VYVGART™
(efgartigimod alfa-fcab)

Frequently Asked Questions

The first and only IgG Fc-antibody fragment for the treatment of **generalized myasthenia gravis (gMG)** in adult patients who are anti-acetylcholine receptor (AChR) antibody positive[1,2]

VYVGART: recharging the neuromuscular junction[3,4]

VYVGART binds to and blocks the neonatal Fc receptor (FcRn), resulting in the reduction of immunoglobulin G (IgG) antibodies, including AChR autoantibodies.[1]

Fc=fragment, crystallized.

Patient portrayal

INDICATION

VYVGART™ (efgartigimod alfa-fcab) is indicated for the treatment of generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infection

VYVGART may increase the risk of infection. The most common infections observed in Study 1 were urinary tract infection (10% for VYVGART vs 5% for placebo) and respiratory tract infection (33% for VYVGART vs 29% for placebo).

Please see additional Important Safety Information throughout and full Prescribing Information.

AChR=acetylcholine receptor; Fc=fragment, crystallized; gMG=generalized myasthenia gravis; IgG=immunoglobulin G; MG-ADL=Myasthenia Gravis Activities of Daily Living.

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What is the neonatal Fc receptor (FcRn), and what role does it play in gMG?

FcRn is a receptor present in several cell types, including vascular endothelial cells, that plays a key role in gMG by reducing the clearance and prolonging the half-life of IgG antibodies.[5]

FcRn binds IgG antibodies, including the AChR autoantibodies that drive gMG, preventing them from being destroyed in the lysosome.[5] In doing so, FcRn helps maintain high levels of circulating IgG antibodies, including AChR autoantibodies that attack structures such as AChR and damage the NMJ.[5-7]

The resulting damage and dysfunction contribute to the chronic, debilitating, and potentially life-threatening muscle weakness seen in gMG.[8,9]

What is the IgG Fc-antibody fragment?

VYVGART is the Fc portion of an IgG antibody,* engineered for affinity to FcRn in order to facilitate the targeted reduction of IgG antibodies, including AChR autoantibodies.[1,10]

*Human IgG-derived.

AChR=acetylcholine receptor; Fc=fragment, crystallized; gMG=generalized myasthenia gravis; IgG=immunoglobulin G; NMJ=neuromuscular junction.

IMPORTANT SAFETY INFORMATION (cont'd)

Infection

Patients on VYVGART vs placebo had below normal levels for white blood cell counts (12% vs 5%, respectively), lymphocyte counts (28% vs 19%, respectively), and neutrophil counts (13% vs 6%, respectively). The majority of infections and hematologic abnormalities were mild to moderate in severity. Delay VYVGART administration in patients with an active infection until the infection is resolved; monitor for clinical signs and symptoms of infections. If serious infection occurs, administer appropriate treatment and consider withholding VYVGART until the infection has resolved.

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Did the ADAPT clinical trial include patients with different levels of disease severity?

Most patients in the ADAPT clinical trial had mild to moderate disease, according to the Myasthenia Gravis Foundation of America (MGFA) classification.[10]

At baseline, of the 167 patients studied[1,10]:

- **40%** in the VYVGART arm had **mild** disease (class II) vs **37%** in the placebo arm
- **56%** in the VYVGART arm had **moderate** disease (class III) vs **59%** in the placebo arm
- **4%** in the VYVGART arm had **severe** disease (class IV) vs **4%** in the placebo arm

There were no patients in the trial who were class I (only ocular symptoms) or class V (in crisis).[1,10]

Did the trial exclude patients with specific conditions?

Patients who had active hepatitis B, were seropositive for hepatitis C, were seropositive for HIV with low CD4 count, had severe infections, or had evidence of any significant serious malignant disease were not eligible to participate in the ADAPT clinical trial.[11]

Patients who were classified as MGFA class I or class V, who had a history of autoimmune disease other than gMG, or who were pregnant or lactating or intending to become pregnant, were also excluded from the trial.[1,10]

IMPORTANT SAFETY INFORMATION (cont'd)

Immunization

Immunization with vaccines during VYVGART treatment has not been studied; the safety with live or live-attenuated vaccines and the response to immunization with any vaccine are unknown. Because VYVGART causes a reduction in immunoglobulin G (IgG) levels, vaccination with live-attenuated or live vaccines is not recommended during VYVGART treatment. Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with VYVGART.

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Did patients in the ADAPT clinical trial receive any treatment in addition to VYVGART or placebo?

Patients in the clinical trial remained on stable doses of their current gMG treatment, such as NSISTs, steroids, or acetylcholinesterase inhibitors, in combination or alone, in addition to VYVGART or placebo.[1*†]

Treatments at study entry (percentage of patients in each arm)[1]:

How was response assessed in the ADAPT clinical trial?

The primary endpoint was assessed using the MG-ADL scale, a patient-reported outcome measure. The MG-ADL scale assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment.[1,12]

Patients were considered responders if they achieved a ≥2-point reduction in the total MG-ADL score compared to the treatment cycle baseline for at least 4 consecutive weeks during the first treatment cycle (by week 8), with the first reduction occurring no later than 1 week after the last infusion of the cycle. In the clinical trial, a treatment cycle was defined as 4 once-weekly 1-hour IV infusions with at least 5 weeks of follow-up.[1,10]

*All patients received stable doses of their current gMG treatment.
†All patients received an initial cycle, with subsequent cycles administered based on individual clinical evaluation when their MG-ADL score was at least 5 (with >50% MG-ADL nonocular) and if the patient was an MG-ADL responder, when they no longer had a clinically meaningful decrease (defined as having a ≥2-point improvement in total MG-ADL score) compared to baseline. The minimum time between treatment cycles, specified by study protocol, was 50 days. A maximum of 3 cycles were possible in the 26-week study.
gMG=generalized myasthenia gravis; MG-ADL=Myasthenia Gravis Activities of Daily Living; NSIST=nonsteroidal immunosuppressive therapy.

IMPORTANT SAFETY INFORMATION (cont'd)

Hypersensitivity Reactions

Hypersensitivity reactions, including rash, angioedema, and dyspnea, were observed with VYVGART. In clinical trials, hypersensitivity reactions were mild or moderate, occurred within 1 hour to 3 weeks of administration, and did not lead to treatment discontinuation. Monitor patients during administration and for 1 hour thereafter for clinical signs and symptoms of hypersensitivity reactions. If a hypersensitivity reaction occurs during administration, discontinue VYVGART infusion and institute appropriate supportive measures if needed.

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The secondary endpoint was determined using the physician-reported QMG score. QMG total score is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.[1,12]

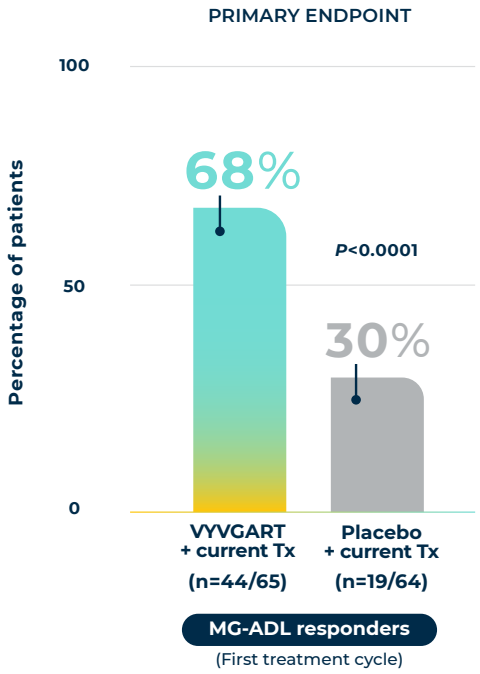
Patients were considered responders if they achieved a ≥3-point reduction in the total QMG score compared to the treatment cycle baseline for at least 4 consecutive weeks during the first treatment cycle (by week 8), with the first reduction occurring no later than 1 week after the last infusion of the cycle.[1]

What was the primary endpoint of the ADAPT clinical trial?

The primary endpoint was the percentage of anti-AChR antibody positive patients who were MG-ADL responders, defined as a patient with a ≥2-point reduction in the total MG-ADL score compared to the treatment cycle (by week 8), baseline for at least 4 consecutive weeks during the first treatment cycle, with the first reduction occurring no later than 1 week after the last infusion of the cycle.[1]

Did VYVGART meet its primary endpoint?

Yes, **68% (n=44/65) of anti-AChR antibody positive patients** treated with **VYVGART** were responders who experienced improvement in daily function (MG-ADL) vs **30% (n=19/64)** with placebo **(*P*<0.0001)**.[1,10]



AChR=acetylcholine receptor; gMG=generalized myasthenia gravis; MG-ADL=Myasthenia Gravis Activities of Daily Living; QMG=quantitative myasthenia gravis; Tx=treatment.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common (≥10%) adverse reactions with VYVGART were respiratory tract infection, headache, and urinary tract infection.

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Are there any contraindications to VYVGART?

VYVGART has no contraindications.[1]

Does VYVGART increase the risk of infections?

VYVGART may increase the risk of infection. The most common infections observed in the ADAPT clinical trial were urinary tract infection (10% vs 5%) and respiratory tract infections (33% vs 29%). A higher frequency of patients who received VYVGART compared to placebo were observed to have below normal levels for white blood cell counts (12% vs 5%), lymphocyte counts (28% vs 19%), and neutrophil counts (13% vs 6%). The majority of infections and hematologic abnormalities were mild to moderate in severity.[1]

Delay administering VYVGART in patients with an active infection until the infection is resolved, and monitor for clinical signs and symptoms of infections during treatment with VYVGART. If serious infection occurs, administer appropriate treatment and consider withholding VYVGART until the infection has resolved.[1]

Does VYVGART have any effect on the COVID-19 vaccine?

As with all vaccines, immunization with the COVID-19 vaccine during treatment with VYVGART has not been studied. The safety of immunization with live or live-attenuated vaccines and the response to immunization with any vaccine is unknown.[1]

For patients who are on treatment with VYVGART, vaccination with live-attenuated or live vaccines is not recommended. For all other vaccines, evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with VYVGART.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

Pregnancy

As VYVGART is expected to reduce maternal IgG antibody levels, reduction in passive protection to the newborn is anticipated. Risks and benefits should be considered prior to administering live or live-attenuated vaccines to infants exposed to VYVGART in utero.

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What can my patient expect in terms of tolerability?

The most common ARs observed in the clinical trial for VYVGART vs placebo were respiratory tract infection (33% vs 29%), headache (32% vs 29%), urinary tract infection (10% vs 5%), paraesthesia (7% vs 5%), and myalgia (6% vs 1%).[1]*

A higher frequency of patients who received VYVGART compared to placebo were observed to have below normal levels for white blood cell counts (12% vs 5%), lymphocyte counts (28% vs 19%), and neutrophil counts (13% vs 6%).[1]

The majority of infections and hematologic abnormalities were mild to moderate in severity.[1]

*ARs in ≥5% of patients treated with VYVGART and more frequently than placebo. Headache includes migraine and procedural headache. Paraesthesia includes oral hypoesthesia, hypoesthesia, and hyperesthesia.
AR=adverse reaction.

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

Lactation

There is no information regarding the presence of VYVGART in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VYVGART and any potential adverse effects on the breastfed infant from VYVGART or from the underlying maternal condition.

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Are any vaccinations required to begin treatment with VYVGART?

Patients should be advised to complete age-appropriate vaccines according to immunization guidelines prior to initiation of a new treatment cycle with VYVGART. Vaccination with live-attenuated or live vaccines is not recommended during treatment with VYVGART. No specific vaccinations were required in the ADAPT clinical trial inclusion criteria.[1,10]

How is VYVGART administered?

VYVGART is administered in treatment cycles of once-weekly 1-hour IV infusions for 4 weeks.[1] Infusions can be administered in a physician's office, at an infusion center, or at a patient's home with assistance from a nurse.*

*Home infusions may be available for patients with insurance coverage for this service. Please contact the patient's insurance provider directly.

How do I determine the appropriate dose for my patient?

The dose of VYVGART required is based on the patient's bodyweight and the recommended dose of 10 mg/kg. In patients weighing 120 kg or more, the recommended dose of VYVGART is 1200 mg (3 vials) per infusion.[1]

For more information on preparing and administering VYVGART, please refer to the VYVGART Dosing Guide or full Prescribing Information.

What is the dosing schedule for VYVGART?

VYVGART is a treatment for the management of gMG in anti-AChR antibody positive adult patients, administered in treatment cycles of once-weekly 1-hour IV infusions for 4 weeks.[1]

Subsequent treatment cycles should be administered based on clinical evaluation.[1]

The safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established.[1]

AChR=acetylcholine receptor; gMG=generalized myasthenia gravis.

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Infection

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For the overall VYVGART-treated population in the clinical trial, the median time to the second treatment cycle was 7 weeks after the last infusion.[1]*

The mean and median times to the second treatment cycle were 94 days and 72 days from the initial infusion of the first treatment cycle, respectively, for VYVGART-treated patients.[1]

Can I adjust the infusion schedule?

Infusions of VYVGART are administered in treatment cycles of once-weekly 1-hour IV infusions for 4 weeks. If a scheduled infusion is missed, VYVGART may be administered up to 3 days before or after the scheduled date. Thereafter, resume the original dosing schedule until the treatment cycle is completed.[1]

Are any dosing adjustments needed for patients with renal or hepatic impairment?

No dose adjustments are needed for patients with mild renal impairment or hepatic impairment.[1]

How do I monitor patients for subsequent treatment cycles?

Administer subsequent treatment cycles based on clinical evaluation; the safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established.[1]

*Time to the second treatment cycle was defined as time to return to a <2-point improvement in MG-ADL from baseline, from the last infusion of the first treatment cycle.
MG-ADL=Myasthenia Gravis Activities of Daily Living.

IMPORTANT SAFETY INFORMATION (cont'd)

Infection

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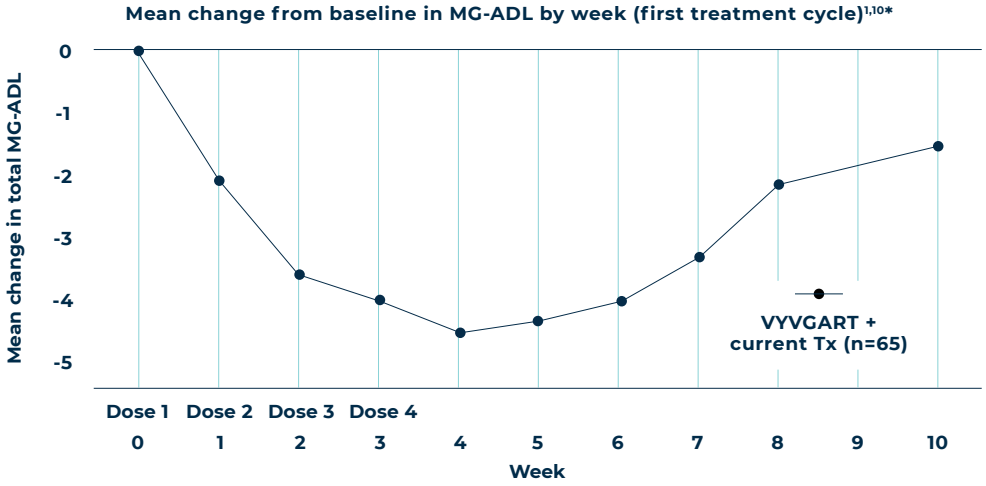

In addition, encouraging patients to track their gMG symptoms and any adverse reactions during treatment may be helpful for scheduling subsequent visits and treatment cycles.

What are the storage and handling requirements for VYVGART?

Store VYVGART vials refrigerated at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light until time of use. Do not freeze, and do not shake.[1]

*Clinical trial data from anti-AChR antibody positive VYVGART-treated population.
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References: 1. VYVGART. Prescribing information. argenx US Inc; 2021. **2.** Wolfe GI et al. *J Neurol Sci*. 2021; 430:118074. doi:10.1016/j.jns.2021.118074 **3.** Koneczny I, Herbst R. *Cells*. 2019;8(7):671. doi:10.3390/cells8070671 **4.** Howard JF Jr et al. *Neurology*. 2019;92(23):e2661-e2673. doi:10.1212/WNL.0000000000007600 **5.** Roopenian DC, Akilesh S. *Nat Rev Immunol*. 2007;7(9):715-725. doi:10.1038/nri2155 **6.** Ward ES, Ober RJ. *Trends Pharmacol Sci*. 2018;39(10):892-904. doi:10.1016/j.tips.2018.07.007 **7.** Ulrichts P et al. *J Clin Invest*. 2018;128(10):4372-4386. doi:10.1172/JCI97911 **8.** Behin A, Le Panse R. *J Neuromuscul Dis*. 2018;5(3):265-277. doi:10.3233/JND-170294 **9.** Huijbers MG et al. *J Intern Med*. 2014;275(1):12-26. doi:10.1111/joim.12163 **10.** Howard JF Jr et al. *Lancet Neurol*. 2021;20(7):526-536. doi:10.1016/S1474-4422(21)00159-9 **11.** Data on file, argenx US Inc. November 2021. **12.** Wolfe GI et al. *Neurology*. 1999;52(7):1487-1489. doi:10.1212/wnl.52.7.1487

IMPORTANT SAFETY INFORMATION (cont'd)

Immunization

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USE IN SPECIFIC POPULATIONS

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Please see the full Prescribing Information.

You may report side effects to the US Food and Drug Administration by visiting http://www.fda.gov/medwatch or calling 1-800-FDA-1088. You may also report side effects to argenx US, Inc, at 1-833-argx411 (1-833-274-9411).

For more information about VYVGART and to learn how to contact an argenx representative, please visit VYVGARTHCP.com

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