Health Technology Briefing
March 2024

Troriluzole for spinocerebellar ataxia

Company/Developer	Biohaven Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 13450	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Troriluzole is in development for the treatment of adults with spinocerebellar ataxia (SCA). SCAs are a group of ataxias (lack of muscular control) which are inherited from parents. SCAs do not usually begin until adulthood and can affect people from the age of 25 up to 80, depending on the type of SCA. The symptoms vary depending on the type of SCA but can include problems with balance and co-ordination, increasingly slurred, slow and unclear speech, difficulty swallowing, muscle stiffness and cramps, loss of sensation in the hands and feet, memory loss, difficulties with spoken language, slow eye movement and reduced bladder control. There is no cure for SCA, and no specific treatments are currently available to slow or stop disease progression. Therefore, there is an unmet need for specific medicinal treatments to support patients with SCA.

Troriluzole is a medicinal product administered orally. Following administration, troriluzole is converted into the active form of the drug called riluzole. The way in which riluzole works is not fully understood but it is possible that by interacting with neurotransmitters (chemical messengers found in the brain and nervous system) the symptoms of SCA are reduced. Troriluzole has been reported to have consistent treatment benefits in patients with genotype SCA3. If licensed, troriluzole would offer a novel treatment for patients with SCA.

Proposed Indication

The treatment of spinocerebellar ataxia (SCA) in adults.[1-4]

Technology

Description

Troriluzole (BHV-4157) is a formulation comprised of a prodrug form of the benzothiazole derivative riluzole. Following oral administration, troriluzole is converted into the active form riluzole.[5] While the mechanism of action of riluzole is unknown, its pharmacological activities, some of which may be related to its effect, include the following: an inhibitory effect on glutamate release; inactivation of voltage-dependent sodium channels; and interference with intracellular events that follow transmitter binding at excitatory amino acid receptors.[5] These activities may result in myorelaxation and sedation due to the blockade of glutamatergic neurotransmission.[5]

Troriluzole is currently in currently in phase III clinical development of adult patients with SCA. In this trial, troriluzole is administered orally in doses of 200 mg once daily for 48 weeks.[2] In a phase IIb/III trial for the use of troriluzole in adult patients with SCA a dose of 140mg was administered orally once daily.[1]

Key Innovation

There is no cure for SCA and no specific treatments are available to slow or stop disease progression.[6-8] Treatment for SCA is therefore symptomatic and supportive, usually involving a multidisciplinary team to form a care plan.[7] This demonstrates an unmet need for specific pharmacological treatments to support patients with SCA.[8] Troriluzole is a prodrug of riluzole which is suggested to modulate ion channels.[5,9] As ion channel dysfunction is a common theme in SCA, troriluzole presents itself as a specific, pharmacologic, symptomatic therapy for SCA.[9] Therefore, if licensed, troriluzole could offer a novel treatment option for patients with SCA.

Regulatory & Development Status

Troriluzole does not currently have marketing authorisation in the EU/UK for any indication.

Troriluzole is currently in phase II/III clinical development for obsessive compulsive disorder,[10,11] and newly diagnosed and recurrent glioblastoma[12] as well as phase III clinical development for generalised anxiety disorder.[13]

Troriluzole has the following regulatory designations/awards:

- An orphan drug designation for spinocerebellar ataxia by the EMA in December 2021.[14]
- A Fast Track designation by the FDA[15]

Patient Group

Disease Area and Clinical Need

SCAs are a group of hereditary ataxias that usually do not begin until adulthood and can affect people from the age of 25 up to 80, depending on the type of SCA.[16] SCA can be inherited in both an autosomal dominant or recessive manner.[17] SCAs The symptoms vary depending on the type of SCA but can include: problems with balance and co-ordination, increasingly slurred, slow and unclear speech, difficulty swallowing, muscle stiffness and cramps, loss of sensation in the hands and feet, memory loss, difficulties with spoken language, slow eye movement and reduced bladder control.[16] The most common subtype, SCA3, also called Machado-Joseph Disease (MJD-III), is a rare, inherited, ataxia (lack of muscular control)

affecting the central nervous system and characterised by the slow degeneration of particular areas of the brain called the hindbrain.[18] The gene responsible for SCA3 has been identified and mapped to Gene Map Locus; 14q24.3-q31.[18] The onset of symptoms of SCA3 varies; patients with SCA3 may eventually become crippled and/or paralysed but their intellect remains intact.[18]

The global prevalence of SCA is estimated to be 3 in 100,000, however, a wide regional variation exists.[19] SCA3 is the most common dominant ataxia worldwide, with an overall average prevalence of 1–5/100,000.[20] In England, 2022-23, there were 30 finished consultant episodes (FCE) and 22 admissions for other hereditary ataxias (ICD-10 code G11.8), which resulted in 84 FCE bed days and 6 day cases.[21]

Recommended Treatment Options

There is no treatment option recommended by the National Institute for Health and Care Excellence (NICE) for SCA. There is no cure for SCA and no specific approved pharmacological treatment options available to slow or stop disease progression.[6,22] Treatment for SCA is therefore symptomatic and supportive often including speech and language therapy, physiotherapy and muscle relaxant medication such as baclofen or tizanidine.[7,23] Ataxia UK has clinical guidelines which outline potential treatments for various symptoms.[17]

Clinical Trial Information

Trial	NCT03701399; A Phase III, Long-Term, Randomized, Double-blind, Placebo-controlled Trial of Troriluzole in Adult Subjects With Spinocerebellar Ataxia. **Phase III –** Active, not recruiting **Locations:** USA and China **Study completion date (actual):** October 2025
Trial Design	Randomised, parallel-assignment, placebo-controlled, triple-blind
Population	N = 218 (actual); adults aged 18 to 75 years with a known or suspected diagnosis of the following specific hereditary ataxias: SCA1, SCA2, SCA3, SCA6, SCA7, SCA8 and SCA10
Intervention(s)	Oral troriluzole (200 mg once daily)
Comparator(s)	Oral placebo (200 mg)
Outcome(s)	Primary outcome: Change from Baseline in the total score of the Modified Functional Scale for the Assessment and Rating of Ataxia (f-SARA) after 48 weeks of treatment. See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	NCT02960893; A Phase IIb/III, Randomized, Double-blind, Placebo-controlled Trial of Troriluzole in Adult Subjects With Spinocerebellar Ataxia **Phase IIb/III –** Active, not recruiting **Location:** USA **Study completion date:** September 2024
Trial Design	Randomised, parallel-assignment, controlled, placebo-controlled, double-blind
Population	N = 141 (actual); adults aged 18 to 75 years with a known or suspected diagnosis of the following specific hereditary ataxias: SCA1, SCA2, SCA3, SCA6, SCA7, SCA8 and SCA10
Intervention(s)	Randomisation phase: oral troriluzole (140 mg once daily) Extension phase: oral troriluzole (140 mg once daily)
Comparator(s)	Randomisation phase: matched placebo
Outcome(s)	Primary outcome: Change from baseline in total score on the Scale for the Assessment and Rating of Ataxia (SARA) at randomisation phase week 8 See trial record for full list of other outcomes.
Results (efficacy)	See trial record.
Results (safety)	See trial record.

Estimated Cost

The cost of troriluzole is not yet known.

Relevant Guidance

NICE Guidance

No relevance guidance identified.

NHS England (Policy/Commissioning) Guidance

No relevance guidance identified.

Other Guidance

Ataxia UK. Management of the ataxias towards best clinical practice. 2016.[17]

Additional Information

Biohaven Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge

pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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