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Newcastle University

Health Technology Briefing
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Efgartigimod PH20 SC for treating chronic inflammatory demyelinating polyradiculoneuropathy

Company/Developer	Argenx BVBA

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 29647	NICE ID: Not available	UKPS ID: 671747

Licensing and Market Availability Plans

Currently in phase II clinical development.

Summary

Efgartigimod PH20 SC are currently in clinical development for the treatment of adults with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). CIDP is a neurological disorder that leads to progressive weakness and reduced senses in the arms and legs. It is caused by damage to the fat protecting the nerves. Symptoms of CIDP include tingling or no feeling in the fingers or toes, weakness in the arms and legs, loss of reflexes and fatigue. CIDP most commonly occurs between ages 40 and 60, but can also affect children and the elderly, and is more common in men. Treatment options for CIDP are currently limited.

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 CIDP. It is co-formulated with recombinant human hyaluronidase (rHuPH20), which helps to facilitate rapid delivery and dispersion of efgartigimod alfa. If licensed, efgartigimod alfa with rHuPH20 will offer a new treatment option to adults with CIDP.

Proposed Indication

Treatment of adults with chronic inflammatory demyelinating polyneuropathy (CIDP).[1,2]

Technology

Description

Efgartigimod alfa (Vyvgart, ARGX-113) is a human recombinant immunoglobulin G1 (IgG1) antibody fragment that binds to the neonatal Fc receptor (FcRn), thereby reducing the levels of circulating IgG, including pathogenic IgG autoantibodies, and improving neuromuscular transmission.[3] Recombinant human PH20 hyaluronidase (rHuPH20) is used to facilitate dispersion of subcutaneously delivered fluids and drugs.[4] The glycosaminoglycan hyaluronan forms a gel-like substance, which presents a barrier to bulk fluid flow in the subcutaneous (SC) space, limiting SC drug delivery volume and administration rates. rHuPH20 acts locally to temporarily remove this barrier, facilitating rapid SC 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 II clinical development for the treatment of adults with CIDP (NCT04280718, ADHERE+; NCT04281472 (ADHERE.[1,2] In both trials, efgartigimod alfa is subcutaneously co-administered with rHuPH20.[1]

Key Innovation

Most CIDP patients require treatment and intravenous immunoglobin (IVIg), which is the preferred first-line therapy.[7] However, the costs of immunoglobin means CIDP has a significant economic burden.[8] Glucocorticoids and plasma exchange are used less due to side effects from chronic use or, in the case of glucocorticoids, invasiveness of the procedure and access. In the case of plasma exchange, access is limited to specialised centres. Other immunosuppressant agents are typically only used in patients ineligible for or refractory to IVIg, glucocorticoids or plasma exchange.[7] If licenced Efgartigimod PH20 SC will offer a new treatment option to patients with CIDP.

Regulatory & Development Status

Efgartigimod alfa is currently authorised for use in the EU for the treatment of adults with generalized myasthenia gravis.[9] 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:[10]

- primary Immune thrombocytopenia
- generalized myasthenia gravis
- pemphigus (vulgaris or foliaceus)
- bullous pemphigoid
- active idiopathic inflammatory myopathy

Efgartigimod PH20 SC is also in phase II clinical development for bullous pemphigoid and active idiopathic inflammatory myopathy.[11]

Efgartigimod alfa has the following regulatory designations/awards:

- an orphan drug in the EU in 2022 for treating CIDP in adults.[12]

Patient Group

Disease Area and Clinical Need

CIDP is a neurological disorder characterised by progressive weakness and impaired sensory function in the arms and legs; this includes the loss of reflexes. It is considered an autoimmune disorder, where the immune system begins to attack the peripheral nerves and damages the myelin sheath, though the exact mechanism by which this happens is still not clearly defined. CIDP is a rare disorder that can affect any age group and the onset of the disorder may begin during any decade of life. CIDP affects males twice as often as females and the average age of onset is 50.[13-15] The chief symptoms of CIDP are slowly progressive (over at least two months) symmetric weakness of both muscles around the hip and shoulder as well as of the hands and feet (both proximal and distal muscles). Nerve signals become altered causing impairment in motor function and/or abnormal, or loss of, sensation. There are usually some alterations of sensation causing loss of co-ordination, numbness, tingling or prickling sensations. Other symptoms of CIDP include fatigue, burning, pain, clumsiness, difficulty swallowing and double vision.[15]

Up to 650 people are diagnosed with CIDP each year in the UK.[16] The prevalence of CIDP is estimated to be around 5-7 cases per 100,000 individuals.[15] In England, 2022-23, there were 20,133 finished consultant episodes (FCE) and 19,709 admissions for other inflammatory polyneuropathies (ICD-10 = G618), of which CIDP makes up a percentage, which resulted in 18,827 day cases and 8,732 FCE bed days.[17]

Recommended Treatment Options

There are currently no NICE approved pharmacological treatment options for CIDP. The European Academy of Neurological/Peripheral nerve society suggested treatments for CIDP include corticosteroids, immunoglobulin therapy or plasma exchange.[18]

Clinical Trials

Trial	**ADHERE; NCT04281472; EudraCT2019-003076-39;** A Phase 2 Trial to Investigate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 SC in Adult Patients With Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) **Phase II** - Completed **Locations:** 14 EU countries, UK, US and other countries **Study completion date:** May 2023	**ADHERE+; NCT04280718; EudraCT2019-003107-35;** Open-label Extension of the ARGX-113-1802 Trial to Investigate the Long-term Safety, Tolerability, and Efficacy of Efgartigimod PH20 SC in Patients With Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) **Phase II -** Active, not recruiting **Locations:** 13 EU countries, UK, US and other countries **Primary completion date:** March 2027
Trial Design	Randomised, parallel assignment, placebo-controlled, quadruple-blind	Single group assignment, open-label
Population	N = 322; men and women aged 18 years and over, diagnosed with probable or definite CIDP	N = 226; men and women aged 18 and over who have previously completed the week 48 visit of Stage B of the ARGX-113-1802 (NCT04281472) trial and considered

		eligible for treatment with subcutaneous efgartigimod PH20
Intervention(s)	Stages A and B: efgartigimod PH20 (subcutaneous administration)	Efgartigimod PH20 (subcutaneous administration)
Comparator(s)	Stage A: patients receiving efgartigimod PH20 (subcutaneous administration) during stage A Stage B: placebo	-
Outcome(s)	Primary outcome measures: • Stage A: Percentage of patients with confirmed evidence of clinical improvement (ECI) [Time frame: up to 12 weeks during the open-label stage A] • Stage B: Time to first adjusted INCAT deterioration compared to Stage B baseline [Time frame: up to 48 weeks during the randomised placebo-controlled stage B] See trial for full list of all outcomes	Primary outcome measures: • Incidence of treatment-emergent adverse events and serious adverse events [Time frame: up to 48 weeks per cycle (each cycle is 48 weeks) until the end of the study] See trial record for full list of all outcomes.
Results (efficacy)	Efgartigimod alfa showed a 61% reduction in risk of relapse compared with placebo (HR 0.39; 95% CI 0.25 to 0.61). Efgartigimod alfa patients had a lower relapse rate compared to placebo at weeks 24 (26% versus 54%) and 48 (34% versus 60%). Efgartigimod alfa patients experienced longer time to relapse compared to those on placebo with a rapid separation of the Kaplan–Meier curves beginning at week 4 and sustained through week 48. Efgartigimod alfa patients demonstrated a clinically meaningful mean improvement of 7.7 points on the Inflammatory Rasch-bult Overall Disability Scale (I-RODS) and 12.3 kPa on grip strength in Stage A. This clinically meaningful benefit was maintained in stage B by treated patients and	

	lost in placebo patients. Clinical benefit was observed across all efficacy scales and patient subgroups, regardless of prior therapy.[19]	
Results (safety)	Efgartigimod alfa was well-tolerated with a safety profile consistent with prior clinical trials and the known profile of efgartigimod alfa. The most frequent treatment-related adverse event was injection site reactions, which occurred in a lower percentage of patients than previous efgartigimod alfa trials (20% in stage A; 10% in stage B). All ISRs were mild to moderate and resolved over time.[19]	

Estimated Cost

The cost of Efgartigimod PH20 SC is currently unknown.

Relevant Guidance

NICE Guidance

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NHS England (Policy/Commissioning) Guidance

- NHS England. Commissioning criteria policy for the use of therapeutic Immunoglobulin. 2021. [CG98]
- NHS England. Clinical Commissioning Policy Rituximab for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN) & vasculitis of the peripheral nervous system (adults). 2021
- NHS England. Clinical Commissioning Policy Rituximab for the treatment of IgM paraproteinaemic demyelinating peripheral neuropathy in adults. 2021. [211001P]
- NHS England. Clinical Commissioning Policy Rituximab therapy for the treatment of nodal/paranodal antibody positive inflammatory/autoimmune neuropathy in adults and postpubescent children. 2021. [210602P]

Other Guidance

- Van den Bergh, van Doorn, Hadden et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force—Second revision. 2021.[18]
- NHS Scotland. Clinical guidelines for immunoglobulin use. 2012.[20]

Additional Information

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