Product Monograph

Including Patient Medication Information

PrVYVGART® SC

Efgartigimod alfa injection

1000 mg/5 mL (200 mg/mL) solution in single-use prefilled syringe

Subcutaneous use

Professed Standard

Neonatal Fc Receptor Antagonist

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

Imported by:
Quality & Compliance Services Inc.
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Recent Major Label Changes

Not applicable.

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Health Professional Information

1 Indications

VYVGART® SC (efgartigimod alfa injection) is indicated:

- for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
- as a monotherapy for adult patients with active chronic inflammatory demyelinating polyneuropathy (CIDP).

1.1 Pediatrics

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

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Twenty two percent of patients (12/55 patients with gMG and 25/111 patients with CIDP) aged 65 and over were treated with VYVGART SC in randomized controlled studies. Although no apparent age-related differences were observed in efficacy and safety, the number of patients aged 65 and over is insufficient to determine whether they respond differently from younger adult patients.

2 Contraindications

VYVGART SC is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation (efgartigimod alfa, hyaluronidase), 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

4.1 Dosing Considerations

VYVGART SC is a ready to use solution for injection in a single-use prefilled syringe which does not need to be diluted. VYVGART SC is for subcutaneous use only. Do not administer VYVGART SC intravenously.

4.2 Recommended Dose and Dosage Adjustment

Generalized Myasthenia Gravis

The recommended dose of VYVGART SC is 1000 mg efgartigimod alfa administered subcutaneously in cycles of once weekly injections for 4 weeks.

Administer subsequent treatment cycles according to clinical evaluation. The frequency of VYVGART SC treatment cycles may vary by patient.

For patients currently receiving efgartigimod alfa intravenously, the solution for subcutaneous injection may be used as an alternative. It is recommended to switch between formulations at the start of a new treatment cycle. No safety and efficacy data in patients switching formulations during the same cycle is available.

Chronic Inflammatory Demyelinating Polyneuropathy

The recommended dose of VYVGART SC is 1000 mg efgartigimod alfa administered subcutaneously as once-weekly injections.

For patients transitioning from other CIDP therapies, VYVGART SC treatment should preferably be initiated before the clinical effect of these prior therapies starts to decrease.

Clinical response is usually achieved within 3 months of initiation of treatment with VYVGART SC. Clinical evaluation should be considered 3-6 months after treatment initiation to assess the treatment effect and at regular intervals thereafter.

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

Geriatrics (≥ 65 years of age): Clinical studies of VYVGART SC did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger adult patients (see 1.2 Geriatrics).

Renal Impairment: No dose adjustment of VYVGART SC 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 m²) and severe renal impairment (eGFR <30 mL/min/1.73 m²) on pharmacokinetic parameters of VYVGART SC (see 10 Clinical Pharmacology).

4.3 Reconstitution

Parenteral Products:

No reconstitution is required for VYVGART SC.

4.4 Administration

Initially, VYVGART SC must be administered by a healthcare professional. After proper instruction in subcutaneous injection technique, a patient may self-inject VYVGART SC using the prefilled syringe or the patient's caregiver may administer VYVGART SC if a healthcare professional determines that it is appropriate (see Instructions for Use).

During the administration of efgartigimod alfa, appropriate treatment for injection and hypersensitivity-related reactions should be readily available.

- Take the VYVGART SC prefilled syringe out of the refrigerator at least 30 minutes before injecting to allow it to reach room temperature. Do not use external heat sources.
- Visually inspect that the prefilled syringe solution is yellowish, clear to opalescent and devoid of particulate matter. If visible particles are observed, the prefilled syringe must not be used.
- Use aseptic technique when preparing for and during administering VYVGART SC. Do not shake the prefilled syringe. Each prefilled syringe is for single-use only.
- To administer VYVGART SC prefilled syringe, use a safety needle 25G, 5/8 inches (16mm) length thin wall which is not included in the pack.
- Connect the syringe to the needle.
- Choose an injection site on the abdomen (at least 2 inches (5 cm) away from the navel).
    - Do not inject into areas where the skin is red, bruised, tender, hard, or into areas where there are moles or scars.
    - Rotate injection sites for subsequent administrations.

- Inject VYVGART SC prefilled syringe subcutaneously into a pinched skin area at an angle of 45 to 90 degrees for approximately 20 to 30 seconds.
- VYVGART SC does not contain preservatives. Administer immediately after preparation. Discard any unused portions of medicine remaining in the syringe.
- Hypersensitivity-related reactions, including anaphylaxis and localized injection site reactions may occur after VYVGART SC is administered. Monitor patients/self-monitor for clinical signs and symptoms of these reactions, see 7 Warnings and Precautions, Sensitivity, Resistance.

4.5 Missed Dose

An interval of at least 3 days should be observed between two consecutive administrations. When administrations cannot be done at the scheduled time point, they should be performed as soon as possible and at least 3 days ahead of the following administration. If there are less than 3 days to the next administration, the missed dose should be skipped and the next dose should be administered at the scheduled time point.

5 Overdose

There are no known specific signs and symptoms of overdose with VYVGART SC. 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 SC.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

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
Subcutaneous	Solution, 200 mg/mL efgartigimod alfa	Hyaluronidase (rHuPH20), L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, sodium chloride, sucrose, water for injection

Description

VYVGART SC (efgartigimod alfa injection) is a sterile, preservative-free, yellowish, clear to opalescent solution for subcutaneous injection. VYVGART SC is supplied as 1000 mg efgartigimod alfa per 5 mL (200 mg/ml) in a single-use prefilled syringe.

Hyaluronidase (human recombinant) is an endoglycosidase used to increase the dispersion and absorption of co-administered drugs when administered subcutaneously.

7 Warnings and Precautions

Immune

Infections

As VYVGART SC 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 SC. Delay VYVGART SC administration in patients with an active infection until the infection is resolved. If a serious infection occurs, administer appropriate treatment and consider withholding VYVGART SC until the infection has resolved.

Immunization

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

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

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

Reproductive Health

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

Sensitivity/Resistance

Injection-related reactions and hypersensitivity, including anaphylaxis

Hypersensitivity reactions such as rash, pruritus or anaphylactic reactions may occur. In clinical trials, these were mild to moderate. (Self-) monitor for clinical signs and symptoms of hypersensitivity reactions for 30 minutes after administration. Cases of anaphylaxis were reported in the post-market setting. Should a reaction occur, institute appropriate supportive measures. Subsequent injections may be cautiously administered, based on clinical evaluation. If an anaphylactic reaction is suspected, administration of VYVGART SC should be immediately discontinued and appropriate medical treatment initiated.

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 Pregnancy

There are no available clinical data on the use of VYVGART SC during pregnancy.

Treatment of pregnant women with VYVGART SC should only be considered if the clinical benefit outweighs the risks.

No reproductive and developmental toxicity studies have been conducted with subcutaneously administered efgartigimod co-formulated with hyaluronidase (rHuPH20). Reproductive and developmental toxicity studies were conducted in rats and rabbits administered efgartigimod by IV injection. Reproductive and developmental toxicity studies were conducted in mice administered rHuPH20 by SC injection. 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 SC may be transmitted from the mother to the developing fetus. As VYVGART SC is expected to reduce maternal IgG antibody levels and 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 SC *in utero*.

7.1.2 Breastfeeding

There is no information regarding the presence of efgartigimod alfa 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 SC should be considered, as well as any potential adverse effects on the breastfed infant from VYVGART SC or from the underlying maternal condition.

7.1.3 Pediatrics

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

7.1.4 Geriatrics

Geriatrics (≥ 65 years of age): Twelve (12/55 patients with gMG) and twenty-five (25/111 patients with CIDP) aged 65 and over were treated with VYVGART SC in a randomized controlled parallel group study and a randomized placebo-controlled study. Although no apparent age-related differences were observed in efficacy and safety, 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

Generalized Myasthenia Gravis (gMG)

The safety of efgartigimod alfa in patients with gMG was established in a double blinded placebo-controlled study (ARGX-113-1704, VYVGART) and its open-label extension, and in an active-controlled study (ARGX-113-2001, VYVGART and VYVGART SC) and its open label extension.

In the placebo-controlled Phase 3 Study ARGX-113-1704, as reported in the Product Monograph for VYVGART (IV formulation), the most common adverse reactions (≥ 10%) seen in patients who received at least one dose of VYVGART (IV formulation) included headache (reported by 32% of VYVGART-treated patients and 29% 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).

In study ARGX-113-2001, 110 patients were randomized and received one cycle of once weekly administrations for 4 weeks, of either VYVGART SC (n=55) or VYVGART (IV formulation) (n=55) at recommended doses. Injection site reactions (ISRs) occurred in 33% of patients receiving VYVGART SC. These were injection site rash, injection site erythema, injection site pruritus and injection site pain. All ISRs were mild to moderate in severity and did not lead to treatment discontinuation. The majority occurred within 24 hours after administration and resolved spontaneously. Most ISRs occurred during the first treatment cycle. The incidence of ISRs decreased with each subsequent cycle.

The most frequently observed adverse reactions in patients treated with VYVGART IV (≥ 10%) were upper respiratory tract infections and urinary tract infections. The most frequently observed adverse reactions in patients treated with VYVGART SC (≥ 10%) were injection site reactions.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

In a placebo-controlled study in patients with CIDP (ARGX-113-1802, stage B), 221 patients were randomized and received once-weekly administration of either VYVGART SC at 1000 mg subcutaneously (n=111) or placebo (n=110). The mean (SD) duration of treatment with VYVGART SC in stage B was 25.1 (17.17) weeks. The overall safety profile observed in patients with CIDP treated with VYVGART SC was generally consistent with the overall safety profile of VYVGART SC and of VYVGART (IV formulation). In Part A, the most common adverse reactions were injection site erythema (10.2%). None of these events led to discontinuation of study treatment. In Part B, the most common adverse reactions were COVID-19 (17.1%). None of these events led to discontinuation of study treatment. The overall safety profile of continuous weekly administrations of VYVGART SC in CIDP was generally consistent with the known safety profile of cyclic administration of the intravenous formulation in gMG.

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.

Generalized Myasthenia Gravis (gMG)

Information in this section from study ARGX-113-1704 reports data from a separate Product Monograph for VYVGART (IV formulation)

Study ARGX-113-1704

In the placebo-controlled Phase 3 study (ARGX-113-1704) 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. 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 in 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		
Headache*	27 (32)	24 (29)
Musculoskeletal and connective tissue disorders		
Myalgia	5 (6)	1 (1)

**Headache includes migraine and procedural headache (for IV formulation only)*

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).

Study ARGX-113-2001

In study ARGX-113-2001, the most common adverse reactions (reported in at least 10% of VYVGART SC-treated patients) were injection site reactions. See 8.1 Adverse Reaction Overview. The overall safety profile for VYVGART SC was generally consistent with the safety profile of VYVGART (IV formulation).

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

In a placebo-controlled study in patients with CIDP (ARGX-113-1802, stage B), 221 patients were randomized and received once-weekly administration of either EFG SC at 1,000 mg / 11,200 Units subcutaneously (n=111) or placebo (n=110). The mean (SD) duration of treatment with VYVGART SC in stage B was 25.1 (17.17) weeks.

The overall safety profile observed in patients with CIDP treated with VYVGART SC was generally consistent with the known safety profile of VYVGART. The most common adverse reactions were injection site reactions, which occurred in 15% of VYVGART SC-treated patients compared to 6% of patients who received placebo. The most common of these injection site reactions were injection site bruising and injection site erythema. All injection site reactions were mild to moderate in severity. Most injection site reactions occurred during the first 3 months of treatment.

8.3 Less Common Clinical Trial Adverse Reactions

Generalized Myasthenia Gravis (gMG)

Information in this section reports data from a separate Product Monograph for VYVGART (IV formulation).

Less common clinical trial adverse reactions occurring in <5% of patients with gMG treated with VYVGART and more frequently than in placebo-treated patients (≥ 2 patients) in Study ARGX-113-1704 are as follows:

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

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Less common clinical trial adverse reactions occurring in <5% of patients with CIDP treated with VYVGART SC and more frequently than in placebo-treated patients (≥ 3 patients) in Study ARGX-113-1802 Stage B is as follows:

General Disorders and Administration Site Conditions: Influenza like illness

8.5 Post-Market Adverse Reactions

Immune System Disorders: Hypersensitivity reactions including anaphylaxis and hypotension, and injection-related reactions.

9 Drug Interactions

9.2 Drug Interactions Overview

Clinical drug interactions studies have not been performed with VYVGART SC.

9.4 Drug-Drug Interactions

VYVGART SC 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.

Myasthenia Gravis

gMG patients receiving VYVGART SC 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 SC.

CIDP

Interactions with other drugs have not been established in CIDP patients.

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 double-blind- placebo-controlled study ARGX-113-1704 in gMG patients using VYVGART (IV formulation), the pharmacological effect of efgartigimod alfa was assessed by measuring the decrease in serum total IgG levels and AChR autoantibody (AChR-Ab) levels. In patients who were tested positive for AChR-ab and treated with efgartigimod alfa at the recommended dose and schedule, 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-ab levels followed a similar time course.

In study ARGX-113-2001, the pharmacological effect of the subcutaneous formulation of VYVGART SC at 1000 mg was compared to VYVGART (IV formulation) at 10 mg/kg in gMG patients. Maximum mean percentage decreases in AChR-Ab levels of 62.2% and 59.6% were observed, one week after the last administration, in the VYVGART SC and VYVGART (IV formulation) groups, respectively.

In ARGX-113-1802, in patients with CIDP receiving continuous once-weekly administration of VYVGART SC at 1000 mg, the mean percent change from baseline in total IgG levels was sustained from week 4

(Day 29) throughout the treatment period (mean percentage reduction from baseline in total IgG levels ranging between 66.8 to 71.6%).

10.3 Pharmacokinetics

The pharmacokinetics profile of efgartigimod alfa is linear, independent of dose or time, with minimal accumulation. Pharmacokinetic parameters in healthy subjects, patients with gMG and with CIDP were comparable.

In healthy subjects receiving subcutaneously 1000 mg efgartigimod alfa (EFG SC) once weekly for 4 weeks, mean maximum concentrations (C_{max}) and mean trough concentrations (C_{trough}) were 50.1 mcg/mL and 19.3 mcg/mL after the fourth administration. The $AUC_{0\text{-}168h}$ following one cycle of subcutaneous and intravenous administrations at the recommended doses was comparable.

In patients with CIDP receiving continuous administration of EFG SC once weekly, mean C_{trough} ranged from 14.9 to 20.1 mcg/mL.

Distribution

The volume of distribution is 15 to 20L. This exceeds the blood volume, indicating distribution to well perfused organs and tissue water, consistent with that of an antibody fragment.

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, race and body weight:** Based on a population PK analyses, the pharmacokinetics of efgartigimod were not affected by age (19 – 84 years) and race. The effect of gender and body weight on the pharmacokinetics of efgartigimod was not clinically relevant.
- **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/1.73 m²) had 11% to 21% increase in exposure relative to the exposure in patients with normal renal function (eGFR ≥90 mL/min/1.73 m²). Clinical data shows that mild renal impairment does not impact the safety profile of efgartigimod alfa. There is insufficient data on the impact of moderate renal impairment (eGFR 30-59 mL/min/1.73 m²) and severe renal impairment (eGFR <30 mL/min/1.73 m²) on pharmacokinetic parameters of efgartigimod alfa.

10.4 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.

gMG Studies

In Study ARGX-113-1704, which used the IV formulation (VYVGART) as reported in the VYVGART Product Monograph, antibodies to efgartigimod alfa were detected in 17/83 (21%) of patients. Neutralizing antibodies were detected in 6/83 (7%) of patients treated with VYVGART.

In study ARGX-113-2001, pre-existing antibodies that bind to efgartigimod alfa were detected in 12/110 (11%) of patients with gMG. Antibodies to efgartigimod alfa were detected in 19/55 (35%) of patients in the VYVGART SC treatment group compared to 11/55 (20%) of patients in the VYVGART (IV formulation) treatment group. Neutralizing antibodies to efgartigimod alfa were detected in 2/55 (4%) of patients in both the VYVGART SC and VYVGART (IV formulation) treatment groups. 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.

CIDP Studies

In study ARGX-113-1802, antibodies to efgartigimod alfa were detected in 20/317 (6.3%) of patients treated with VYVGART SC in Stage A, and in 2/111 (1.8%) of patients treated with VYVGART SC in Stage B. Neutralizing antibodies to efgartigimod alfa were detected in 1/317 (0.3%) of patients in Stage A only.

There was no apparent impact of antibodies to VYVGART SC on clinical efficacy or safety, nor on pharmacokinetics and pharmacodynamic parameters.

11 Storage, Stability and Disposal

VYVGART SC (efgartigimod alfa injection) is a sterile, preservative-free, yellowish, clear to opalescent solution for subcutaneous injection and is supplied as 200 mg/mL in one single-use prefilled syringe.

Store VYVGART SC unopened prefilled syringes refrigerated for up to 18 months at 2°C to 8°C in the original carton to protect from light until time of use. Unopened prefilled syringes may be stored at room temperature up to 30°C in the original carton for a single period of up to 1 month after removing them from the refrigerator or until the expiration date on the carton, whichever occurs first. Do not shake the syringe. Do not freeze.

12 Special Handling Instructions

Discard any unused portion of VYVGART SC remaining in the syringe in accordance with local requirements.

Part 2: 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, colourless 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 Clinical Trials by Indication

Generalized Myasthenia Gravis (gMG)

Information in this section pertaining to study ARGX-113-1704 conducted with the IV formulation reports data from a separate Product Monograph for VYVGART (IV formulation).

The efficacy of VYVGART for the treatment of gMG in adults who are AChR antibody positive was established in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial (ARGX-113-1704).

The efficacy of VYVGART SC in patients with gMG is based on bridging from VYVGART (IV formulation) to VYVGART SC using pharmacodynamic endpoints (study ARGX-113-2001). ARGX-113-2001 was a 10 week, multicenter, randomized, open-label, parallel-group study conducted in adult patients with gMG to evaluate the non-inferiority of the pharmacodynamic effect of VYVGART SC compared to VYVGART (IV formulation).

Table 3: Summary of Patient Demographics for Clinical Trials in Generalized 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	VYVGART (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

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
ARGX-113-2001	Phase 3, randomized, open-label, parallel-group	VYVGART SC 1000 mg VYVGART (IV formulation) 10 mg/kg 1 cycle of 4 once-weekly administrations and a 7-week follow-up	110 patients randomized AChR-Ab seropositive: 91 AChR-Ab seronegative: 19 VYVGART SC: 55 VYVGART: 55	53.4 years (19 – 84 years)	65 females/ 45 males

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

Study ARGX-113-1704

The information pertaining to Study ARGX-113-1704 is reported from the VYVGART (IV formulation) Product Monograph.

Study ARGX-113-1704 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.

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

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

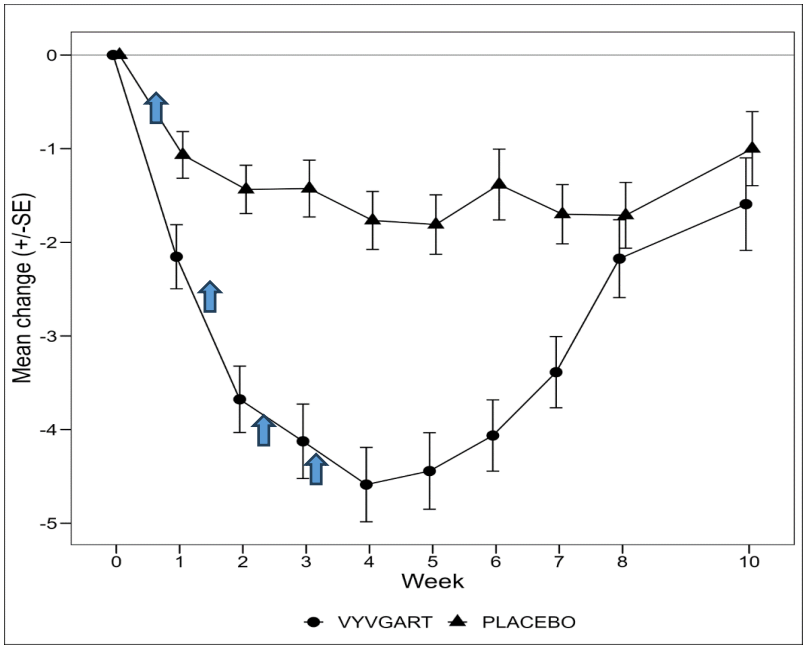
Primary & Secondary Endpoints	Population	VYVGART (n/N) (%)	Placebo (n/N) (%)	P-value[a]	Difference VYVGART-Placebo (95% CI)[a]
MG-ADL Responders	AChR-Ab seropositive	44/65 (67.7)	19/64 (29.7)	< 0.0001	38.0 (22.1; 54.0)
QMG Responders	AChR-Ab seropositive	41/65 (63.1)	9/64 (14.1)	< 0.0001	49.0 (34.5;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

Study ARGX-113-2001

Study ARGX-113-2001 enrolled patients who met the same criteria at screening as study ARGX-113-1704.

A total of 110 patients were randomized and received one cycle of once weekly administrations for 4 weeks, of either VYVGART SC 1000 mg (1000 mg efgartigimod alfa) (n=55) or VYVGART (IV formulation) at 10 mg/kg (n=55). All patients were on stable doses of myasthenia gravis therapy prior to screening, that included AChE inhibitors, steroids or non-steroidal immunosuppressive therapy (NSISTs), either in combination or alone.

Baseline characteristics were similar between treatment groups and to those of study ARGX-113-1704, including median age at diagnosis (53 years in VYVGART SC group and 59 years in VYVGART group), gender [most were female - 56% (VYVGART SC) versus 62% (VYVGART)], race [most patients were white - 91% (VYVGART SC) and 93% (VYVGART)] and median time since diagnosis [4.4 years VYVGART SC and 4.6 years (VYVGART)]. Median MG-ADL total score was 8.0 in both treatment groups, and median QMG total score was 15 and 16 in the VYVGART SC and VYVGART groups, respectively.

The majority of patients were positive for antibodies to AChR (AChR-Ab): 82% in VYVGART SC group and 84% in VYVGART group.

During the study, over 80% of patients in each group received AChE inhibitors, over 60% of patients in each group received steroids and over 40% in each treatment group received NSISTs, at stable doses. At study entry, approximately 56% of patients in each treatment group had no previous exposure to NSISTs.

The primary endpoint was the comparison of the percent reduction from baseline in total IgG levels at week 4 (day 29) between both treatment groups in the overall gMG population. Non-inferiority evaluation was based on a percent reduction from baseline in total IgG levels at week 4 (day 29) using a margin of 10%. The results for the primary endpoint demonstrated non-inferiority of VYVGART SC to VYVGART, as presented in Table 5.

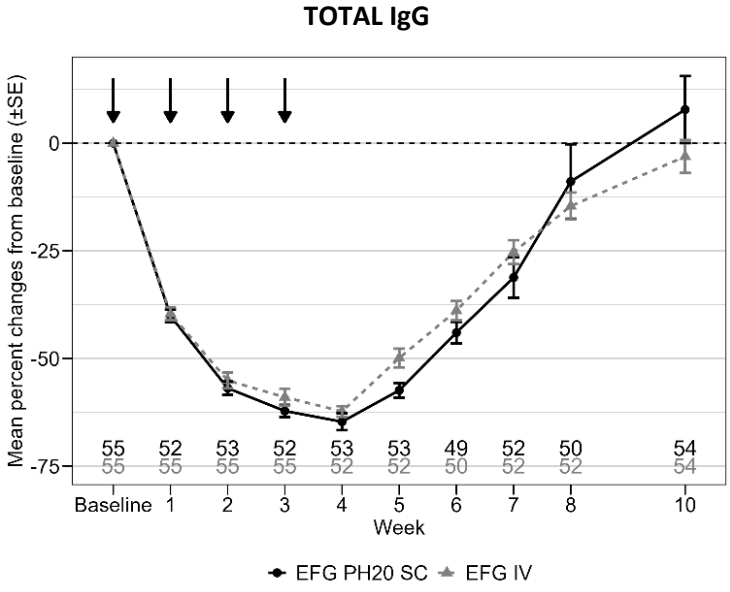
Table 5: ANCOVA Analysis of Percent Change From Baseline in Total IgG Level at Day 29

VYVGART SC			VYVGART			VYVGART SC versus VYVGART		
N	**LS Mean**	**95% CI**	**N**	**LS Mean**	**95% CI**	**LS of Mean difference**	**95% CI**	**p-value**
Overall population (mITT)								
55	-64.4	-68.09, -60.61	55	-60.7	-64.49, -57.00	-3.6	-8.91, 1.69	<0.0001

AChR-Ab=acetylcholine receptor – antibody; ANCOVA=analysis of covariance; CI = confidence interval; EFG SC: efgartigimod alfa subcutaneous; EFG IV: efgartigimod alfa intravenous; LS=least squares; mITT=modified intent-to-treatment analysis set; N= number of patients per group that were included in the ANCOVA analysis; p<0.0001 for non-inferiority.

Figure 2 shows the percent change from baseline in total IgG for the VYVGART SC and VYVGART groups in the mITT population.

Figure 2: Mean (SE) Percent Change From Baseline in Total IgG (mITT Analysis Set) – (Study ARGX-113-2001)



The arrow shows the administrations; the upper row of numbers shows the number of patients in EFG SC vial group, the lower row of numbers shows the number of patients in EFG IV group.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Study ARGX-113-1802

The efficacy of VYVGART SC for the treatment of adults with CIDP was demonstrated in a prospective, multicenter study (ARGX-113-1802) conducted in 2 treatment stages: an open-label period to identify VYVGART SC responders (stage A) who then entered a randomized, double-blind, placebo-controlled, withdrawal period (stage B).

Table 6: Summary of Patient Demographics for VYVGART SC Clinical Trial in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
ARGX-113-1802	Phase 2 study in 2 stages Stage A: open-label Stage B: randomized-withdrawal, double-blinded, placebo-controlled	VYVGART SC and placebo; Stage A: VYVGART SC 1000 mg once weekly; 4-12 weeks with an optional one additional week Stage B: VYVGART SC 1000 mg or placebo once weekly; up to 48 weeks	Stage A: 322 enrolled and received VYVGART SC Stage B: 221 randomized • VYVGART SC: 111 • Placebo: 110	Stage A: 54 years (20 – 82 years) Stage B: 52.9 years (20 – 82 years)	Stage A: 114 females 208 males Stage B: 79 females 142 males

Eligible patients had been either on or off CIDP treatment during the 6 months prior to study entry; some patients were true treatment-naïve and had never received any CIDP medications. Those on prior CIDP treatment as well as those off CIDP treatment with no documented evidence of recent CIDP deterioration, entered a treatment-free run-in period, and patients who demonstrated evidence of clinically meaningful deterioration then entered Stage A of the study. Those off CIDP treatment who had recent documented evidence of CIDP deterioration, skipped the run-in period and entered straight into Stage A.

A total of 322 patients enrolled in stage A received up to 12 once weekly injections of VYVGART SC at 1000 mg (1000 mg efgartigimod alfa) until evidence of clinical improvement (ECI) occurred at 2 consecutive study visits. Subsequently, the patients with confirmed ECI entered Stage B of the study and were randomised to receive weekly administrations of either VYVGART SC (111 patients) or placebo (110 patients). ECI was defined as clinical improvement on adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) or improvement on Inflammatory Rasch-built Overall Disability Scale (I-RODS) / Grip Strength in patients who deteriorated on these scales only prior to Stage A. The INCAT is a scale used to assess the impact of CIDP on daily upper and lower limb function, and is composed of the arm score and leg score (0 to 5 points for each). A total score on the INCAT ranges from 0 to 10 points with a higher number representing more disability. The aINCAT disability score, identical to the INCAT disability score but with changes in the upper limb function from 0 (normal) to 1 (minor symptoms) excluded, was used to assess efficacy for VYVGART SC for the treatment of CIDP.

Stage A included 228 patients currently receiving standard-of-care therapy and 94 patients who were classified as follows: 31 as strictly treatment naive, 56 as off corticosteroids, IVIg or SCIg for at least 6 months prior to screening, and 7 participants were off CIDP therapy other than corticosteroids, IVIg or SCIg for at least 6 months. Reasons that participants did not roll over to Stage B included lack of efficacy (11.2%), Stage B events required for primary analysis achieved (6.8%), adverse event (6.2%) and participant withdrawal (3.4%). A total of 221 patients were randomized in stage B, with 111 receiving VYVGART SC at 1000 mg and 110 receiving placebo once weekly. Stage B included:

- 146 patients currently receiving standard-of-care therapy, and
- 75 patients who had either not received prior treatment for CIDP (28 patients) or were not treated with standard-of-care therapy for at least 6 months before study entry (47 patients).

Baseline characteristics of stage B were similar between treatment groups. Patients had a median age of 55 years (56.0 years in VYVGART SC group and 54.5 years in placebo group), a median time since CIDP diagnosis of 2.2 years and a median INCAT score of 3.0. Sixty-four percent were male (66% in VYVGART SC group and 63% in placebo group) and 65% were White (66% in VYVGART SC group and 65% in placebo group).

Study Results

In stage A, the primary endpoint was the percentage of responders with the time to the first ECI as secondary endpoint. The results are presented in Table 7.

Table 7: Evidence of Clinical Improvement In Patients With CIDP In ARGX-113-1802 Stage A – ECI Responders And Time To Initial Confirmed ECI

	Stage A
	VYVGART SC (N=322)
ECI Responders (patients with confirmed clinical improvement) n/N (%) (95% CI)	214/322 (66.5%) (61.0; 71.6)
Time to initial confirmed ECI in days median (95% CI)	43.0 (31.0; 51.0)

n=number of patients for whom the observation was reported; N=number of patients in the analysis set

In stage B, the primary endpoint was defined as the time to the occurrence of the first evidence of clinical deterioration (≥ 1-point increase in aINCAT compared to stage B baseline, which was confirmed at a consecutive visit after the first 1-point increase in aINCAT or not confirmed for patients with ≥ 2-point increase in aINCAT compared to stage B baseline). Patients who had clinical deterioration or completed week 48 in Stage B without clinical deterioration were withdrawn from the placebo-controlled portion of the study. The study stopped when 88 events of clinical deterioration occurred for the primary endpoint analysis.

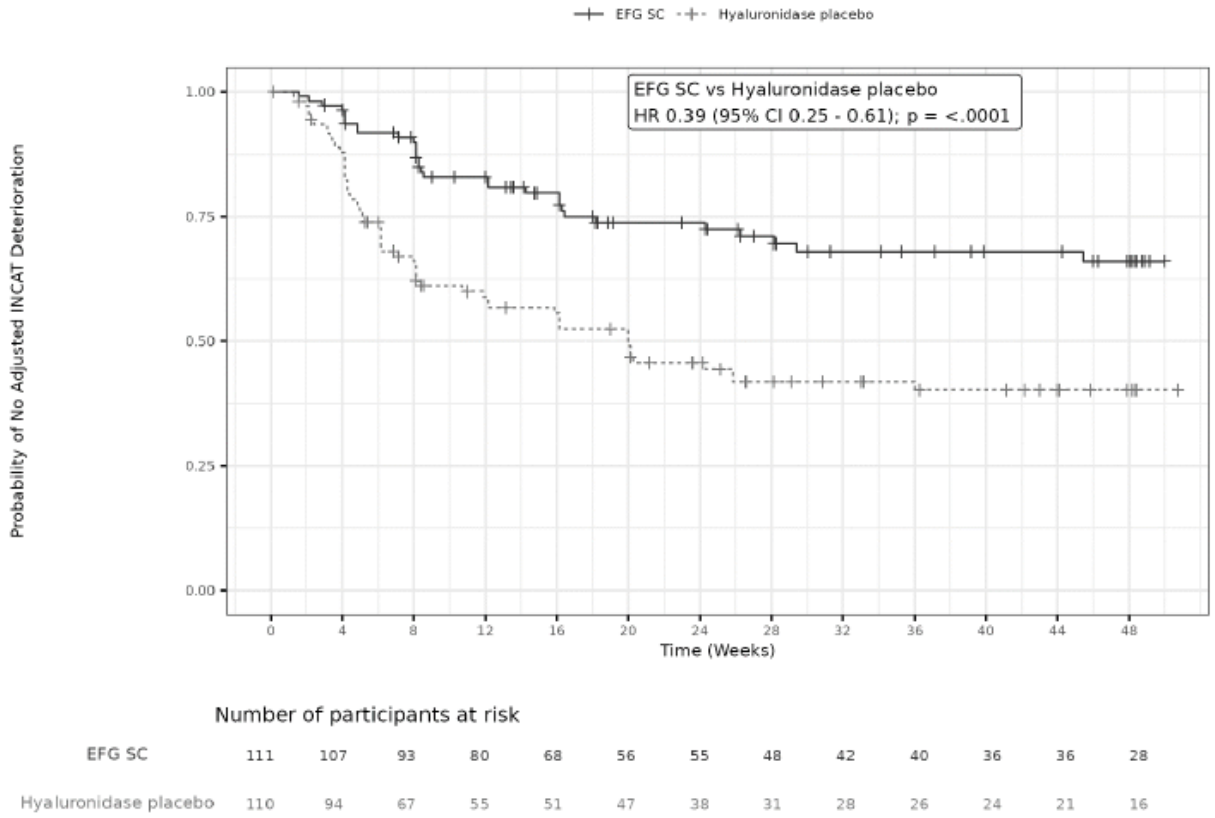
Patients who received VYVGART SC remained relapse-free (i.e., no clinical deterioration) significantly longer compared to patients who received placebo, as demonstrated by a hazard ratio of 0.394 [95% CI (0.253; 0.614) p=0.000039] which represents a 61% risk reduction for deterioration in patients treated with VYVGART SC. The results are presented in Table 8 and Figure 3.

Table 8: First Evidence of Clinical Deterioration In Patients With CIDP In ARGX-113-1802 Stage B - Time To 1st aINCAT Increase

	Stage B	
	VYVGART SC (N=111)	**Placebo (N=110)**
Time to 1st aINCAT increase (clinical deterioration) in days Hazard ratio (95% CI)	0.394 (0.253; 0.614) p-value < 0.0001	
Median time (95% CI)	NC (NC; NC)	140.0 (75.0; NC)

NC: not calculated; N=number of patients in the analysis set; Cox Proportional Hazards Regression Model stratified for prior CIDP medication and change of adjust INCAT Score during Stage A

Figure 3: Time to the First aINCAT Deterioration (Kaplan-Meier Curve) In Patients With CIDP In Study ARGX-113-1802 stage B



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 IV dose 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 recommended human IV dose of 10 mg/kg, on a body weight (mg/kg) basis.

In a 12-week repeat-dose bridging study, cynomolgus monkeys were administered 30 or 100 mg/kg efgartigimod by SC injection (yielding exposures approximately 2- or 5-times the recommended human SC dose of 1000 mg, on a body weight [mg/kg] basis, respectively) with or without hyaluronidase (± rHuPH20) once weekly (total of 13 injections). Some monkeys were observed for an additional 12-week recovery period. Enlarged spleens and lymph nodes were observed in animals administered efgartigimod SC ± rHuPH20 with no relation to dose or severity of microscopic findings. Lymphoid hyperplasia was noted in animals from both test and control groups in various lymph organs (bone marrow, spleen, lymph nodes) with a higher incidence and severity in animals treated with efgartigimod SC ± rHuPH20, without apparent dose-response. At the end of the recovery period, enlarged lymph nodes were observed in 3 of the 12 animals administered efgartigimod SC ± rHuPH20. Most animals receiving efgartigimod SC ± rHuPH20 were positive for anti-drug antibodies. Local signs of inflammation at the SC injection sites were reported at all doses of efgartigimod ± rHuPH20 and included accumulation of subcutaneous proteinaceous material, edema, hematoma, and lymphocytic perivascular infiltration which were partially resolved at the end of the recovery period. A NOAEL could not be established for this study.

In a local tolerance study the rabbits received a single injection of 1 mL SC and also 0.25 mL intramuscular (IM) of efgartigimod SC, formulated at a concentration of 180 mg/mL efgartigimod co-formulated with hyaluronidase. This study did not reveal any test-item-related changes following macroscopic and histopathological examination of the injection sites, and did not result in erythema, eschar, or edema as evaluated by Draize scoring.

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

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

Reproductive and Developmental Toxicology:

No reproductive and developmental toxicity studies have been conducted with subcutaneously administered efgartigimod co-formulated with hyaluronidase (rHuPH20).

Reproductive and development toxicity studies were conducted for efgartigimod alfa administered 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 recommended human IV dose 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 (30 or 100 mg/kg/day IV injection) tested are 3- and 10-times the recommended human IV dose of 10 mg/kg, on a body weight (mg/kg) basis, respectively.

An embryo-fetal development study was conducted in female rats and rabbits. Efgartigimod alfa was administered at a dose of 30 or 100 mg/kg/day by IV injection 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 recommended human IV dose of 10 mg/kg, on a body weight (mg/kg) basis, respectively.

Female rats received efgartigimod alfa at a dose of 30 or 100 mg/kg/day by IV injection 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 recommended human IV dose of 10 mg/kg, on a body weight (mg/kg) basis, respectively.

In an embryofetal development study conducted with pregnant mice, hyaluronidase (rHuPH20) administered at doses of 3, 9, or 18 mg/kg by SC injection once per day from GD 6 to 15 resulted in reduced fetal weight and increased resorptions. Embryofoetal toxicity leading to fetal loss may be due to rHuPH20 interference with fetal heart development. The NOAEL was determined to be 3 mg/kg, approximately 1800-times the recommended SC dose of hyaluronidase in VYVGART SC on a U/kg basis.

17 Supporting Product Monographs

VYVGART (efgartigimod alfa for injection, 20 mg/mL solution), Submission Control Number 282197, Product Monograph, argenx BV. (2025-07-17)

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrVYVGART® SC

1000 mg/5 mL (200 mg/mL) solution in single-use prefilled syringe

Subcutaneous use

This Patient Medication Information is written for the person who will be taking **VYVGART SC**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **VYVGART SC**, talk to a healthcare professional**.**

What VYVGART SC is used for:

gMG

VYVGART SC is used to treat adults with generalised Myasthenia Gravis (gMG). gMG is 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 SC can improve the ability of muscles to contract and reduce the symptoms of the disease and their impact on daily activities.

CIDP

VYVGART SC is also used to treat adults with chronic inflammatory demyelinating polyneuropathy (CIDP), a form of autoimmune disease. CIDP causes muscle weakness and/or numbness mainly in the legs and arms. VYVGART SC can protect the nerves from being attacked and reduce the symptoms of the disease and their impact on daily activities.

How VYVGART SC works:

VYVGART SC 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.

The ingredients in VYVGART SC are:

Medicinal ingredients: efgartigimod alfa

Non-medicinal ingredients: Hyaluronidase (rHuPH20), L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, sodium chloride, sucrose, and water for injection

VYVGART SC comes in the following dosage form:

1000 mg efgartigimod alfa per 5 mL in a single-use prefilled syringe, for subcutaneous (under the skin) administration

Do not use VYVGART SC if:

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take VYVGART SC. 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 SC.
- are pregnant or plan to become pregnant. It is not known if VYVGART SC will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if VYVGART SC passes into your breast milk.
- have had an allergic reaction to VYVGART SC in the past.

Other warnings you should know about:

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

VYVGART SC may cause serious side effects, including:

- Infections: VYVGART SC 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 SC 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 SC 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 SC.

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

The following may also interact with VYVGART SC:

No relevant drug-drug interactions are known, however, use of VYVGART SC with medications that bind to the 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 SC:

The initial injection(s) will be administered by a healthcare professional. After that, you may administer VYVGART SC by yourself, following proper training, or it may be administered by your caregiver or by a healthcare professional. VYVGART SC is administered subcutaneously (under the skin) in the stomach area (abdomen). (see Instructions for Use)

Usual dose:

Generalized Myasthenia Gravis (gMG)

The recommended dose is 1000 mg efgartigimod alfa administered subcutaneously (under the skin) in cycles of once weekly injections for 4 weeks. Your doctor will determine when further treatment cycles are needed.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The recommended dose is 1000 mg efgartigimod alfa administered subcutaneously (under the skin) as once-weekly injections.

Overdose:

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

If you think you, or a person you are caring for, have taken too much VYVGART SC, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed Dose:

If you miss a dose, you should administer the missed dose as soon as possible and at least 3 days ahead of the next dose. If there are less than 3 days to the next administration, the missed dose should be skipped and the next dose should be administered at the scheduled time.

What are possible side effects from using VYVGART SC?

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

Side effects and what to do about them

Frequency/Side Effect/Symptom	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	✓		
Injection Site Reactions: redness of the skin	✓		
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 VYVGART SC unopened prefilled syringes in a refrigerator at 2°C to 8°C in the original carton for up to 18 months. Unopened prefilled syringes may be stored at room temperature up to 30°C in the original carton for a single period of up to 1 month after removing them from the refrigerator or until the expiration date on the carton, whichever occurs first.

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

Keep out of reach and sight of children.

If you want more information about VYVGART SC:

- 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.

Date of Authorization: 2025-11-03

Instructions for Use (Prefilled Syringe)

PrVYVGART® SC

Efgartigimod alfa injection

1000 mg/5 mL (200 mg/mL) solution in single-use prefilled syringe

Subcutaneous use

Important Information You Need to Know Before Injecting VYVGART SC

- **VYVGART SC is for subcutaneous (under the skin) injection only.**
- **Be sure to read and understand this Instructions for Use before injecting VYVGART SC**. Your healthcare provider should show you or your caregiver how to prepare and inject VYVGART SC the right way before using it for the first time. Ask your healthcare provider if you have any questions.
- **The prefilled syringe is for single-use only** and cannot be reused.
- **Do not** use VYVGART SC if it has been at room temperature for longer than 1 month.
- **Do not** use the prefilled syringe if it is expired.
- **Do not** use the prefilled syringe if it is damaged. Return damaged prefilled syringes to the specialty pharmacy.
- **Do not** use a prefilled syringe if the medicine is discoloured or contains particles. **The medicine should look** clear to light yellow in colour. A little cloudiness is normal.
- **Do not** shake the prefilled syringe.

Storing VYVGART SC

- **Store VYVGART SC in the refrigerator** between 2°C to 8°C (see Figure A).
- **Keep the prefilled syringes in the original carton** to protect them from light.
- **Keep VYVGART SC and all medicines out of the reach of children.**

Do not freeze the prefilled syringes or store them in direct sunlight.

Do not use a prefilled syringe that has been frozen or left in direct sunlight.

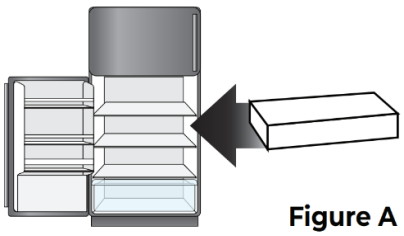
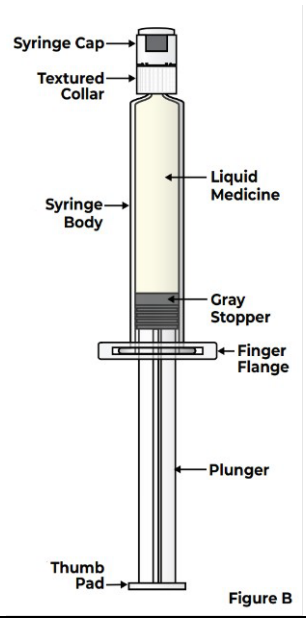
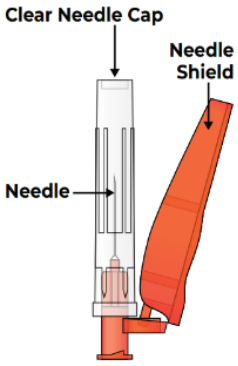


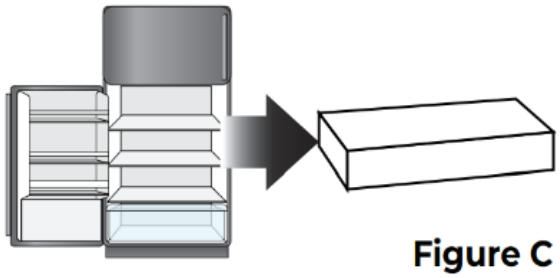
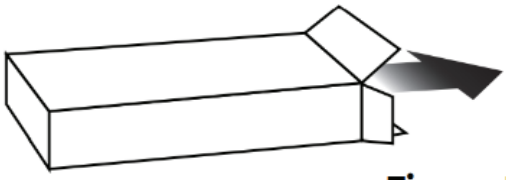
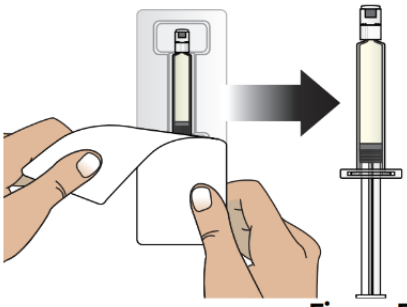
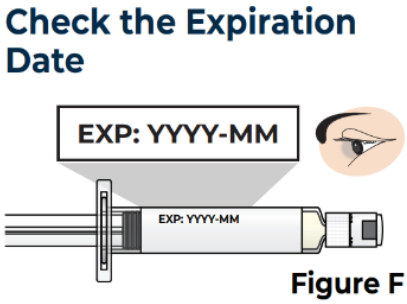
Figure A

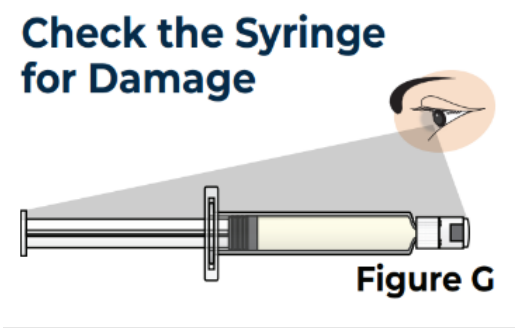
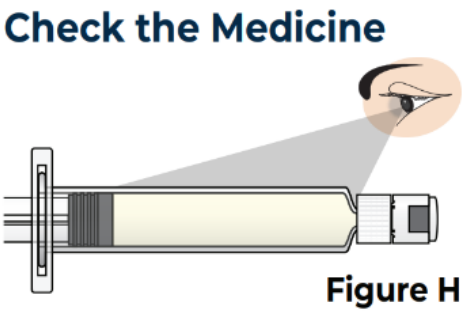
Prefilled syringe parts

	 Figure B

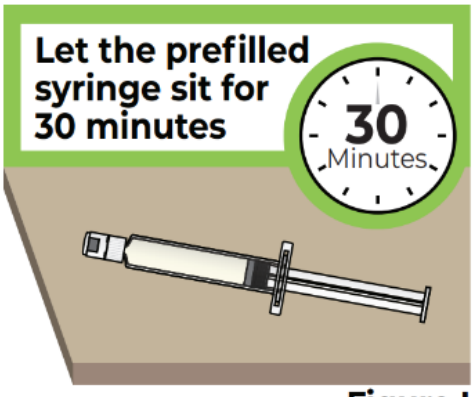
Safety Needle (Not provided with syringe) 25G, 5/8” length, thin wall	

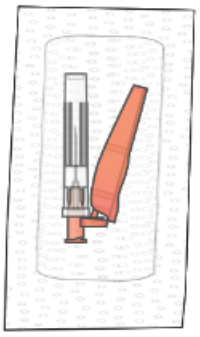
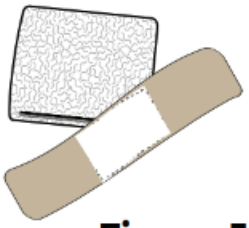
Gather & Check Supplies

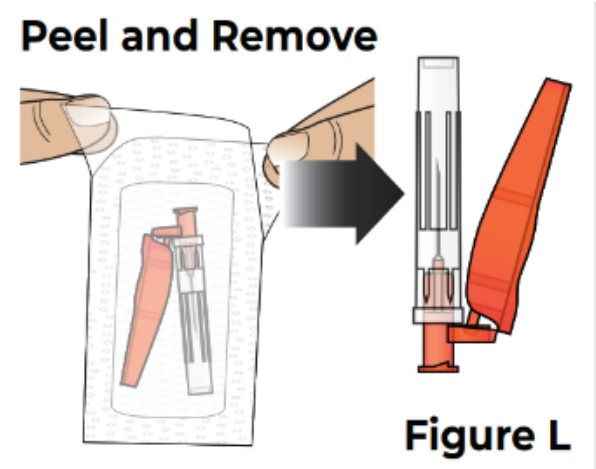
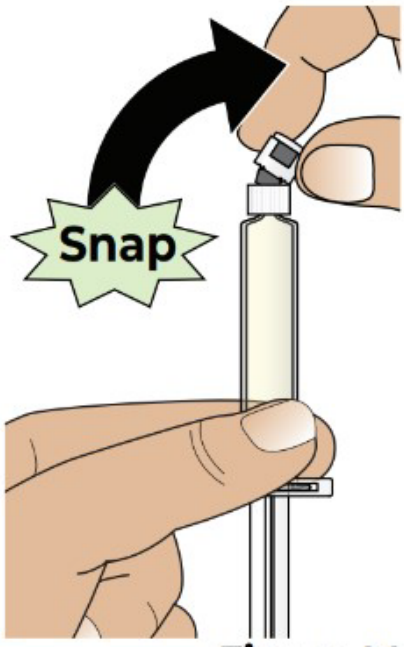
1 Remove the carton from the refrigerator	
1.1 Remove the prefilled syringe carton from the refrigerator (see Figure C).	 Figure C
1.2 Remove 1 prefilled syringe from the carton (see Figure D) and place any remaining prefilled syringes back into the refrigerator for later use.	 Figure D
1.3 Remove the prefilled syringe from the tray (see Figure E).	 Figure E
2 Check the prefilled syringe before use	
2.1 Check the expiration date on the prefilled syringe label (see Figure F). **Do not** use the prefilled syringe if the expiration date has passed.	 Figure F

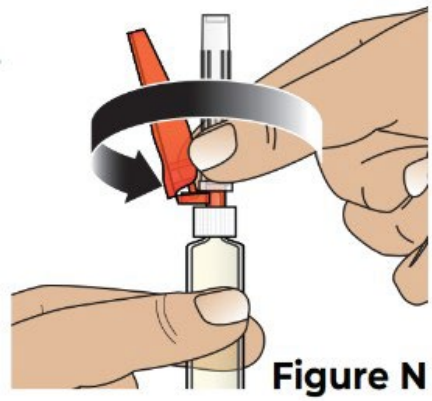
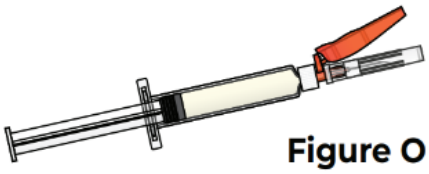
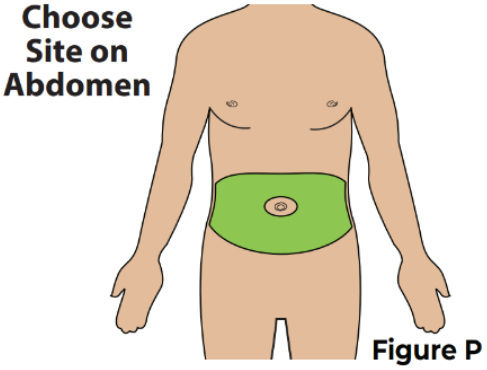
2.2 Check the condition of the prefilled syringe and the prefilled syringe cap (see Figure G). **Do not** use the prefilled syringe if it is cracked, broken, damaged, or if the cap is missing.	 Figure G
2.3 Check the appearance of the medicine in the prefilled syringe (see Figure H). **The medicine should look** clear to light yellow in colour. A little cloudiness is normal. **Do not** use the prefilled syringe if the medicine is discoloured or contains particles.	 Figure H

Prepare for the Injection

3 Allow the prefilled syringe to warm to room temperature	
3.1 Place the prefilled syringe on a clean flat surface and **let it sit for at least 30 minutes,** to allow it to warm to room temperature (see Figure I). **Do not** attempt to warm the prefilled syringe in any other way. **Do not** use VYVGART SC if it has been at room temperature for longer than 1 month.	 Figure I

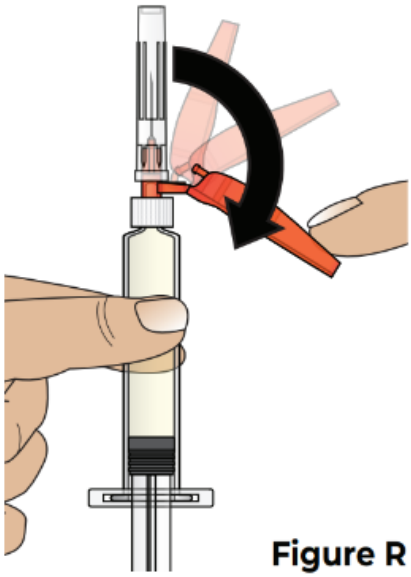
4 Gather supplies & wash hands	
4.1 Gather the following supplies that are **not provided** with the prefilled syringe (see Figure J).	• **Safety Needle**  • **Alcohol Swab**  • **Sharps Disposal Container**  • **Sterile Gauze and/or Bandage** (As Needed)  **Figure J**
4.2 Wash hands with soap and water (see Figure K).	 **Figure K**

5 Snap off the prefilled syringe cap & attach the needle	
5.1 Carefully open the needle package and remove the needle (see Figure L). Throw away the packaging into household trash.	 Figure L
5.2 Bend the prefilled syringe cap to one side to snap it off and remove it from the prefilled syringe (see Figure M). Throw away the syringe cap. **Do not** touch the tip of the prefilled syringe after the cap has been removed.	 Figure M

5.3 Hold the prefilled syringe in one hand, and **attach the needle to the prefilled syringe by twisting it on** (clockwise/to the right) until you feel resistance (see Figure N). The needle is now attached to the prefilled syringe (see Figure O).	 Figure N  Figure O
6 Choose & clean the injection site on abdomen	
6.1 Choose an injection site on the abdomen (belly area) at least two inches away from the belly button (navel) (see Figure P). **Rotate** (change) the injection site for each injection. **Do not** inject into skin that is irritated, red, bruised, infected, or scarred. **Do not** inject into a vein. VYVGART SC is for subcutaneous (under the skin) injection only.	 Figure P

6.2 Clean the chosen injection site with an alcohol swab and let it air dry (see Figure Q). **Do not** blow on or touch the injection site after it has been cleaned.	 Figure Q

Inject VYVGART SC

7 Pull back the needle shield & remove the needle cap	
7.1 Pull the needle shield back (see Figure R). **Note:** The needle shield will be used after the injection to cover the needle and protect from needle-stick injuries.	 Figure R

7.2 Hold the prefilled syringe body and **remove the clear needle cap by pulling it straight off** of the needle (see Figure S).

Throw away the needle cap into household trash.

Do not recap the needle.

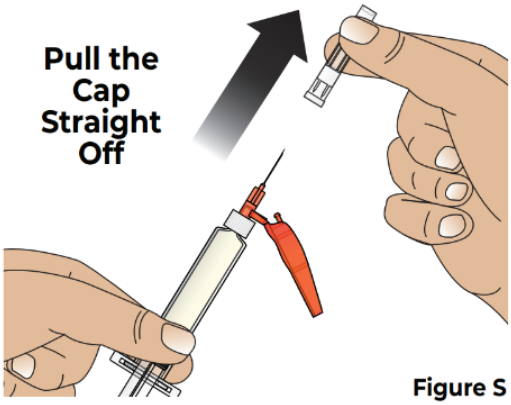


Figure S

8 Give the injection

8.1 Pinch the cleaned injection site (Figure T).

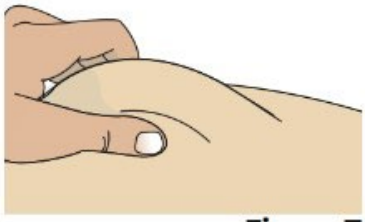


Figure T

While pinching the skin, **insert the needle at a 45 to 90 degree angle** all the way into the pinched skin (see Figure U).

Then release the pinched skin.

Do not pinch the skin too tightly as this can cause bruising.

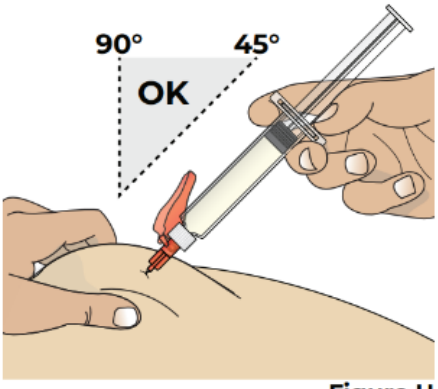


Figure U

8.2 Slowly press the plunger down all the way until it stops to inject the medicine (see Figure V).

It will take approximately 20-30 seconds to inject all of the medicine.

You will feel resistance as you press down. Inject more slowly in case of discomfort.

It is ok if you need to pause or change your grip during the injection.

Do not try to force the plunger down quickly as this will make the plunger harder to press.

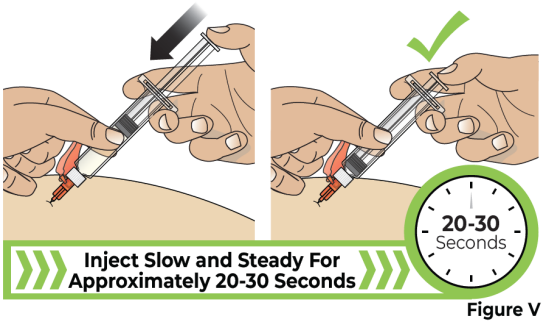


Figure V

8.3 After all the liquid medicine is injected, **remove the needle from the skin** by pulling it out straight out without changing the angle (see Figure W).

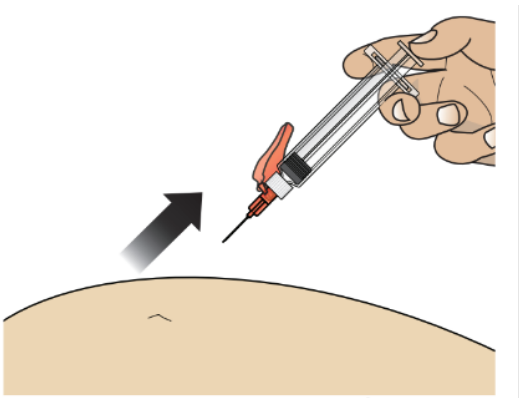
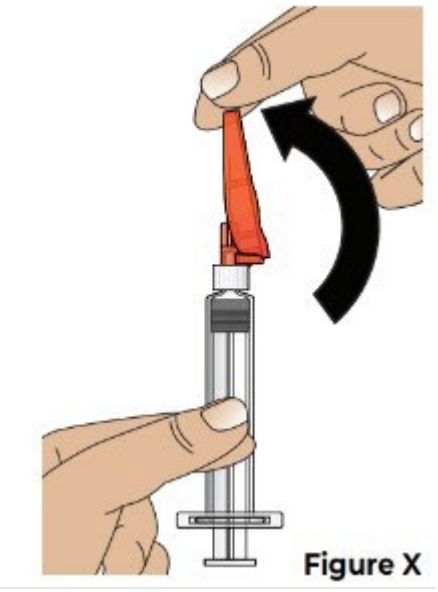
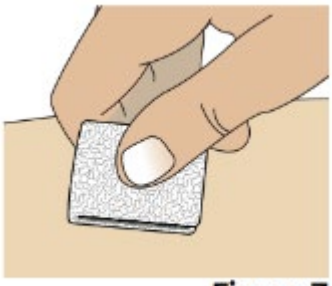


Figure W

Dispose of the Used Syringe

9 Cover the needle & throw away the used syringe	
9.1 Carefully push the needle shield over the needle until it snaps into place and covers the needle (see Figure X). This helps to prevent needle-stick injuries. **Do not** recap the needle using the needle cap; only use the needle shield to cover the needle.	 Figure X
9.2 Throw away the used syringe, with the needle still attached**, into a sharps disposal container** right away after use (see Figure Y). **Do not** throw away (dispose of) loose needles and syringes in your household trash.	 Figure Y

10 Treat the injection site	
10.1 If there is a small amount of blood or liquid at the injection site, press a gauze over the injection site until the bleeding stops (see Figure Z). If needed, you may apply a small adhesive bandage.	 **Figure Z**

Additional disposal information

If you do not have an sharps disposal container, you may use a household container that is:
• made of a heavy-duty plastic,
• can be closed with a tight-fitting, puncture-resistant lid without sharps being able to come out,
• upright and stable during use,
• leak-resistant, and
• properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be local laws about how you should throw away used needles and syringes.

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Always keep the sharps disposal container out of the reach of children.