marketing Authorisation in the EU/UK for any indication.

Riluzole (film-coated tablet and oral suspension) currently has Marketing Authorisation in the EU/UK to extend life or the time to mechanical ventilation for patients with ALS.[9-11]

Riluzole oral film is not currently in clinical development for any other indications.[12]

Patient Group

Disease Area and Clinical Need

Motor neurone disease (MND) is a rare disease that affects the brain and nerves, causing weakness that worsens over time.[13] ALS is a form of MND and the most common type in the UK.[14] ALS is a neurodegenerative disorder characterised by the progressive degeneration and eventual death of nerve cells (neurons) in the brain, brainstem and spinal cord. ALS affects both the upper and lower motor neurons so that the transmission of messages is interrupted and muscles gradually weaken and waste away. As a result, the ability to initiate and control voluntary movement is lost. ALS affects the muscles needed to

move the arms and legs, to speak and swallow, to support the neck and trunk, and to breathe. The symptoms of ALS progress over time and, ultimately, the disease leads to ventilatory failure because affected individuals lose the ability to control muscles in the chest and diaphragm. Approximately 10 percent of all cases of ALS are hereditary, and more than 25 genes have been associated with the disease. However, the underlying cause of sporadic ALS is not known.[15]

MND affects around two in every 100,000 people in the UK each year. There are about 5,000 people living with the condition in the UK at any one time.[16] Patients with ALS account for approximately 60-70% of the total MND cases, meaning there are about 3,000-3,500 people living with ALS in the UK at any one time.[16,17] In England (2020-21), there were 3,428 finished consultant episodes (FCEs) and 2,129 admissions for motor neuron disease (ICD-10 code G12.2) which resulted in 14,700 FCE bed days and 788 day cases.[18]

Recommended Treatment Options

There is currently no cure for ALS and no effective treatment to halt or reverse the progression of the disease. Management of ALS consists of symptomatic and palliative care.[19,20]

Riluzole (oral tablet or suspension) is currently the only drug licensed for treating ALS in the UK. The licensed indication of riluzole is to extend life or the time to mechanical ventilation for individuals with ALS.[20]

Clinical Trial Information

Trial	NCT04819438; Comparative Bioavailability Study of a New Riluzole Orodispersible Film vs. a Marketed Oral Reference (Rilutek® Tablets) in Healthy Male and Female Volunteers **Phase I** – Completed **Location:** Switzerland **Study completion date:** March 2021
Trial Design	Randomized, crossover assignment, open-label
Population	N=54; Healthy male and female volunteers; Aged 18 to 55 years
Intervention(s)	Riluzole 50mg oral film
Comparator(s)	Riluzole 50mg tablet
Outcome(s)	**Primary outcomes:** – Evaluation of the bioequivalent rate (Cmax) of absorption of riluzole after replicate single dose administration of test and reference. [Time frame: 36 hours after the drug treatment] – Evaluation of the bioequivalent extent (AUC0-t) of absorption of riluzole after replicate single dose administration of test and reference. [Time frame: 36 hours after the drug treatment] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of riluzole oral film was confidential at the time of producing this briefing.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Tofersen for treating amyotrophic lateral sclerosis caused by SOD1 gene mutations (GID-HST10050). Expected date of issue to be confirmed.
- NICE technology appraisal. Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease (TA20). January 2001.
- NICE guideline. Motor neurone disease: assessment and management (NG42). February 2016; updated: July 2019.
- NICE quality standard. Motor neurone disease (QS126). July 2016.
- NICE interventional procedures guidance. Intramuscular diaphragm stimulation for ventilator-dependent chronic respiratory failure caused by motor neurone disease (IPG593). September 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/S/a.
- NHS England. 2013/14 NHS Standard Contract for Specialised rehabilitation for patients with highly complex needs (All ages). D02/S/a

Other Guidance

- Regional Medicines Optimisation Committee North. RMOC Shared Care Work Plan - Riluzole for patients within adult services.[21]
- Royal College of General Practitioners and Motor Neurone Disease Association. Motor neurone disease: a guide for GPs and primary care teams. 2018.[22]

Additional Information

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