PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrVYVGART®

Efgartigimod alfa for injection

400 mg/20 mL (20 mg/mL) solution, for intravenous use

Professed Standard

Neonatal Fc Receptor Antagonist

Manufactured by:
argenx BV
Industriepark Zwijnaarde 7
9052 Zwijnaarde (Ghent)
Belgium

Imported by:
Quality & Compliance Services Inc.
220-2000 Argentia Road, Plaza 2
Mississauga ON L5N 1V8
Canada

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RECENT MAJOR LABEL CHANGES

7 Warnings and Precautions, Immune [2025-06]

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

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

1.1 Pediatrics

Pediatrics (< 18 years of age): The safety and efficacy of VYVGART in children and adolescents below the age of 18 years has not been established. VYVGART is not indicated for use in pediatric patients.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Eleven (11/84 – 13%) patients aged 65 and over were treated with VYVGART in the placebo-controlled study. The number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger adult patients.

2 CONTRAINDICATIONS

Vyvgart is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

Dilute Vyvgart prior to administration. Administer via intravenous infusion only. See 4.3 Reconstitution.

The recommended dosage of Vyvgart is 10 mg/kg administered as an intravenous infusion over one hour once weekly for 4 weeks (one treatment cycle). 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 frequency of Vyvgart treatment cycles may vary by patient. The safety of initiating subsequent cycles sooner than 4 weeks from the last infusion of the previous treatment cycle has not been established.

Pediatrics (< 18 years of age): The safety and efficacy of Vyvgart in children and adolescents below the age of 18 years has not been established. Vyvgart is not indicated for use in pediatric patients.

Geriatrics (≥ 65 years of age): Eleven (11/84 – 13%) patients aged 65 and over were treated with Vyvgart in the placebo-controlled study. The number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger adult patients.

Renal Impairment: No dose adjustment of Vyvgart is needed for patients with mild renal impairment. There is very limited safety and efficacy data in patients with moderate renal impairment (eGFR 30-59mL/min/1.73 m^2) and no safety and efficacy data in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2). (see 10 CLINICAL PHARMACOLOGY)

4.3 Reconstitution

Parenteral Products:

Prior to administration, Vyvgart single-use vials require dilution in 0.9% Sodium Chloride Injection, USP, to make a total volume to be administered of 125 mL.

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-use only.

Discard any unused portion in accordance with local requirements.

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. Each vial contains a total of 400 mg of Vyvgart at a concentration of 20 mg per mL. See 4.2 Recommended Dose and Dosage Adjustment.
- Gently withdraw the calculated dose of Vyvgart from the vial(s) with a sterile syringe and needle. Discard any unused portion of the vials in accordance with local requirements.
- 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. See 11 STORAGE, STABILITY AND DISPOSAL.

4.4 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 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 infusion reactions. Should a reaction occur, discontinue the infusion and institute

appropriate supportive measures, if needed. Once resolved, and based on the severity of the reaction, administration may be cautiously resumed, if needed at a slower rate based on clinical evaluation. See 7 WARNINGS AND PRECAUTIONS.

- Other medications should not be injected into infusion side ports or mixed with Vyvgart.

4.5 Missed Dose

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.

5 OVERDOSAGE

There are no known specific signs and symptoms of overdose with Vyvgart. In the event of an overdose the adverse events are not expected to be different from those observed at the recommended dose. Patients should be monitored for adverse reactions and appropriate symptomatic and supportive treatment initiated. There is no specific antidote for overdose with Vyvgart.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	20 mg/mL efgartigimod alfa solution	L-arginine hydrochloride, sodium chloride, sodium phosphate dibasic anhydrous, sodium phosphate monobasic monohydrate polysorbate 80, water for injection

Description

Vyvgart (efgartigimod alfa for 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-use vial.

7 WARNINGS AND PRECAUTIONS

Immune

Infections

As Vyvgart causes a reduction in IgG levels, the risk of infections may increase. The most common infections observed in clinical trials were upper respiratory tract infections and urinary tract infections. While the majority of infections were mild to moderate in severity, serious infections were reported. See 8.2 Clinical Trial Adverse Reactions. Monitor for clinical signs and symptoms of infections during treatment with Vyvgart. Delay Vyvgart administration in patients with an active infection until the infection is resolved. If a serious infection occurs, administer appropriate treatment and consider withholding Vyvgart until the infection has resolved.

Immunization

Administer all vaccines according to immunization guidelines at least 4 weeks before initiation of treatment with Vyvgart.

The safety of immunization with live vaccines and the immune response to vaccination during treatment with Vyvgart are unknown. Because Vyvgart causes a reduction in IgG levels, vaccination with live vaccines is not recommended during treatment with Vyvgart.

For all other vaccines, vaccination should take place at least 2 weeks after the last infusion of a treatment cycle and 4 weeks before initiating the next cycle.

Reproductive Health: Female and Male Potential

- **Fertility**
  There is no clinical experience with Vyvgart use and its potential effect on fertility.

Sensitivity/Resistance

Hypersensitivity and Infusion related reactions

Hypersensitivity reactions such as rash, pruritis or anaphylactic reactions may occur. In clinical trials, infusion-related reactions were mild or moderate and did not lead to treatment discontinuation. Monitor patients during administration and for 1 hour thereafter for clinical signs and symptoms of infusion reactions. Should a reaction occur, discontinue the infusion and institute appropriate supportive measures, if needed. Once resolved, and based on the severity of the reaction, administration may be cautiously resumed, if needed at a slower rate based on clinical evaluation (See 4.4 Administration).

Patients should be informed of the signs and symptoms of hypersensitivity reactions and advised to contact their healthcare provider immediately should they occur.

7.1 Special Populations

7.1.1 Pregnant Women

There are no available clinical data on the use of Vyvgart during pregnancy. Reproductive and developmental toxicity studies were conducted in rats and rabbits. See 16 NON CLINICAL TOXICOLOGY.

Monoclonal antibodies are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third trimester. Therefore, Vyvgart may be transmitted from the mother to the developing fetus. As Vyvgart is expected to reduce maternal IgG antibody levels, and is also expected to inhibit the transfer of maternal antibodies to the fetus, 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*.

7.1.2 Breast-feeding

There is no information regarding the presence of Vyvgart 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. A risk to the breastfed newborn/infant cannot be excluded.

The developmental and health benefits of breastfeeding and the mother's clinical need for Vyvgart should be considered, as well as any potential adverse effects on the breastfed infant from Vyvgart or from the underlying maternal condition.

7.1.3 Pediatrics

Pediatrics (<18 years): The safety and efficacy of Vyvgart in children and adolescents below the age of 18 years has not been established. Vyvgart is not indicated for use in pediatric patients.

7.1.4 Geriatrics

Geriatrics (≥ 65 years of age): Eleven (11/84 – 13%) patients aged 65 and over were treated with Vyvgart in the placebo-controlled study. The number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger adult patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

In the placebo-controlled Phase 3 Study ARGX-113-1704 (Study 1704), the most common adverse reactions (≥ 10%) seen in patients who received at least one dose of Vyvgart included headache (reported by 29% of Vyvgart-treated patients and 28% of placebo-treated patients), upper respiratory tract infection (reported by 11% of Vyvgart-treated patients and 5% of placebo-treated patients), and urinary tract infection (reported by 10% of Vyvgart-treated patients and 5% of placebo-treated patients) (Table 2). Adverse reactions of severity Grade ≥3 (according to the Common Terminology Criteria for Adverse Events) were reported by 11% (9/84) of Vyvgart-treated patients and 10% (8/83) of placebo-treated patients. The proportion of patients treated with Vyvgart who discontinued treatment due to adverse reactions was 4% (3/84).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In the placebo-controlled Phase 3 study (Study 1704) in patients with gMG, 84 patients received Vyvgart 10 mg/kg. See 14 CLINICAL TRIALS. The frequency of Vyvgart treatment cycles at the recommended dose regimen varied by patient. See 4 DOSAGE AND ADMINISTRATION. The safety of initiating subsequent cycles sooner than 4 weeks from the last infusion of the previous treatment cycle has not been established.

A total of 21/84 (25%) patients on Vyvgart received a single treatment cycle, 56/84 (67%) patients received 2 treatment cycles, and 7/84 (8%) patients received 3 treatment cycles. 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.

Adverse reactions reported in at least 5% of patients treated with Vyvgart and more frequently than placebo (≥ 3 patients) are summarized Table 2.

Table 2: Adverse Reactions Reported in ≥ 5% of Patients with Myasthenia Gravis Treated With Vyvgart and More Frequently Than in Placebo-Treated Patients (≥ 3 patients) in Study ARGX-113-1704

Adverse reaction	**Vyvgart** (N=84) n (%)	**Placebo** (N=83) n (%)
Infections and infestations		
Bronchitis	5 (6)	2 (2)
Upper respiratory tract infection	9 (11)	4 (5)
Urinary tract infection	8 (10)	4 (5)
Injury, poisoning and procedural complications		
Procedural headache	4 (5)	1 (1)
Musculoskeletal and connective tissue disorders		
Myalgia	5 (6)	1 (1)

Infections

The most frequently reported adverse reactions were infections. Overall, treatment emergent infections were reported in 46% (n=39) of patients treated with Vyvgart and 37% (n=31) of patients treated with placebo. The most reported infections were upper respiratory tract infections and urinary tract infections. 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 hematology abnormalities were mild to moderate in severity. Serious infections have been reported in patients treated with Vyvgart.

Procedural headache

Procedural headache was reported in 4.8% of the patients treated with Vyvgart and 1.2% of patients treated with placebo. Procedural headache was reported when a headache was judged to be temporally related to the intravenous infusion of Vyvgart. All were mild or moderate except one event which was reported as severe (Grade 3).

8.3 Less Common Clinical Trial Adverse Reactions (occurring in <5% of Patients with Myasthenia Gravis treated with Vyvgart and more frequently than in placebo-treated patients (≥ 2 patients) in Study ARGX-113-1704)

Eye Disorders: visual impairment
General Disorders and Administration Site Conditions: pain
Immune System Disorders: seasonal allergy
Infections and Infestations: ear infection, sinusitis
Injury, Poisoning and Procedural Complications: skin abrasion
Nervous System Disorders: migraine, hypoesthesia

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Clinical drug interactions studies have not been performed with Vyvgart.

9.4 Drug-Drug Interactions

Vyvgart may decrease concentrations of compounds that bind to the human FcRn, such as, immunoglobulin products, monoclonal antibodies, or antibody derivates containing the human Fc domain of the IgG subclass. Patients receiving Vyvgart while concomitantly on treatment with these products should be closely monitored for the altered efficacy response to these products. If possible, it is recommended to postpone initiation of treatment with these products to two weeks after the last dose of any given treatment cycle of Vyvgart.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Efgartigimod alfa is a human IgG1 antibody fragment that binds to neonatal Fc receptor (FcRn) and inhibits its interaction with IgG. This results in increased degradation of IgG and reduction of circulating IgG and pathological IgG autoantibodies.

10.2 Pharmacodynamics

In the placebo-controlled study in gMG patients (see 14 CLINICAL TRIALS), the pharmacological effect of efgartigimod alfa was assessed by measuring the decrease in serum IgG levels and AChR autoantibody levels. In patients who were tested positive for AChR antibodies and treated with efgartigimod alfa at the recommended dose and schedule (see 4 DOSAGE AND ADMINISTRATION), the mean percentage decrease in total IgG levels compared to baseline reached 61% one week after the last infusion of the initial treatment cycle and returned to baseline levels 9 weeks after the last infusion. Decrease in AChR autoantibody levels followed a similar time course.

10.3 Pharmacokinetics

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

Distribution:

The volume of distribution is 15 to 20L.

Metabolism:

Efgartigimod alfa 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).

Elimination

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

Special Populations and Conditions

- **Age, gender, and race:** A population pharmacokinetics analysis assessing the effect of age, gender, and race did not suggest clinically significant impact of these covariates on efgartigimod alfa exposures.
- **Hepatic Insufficiency:** No dedicated pharmacokinetic study has been performed in patients with hepatic impairment. Hepatic impairment is not expected to affect the pharmacokinetics of efgartigimod alfa.
- **Renal Insufficiency:** No dedicated pharmacokinetic study has been performed in patients with renal impairment. Based on a population PK analysis of data from the Vyvgart clinical studies, patients with mild renal impairment (eGFR 60-89 mL/min/1.73m^2) had 22% increase in exposure relative to the exposure in patients with normal renal function. The impact of moderate renal impairment (eGFR < 60 mL/min/1.73m^2) on Vyvgart exposure could not be assessed since the number of patients was too small (N = 3).

11 STORAGE, STABILITY AND DISPOSAL

Vyvgart (efgartigimod alfa for 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-use vial.

Store Vyvgart vials refrigerated at 2°C to 8°C in the original carton to protect from light until time of use. Do not freeze. Do not shake.

See 4.3 Reconstitution for information on stability and storage of the diluted solutions of Vyvgart.

12 SPECIAL HANDLING INSTRUCTIONS

Discard the vial containing unused portion of Vyvgart in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: efgartigimod alfa

Chemical name: efgartigimod; human recombinant immunoglobulin G1 Abdeg™ Fc fragment

Molecular formula and molecular mass: The theoretical mass for efgartigimod is 53,915 Da based on the lysine clipped amino acid sequence with 2 x G0F glycans at 100% occupancy, and has been confirmed by peptide mapping experiments.

Structural formula: The efgartigimod Fc fragment is a homodimer consisting of two identical peptide chains each consisting of 227 amino acids. The peptide chains are linked together by two interchain disulfide bonds at positions Cys_{226} and Cys_{229}. Every peptide chain includes two intrachain disulfide bonds at positions Cys_{261}-Cys_{321} and Cys_{367}-Cys_{425}. Efgartigimod contains an N-glycosylation site at position Asn_{297} with the predominant glycan being of the G0F format. The C-terminal lysine is predominantly clipped.

Physicochemical properties: Efgartigimod is a clear to slightly opalescent, colorless to slightly yellow solution that has an extinction coefficient (280 nm) that is theoretically 1.33 $mg/mL^{-1}cm^{-1}$ and was experimentally seen as 1.44 $mg/mL^{-1}cm^{-1}$. The pI (isoelectric point) of the main isoform is approximately 7.2.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Table 3: Summary of Patient Demographics for Clinical Trials in Myasthenia Gravis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
ARGX-113-1704	Phase 3 randomized double-blinded placebo-controlled	EFG IV solution Cycles of 10 mg/kg EFG or PBO every week x 3 weeks (4 infusions total) for up to 28 weeks	167 patients randomized AChR-Ab seropositive: 129 AChR-Ab seronegative: 38 EFG arm: 84 PBO arm: 83	EFG arm: 45.9 years (19 – 78 years) PBO arm: 48.2 years (19 – 81 years)	EFG arm: 63 females / 21 males PBO arm: 55 females / 28 males

EFG = efgartigimod alfa; IV = intravenous; PBO = placebo; AChR-Ab = acetylcholine receptor antibody

The efficacy of Vyvgart for the treatment of generalized myasthenia gravis (gMG) in adults was

established in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial.

Study 1704 enrolled patients who met the following criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of ≥ 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 1704 and were randomized to receive either Vyvgart 10 mg/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 (77% in each group) tested positive for antibodies to AChR (AChR-Ab). Of the 38 (23%) patients that tested negative for AChR-Ab, 3 patients in each treatment group tested positive for MuSK autoantibodies.

During the study, 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. At study entry, approximately 30% of patients in each treatment group had no previous exposure to NSISTs.

Patients were treated with Vyvgart at the recommended dosage regimen and received a maximum of 3 treatment cycles. See 4.2 Recommended Dose and Dosage Adjustment.

14.2 Study Results

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 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 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 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 seropositive population. A key 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 population. Results are shown in Table 4. This was also assessed in the overall population.

Table 4: Results in Cycle 1 of Study ARGX-113-1704 in AChR-Ab positive patients with Myasthenia Gravis (mITT analysis set)

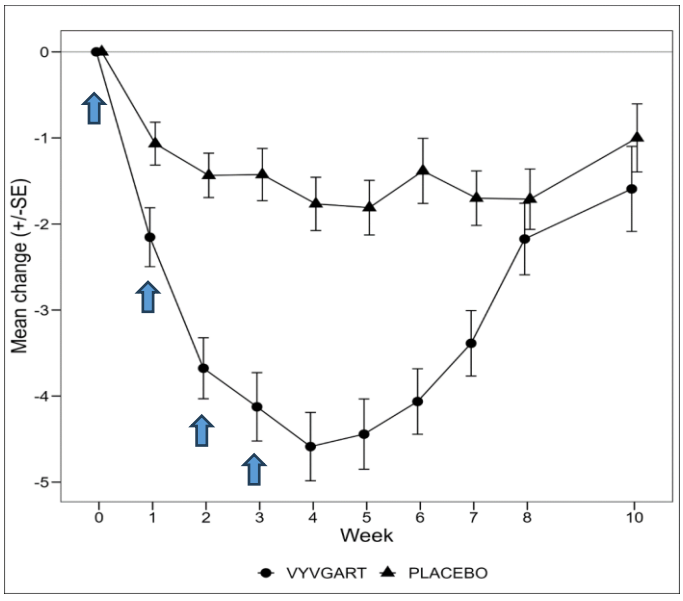
Primary & Secondary Endpoints	Population	Efgartigimod (n/N) (%)	Placebo (n/N)(%)	P-value[a]	Difference Efgartigimod alfa-Placebo (95% CI)[a]
MG-ADL Responders	AChR-Ab seropositive	44/65 (67.7)	19/64 (29.7)	< 0.0001	38.0 (22.1; 54.0)
QMG Responders	AChR-Ab seropositive	41/65 (63.1)	9/64 (14.1)	< 0.0001	49.0 (34.5; 63.5)

MG-ADL=Myasthenia Gravis Activities of Daily Living; AChR-Ab=acetylcholine receptor-antibody QMG=Quantitative Myasthenia Gravis; n=number of patients for whom the observation was reported; N=number of patients in the analysis set; CI=confidence interval; mITT=modified Intention to Treat

[a] Based on the difference in proportions

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

Figure 1: Mean Change From Baseline in Total MG-ADL Over Time During Cycle 1 in AChR-Ab Positive Patients (mITT Analysis Set) (the arrows indicate the visits where Vyvgart or placebo were administered)



In patients who responded to treatment, the duration of responder status was 5 weeks in 5/44 (11%) patients, 6 to 7 weeks in 14/44 (32%) of patients, 8 to 11 weeks in 10/44 (23%) patients and 12 weeks or more in 15/44 (34%) patients, in the AChR-Ab seropositive MG-ADL responders.

14.4 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In Study 1704, antibodies to Vyvgart were detected in 17/83 (21%) patients. Neutralizing antibodies were detected in 6/83 (7%) patients treated with Vyvgart. Data was not sufficient to conclude whether there is clinically meaningful impact of antibodies to Vyvgart on the efficacy, safety, pharmacokinetics and pharmacodynamic of Vyvgart.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

In a 4-week repeat-dose toxicity study rats were treated with efgartigimod alfa at doses of 0 (0.9% sodium chloride solution), 10, 30, or 100 mg/kg administered by IV injection once every 2 days (total of 15 IV doses). Findings of Kupffer cell hypertrophy/hyperplasia was seen in male and female rat liver at 100 mg/kg that were considered of uncertain relationship to treatment. The no-observed-adverse effect-level (NOAEL) was established at 30 mg/kg, approximately 3 times the recommended human dose (RHD) of 10 mg/kg, on a body weight (mg/kg) basis.

In the pivotal 26-week toxicity study of efgartigimod alfa, cynomolgus monkeys received IV infusions at doses of 0 (vehicle), 10, 30, and 100 mg/kg once per week (total of 27 infusions). Enterocolitis was reported in 2 low-dose monkeys and 1 high-dose monkey, with greater severity observed at the high dose. The diarrhea observed in the high-dose monkey was accompanied by myeloid hyperplasia in the bone marrow of the sternum. Findings have uncertain relationship to treatment. The NOAEL was established at 100 mg/kg, approximately 10 times the human dose RHD of 10 mg/kg, on a body weight (mg/kg) basis.

Carcinogenicity: No studies have been conducted to assess the carcinogenic potential of efgartigimod alfa.

Genotoxicity: No studies have been conducted to assess the genotoxic potential of efgartigimod alfa.

Reproductive and Developmental Toxicology:

Reproductive and development toxicity studies were conducted for efgartigimod alfa given by IV bolus injection once per day at doses of 0 (vehicle), 30, or 100 mg/kg in rats and rabbits. For all studies, the NOAEL was established at 100 mg/kg , approximately 10 times the RHD of 10 mg/kg, on a body weight (mg/kg) basis. Efgartigimod alfa concentrations in maternal milk and sera of fetuses or F1 offspring were not assessed. The potential effect of efgartigimod alfa on FcRn-mediated transfer of maternal antibodies to the fetus was not assessed.

A fertility study was conducted in male and female rats. Males were dosed from 4 weeks before mating and up to day 43 of the study, and females were dosed 2 weeks before mating and up to day 7 of gestation. Efgartigimod alfa did not adversely affect male and female fertility. The doses tested are 3 and 10 times the RHD of 10 mg/kg, on a body weight (mg/kg) basis.

An embryo-fetal development study was conducted in female rats and rabbits. Efgartigimod alfa was administered from gestation day 6 through 17 in rats and gestation day 6 through 28 in rabbits. There

is no evidence of adverse developmental outcomes following the administration of efgartigimod alfa in rats and rabbits. In rabbits only, abortions were reported (2 in the low dose group, 1 in the high dose group) at an incidence that was comparable to historical control data of the test facility. These abortions were considered to be spontaneous occurrences. One low-dose rabbit presented with a contained liver lesion where an infectious cause could not be excluded. The doses tested are 3 and 10 times the RHD of 10 mg/kg, on a body weight (mg/kg) basis.

Female rats received efgartigimod alfa from day 6 of gestation to day 21 of lactation. Ataxia was observed in 4 F1 pups of 1 high-dose F0 female, with uncertain relationship to treatment. Overall, the results show that efgartigimod alfa had no effect on the pregnancy of the female rats, or on the development of both the pre- and postnatal F1 and F2 generation pups. The doses tested are 3 and 10 times the RHD of 10 mg/kg, on a body weight (mg/kg) basis.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrVYVGART®

Efgartigimod alfa for injection

Read this carefully before you start taking **Vyvgart**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Vyvgart.**

What is Vyvgart used for?

Vyvgart is used to treat adults with generalised Myasthenia Gravis (gMG), an autoimmune disease that causes muscle weakness. gMG can affect multiple muscle groups throughout the body. The condition can also lead to shortness of breath, extreme fatigue and difficulties swallowing.

In patients with gMG, IgG autoantibodies attack and damage proteins at the neuromuscular junction. Because of this damage, the nerves are not able to make the muscles contract as well as normal, leading to muscle weakness and difficulty moving. By binding to the neonatal Fc receptor (FcRn) protein and reducing autoantibody levels, Vyvgart can improve the ability of muscles to contract and reduce the symptoms of the disease and their impact on daily activities.

How does Vyvgart work?

Vyvgart contains the active substance efgartigimod alfa. Efgartigimod alfa binds to and blocks a protein in the body called FcRn. By blocking FcRn, efgartigimod alfa decreases the level of IgG autoantibodies which are proteins of the immune system that attack parts of a person's own body by mistake.

What are the ingredients in Vyvgart?

Medicinal ingredients: efgartigimod alfa

Non-medicinal ingredients: L-arginine hydrochloride, sodium chloride, sodium phosphate dibasic anhydrous, sodium phosphate monobasic monohydrate polysorbate 80, water for injection

Vyvgart comes in the following dosage forms:

400 mg/20 mL (20 mg/mL) solution, for intravenous use

Do not use Vyvgart if:

- you are allergic to efgartigimod alfa or any other ingredients in Vyvgart.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Vyvgart. Talk about any health conditions or problems you may have, including if you:

- have a history of infection or think you have an infection.
- have had a recent vaccination or are scheduled to receive any vaccinations. You should receive any required vaccines at least 4 weeks before you start treatment with Vyvgart.
- are pregnant or plan to become pregnant. It is not known if Vyvgart will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Vyvgart passes into your breast milk.

- have had an allergic reaction to Vyvgart in the past.

Other warnings you should know about:

It is not known whether Vyvgart may affect your fertility. Talk to your healthcare practitioner if you are planning on having children**.**

Vyvgart may cause serious side effects, including:

- Infections: Vyvgart may increase the risk of infection. Tell your healthcare professional 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 of secretion, 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, itchiness, and shortness of breath. Tell your healthcare professional immediately about any undesirable reactions to Vyvgart.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Vyvgart:

No relevant drug-drug interactions are known, however, use of Vyvgart with medications that bind to the human FcRn (e.g., immunoglobulin products, monoclonal antibodies, or antibody derivates containing the human Fc domain of the IgG subclass) may reduce effectiveness of such medications. Inform your healthcare professional of any other medications you are taking.

How to take Vyvgart:

Vyvgart will be given to you by a healthcare professional. The product will be diluted and administered from a drip bag through a tube directly into one of your veins.

Usual dose:

The dose you receive will depend on your bodyweight and will be administered in cycles of one infusion per week for 4 weeks. Your doctor will determine when further treatment cycles are needed.

Overdose:

If you suspect that you have been accidentally administered a higher dose of Vyvgart than prescribed, please contact your healthcare professional.

If you think you, or a person you are caring for, have taken too much Vyvgart, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget an appointment, please contact your healthcare professional immediately.

Interrupting or stopping treatment with Vyvgart may cause your gMG symptoms to come back. Please speak to your doctor before stopping Vyvgart. Your healthcare professional will discuss the possible side effects and risks with you. Your healthcare professional will also want to monitor you closely.

What are possible side effects from using Vyvgart?

These are not all the possible side effects you may have when taking Vyvgart. If you experience any side effects not listed here, tell your healthcare professional.

Side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Upper Respiratory Tract Infection: nose and throat	✓		
COMMON			
Urinary Tract Infection: pain or a burning sensation during urination		✓	
Bronchitis: inflammation of the airways in the lungs		✓	
Myalgia: muscle pain	✓		
Headache during or after the administration	✓		

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store in a refrigerator at 2°C to 8°C in the original carton.

Do not freeze. Do not shake. Protect from light.

Do not use if visible particles are observed and/or the liquid in the vial is discoloured.

Keep out of reach and sight of children.

If you want more information about Vyvgart:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html, or by calling 1-800-731-8917.

This leaflet was prepared by argenx BV.

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