# Health Technology Briefing
# February 2023

## Pegcetacoplan for treating amyotrophic lateral sclerosis

| Company/Developer | Swedish Orphan Biovitrium AB |
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☐ New Active Substance ☒ Significant Licence Extension (SLE)

| NIHRIO ID: 30577 | NICE ID: 10594 | UKPS ID: Not Available |
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## Licensing and Market Availability Plans

Currently in phase II clinical development.

## Summary

Pegcetacoplan is in clinical development for the treatment of patients with amyotrophic lateral sclerosis (ALS), a form of motor neurone disease. 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. Currently, there is no cure for ALS and few treatments available, none of which have a profound effect on survival.

Pegcetacoplan is made of two synthetic peptides (short chains of amino acids) linked together, which target and attach to the C3 complement protein, which is a part of the body's defence system called the 'complement system'. Elevated levels of C3 may play a role in the progression of ALS and pegcetacoplan may offer a new treatment approach for people living with ALS by controlling complement activation at the level of C3. Pegcetacoplan is administered subcutaneously. If licenced, pegcetacoplan will offer an additional treatment option for people with ALS who currently have no effective therapies available.

## Proposed Indication

Treatment for adults (18 years and older) with sporadic amyotrophic lateral sclerosis (ALS).[1]

## Technology

### Description

Pegcetacoplan (Aspaveli, Empaveli, APL-2) is a symmetrical molecule comprised of two identical pentadecapeptides covalently bound to the ends of a linear 40-kDa PEG (polyethylene glycol) molecule. The peptide moieties bind to complement C3 and exert a broad inhibition of the complement cascade. Pegcetacoplan binds to complement protein C3 and its activation fragment C3b with high affinity, thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation.[2]

Pegcetacoplan is currently in clinical development for the treatment of ALS. In the phase II clinical trial (MERIDIAN, NCT04579666) patients are given 1,080mg pegcetacoplan administered subcutaneously (SC) twice weekly.[1]

### Key Innovation

Currently, there is no cure for ALS and few treatments available, none of which have a profound effect on survival.[3] Riluzole is currently the only drug licensed for treating ALS in the UK, however, it can only slow the progression for a few months and cannot reverse damage to motor neurons.[3-5]

Studies suggest that elevated levels of C3 may play a role in the progression of ALS, a neurodegenerative disease that leads to progressive muscle weakness and paralysis. Pegcetacoplan may offer a new treatment approach for people living with ALS.[6] It has been designed to target C3, a central protein in the complement cascade. Increased levels of C3 have been found at the motor end plate (also called the neuromuscular junction) where nerves and muscles meet. It is thought that reducing the activation of C3 may result in less C3 depositing at the motor end plate, which may reduce inflammation, and this may slow the progression of ALS.[7] If licenced, pegcetacoplan will offer an additional treatment option for people with ALS who currently have no effective therapies available.

### Regulatory & Development Status

Pegcetacoplan has Marketing Authorisation in the EU/UK for the treatment of paroxysmal nocturnal haemoglobinuria (PNH).[8]

Pegcetacoplan is also in phase II/III clinical development for a number of indications, some of which include:[9]

- Transplant-associated thrombotic microangiopathy
- PNH (paediatric)
- Cold agglutin disease
- Geographic atrophy

## 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.[10] ALS is a form of MND.[11] 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. 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.[12] Nearly all cases of ALS are considered sporadic. This means the disease seems to occur at random with no clearly associated risk factors and no family history of the disease.[13]

ALS has a reported incidence of 1–2/100,000 person-years. It is estimated that there are 5,000 people with ALS in the UK at any one time.[14] ALS is the most common type of MND in the UK accounting for approximately 60-70% of the total MND cases.[15] Estimated incidence rates for sporadic ALS are between 5-20% of all ALS cases.[16] In England, 2021-22, there were 4,406 finished consultant episodes (FCEs) and 2,694 admissions for MND (ICD-10 code G12.2) which resulted in 21,826 FCE bed days and 1,029 day cases.[17]

### Recommended Treatment Options

Management of ALS consists of symptomatic and palliative care.[4,18] 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.[4]

## Clinical Trial Information

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| Trial | **MERIDIAN**, NCT04579666, EudraCT 2019-003797-10; A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Pegcetacoplan in Subjects With Amyotrophic Lateral Sclerosis (ALS)<br>**Phase II** – Active, not recruiting<br>**Locations:** 9 EU countries, UK, USA and other countries<br>**Primary completion date:** March 2023 |
| Trial Design | Randomised, parallel-assignment, quadruple-blind, placebo-controlled |
| Population | N=249 (actual); Subjects with sporadic ALS diagnosed as definite, probable, or laboratory-supported probable as defined by the revised El Escorial criteria; Aged 18 years and older |
| Intervention(s) | Pegcetacoplan (SC) 1,080mg |
| Comparator(s) | Matched placebo |
| Outcome(s) | Primary outcome measure:<br>• Combined assessment of function and survival (CAFS) [Time frame: week 52]<br>See trial record for full list of other outcomes |
| Results (efficacy) | - |
| Results (safety) | - |

## Estimated Cost

Pegcetacoplan is already marketed in the UK for the treatment of PNH; a 1080mg/20ml solution for infusion vial costs £3,100.00.[19]

## Relevant Guidance

### NICE Guidance

- 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.

### 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

- Royal College of General Practitioners and Motor Neurone Disease Association. Motor neurone disease: a guide for GPs and primary care teams. 2018.[20]

## Additional Information

Swedish Orphan Biovitrium AB 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.

## References

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