Health Technology Briefing
December 2023

Efgartigimod PH20 SC for adults with primary immune thrombocytopenia

Company/Developer	Argenx BVBA

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 30972	NICE ID: Not available	UKPS ID: 671746

Licensing and Market Availability Plans

Currently in phase II clinical development.

Summary

Efgartigimod PH20 SC is currently in phase 3 development for the treatment of adults with primary immune thrombocytopenia (ITP). ITP is a rare disorder that makes the blood clot poorly due to low levels of platelets, the cells that plug wounds. ITP can cause bleeding under the skin, in the mouth, nose or other organs. It is caused through a malfunction in the immune system that attacks and destroys platelets. The exact trigger is unknown but some cases are linked to infections, drugs or other diseases. ITP is currently treated with drugs that suppress the immune system, boost platelet production, or prevent bleeding.

Efgartigimod alfa works by blocking a protein in the body called the neonatal Fc receptor (FcRn). By blocking FcRn, efgartigimod alfa decreases the level of IgG antibodies, which are proteins of the immune system that attack parts of a person's own body by mistake. This allows the damaging IgGs to be broken down and removed from the body much more quickly, which is expected to increase the levels of platelets in the blood and therefore improve symptoms of the ITP. It is co-formulated with recombinant human hyaluronidase (rHuPH20), which helps to facilitate rapid delivery and dispersion of efgartigimod alfa. If licensed, efgartigimod alfa PH20 SC will offer a new treatment option to adults with primary ITP.

Proposed Indication

Treating adult patients with primary immune thrombocytopenia (ITP).[1,2]

Technology

Description

Efgartigimod alfa is a human recombinant immunoglobulin G1 (IgG1) antibody fragment that binds to the neonatal Fc receptor (FcRn), reducing levels of circulating IgG, including pathogenic IgG autoantibodies, and improving neuromuscular transmission.[3] Recombinant human PH20 hyaluronidase (rHuPH20) is used to facilitate dispersion of fluids and drugs administered subcutaneously.[4] The glycosaminoglycan hyaluronan forms a gel-like substance, presenting a barrier to bulk fluid flow in the subcutaneous space, limiting subcutaneous drug delivery volume and administration rates. rHuPH20 acts locally to temporarily remove this barrier, facilitating rapid subcutaneous delivery of large volumes and/or high doses of sequentially or co-administered therapeutics.[5] Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes.[6]

Efgartigimod PH20 SC is currently in phase III development for the treatment of adult patients with primary ITP who have received at least two prior ITP treatments or one prior and one concurrent treatment with response to at least one (NCT04687072, ADVANCE SC; NCT04812925, ADVANCE SC+).[1,2,7] ADVANCE SC compares efgartigimod PH20 SC with a matched placebo, while ADVANCE SC+ is a single arm trial.[1,2] In ADVANCE SC+, efgartigimod (fixed dose of 1,000 mg) co-formulated with PH20,.[2,7]

Key Innovation

There are limited recommended treatment options for treating adults with primary ITP. Approximately 80% of adult patients with ITP have treatment failure with corticosteroids or become dependent on them and require second-line therapy. Several new and effective therapies have been introduced during the past decade and our understanding of disease burden and its effect on quality of life has expanded.[8] Based on the results of previous phase II (NCT03102593) and phase III (NCT04188379) clinical trials with intravenous efgartigimod alfa to treat ITP in adults,[9,10] a new subcutaneous (SC) formulation (efgartigimod PH20 SC) has been developed to offer additional flexibility and convenience for patients.[7,11]

Regulatory & Development Status

Efgartigimod alfa is currently authorised for use in the EU for the treatment of adults with generalized myasthenia gravis.[12] rHuPH20 does not currently have marketing authorisation in the EU/UK for any indication. Efgartigimod PH20 SC does not currently have marketing authorisation in the EU/UK for any indication.

Efgartigimod PH20 SC is currently in phase III clinical development for the following indications:[13]

- generalised myasthenia gravis
- pemphigus (foliaceus or vulgaris)
- bullous pemphigoid
- active idiopathic inflammatory myopathy

Efgartigimod PH20 SC is also in phase II clinical development for:[14]

- chronic inflammatory demyelinating polyneuropathy
- bullous pemphigoid

- active idiopathic inflammatory myopathy

Efgartigimod alfa has an orphan drug in the EU in 2019 for treating ITP.[15]

Patient Group

Disease Area and Clinical Need

Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder characterised by abnormally low levels of platelets, blood cells that help maintain the integrity of the walls of blood vessels and help prevent and stop bleeding..[16] It is usually caused by something going wrong with the immune system. Inherited thrombocytopenias are uncommon but are under-diagnosed.[16] The condition may develop after a viral infection, vaccination or after taking certain medications, though the cause is often unknown.[17] ITP can occur at any age, though is most prevalent over the age of 60 years. Between adolescence and 60 years of age, the condition is more common in females.[16] People with ITP may show no symptoms when their low platelet count is first discovered, or bleeding symptoms may appear first before the low platelet count is discovered. Symptoms may include: skin that bruises easily or spontaneously; a rash of small red dots, representing small haemorrhages; bleeding from the gums; frequent, long-lasting nose bleeds that are hard to stop; blood blisters inside the cheeks; and excessive and/or prolonged menstrual bleeding. Less commonly, people with ITP may have signs of internal bleeding with blood in the urine, vomit or bowel movements, while in rare cases there may be serious bleeding into the brain (intracranial haemorrhage). The frequency of intracranial haemorrhage increases in adults aged over 60. Bleeding can lead to anaemia, which may cause fatigue and impair quality of life.[16]

About six in every 100,000 adults in the UK have ITP.[17] A total of 25,805 patients (mean age 59 years; females 57.8%) with a diagnosis were identified in England between 2003 and 2014.[18] In England in 2022-23, there were 427 finished consultant episodes (FCE) and 383 admissions for other primary thrombocytopenia (ICD-10 = D69.4), of which ITP makes up a subset of the population, which resulted in 450 FCE bed days and 286 day cases.[19]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends Avatrombopag or Fostamatinib for ITP.[20,21]

Clinical Trial Information

Trial	**ADVANCE SC**, NCT04687072, A Phase 3, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and the Safety of Efgartigimod (ARGX-113) PH20 Subcutaneous in Adult Patients With Primary Immune Thrombocytopenia. **Phase III** - Active, not recruiting. **Locations:** 14 EU countries, UK, US and other countries **Primary completion date:** October 2023
Trial Design	Randomised, parallel assignment, placebo-controlled, quadruple-blind
Population	N = 207 (actual); participants aged 18 years or over with a confirmed of primary ITP with prior response to previous ITP therapy and a documented history of a platelet count of < 30×10 E9/L.

Intervention(s)	Efgartigimod PH20 (subcutaneously administered)
Comparator(s)	Placebo PH20 (subcutaneously administered)
Outcome(s)	Primary outcome measures: • Proportion of patients with chronic ITP with a sustained platelet count response defined as achieving platelet counts f ≥50×10 E9/L for at least 4 of the 6 visits between week 19 and week 24 of the trial [Time frame: up to 5 weeks (between week 19 -24)] See trial record for full list of outcome measures.
Results (efficacy)	-
Results (safety)	-

Trial	**ADVANCE SC+,** NCT04812925; A Phase 3, Multicenter, Open-Label, Long-Term Trial to Evaluate the Safety and Efficacy of Efgartigimod (ARGX-113) PH20 Subcutaneous in Adult Patients With Primary Immune Thrombocytopenia **Phase III** - Recruiting. **Locations:** 10 EU countries, UK, US, and other countries. **Primary completion date:** October 2026
Trial Design	Single group assignment, open label
Population	N = 156 (estimated); men and women aged 18 and over who were previously enrolled in the ARGX-113-2004 trial and completed the 24-week trial period.
Intervention(s)	Efgartigimod PH20 (subcutaneously administered)
Comparator(s)	-
Outcome(s)	Primary outcome measures: • Incidence, frequency and severity of adverse effects (AEs), AEs of special interest (AESIs) [Time frame: 216 weeks] • Vital sign measurement: blood pressure in the overall population [Time frame: 216 weeks] • ECG: PR, QT and QRS interval in the overall population [Time frame: 216 weeks] • Laboratory and safety evaluations: CRP analysis in the overall population [Time frame: 216 weeks] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of Efgartigimod PH20 SC is currently unknown.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Avatrombopag for treating primary chronic immune thrombocytopenia (TA853). December 2022.
- NICE technology appraisal. Fostamatinib for treating refractory chronic immune thrombocytopenia (TA835). October 2022.

NHS England (Policy/Commissioning) Guidance

No relevant guidance found.

Other Guidance

- Song F, Al-Samkari H. Management of Adult patients with Immune Thrombocytopenia (ITP): A review on Current Guidance and Experience from Clinical Practice. 2022.[22]
- Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. 2019.[23]
- Provan D, Arnold DM, Bussel JB, Chong BH, Cooper N, et al. Updated international consensus on the investigation and management of primary immune thrombocytopenia. 2019.[24]

Additional Information

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