

Category

Best Biotechnology Product

Drug / Device Name

VYVGART®

Compound/ Tech Name

efgartigimod alfa-fcab

Trade Name

\$ARGX

Date of Approval

2021-12-17

Indications

VYVGART® (efgartigimod alfa-fcab) is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating immunoglobulin G (IgG) autoantibodies. It is the first and only approved FcRn blocker. VYVGART is approved in the United States, the EU, the UK, and Israel for the treatment of adults with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive and in Japan for the treatment of adults with gMG who do not have sufficient response to steroids or non-steroidal immunosuppressive therapies (ISTs). VYVGART is being studied in adults with primary immune thrombocytopenia (ITP) and other IgG autoantibody-mediated diseases.

The most common adverse events in the pivotal Phase 3 ADAPT trial were respiratory tract infection (33% vs. 29% placebo), headache (32% vs. 29% placebo), and urinary tract infection (10% vs. 5% placebo).

See Important Safety Information and full Prescribing Information at the following link for additional information: <https://argenx.com/product/vyvgart-prescribing-information.pdf>

Therapeutic Categories

Immunology

Attached Files:

- [vyvgartprescribinginformation.pdf](#)

Background information and need for drug/device

For generations, people living with myasthenia gravis (MG) have faced both the debilitating symptoms of this incurable disease, and frustration and despondency over their lack of treatment options. MG is a rare, chronic neuromuscular autoimmune disease characterized by debilitating and potentially life-threatening muscle weakness and fatigue. MG usually begins with eye muscle weakness, but over 85% of people progress to gMG within 24 months, where muscles throughout the body may be affected.[1] Approximately 85% of people with gMG are 'AChR-positive' [2] – meaning they have harmful IgG

autoantibodies in their blood that interfere with the AChR, a key component of the neuromuscular junction. An estimated 65,000 people in the U.S., 20,000 people in Japan, and 150,000 people in Europe are living with MG [3, 4], though many cases still go undiagnosed.

gMG patients face immense burdens. People living with AChR antibody positive gMG experience symptoms of extreme muscle weakness and fatigue that lead to difficulties with facial expression, speech, swallowing, vision and mobility. In life-threatening cases, gMG can affect muscles responsible for breathing. Symptoms vary significantly from patient to patient, and in the same patient at different times. The waxing and waning nature of gMG symptoms make it highly unpredictable and can have a significant impact on a person's quality of life. Because the disease is not progressive, patients can enter and exit periods of exacerbation or crisis where they require aggressive treatments that must work quickly to provide relief. Patients have typically been treated with steroids and immunosuppressive therapies, but in many cases, the side effects of these treatments are worse than symptoms of the disease. Furthermore, gMG affects more than a person's muscles – many patients struggling with this disease are also diagnosed with depression and/or anxiety.

[1] Hehir M. Generalized myasthenia gravis: classification, clinical presentation, natural history, and epidemiology, *Neurol Clin.* 2018; 36: 253-260

[2] Behin et al. New Pathways and Therapeutics Targets in Autoimmune Myasthenia Gravis. *J Neuromusc Dis* 5. 2018. 265-277

[3] Gilhus N. Myasthenia gravis — autoantibody characteristics and their implications for therapy. *Nature Reviews Neurology.* 2016. 12:259-269. Carr AS. Generalized myasthenia gravis. *BMC Neurol.* 2019; 10:46-54

[4] Orphanet. Myasthenia Gravis. [https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=667&Disease_Disease_Search_diseaseGroup=myasthenia&Disease_Disease_Search_diseaseType=Pat&Disease\(s\)/group%20of%20diseases=Myasthenia-gravis&title=Myasthenia%20gravis&search=Disease_Search_Simple](https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=667&Disease_Disease_Search_diseaseGroup=myasthenia&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group%20of%20diseases=Myasthenia-gravis&title=Myasthenia%20gravis&search=Disease_Search_Simple). 2020. Accessed October 23, 2020.

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- 2023 prix galien submission_upload_VYVGART_Background.docx
- argenx 2023 Prix Galien Award Submission_Reference links.docx

History of the development of the drug/device

VYVGART is an FcRn antagonist designed to reduce the presence of pathogenic IgG antibodies, which mediates gMG.

Efgartigimod (ARGX-113) was developed based on the foundational research of Prof. E. Sally Ward, Ph.D., during her tenure at UT Southwestern in the mid-1990s. Prof. Ward pioneered research identifying the role of FcRn as a key receptor involved in the long persistence and tissue penetration of IgG antibodies in the human body. In close collaboration with Prof. Ward, MG patients and advocacy groups, argenx designed efgartigimod as an FcRn antagonist - addressing a root mechanism of IgG-mediated neuromuscular degradation, rather than merely treating its symptoms like existing therapeutics. argenx engineered efgartigimod to be a human IgG1 antibody fragment that binds to FcRn in a way that blocks it from binding to pathogenic IgGs and recycling them back into the immune system. Blocking FcRn in this manner prevents continuous IgG recycling, which ultimately

reduces the level of pathogenic IgG autoantibodies in a person's immune system.

VYVGART has seen impressive commercial success and rapid adoption, netting \$400M+ in sales and 3,000+ patients on drug in the first year of commercial availability and reporting \$218M in sales for Q12023.

The FDA approval of VYVGART was based on positive results from the randomized, double-blind, placebo-controlled, multi-center, global Phase 3 ADAPT trial evaluating the safety and efficacy of efgartigimod in patients with gMG, first reported in May 2020 and published in the July 2021 issue of The Lancet Neurology. The trial demonstrated 40% of patients treated with efgartigimod achieved minimal symptom expression defined as MG-ADL scores of zero (symptom free) or one, compared to 11.1% of patients who received placebo. Among AChR-Ab+ responders, 84.1% showed clinically meaningful improvement on the MG-ADL score within the first two weeks of treatment. The safety profile of efgartigimod was comparable to placebo.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

VYVGART is the first approved therapy of its kind, representing a new beginning for the AChR-antibody positive gMG community and many people living with other IgG-mediated autoimmune diseases. It is the first-and-only approved neonatal Fc receptor (FcRn) blocker in the U.S., Japan, the EU, the UK, and Israel, establishing and leading a new class of drugs, as well as the first approved therapy designed specifically to reduce pathogenic IgGs, the underlying driver of gMG and a broad spectrum of other autoimmune diseases. None of the commonly used treatments for gMG target the root driver of the disease in this way, which has led to historically suboptimal treatment outcomes, and a forced complacency in both healthcare providers (HCPs) and patients.

Every patient's journey with gMG is unique, so argenx engaged the patient community early in the clinical development process for efgartigimod and learned that personalized care was vital to patients, families and treaters. With the patient experience top of mind, argenx designed the Phase 3 ADAPT trial to incorporate and address these insights and created the dosing regimen of VYVGART based on individual response to the therapy. This offers an individualized dosing approach based on the frequency of a patient's symptoms, so treaters can tailor treatment based on their patients' dynamic needs.

VYVGART and its individualized treatment approach represents a new age of treatment for people living with AchR-antibody positive gMG, and argenx's approach to the development of VYVGART has also informed argenx's clinical development programs currently underway in other autoimmune disease indications. FcRn represents unifying, foundational biology with the potential to address upwards of 100 autoimmune diseases that are also mediated by pathogenic IgGs. With this pipeline-in-a-product potential, argenx has demonstrated proof of concept in seven autoimmune indications and intends to be active in 15 indications by 2025.

Please provide appropriate references (ie Pubmed links)

<https://pubmed.ncbi.nlm.nih.gov/34146511/>

<https://pubmed.ncbi.nlm.nih.gov/31385879/>

<https://pubmed.ncbi.nlm.nih.gov/31118243/>

<https://pubmed.ncbi.nlm.nih.gov/30040076/>

<https://www.mg-united.com/a-mystery-to-me/>