# Health Technology Briefing
# May 2022

# ABP 959 for treating paroxysmal nocturnal haemoglobinuria

| Company/Developer | Amgen Ltd. |
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☒ New Active Substance ☐ Significant Licence Extension (SLE)

| NIHRIO ID: 27072 | NICE ID: 10250 | UKPS ID: Not Available |
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## Licensing and Market Availability Plans

Currently in phase III clinical development.

## Summary

ABP 959 is in development for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). PNH is a rare condition, which occurs due to a genetic mutation within stem cells in the bone marrow. In PNH, red blood cells lack specific proteins on their surface which normally protect them from being destroyed (a process called haemolysis) by the body's normal defence system. PNH is characterised by the presence of brownish urine. The characteristic colour of urine is due to the presence of products from destroyed red blood cells. Patients have a low count of red blood cells, and may have blood clots in the large vessels. The exact cause of PNH is not fully understood but it is known that the genetic mutation is acquired. PNH can be potentially life threatening, and thrombosis (blood clot) is recognised as the leading cause of death in PNH patients. There are currently few treatment options available for PNH and current treatments can be expensive.

ABP 959 is an eculizumab biosimilar (a type of medicinal product that is highly similar to another biological medicine already licenced for use). In the human body there are a group of proteins called the complement system, which promotes inflammation and can destroy cells in the body (including cells that cause disease). ABP 959 is an antibody that binds to the human C5, a complement protein with capacity to start an inflammatory reaction in humans resulting in the destruction of blood cells. ABP 959 acts in a similar way to the reference product eculizumab in blocking C5 and preventing it from splitting into pro-inflammatory components, and therefore the subsequent cell breakdown. If licenced, ABP 959 will offer an additional treatment option for patients with PNH, having shown similar efficacy and safety to eculizumab in a phase III trial.

## Proposed Indication

Subjects with Paroxysmal Nocturnal Haemoglobinuria (PNH).[1]

## Technology

### Description

ABP 959 is in development as a biosimilar to eculizumab, a recombinant humanised monoclonal immunoglobulin G2/4k chimeric monoclonal antibody that binds to the human C5 complement protein.[2] This inhibits C5 cleavage to C5a and C5b, preventing the generation of the terminal complement complex C5b-9 mediated proinflammatory signalling pathways and thrombus formation.[3] In PNH patients, uncontrolled terminal complement activation and the resulting complement-mediated intravascular haemolysis are blocked with eculizumab treatment.[4]

ABP 959 is currently in phase III clinical development for the treatment of PNH. In the phase III study (NCT03818607), patients will receive an intravenous (IV) infusion of ABP 959.[1]

### Key Innovation

ABP 959 has demonstrated pharmacokinetic and pharmacodynamic bioequivalence to eculizumab. Safety and immunogenicity profiles were also similar.[5,6] Comparison of C5 binding profiles and effects on the terminal complement complex formation inhibition and haemolysis inhibition have also showed that ABP 959 and eculizumab have similar biological and functional properties relevant to the clinical mechanisms of action.[3] If licenced, ABP 959 will offer an additional treatment option for patients with PNH, showing similar efficacy and safety to eculizumab.

### Regulatory & Development Status

ABP 959 does not currently have Marketing Authorisation in the EU/UK for any indication.

ABP 959 is not currently in phase II or III trials for any other indication.

## Patient Group

### Disease Area and Clinical Need

PNH is a rare condition that manifests with haemolytic anaemia, thrombosis, and peripheral blood cytopenias due to bone marrow failure.[7] PNH occurs due to a mutation in a gene called PIG-A within stem cells in the bone marrow. These stem cells give rise to red blood cells, white blood cells and platelets, therefore, when the PIG-A mutation occurs all cells derived from the affected stem cell carry the mutation. Mutated blood cells are deficient in a class of proteins called GPI-anchored proteins. Some of these proteins protect red blood cells from destruction and many clinical PNH manifestations result from a deficiency in GPI-anchored proteins.[8] The exact cause of PNH is not fully understood, but it is known that the PIG-A mutation is acquired and not present from birth.[9] It can occur at any age, but is usually diagnosed in young adulthood.[10] Symptoms of PNH can show a large amount of variation. Some people exhibit no symptoms, yet others may be affected by a number of different symptoms and complications. Common symptoms include; haemoglobinuria (dark or black urine due to haemoglobin in the urine), anaemia, breathlessness, difficulty swallowing, abdominal pain, erectile dysfunction in men, fatigue, jaundice, kidney damage and blood clots.[11] PNH can be potentially life-threatening and thrombosis is recognised as the leading cause of death in PNH patients.[12]

The incidence of PNH in Great Britain has been estimated as approximately 1 in 770,000 each year, with a predicted prevalence of approximately 1 in 62,500.[13] It is estimated that there are about 650 to 900 people in England with PNH.[13,14] In England (2020/21), there were 431 hospital admissions with primary diagnosis of PNH (ICD-10 code: D59.5), and 445 finished consultant episodes (FCEs), resulting in 104 FCE bed days and 390 day cases.[15]

### Recommended Treatment Options

For treating PNH in adults the National Institute for Health and Care Excellence (NICE) currently recommends the following treatment options:

- Ravulizumab [16]
- Pegcetacoplan[17]

Eculizumab was approved in 2007 by the European Medicines Agency (EMA) for the treatment of PNH in adults and children.[18] Eculizumab is recommended for reducing haemolysis in PNH patients with a history of blood transfusions (under expert supervision) and is commissioned by NHS England for the treatment of PNH in adults and adolescents as a highly specialised service.[19,20] However, there have been concerns about the cost effectiveness of eculizumab as a treatment option for PNH and it is not currently recommended within NHS Scotland.[21]

## Clinical Trial Information

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| Trial | **DAHLIA, NCT03818607, 2017-001418-27;** A Randomized, Double-Blind, Active-Controlled Phase 3 Study Evaluating the Efficacy and Safety of ABP 959 Compared With Eculizumab in Adult Subjects With Paroxysmal Nocturnal Haemoglobinuria (PNH)<br>**Phase III** – Active, not recruiting<br>**Locations:** 10 EU countries, UK, USA, and other countries<br>**Primary completion date:** July 2022 |
| Trial Design | Randomised, crossover assignment, double-blinded, active-controlled |
| Population | N=42; historical diagnosis of paroxysmal nocturnal haemoglobinuria; administration of eculizumab for ≥ 6 months and currently receiving 900 mg of eculizumab |
| Intervention(s) | ABP 959 (IV infusion) |
| Comparator(s) | Eculizumab (IV infusion) |
| Outcome(s) | Primary outcomes:<br>• Haemolysis as measured by lactate dehydrogenase (LDH) (Parallel Comparison) [Time Frame: 12 months]<br>• Haemolysis as measured by LDH (Crossover Comparison) [Time Frame: 18 months]<br>See trial record for full list of other outcomes |
| Results (efficacy) | - |
| Results (safety) | - |

## Estimated Cost

The cost of ABP 959 is not yet known.

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal. Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria (TA778). March 2022.
- NICE technology appraisal. Ravulizumab for treating paroxysmal nocturnal haemoglobinuria (TA698). May 2021.

### NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Paroxysmal Nocturnal Haemoglobinuria Service (Adults and Adolescents). B05/S(HSS)/a

### Other Guidance

- PNH Education and Study Group. PESG PNH diagnosis, follow-up and treatment guidelines. 2016.[22]

## Additional Information

Amgen 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.

## References

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