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Health Technology Briefing
January 2023

Efgartigimod alfa (subcutaneous injection) for treating generalised myasthenia gravis

Company/Developer	Argenx BVBA

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 31251	NICE ID: 11835	UKPS ID: 667521

Licensing and Market Availability Plans

Subcutaneous administration of efgartigimod alfa is currently in Phase III trials.

Summary

Efgartigimod alfa is currently in clinical development for the treatment of adults with generalised myasthenia gravis (gMG). gMG is a rare, long-term autoimmune disorder that leads to muscle weakness and tiredness, which can be seriously debilitating and life-threatening, affecting eye alignment, swallowing, speech, mobility and respiratory function. These symptoms can significantly impair independence and quality of life. Currently, there are few treatment options for gMG, and medicines that can take a long time to work and result in side-effects, which can limit their use.

Efgartigimod alfa is a modified human antibody (a protein produced by the immune system) fragment that is administered under the skin. In patients with myasthenia gravis, the body produces antibodies against the neurotransmitter receptors. This medicine works by blocking a protein called FcRn, which attaches to these antibodies and protects them from degradation. Blocking FcRn leads to the decrease in the level of the antibodies that damage the acetylcholine receptors; this is expected to restore the normal contraction of the muscles. If licensed, efgartigimod alfa given as an injection under the skin will offer a treatment option for gMG and reduce the treatment burden for these patients.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Efgartigimod alfa is indicated for treating adults with generalised myasthenia gravis (gMG).[1,2]

Technology

Description

Efgartigimod alfa works by attaching to and blocking the actions of the protein called the neonatal Fc receptor (FcRn), which is involved in regulating antibody levels within the blood.[3] In people with myasthenia gravis, the immune system produces antibodies that work against a self-protein called the acetylcholine receptor (AChR), which acts as a receiver for a chemical signal released from the nerve when a muscle is used.[3,4] In blocking FcRn, efgartigimod alfa decreases the levels of autoantibodies and thus improves the muscles' ability to contact.[3]

Efgartigimod alfa is being evaluated in treating patients with gMG. In a Phase III trial (NCT04735432; ADAPTsc),[1] efgartigimod alfa is being administered subcutaneously to adults aged 18 years and older with gMG at fixed weekly dose of 1,000 mg per injection for one treatment cycle consistent of four doses at weekly intervals.[5]

Key Innovation

Current treatments for gMG can include immune-suppressants and anticholinesterases.[6] However, many of these treatments are associated with long-term side-effects, which can be intolerable for patients, as well as taking several months to become effective.[7,8]

A previous clinical trial of intravenous efgartigimod alfa demonstrated positive efficacy and safety results in patients with gMG.[9] The efficacy and safety of subcutaneous administration of efgartigimod alfa is now being evaluated against intravenous efgartigimod alfa in a Phase III clinical trial (NCT04735432; ADAPTsc),[1] while another Phase III clinical trial is evaluating the safety and tolerability of subcutaneous administration of efgartigimod alfa (NCT04818671; ADAPTsc+).[2] It is anticipated that the availability of a subcutaneous formulation of efgartigimod alfa will provide additional options and flexibility for patients.[5] If licensed, subcutaneous efgartigimod alfa will offer an additional treatment option for adults with gMG who currently have few well tolerated effective therapies available.

Regulatory & Development Status

Efgartigimod alfa does not currently have Marketing Authorisation in the EU/UK for any indication.

Subcutaneous efgartigimod alfa is in phase II/III for:

- myasthenia gravis[1,2]
- bullous pemphigoid[10]
- primary immune thrombocytopenia[11,12]
- chronic inflammatory demyelinating polyneuropathy (CIDP)[13,14]
- pemphigus (vulgaris or foliaceus)[15,16]
- active idiopathic inflammatory myopathy[17]

Efgartigimod alfa has the following regulatory designations/awards:

- an orphan drug in the EU in 2018 for myasthenia gravis;[18]

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- a PIM designation by the MHRA in November 2021[19]

Patient Group

Disease Area and Clinical Need

Myasthenia gravis (MG) develops in adults due to a defect in the immune system.[4] In people with MG, the immune system produces antibodies that damage receptors, meaning that muscles are not able to contract as well as usual.[3] MG most commonly affects the muscles controlling the eyes and eyelids; if the weakness is limited to the ocular muscles, this is termed ocular myasthenia.[20] Oropharyngeal weakness in people with MG may also affect chewing, swallowing and speaking.[20] In gMG, limb girdle weakness is generally more pronounced in the proximal rather than the distal muscle groups.[20] The most common symptoms of MG are drooping eyelids, double vision, difficulty in making facial expressions, problems with chewing and swallowing, slurred speech, weak arms, legs or neck, and shortness of breath and, occasionally, serious breathing difficulties.[21] Symptoms can become more severe with tiredness and can be triggered by factors such as stress, infections and certain medicines in some people.[22] Most individuals with MG have no family history of the condition.[23]

In the UK, MG affects about 15 in every 100,000 people.[24] Although it can affect people of any age, MG typically starts in women under 40 and men over 60.[21] Disease progression can be variable but usually progresses in the first few years, with weakness involving more muscles occurring during the first three years.[25] In England (2021-22), there were 5,199 finished consultant episodes (FCE) for MG (G70.0) leading to 3,838 admissions, 2,383 day cases and 16,170 FCE bed days.[26]

Recommended Treatment Options

The British National Formulary (BNF) recommends the following current pharmacological treatment options for gMG.[6]

- Prednisolone is given as immunosuppresant therapy
- Azathioprine can be started at the same time as as a corticosteroid
- Ciclosporin, methotrexate or mycophenolate mofetil can be used in patients who are unresponsive or intolerant to other treatments
- Anticholinesterases (neostigmine and pyridostigmine bromide) as an adjunct to immunosuppresant therapy

In addition, surgery may be undertaken to remove the thymus gland, a gland in the chest linked to MG; this can improve symptoms in some people with an unusually large thymus.[21]

Clinical Trial Information

Trial	**ADAPTsc; NCT04735432, EudraCT - 2020-004085-19**; A Phase 3, Randomized, Open-Label, Parallel-Group Study to Compare the Pharmacodynamics, Pharmacokinetics, Efficacy, Safety, Tolerability, and Immunogenicity of Multiple

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	Subcutaneous Injections of Efgartigimod PH20 SC With Multiple Intravenous Infusions of Efgartigimod in Patients with Generalized Myasthenia Gravis **Phase III** - Completed **Location(s):** Seven EU countries, USA, Georgia, Japan and Russia. **Actual study completion date**: December 2021
Trial Design	Randomised, parallel assignment, open-label
Population	N = 111; participants with gMG aged 18 years old or over
Intervention(s)	Subcutaenous injection with efgartigimod PH20
Comparator(s)	Intravenous infusion of efgartigimod
Outcome(s)	Percentage change from baseline in total immunoglobin (IgG) levels at day 29 [Time frame: at day 29] See trial record for full list of other outcomes
Results (efficacy)	Subcutaneous efgartigimod demonstrated a mean total IgG reduction of 66.4% from baseline at day 29 compared with 62.2% with IV formulation.[5] Consistent results were shown across the population, including people with acetylcholine receptor antibodies and people where acetylcholine receptor antibodies were not detected.[5]
Results (safety)	Subcutaneous efgartigimod demonstrated a safety profile consistent with the Phase III ADAPT study.[27] It was generally well-tolerated, with the most frequent adverse events being injection site reactions; these were mild and resolved over time.[27]

Clinical Trial Information	
Trial	**ADAPTSC+; NCT04818671, EudraCT - 2020-004086-38;** A Long-Term, Single-Arm, Open-label, Multicenter Phase 3 Study to Evaluate the Safety and Tolerability of Multiple Subcutaneous Injections of Efgartigimod PH20 SC in Patients With Generalized Myasthenia Gravis **Phase III** – Active, not recruiting **Location(s):** Seven EU countries, USA and other countries **Primary completion date**: April 2023
Trial Design	Single group assignment, open-label
Population	N = 183; adults with generalised myasthenia gravis aged 18 or over who have previously participated in ARGX-113-2001 (NCT04735432) or ARGX-113-1705 and are eligible for roll over.
Intervention(s)	Subcutaneous injection with efgartigimod PH20 SC
Comparator(s)	-
Outcome(s)	• Incidence and severity of adverse events [Time frame: up to 2 years] • Incidence of serious adverse events [Time frame: up to 2 years] • Incidence of adverse events of special interest [Time frame: up to 2 years]

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	See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of efgartigimod is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Zilucoplan for treating antibody positive generalised myasthenia gravis (GID-TA11096). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Rozanolixizumab for treating antibody-positive generalised myasthenia gravis (GID-TA10994). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Efgartigimod for treating generalised myasthenia gravis (GID-TA10986). Expected October 2023.
- NICE technology appraisal in development. Ravulizumab for treating generalised myasthenia gravis (GID-TA10987). Expected July 2023.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Rituximab bio-similar for the treatment of myasthenia gravis (adults). 170084P. September 2018.
- NHS England. 2014/15 NHS Standard Contract for Neuromuscular Operational Delivery Network Specification. D04/ODN/a.
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- NHS England. 2013/14 NHS Standard Contract for Diagnostic Service for Rare Neuromuscular Disorders (All ages). D04/S(HSS)/a.

Other Guidance

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Additional Information

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