

# VYVGART™ (efgartigimod alfa-fcab)

**VYVGART is an FDA-approved treatment for adults with anti-AChR antibody positive generalized myasthenia gravis (gMG)**

AChR=acetylcholine receptor  
Visit [VYVGART.com/glossary](http://VYVGART.com/glossary) for a glossary of terms.

## Doctor Discussion Guide

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### **Start the conversation about your anti-AChR antibody positive gMG symptoms and daily abilities**

- ➔ **Fill out and bring** this guide with you to your next appointment with your neurologist.
- ➔ **Discuss** your current **anti-AChR antibody positive gMG symptoms** and how they impact your **daily abilities** with your doctor.
- ➔ **Ask** your neurologist if VYVGART could be right for you.

#### **What is VYVGART™ (efgartigimod alfa-fcab)?**

VYVGART is a prescription medicine used to treat a condition called generalized myasthenia gravis, which causes muscles to tire and weaken easily throughout the body, in adults who are positive for antibodies directed toward a protein called acetylcholine receptor (anti-AChR antibody positive).

#### **SELECT IMPORTANT SAFETY INFORMATION**

VYVGART may increase the risk of infection. In a clinical study, the most common infections were urinary tract and respiratory tract infections.

**Please see Important Safety Information throughout.**

**Please see accompanying full Prescribing Information or visit [VYVGART.com/PI](http://VYVGART.com/PI).**

## VYVGART (EFGARTIGIMOD ALFA-FCAB) AT A GLANCE

**When added to their current generalized myasthenia gravis (gMG) treatment, VYVGART helped clinical trial participants with anti-AChR antibody positive gMG achieve:**

### Improved daily abilities

**68%** (44 of 65) of participants on VYVGART achieved significant improvement in their ability to perform daily activities\*

### Reduced muscle weakness

**63%** (41 of 65) of participants on VYVGART achieved a significant reduction in muscle weakness†

**VYVGART was evaluated in a global clinical trial of adults with anti-AChR antibody positive gMG.**

**The clinical trial examined the safety and efficacy of VYVGART in 167 adults (18 years or older‡) with gMG. In addition to their current treatment, participants received either VYVGART or a placebo.**

\*Improvement maintained for 4 or more weeks was measured by a decrease of 2 or more points on the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale, with the first reduction occurring no later than 1 week after the last infusion of treatment cycle 1. The MG-ADL scale assesses the impact of gMG on daily functions by measuring 8 signs or symptoms that are commonly affected in gMG. Each item is measured on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents the loss of ability to perform that function. Total scores range from 0 to 24 points, with a higher score showing more severe gMG.

†Improvement maintained for 4 or more weeks was measured by a decrease of 3 or more points on the Quantitative Myasthenia Gravis (QMG) scale, with the first reduction occurring no later than 1 week after the last infusion of treatment cycle 1. The QMG scale assesses muscle weakness in gMG based on 13 items. Each item is assessed on a 4-point scale, where a score of 0 represents no muscle weakness and a score of 3 represents severe muscle weakness. Total scores range from 0 to 39, with a higher score meaning muscle weakness is more severe.

‡Participants in Japan were 20 years or older.

AChR=acetylcholine receptor. Visit [VYVGART.com/glossary](https://www.vyvgart.com/glossary) for a glossary of terms.

## SELECT IMPORTANT SAFETY INFORMATION

More patients on VYVGART vs placebo had below normal levels for white blood cell counts, lymphocyte counts, and neutrophil counts. The majority of infections and blood side effects were mild to moderate in severity. Your health care provider should check you for infections before starting treatment, during treatment, and after treatment with VYVGART.


**Please see Important Safety Information throughout.**

**Please see accompanying full Prescribing Information or visit [VYVGART.com/PI](https://www.vyvgart.com/PI).**

## YOUR ANTI-AChR ANTIBODY POSITIVE GENERALIZED MYASTHENIA GRAVIS (gMG) SYMPTOMS

The **Myasthenia Gravis Activities of Daily Living (MG-ADL)** scale assesses the impact of gMG on daily functions by measuring 8 signs or symptoms that are commonly affected in gMG. Each item is measured on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents the loss of ability to perform that function. Total scores range from 0 to 24 points, with a higher score showing more severe gMG.

## YOUR DAILY ABILITIES

 You can use the space below to describe your anti-AChR antibody positive gMG symptoms and how they impact your daily abilities.

Grade	0	1	2	3	Score (0, 1, 2, or 3)
1. Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	
2. Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
3. Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
4. Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
5. Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
6. Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
7. Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
8. Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	

**MG-ADL score total (Add lines 1-8) =**

In addition to the severity of your anti-AChR antibody positive gMG symptoms and how it impacts your daily abilities, your neurologist may also ask you how frequently you experience each anti-AChR antibody positive gMG symptom.

*This information has been provided for educational purposes only and is not meant to be a substitute for professional medical advice. Patients should not use this information for diagnosing a health condition. Patients should always consult a healthcare professional for medical advice or information about diagnosis and treatment.*

**Source:** Wolfe GI, et al. *Neurology*. 1999;52(7):1487-1489.

## YOUR CURRENT TREATMENT PLAN

1. On its own, my current treatment plan is enough to help me perform daily activities.  
 Yes       No
2. I would be interested in talking to my doctor about whether VYVGART could be right for me.  
 Yes       No
3. Consider your current anti-AChR antibody positive gMG condition. Is it acceptable to you?  
 Yes       No

You can use this space to write down questions and anything else you would like to discuss with your neurologist.

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**Could VYVGART be right for you?**

Learn more at [VYVGART.com](https://www.vyvgart.com).

### SELECT IMPORTANT SAFETY INFORMATION

Tell your health care provider if you have any history of infections. Tell your health care provider right away if you have signs or symptoms of an infection during treatment with VYVGART such as fever, chills, frequent and/or painful urination, cough, pain and blockage of nasal passages/sinus, wheezing, shortness of breath, fatigue, sore throat, excess phlegm, nasal discharge, back pain, and/or chest pain.

**Please see Important Safety Information throughout.**

**Please see accompanying full Prescribing Information or visit [VYVGART.com/PI](https://www.vyvgart.com).**

## IMPORTANT SAFETY INFORMATION

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### What is the most important information I should know about VYVGART™ (efgartigimod alfa-fcab)?

VYVGART may cause serious side effects, including:

- **Infection.** VYVGART may increase the risk of infection. In a clinical study, the most common infections were urinary tract and respiratory tract infections. More patients on VYVGART vs placebo had below normal levels for white blood cell counts, lymphocyte counts, and neutrophil counts. The majority of infections and blood side effects were mild to moderate in severity. Your health care provider should check you for infections before starting treatment, during treatment, and after treatment with VYVGART. Tell your health care provider if you have any history of infections. Tell your health care provider right away if you have signs or symptoms of an infection during treatment with VYVGART such as fever, chills, frequent and/or painful urination, cough, pain and blockage of nasal passages/sinus, wheezing, shortness of breath, fatigue, sore throat, excess phlegm, nasal discharge, back pain, and/or chest pain.
- **Undesirable immune reactions (hypersensitivity reactions).** VYVGART can cause the immune system to have undesirable reactions such as rashes, swelling under the skin, and shortness of breath. In clinical studies, the reactions were mild or moderate and occurred within 1 hour to 3 weeks of administration, and the reactions did not lead to VYVGART discontinuation. Your health care provider should monitor you during and after

treatment and discontinue VYVGART if needed. Tell your health care provider immediately about any undesirable reactions.

Before taking VYVGART, tell your health care provider about all of your medical conditions, including if you:

- Have a history of infection or you think you have an infection
- Have received or are scheduled to receive a vaccine (immunization). Discuss with your health care provider whether you need to receive age-appropriate immunizations before initiation of a new treatment cycle with VYVGART. The use of vaccines during VYVGART treatment has not been studied, and the safety with live or live-attenuated vaccines is unknown. Administration of live or live-attenuated vaccines is not recommended during treatment with VYVGART.
- Are pregnant or plan to become pregnant and are breastfeeding or plan to breastfeed.

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

### What are the common side effects of VYVGART?

The most common side effects of VYVGART are respiratory tract infection, headache, and urinary tract infection.

These are not all the possible side effects of VYVGART. Call your doctor for medical advice about side effects. You may report side effects to the US Food and Drug Administration at 1-800-FDA-1088.

Please see the full Prescribing Information for VYVGART and talk to your doctor.



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## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VYVGART safely and effectively. See full prescribing information for VYVGART.

**VYVGART™ (efgartigimod alfa-fcab) injection, for intravenous use**  
Initial U.S. Approval: 2021

### INDICATIONS AND USAGE

VYVGART is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. (1)

### DOSAGE AND ADMINISTRATION

- Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with VYVGART. (2.1)
- The recommended dosage is 10 mg/kg administered as an intravenous infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, the recommended dose is 1200 mg per infusion. (2.2)
- 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. (2.2)
- Must be diluted with 0.9% Sodium Chloride Injection, USP prior to administration. (2.3)
- Administer as an intravenous infusion over one hour via a 0.2 micron in-line filter. (2.3)

### DOSAGE FORMS AND STRENGTHS

Injection: 400 mg in 20 mL (20 mg/mL) single-dose vial. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

- Infections: Delay administration of VYVGART to patients with an active infection. Monitor for signs and symptoms of infection in patients treated with VYVGART. If serious infection occurs, administer appropriate treatment and consider withholding VYVGART until the infection has resolved. (5.1)
- Hypersensitivity Reactions: Angioedema, dyspnea, and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy. (5.2)

### ADVERSE REACTIONS

Most common adverse reactions ( $\geq 10\%$ ) in patients treated with gMG are respiratory tract infections, headache, and urinary tract infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact argenx at 1-833-argx411 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

Closely monitor for reduced effectiveness of medications that bind to the human neonatal Fc receptor. When concomitant long-term use of such medications is essential for patient care, consider discontinuing VYVGART and using alternative therapies. (7)

### See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2021

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

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

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Recommended Vaccination

Because VYVGART causes transient reduction in IgG levels, immunization with live-attenuated or live vaccines is not recommended during treatment with VYVGART. Evaluate the need to administer age-appropriate immunizations according to immunization guidelines before initiation of a new treatment cycle with VYVGART [see *Dosage and Administration (2.2)* and *Warnings and Precautions (5.1)*].

#### 2.2 Recommended Dose and Dose Schedules

Dilute VYVGART prior to administration. Administer via intravenous infusion only [see *Dosage and Administration (2.3)*].

The recommended dosage of VYVGART is 10 mg/kg administered as an intravenous infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, the recommended dose of VYVGART is 1200 mg (3 vials) per infusion.

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.

If a scheduled infusion is missed, VYVGART may be administered up to 3 days after the scheduled time point. Thereafter, resume the original dosing schedule until the treatment cycle is completed.

#### 2.3 Preparation and Administration Instructions

Prior to administration, VYVGART single-dose vials require dilution in 0.9% Sodium Chloride Injection, USP, to make a total volume to be administered of 125 mL (see *Preparation*).

Check that the VYVGART solution is clear to slightly opalescent and colorless to slightly yellow. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if opaque particles, discoloration, or other foreign particles are present.

Use aseptic technique when preparing the VYVGART diluted solution for intravenous infusion. Each vial is for single-dose only.

Discard any unused portion.

## Preparation

- Calculate the dose (mg), total drug volume (mL) of VYVGART solution required, and the number of vials needed based on the recommended dose according to the patient's body weight [*see Dosage and Administration (2.2)*]. Each vial contains a total of 400 mg of VYVGART at a concentration of 20 mg per mL.
- Gently withdraw the calculated dose of VYVGART from the vial(s) with a sterile syringe and needle. Discard any unused portion of the vials.
- Dilute the withdrawn VYVGART with 0.9% Sodium Chloride Injection, USP to make a total volume of 125 mL for intravenous infusion.
- Gently invert the infusion bag containing the diluted VYVGART without shaking to ensure thorough mixing of the product and the diluent.
- The diluted solution can be administered using polyethylene (PE), polyvinyl chloride (PVC), ethylene vinyl acetate (EVA), or ethylene/polypropylene copolymer bags (polyolefins bags), and with PE, PVC, EVA, or polyurethane/polypropylene infusion lines.

## Storage Conditions of the Diluted Solution

- VYVGART does not contain preservatives. Administer immediately after dilution and complete the infusion within 4 hours of dilution.
- If immediate use is not possible, the diluted solution may be stored refrigerated at 2°C to 8°C (36°F to 46°F) for up to 8 hours. Do not freeze. Protect from light. Allow the diluted drug to reach room temperature before administration. Complete the infusion within 4 hours of removal from the refrigerator. Do not heat the diluted drug in any manner other than via ambient air.

## Administration

- VYVGART should be administered via intravenous infusion by a healthcare professional.
- Visually inspect VYVGART diluted solution for particles or discoloration prior to administration. Do not use if it is discolored, or if opaque or foreign particles are seen.
- Infuse the total 125 mL of diluted solution intravenously over one hour via a 0.2 micron in-line filter.
- After administration of VYVGART, flush the entire line with 0.9% Sodium Chloride Injection, USP.
- 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 administration of VYVGART and institute appropriate supportive measures [*see Warnings and Precautions (5.2)*].
- Other medications should not be injected into infusion side ports or mixed with VYVGART.



### **3 DOSAGE FORMS AND STRENGTHS**

Injection: 400 mg/20 mL (20 mg/mL) as a colorless to slightly yellow, clear to slightly opalescent solution, in a single-dose vial.

### **4 CONTRAINDICATIONS**

None.

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Infections**

VYVGART may increase the risk of infection. The most common infections observed in Study 1 were urinary tract infection (10% of VYVGART-treated patients compared to 5% of placebo-treated patients) and respiratory tract infections (33% of VYVGART-treated patients compared to 29% of placebo-treated patients) [see *Adverse Reactions (6.1) and Clinical Studies (14)*]. A higher frequency of patients who received VYVGART compared to placebo were observed to have below normal levels for white blood cell counts (12% versus 5%, respectively), lymphocyte counts (28% versus 19%, respectively), and neutrophil counts (13% versus 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. During treatment with VYVGART, monitor for clinical signs and symptoms of infections. If serious infection occurs, administer appropriate treatment and consider withholding VYVGART until the infection has resolved.

#### Immunization

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

#### **5.2 Hypersensitivity Reactions**

Hypersensitivity reactions, including rash, angioedema, and dyspnea were observed in VYVGART-treated patients. In clinical trials, hypersensitivity reactions were mild or moderate, occurred within one hour to three 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 [see *Dosage and Administration (2.3)*]. If a hypersensitivity reaction occurs during administration, discontinue VYVGART infusion and institute appropriate supportive measures if needed.

### **6 ADVERSE REACTIONS**

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Infections [see *Warnings and Precautions (5.1)*]

- Hypersensitivity Reactions [see Warnings and Precautions (5.2)]

## 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical studies, the safety of VYVGART has been evaluated in 246 patients who received at least one dose of VYVGART, including 57 patients exposed to at least 7 treatment cycles and 8 patients exposed to at least 10 treatment cycles.

In a placebo-controlled study (Study 1) in patients with gMG, 84 patients received VYVGART 10 mg/kg [see *Clinical Studies (14)*]. Of these 84 patients, approximately 75% were female, 82% were White, 11% were Asian, and 8% were of Hispanic or Latino ethnicity. The mean age at study entry was 46 years (range 19 to 78).

The minimum time between treatment cycles, specified by study protocol, was 50 days. On average, VYVGART-treated patients received 2 cycles in Study 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.

Adverse reactions reported in at least 5% of patients treated with VYVGART and more frequently than placebo are summarized in [Table 1](#). The most common adverse reactions (reported in at least 10% of VYVGART-treated patients) were respiratory tract infection, headache, and urinary tract infection.

**Table 1: Adverse Reactions in  $\geq 5\%$  of Patients Treated with VYVGART and More Frequently than in Placebo-Treated Patients in Study 1 (Safety Population)**

Adverse reaction	VYVGART (N=84) %	Placebo (N=83) %
Respiratory tract infection	33	29
Headache <sup>1</sup>	32	29
Urinary tract infection	10	5
Paraesthesia <sup>2</sup>	7	5
Myalgia	6	1

<sup>1</sup>Headache includes migraine and procedural headache.

<sup>2</sup>Paraesthesia includes oral hypoesthesia, hypoesthesia, and hyperesthesia.

## 6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection,

concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to VYVGART in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In up to 26 weeks of treatment in Study 1, 20% (17/83) of patients developed antibodies to VYVGART. Seven percent (6/83) of patients developed neutralizing antibodies.

Because few patients tested positive for anti-efgartigimod alfa-fcab antibodies and neutralizing antibodies, the available data are too limited to make definitive conclusions regarding immunogenicity and the effect on pharmacokinetics, safety, or efficacy of VYVGART.

## **7 DRUG INTERACTIONS**

### **7.1 Effect of VYVGART on Other Drugs**

Concomitant use of VYVGART with medications that bind to the human neonatal Fc receptor (FcRn) (e.g., immunoglobulin products, monoclonal antibodies, or antibody derivatives containing the human Fc domain of the IgG subclass) may lower systemic exposures and reduce effectiveness of such medications. Closely monitor for reduced effectiveness of medications that bind to the human neonatal Fc receptor. When concomitant long-term use of such medications is essential for patient care, consider discontinuing VYVGART and using alternative therapies.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

There are no available data on the use of VYVGART during pregnancy. There is no evidence of adverse developmental outcomes following the administration of VYVGART at up to 100 mg/kg/day in rats and rabbits (see Data).

The background rate of major birth defects and miscarriage in the indicated population is unknown. In the U.S. general population, the estimated background rate of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Clinical Considerations

##### *Fetal/Neonatal Adverse Reactions*

Monoclonal antibodies are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third semester. Therefore, efgartigimod alfa-fcab may be transmitted from the mother to the developing fetus.

As VYVGART is expected to reduce maternal IgG antibody levels, reduction in passive protection to the newborn is anticipated. Risk and benefits should be considered prior to administering live or live-attenuated vaccines to infants exposed to VYVGART in utero [see *Warnings and Precautions (5.1)*].

#### Data

## *Animal Data*

Intravenous administration of efgartigimod alfa-fcab (0, 30, or 100 mg/kg/day) to pregnant rats and rabbits throughout organogenesis resulted in no adverse effects on embryofetal development in either species. The doses tested are 3 and 10 times the recommended human dose (RHD) of 10 mg/kg, on a body weight (mg/kg) basis.

Intravenous administration of efgartigimod alfa-fcab (0, 30, or 100 mg/kg/day) to rats throughout gestation and lactation resulted in no adverse effects on pre- or postnatal development. The doses tested are 3 and 10 times the recommended human dose (RHD) of 10 mg/kg, on a body weight (mg/kg) basis.

## **8.2 Lactation**

### Risk Summary

There is no information regarding the presence of efgartigimod alfa-fcab in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk.

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.

## **8.4 Pediatric Use**

Safety and effectiveness in pediatric patients have not been established.

## **8.5 Geriatric Use**

Clinical studies of VYVGART did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger adult patients.

## **8.6 Renal Impairment**

No dose adjustment of VYVGART is needed for patients with mild renal impairment. There are insufficient data to evaluate the impact of moderate renal impairment (eGFR 30-59 mL/min/1.73 m<sup>2</sup>) and severe renal impairment (eGFR <30 mL/min/1.73 m<sup>2</sup>) on pharmacokinetic parameters of efgartigimod alfa-fcab [see *Clinical Pharmacology* (12.3)].

## **11 DESCRIPTION**

Efgartigimod alfa-fcab is a human immunoglobulin G1 (IgG1) -derived Fc fragment (fragment, crystallized) of the za allotype. The efgartigimod alfa-fcab Fc fragment is a homodimer consisting of two identical peptide chains each consisting of 227 amino acids linked together by two interchain disulfide bonds with affinity for FcRn. The molecular weight of efgartigimod alfa-fcab is approximately 54 kDa.

VYVGART (efgartigimod alfa-fcab) injection is a sterile, preservative free, clear to slightly opalescent, colorless to slightly yellow solution supplied in a single-dose vial for infusion after dilution.

Each 20 mL single-dose vial contains 400 mg of efgartigimod alfa-fcab at a concentration of 20 mg/mL. In addition, each mL of solution contains L-arginine hydrochloride (31.6 mg), polysorbate 80 (0.2 mg), sodium chloride (5.8 mg), sodium phosphate dibasic anhydrous (2.4 mg), sodium phosphate monobasic monohydrate (1.1 mg) and water for injection, USP, at a pH of 6.7.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

Efgartigimod alfa-fcab is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG.

### **12.2 Pharmacodynamics**

In Study 1 [see *Clinical Studies (14)*], the pharmacological effect of efgartigimod alfa-fcab was assessed by measuring the decrease in serum IgG levels and AChR autoantibody levels. In patients testing positive for AChR antibodies and who were treated with VYVGART, there was a reduction in total IgG levels relative to baseline. Decrease in AChR autoantibody levels followed a similar pattern.

### **12.3 Pharmacokinetics**

Efgartigimod alfa-fcab exhibits linear pharmacokinetics, and following single doses of efgartigimod alfa-fcab, exposures increase proportionally up to 50 mg/kg (5 times the recommended dosage).

#### Distribution

The volume of distribution is 15 to 20L.

#### Metabolism and Elimination

Efgartigimod alfa-fcab is expected to be degraded by proteolytic enzymes into small peptides and amino acids.

The terminal half-life is 80 to 120 hours (3 to 5 days).

After a single intravenous dose of 10 mg/kg efgartigimod alfa-fcab in healthy subjects, less than 0.1% of the administered dose was recovered in urine.

#### Specific Populations

##### *Age, Sex, and Race*

A population pharmacokinetics analysis assessing the effects of age, sex, and race did not suggest any clinically significant impact of these covariates on efgartigimod alfa-fcab exposures.

### *Patients with Renal Impairment*

No dedicated pharmacokinetic study has been performed in patients with renal impairment.

A population PK analysis of data from the VYVGART clinical studies indicated that patients with mild renal impairment (eGFR 60-89 mL/min/1.72m<sup>2</sup>) had 22% increase in exposure relative to the exposure in patients with normal renal function [see *Use in Specific Populations (8.6)*].

### *Patients with Hepatic Impairment*

No dedicated pharmacokinetic study has been performed in patients with hepatic impairment. Hepatic impairment is not expected to affect the pharmacokinetics of efgartigimod alfa-fcab.

### Drug Interaction Studies

Clinical drug interactions studies have not been performed with efgartigimod alfa-fcab.

### *P450 Enzymes*

Efgartigimod alfa-fcab is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

### *Drug Interactions with Other Drugs or Biological Products*

Efgartigimod alfa-fcab may decrease concentrations of compounds that bind to the human FcRn [see *Drug Interactions (7.1)*].

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

#### Carcinogenesis and Mutagenesis

No studies have been conducted to assess the carcinogenic potential of efgartigimod alfa-fcab.

No studies have been conducted to assess the genotoxic potential of efgartigimod alfa-fcab.

#### Impairment of Fertility

Intravenous administration of efgartigimod alfa-fcab (0, 30, or 100 mg/kg/day) to male and female rats prior to and during mating and continuing in females through gestation day 7 resulted in no adverse effects on fertility. The doses tested are 3 and 10 times the recommended human dose (RHD) of 10 mg/kg, on a body weight (mg/kg) basis.

## 14 CLINICAL STUDIES

The efficacy of VYVGART for the treatment of generalized myasthenia gravis (gMG) in adults who are AChR antibody positive was established in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial (Study 1; NCT03669588).

Study 1 enrolled patients who met the following criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- MG-Activities of Daily Living (MG-ADL) total score of  $\geq 5$
- On stable dose of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- IgG levels of at least 6 g/L

A total of 167 patients were enrolled in Study 1 and were randomized to receive either VYVGART 10mg/kg (1200 mg for those weighing 120 kg or more) (n=84) or placebo (n=83). Baseline characteristics were similar between treatment groups. Patients had a median age of 46 years at screening (range: 19 to 81 years) and a median time since diagnosis of 9 years. Seventy-one percent were female, and 84% were White. Median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis (QMG) total score was 16. The majority of patients (n=65 for VYVGART; n=64 for placebo) were positive for AChR antibodies.

At baseline, over 80% of patients in each group received AChE inhibitors, over 70% in each treatment group received steroids, and approximately 60% in each treatment group received NSISTs, at stable doses.

Patients were treated with VYVGART at the recommended dosage regimen [see *Dosage and Administration* (2.2)].

The efficacy of VYVGART was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which 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. In this study, an MG-ADL responder was defined as a patient with a 2-point or greater reduction in the total MG-ADL score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of the cycle.

The primary efficacy endpoint was the comparison of the percentage of MG-ADL responders during the first treatment cycle between treatment groups in the AChR-Ab positive population. A statistically significant difference favoring VYVGART was observed in the MG-ADL responder rate during the first treatment cycle [67.7% in the VYVGART-treated group vs 29.7% in the placebo-treated group ( $p < 0.0001$ )].

The efficacy of VYVGART was also measured using the Quantitative Myasthenia Gravis (QMG) total score which 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. In this study, a QMG responder was defined as a patient who had a 3-point or greater reduction in the total QMG score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after last infusion of the cycle.

The secondary endpoint was the comparison of the percentage of QMG responders during the first treatment cycle between both treatment groups in the AChR-Ab positive patients. A statistically significant difference favoring VYVGART was observed in the QMG responder rate during the first treatment cycle [63.1% in the VYVGART-treated group vs 14.1% in the placebo-treated group ( $p < 0.0001$ )].

The results are presented in [Table 2](#).

**Table 2: MG-ADL and QMG Responders During Cycle 1 in AChR-Ab Positive Patients (mITT Analysis Set)**

	<b>VYVGART n=65 %</b>	<b>Placebo n=64 %</b>	<b>P-value</b>	<b>Odds Ratio (95% CI)</b>
MG-ADL Responders	67.7	29.7	< 0.0001	4.951 (2.213, 11.528)
QMG Responders	63.1	14.1	< 0.0001	10.842 (4.179, 31.200)

MG-ADL=Myasthenia Gravis Activities of Daily Living QMG =Quantitative Myasthenia Gravis; mITT=modified intent-to-treat; n=number of patients for whom the observation was reported; CI = confidence interval;

Logistic regression stratified for AChR-Ab status (if applicable), Japanese/Non-Japanese and standard of care, with baseline MG-ADL as covariate / QMG as covariates

Two-sided exact p-value

Figure 1 shows the mean change from baseline on the MG-ADL during cycle 1.



**Figure 1: Mean Change in Total MG-ADL From Cycle 1 Baseline Over Time in AChR-Ab Positive Patients (mITT Analysis Set)**

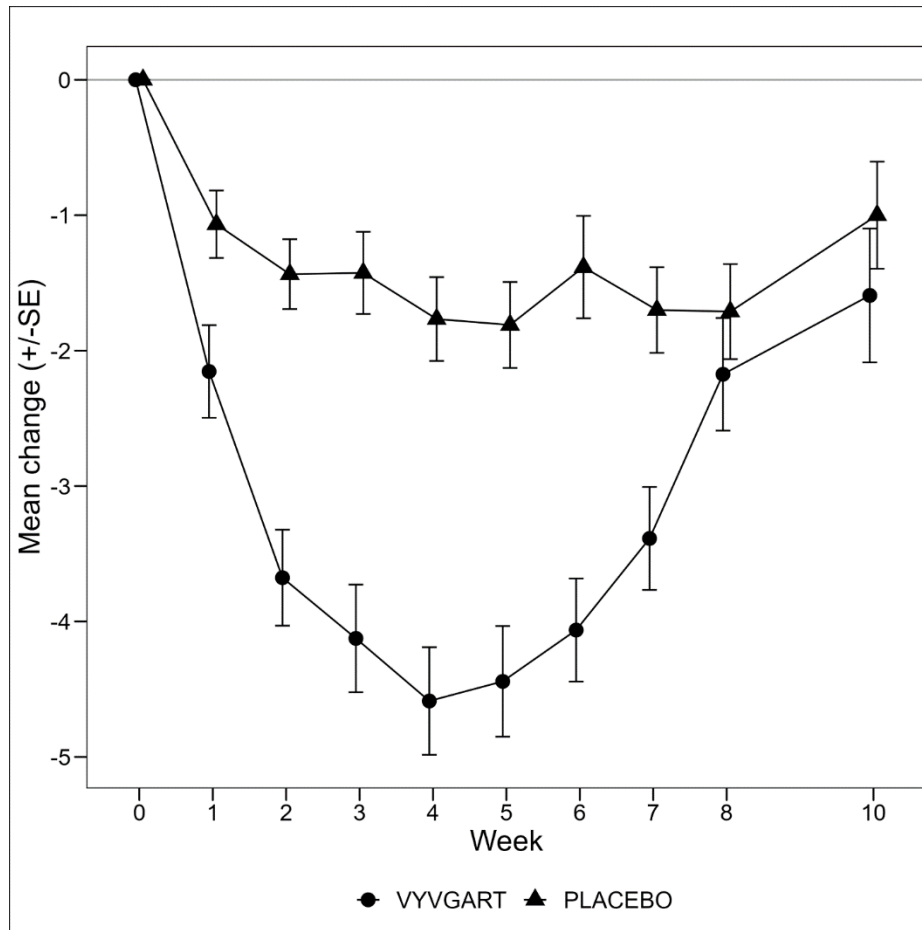
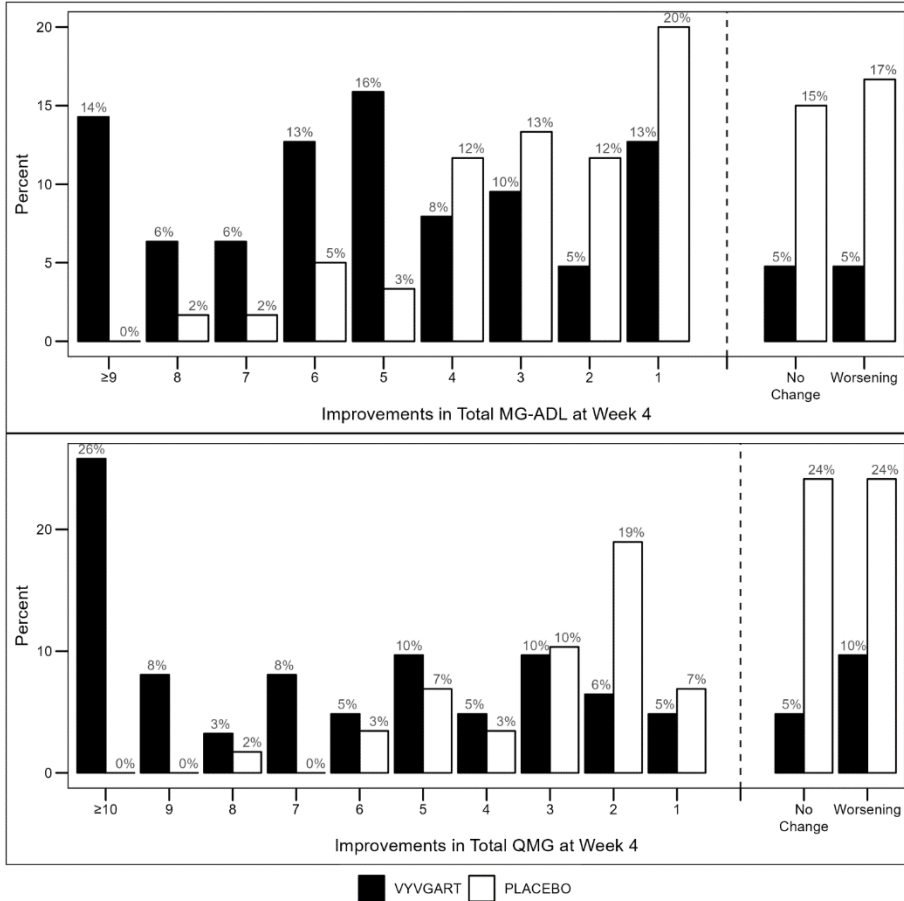


Figure 2 shows the distribution of response on the MG-ADL and QMG during cycle 1, four weeks after the first infusion with VYVGART.

**Figure 2: Percentage of Patients with MG-ADL and QMG Total Score Change 4 Weeks Post Initial Infusion of the First Cycle in AChR-Ab Positive Population**



**16 HOW SUPPLIED/STORAGE AND HANDLING**

VYVGART (efgartigimod alfa-fcab) injection is a preservative free, sterile, colorless to slightly yellow, clear to slightly opalescent solution supplied as 400 mg/20 mL (20 mg/mL) in one single-dose vial per carton (NDC 73475-3041-5).

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. Do not shake.

Refer to *Dosage and Administration* (2.3) for information on stability and storage of the diluted solutions of VYVGART.

## 17 PATIENT COUNSELING INFORMATION

### Infections

Instruct patients to communicate any history of infections to the healthcare provider and to contact their healthcare provider if they develop any symptoms of an infection. Advise patients to complete age-appropriate vaccines according to immunization guidelines prior to initiation of a new treatment cycle with VYVGART. Administration of live or live-attenuated vaccines is not recommended during treatment with VYVGART [see *Warnings and Precautions (5.1)*].

### Hypersensitivity Reactions

Inform patients about the signs and symptoms of hypersensitivity reactions. Advise patients to contact their healthcare provider immediately for signs or symptoms of hypersensitivity reactions [see *Warnings and Precautions (5.2)*].

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