# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 20 mg/mL concentrate for solution for infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of 20 mL contains 400 mg of efgartigimod alfa (20 mg/mL).

Efgartigimod alfa is a human recombinant immunoglobulin G1 (IgG1)-derived Fc fragment produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

Excipient(s) with known effect

Each vial contains 33.2 mg sodium.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate)

Colourless to slightly yellow, clear to slightly opalescent, pH 6.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Vyvgart is indicated as an add-on to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.

### 4.2 Posology and method of administration

Efgartigimod alfa must be administered by a healthcare professional and under the supervision of a physician experienced in the management of patients with neuromuscular disorders.

Posology

The recommended dose is 10 mg/kg as a 1-hour intravenous infusion to be administered in cycles of once weekly infusions for 4 weeks. Subsequent treatment cycles should be administered according to clinical evaluation. The frequency of treatment cycles may vary by patient (see section 5.1).

In the clinical development program, the earliest time to initiate a subsequent treatment cycle was 7 weeks from the initial infusion of the previous cycle.

In patients weighing 120 kg or more, the recommended dose is 1 200 mg (3 vials) per infusion (see section 6.6).

*Missed dose*
If a scheduled infusion is not possible, treatment may be administered up to 3 days before or after the scheduled time point. Thereafter, the original dosing schedule should be resumed until the treatment cycle is completed. If a dose needs to be delayed for more than 3 days, the dose should not be administered to ensure two consecutive doses are given with an interval of at least 3 days.

Special populations

*Elderly*
No dose adjustment is required in patients aged 65 years and older (see section 5.2).

*Renal impairment*
Limited safety and efficacy data in patients with mild renal impairment is available, no dose adjustment is required for patients with mild renal impairment. There is very limited safety and efficacy data in patients with moderate or severe renal impairment (see section 5.2).

*Hepatic impairment*
No data in patients with hepatic impairment are available. No dose adjustment is required in patients with hepatic impairment (see section 5.2).

*Paediatric population*
The safety and efficacy of efgartigimod alfa in paediatric population have not yet been established. No data are available.

Method of administration

This medicinal product should only be administered via intravenous infusion. Do not administer as an intravenous push or bolus injection. It should be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection prior to administration as described in section 6.6.

This medicinal product should be administered over 1 hour. Appropriate treatment for infusion and hypersensitivity-related reactions should be readily available before administration of efgartigimod alfa. In case of infusion reactions, the infusion should be administered at a slower rate, interrupted or can be discontinued (see section 4.4).

*Administration*
- Inspect the solution visually for particulate matter prior to administration.
- Infuse the total 125 mL of diluted medicinal product over 1 hour using a 0.2 µm filter. Administer the full amount of solution, flushing the entire line with sodium chloride 9 mg/mL (0.9%) solution for injection at the end.
- Vyvgart should be administered immediately after dilution and the infusion of diluted solution should be completed within 4 hours of dilution.
- Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C to 8 °C. From a microbiological point of view, unless the method of dilution precludes the risks of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Do not freeze. Allow the diluted medicinal product to reach room temperature before administration. Complete the infusion within 4 hours of removal from the refrigerator. The diluted medicinal product should not be heated in any other manner than via ambient air.
- Should infusion reactions occur, the infusion should be administered at a slower rate, interrupted or discontinued (see section 4.4).
- Other medicinal products should not be injected into infusion side ports or mixed with Vyvgart.

For instructions on dilution of the medicinal product before administration, see section 6.6.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Myasthenia Gravis Foundation of America (MGFA) Class V patients

Treatment with efgartigimod alfa in patients with MGFA Class V (i.e. myasthenic crisis), defined as intubation with or without mechanical ventilation except in the setting of routine postoperative care, has not been studied. The sequence of therapy initiation between established therapies for MG crisis and efgartigimod alfa, and their potential interactions, should be considered (see section 4.5).

Infections

As efgartigimod alfa causes transient reduction in IgG levels the risk of infections may increase (see sections 4.8 and 5.1). The most common infections observed in clinical trials were upper respiratory tract infections and urinary tract infections (see section 4.8). Patients should be monitored for clinical signs and symptoms of infections during treatment with Vyvgart. In patients with an active infection, the benefit-risk of maintaining or withholding treatment with efgartigimod alfa should be considered until the infection has resolved. If serious infections occur, delaying treatment with efgartigimod alfa should be considered until the infection has resolved.

Infusion reactions and hypersensitivity reactions

Infusion reactions such as rash or pruritus may occur. In the clinical trial, infusion reactions were mild to moderate and did not lead to treatment discontinuation. Patients should be monitored during administration and for 1 hour thereafter for clinical signs and symptoms of infusion reactions. Should a reaction occur and based on the severity of the reaction the infusion should be administered at a slower rate, interrupted or discontinued and appropriate supportive measures should be instituted. Once resolved, administration may be cautiously resumed, based on clinical evaluation.
Cases of anaphylactic reaction have been reported in the post-marketing setting. If an anaphylactic reaction is suspected, administration of Vyvgart should be immediately discontinued and appropriate medical treatment initiated. Patients should be informed of the signs and symptoms of hypersensitivity and anaphylactic reactions and advised to contact their healthcare provider immediately should they occur.

Immunisations

All vaccines should be administered according to immunisation guidelines.

The safety of immunisation with live or live-attenuated vaccines and the response to immunisation with these vaccines during treatment with efgartigimod alfa are unknown. For patients that are being treated with efgartigimod alfa, vaccination with live or live-attenuated vaccines is generally not recommended. If vaccination with live or live-attenuated vaccines is required, these vaccines should be administered at least 4 weeks before treatment and at least 2 weeks after the last dose of efgartigimod alfa.
Other vaccines may be administered as needed at any time during treatment with efgartigimod alfa.

Immunogenicity

In the double-blind placebo-controlled study, pre-existing antibodies that bind to efgartigimod alfa were detected in 25/165 (15%) patients with gMG. Treatment-induced antibodies to efgartigimod alfa were detected in 17/83 (21%) patients. In 3 of these 17 patients, treatment-induced anti-drug antibodies (ADAs) persisted until the end of the study. Neutralising antibodies were detected in 6/83 (7%) of patients treated with Vyvgart, including the 3 patients with persisting treatment-induced ADAs. Retreatment did not cause an increase in incidence or titres of efgartigimod alfa antibodies.

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

Immunosuppressant and anticholinesterase therapies

When non-steroidal immunosuppressants, corticosteroids and anticholinesterase therapies are decreased or discontinued, patients should be monitored closely for signs of disease exacerbation.

Excipients with known effect

*Sodium*
This medicinal product contains 33.2 mg sodium per vial, equivalent to 1.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult. This medicinal product will be further prepared for administration with sodium-containing solution (see section 6.6) and this should be considered in relation to the total sodium intake to the patient from all sources per day.

*Polysorbates*
This medicinal product contains 8.2 mg of polysorbate 80 in each vial which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions.

## 4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Efgartigimod alfa may decrease concentrations of compounds that bind to the human neonatal Fc Receptor (FcRn), i.e., immunoglobulin products, monoclonal antibodies, or antibody derivatives containing the human Fc domain of the IgG subclass. If possible, it is recommended to postpone initiation of treatment with these products to 2 weeks after the last dose of any given treatment cycle of Vyvgart. As a precaution, patients receiving Vyvgart while on treatment with these products should be closely monitored for the intended efficacy response of those products.

Plasma exchange, immunoadsorption, and plasmapheresis may reduce circulating levels of efgartigimod alfa.

All vaccines should be administered according to immunisation guidelines.
The potential interaction with vaccines was studied in a nonclinical model using Keyhole limpet hemocyanin (KLH) as the antigen. The weekly administration of 100 mg/kg to monkeys did not impact the immune response to KLH immunisation.
For patients that are being treated with efgartigimod alfa, vaccination with live or live-attenuated vaccines is generally not recommended. If vaccination with live or live-attenuated vaccines is required, these vaccines should be administered at least 4 weeks before treatment and at least 2 weeks after the last dose of a treatment cycle efgartigimod alfa (see section 4.4).

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There is no available data on the use of efgartigimod alfa during pregnancy. Antibodies including therapeutic monoclonal antibodies are known to be actively transported across the placenta (after 30 weeks of gestation) by binding to the FcRn.

Efgartigimod alfa may be transmitted from the mother to the developing foetus. As efgartigimod alfa is expected to reduce maternal antibody levels, and is also expected to inhibit the transfer of maternal antibodies to the foetus, reduction in passive protection to the newborn is anticipated. Therefore, risks and benefits of administering live/live-attenuated vaccines to infants exposed to efgartigimod alfa *in utero* should be considered (see section 4.4).

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

Breast-feeding

There is no information regarding the presence of efgartigimod alfa in human milk, the effects on the breastfed child or the effects on milk production. Animal studies on the transfer of efgartigimod alfa into milk have not been conducted, and therefore, excretion into maternal milk cannot be excluded. Maternal IgG is known to be present in human milk. Treatment of lactating women with efgartigimod alfa should only be considered if the clinical benefit outweighs the risks.

Fertility

There is no available data on the effect of efgartigimod alfa on fertility in humans. Animal studies showed no impact of efgartigimod alfa on male and female fertility parameters (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Vyvgart has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

Summary of the safety profile

The most frequently observed adverse reactions were upper respiratory tract infections and urinary tract infections (10.7% and 9.5%, respectively).

Tabulated list of adverse reactions

The safety of Vyvgart was evaluated in 167 patients with gMG in the Phase 3 double-blind placebo-controlled clinical study.

Adverse reactions are listed in Table 1 by system organ class and preferred term. Frequency categories are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100). rare (≥ 1/10 000 to < 1/1 000) or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 1. Adverse reactions**

| System organ class | Adverse reaction | Frequency category |
|---|---|---|
| **Infections and infestations*** | Upper respiratory tract infections | Very common |
| | Urinary tract infections | Common |
| | Bronchitis | Common |
| **Immune system disorders** | Anaphylactic reaction [a] | Not known |

| System organ class | Adverse reaction | Frequency category |
|---|---|---|
| **Gastrointestinal disorders** | Nausea [a] | Common |
| **Musculoskeletal and connective tissue disorders** | Myalgia | Common |
| **Injury, poisoning and procedural complications*** | Procedural headache | Common |

* See paragraph "Description of selected adverse reactions"
[a] From spontaneous post-marketing reporting

Description of selected adverse reactions

*Infections*

The most frequently reported adverse reactions were infections, and the most reported infections were upper respiratory tract infections (10.7% [n = 9] of patients treated with efgartigimod alfa and 4.8% [n = 4] of patients treated with placebo) and urinary tract infections (9.5% [n = 8] of patients treated with efgartigimod alfa and 4.8% [n = 4] of patients treated with placebo). These infections were mild to moderate in severity in patients who received efgartigimod alfa (≤ Grade 2 according to the Common Terminology Criteria for Adverse Events). Overall, treatment emergent infections were reported in 46.4% (n = 39) of patients treated with efgartigimod alfa and 37.3% (n = 31) of patients treated with placebo. The median time from treatment initiation to emergence of infections was 6 weeks. Incidence of infections did not increase with subsequent treatment cycles. Treatment discontinuation or temporary interruption of treatment due to an infection occurred in less than 2% of patients.

*Procedural headache*

Procedural headache was reported in 4.8% of the patients treated with efgartigimod alfa 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 efgartigimod alfa. All were mild or moderate except one event which was reported as severe (Grade 3).

All other adverse reactions were mild or moderate with the exception of one case of myalgia (Grade 3).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

### 4.9 Overdose

There are no known specific signs and symptoms of overdose with efgartigimod alfa. In the event of an overdose the adverse events that may occur are not expected to be different from those that may be 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 efgartigimod alfa.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, neonatal fragment crystallizable receptor (FcRn) inhibitors, ATC code: L04AL01

Mechanism of action

Efgartigimod alfa is a human IgG1 antibody fragment engineered for increased affinity to the neonatal Fc Receptor (FcRn). Efgartigimod alfa binds to FcRn, resulting in a reduction in the levels of circulating IgG including pathogenic IgG autoantibodies. Efgartigimod alfa does not affect the levels of other immunoglobulins (IgA, IgD, IgE or IgM), and does not reduce those of albumin.

IgG autoantibodies are the underlying cause of the pathogenesis of MG. They impair neuromuscular transmission by binding to acetylcholine receptors (AChR), muscle-specific tyrosine kinase (MuSK) or low-density lipoprotein receptor-related protein 4 (LRP4).

Pharmacodynamic effects

In a double-blind placebo-controlled study in gMG patients, efgartigimod alfa decreased serum IgG levels and AChR autoantibody levels at the recommended dose and schedule (see section 4.2). Maximum 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. Similar effects were also observed for all subtypes of IgG. Decrease in AChR autoantibody levels followed a similar time course with maximum mean percentage decrease of 58% one week after the last infusion and return to baseline levels 7 weeks after the last infusion. Similar changes were observed during the second cycle of the study.

Clinical efficacy and safety

Efficacy of efgartigimod alfa for the treatment of adults with generalised Myasthenia Gravis (gMG) was studied in a 26-week, multicentre randomised double-blind placebo-controlled trial (ARGX-113-1704).

In this study, patients had to meet the following main criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II, III or IV;
- Patients with either positive or negative serologic tests for antibodies to AChR;
- MG-Activities of Daily Living (MG-ADL) total score of ≥ 5;
- On stable doses of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapy (NSIST), either in combination or alone [NSISTs included but were not limited to azathioprine, methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, and cyclophosphamide];
- IgG levels of at least 6 g/L.

Patients with MGFA Class V gMG; patients with documented lack of clinical response to PLEX; patients treated with PLEX, IVIg one month and monoclonal antibodies six months prior to starting treatment; and patients with active (acute or chronic) hepatitis B infection, hepatitis C seropositivity, and diagnosis of AIDS, were excluded from the trials.

A total of 167 patients were enrolled in the study and were randomised to either efgartigimod alfa intravenous (n = 84) or placebo (n = 83). Baseline characteristics were similar between treatment groups, including median age at diagnosis [45 (19-81) years], gender [most were female; 75% (efgartigimod alfa) versus 66% (placebo)], race [most patients were white; 84.4%] and median time since diagnosis [8.2 years (efgartigimod alfa) and 6.9 years (placebo)].

The majority of patients (77% in each group) tested positive for antibodies to AChR (AChR-Ab) and 23% of patients tested negative for AChR-Ab.

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.

Median MG-ADL total score was 9.0 in both treatment groups, and median Quantitative Myasthenia Gravis (QMG) total score was 17 and 16 in the efgartigimod alfa and placebo groups, respectively.

Patients were treated with efgartigimod alfa intravenous 10 mg/kg administered once weekly for 4 weeks and received a maximum of 3 treatment cycles (see section 4.2).

The efficacy of efgartigimod alfa was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which assesses the impact of gMG on daily functions. A total score ranges from 0 to 24 with the higher scores indicating more impairment. In this study, an MG-ADL responder was a patient with ≥ 2-point 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 efgartigimod alfa was also measured using the QMG total score which is a grading system that assesses muscle weakness with a total possible score of 0 to 39 where higher scores indicate more severe impairment. In this study, a QMG responder was a patient who had a ≥ 3-point 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 (C1) between treatment groups in the AChR-Ab seropositive population.

A key secondary endpoint was the comparison of the percentage of QMG responders during C1 between both treatment groups in the AChR-Ab seropositive patients.

**Table 2. MG-ADL and QMG responders during cycle 1 in AChR-Ab seropositive population (mITT analysis set)**

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

AChR-Ab = acetylcholine receptor-antibody; MG-ADL = Myasthenia Gravis Activities of Daily Living; QMG = Quantitative Myasthenia Gravis; mITT = modified intent-to-treat; n = number of patients for whom the observation was reported; N = number of patients in the analysis set; CI = confidence interval;
Logistic regression stratified for AChR-Ab status (if applicable), Japanese/Non-Japanese and standard of care, with baseline MG-ADL as covariate/QMG as covariates
Two-sided exact p-value

Analyses show that during the second treatment cycle MG-ADL responder rates were similar to those during the first treatment cycle (see Table 3).

**Table 3. MG-ADL and QMG responders during cycle 2 in AChR-Ab seropositive population (mITT analysis set)**

| | Population | Efgartigimod alfa n/N (%) | Placebo n/N (%) |
|---|---|---|---|
| MG-ADL | AChR-Ab seropositive | 36/51 (70.6) | 11/43 (25.6) |
| QMG | AChR-Ab seropositive | 24/51 (47.1) | 5/43 (11.6) |

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

Exploratory data shows that onset of response was observed within 2 weeks of initial infusion in 37/44 (84%) patients treated with efgartigimod alfa intravenous in the AChR-Ab seropositive MG-ADL responders.

In the double-blind placebo-controlled study, the earliest possible time to initiating the subsequent treatment cycle was 8 weeks after the initial infusion of the first treatment cycle. In the overall

population the mean time to the second treatment cycle in the efgartigimod alfa intravenous group was 13 weeks (SD 5.5 weeks) and the median time was 10 weeks (8-26 weeks) from the initial infusion of the first treatment cycle. In the open-label extension study the earliest possible time of initiation of the subsequent treatment cycles was 7 weeks.

In patients that responded to treatment, the duration of clinical improvement was 5 weeks in 5/44 (11%) patients, 6-7 weeks in 14/44 (32%) of patients, 8-11 weeks in 10/44 (23%) patients and 12 weeks or more in 15/44 (34%) patients.

## 5.2 Pharmacokinetic properties

Distribution

Based upon population PK data analysis in healthy subjects and patients the volume of distribution is 18 L.

Biotransformation

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

Elimination

The terminal half-life is 80 to 120 hours (3 to 5 days). Based upon population PK data analysis, the clearance is 0.128 L/h. The molecular weight of efgartigimod alfa is approximately 54 kDa, which is at the boundary of molecules that are renally filtered.

Linearity/non-linearity

The pharmacokinetics profile of efgartigimod alfa is linear, independent of dose or time, with negligible accumulation. The geometric mean accumulation ratio based on observed peak concentrations was 1.12.

Special populations

*Age, gender, race and bodyweight*
The pharmacokinetics of efgartigimod alfa were not affected by age (19-78 years), gender and race.

A population pharmacokinetic analysis showed that the effect of bodyweight on efgartigimod alfa exposure was limited at a dose of 10 mg/kg in patients up to 120 kg as well as in patients of 120 kg and above who received a capped dose of 1 200 mg/infusion. There was no effect of bodyweight on the extent of IgG reduction. In the double-blind placebo-controlled study, 5 (3%) patients were over 120 kg. The median bodyweight of patients on efgartigimod alfa in the study was 76.5 kg (min 49; max 229).

*Renal impairment*
No dedicated pharmacokinetic studies have been performed in patients with renal impairment.

The effect of renal function marker estimated glomerular filtration rate [eGFR] as a covariate in a population pharmacokinetic analysis showed a reduced clearance resulting in a limited increase in exposure in patients with mild renal impairment (eGFR 60-89 mL/min/1.73 $m^2$). No specific dose adjustment is recommended in patients with mild renal impairment.

There is insufficient data on the impact of moderate renal impairment (eGFR 30-59 mL/min/1.73 $m^2$) and severe renal impairment (eGFR < 30 mL/min/1.73 $m^2$) on efgartigimod alfa pharmacokinetic parameters.

*Hepatic impairment*
No dedicated pharmacokinetic study has been performed in patients with hepatic impairment.

The effect of hepatic function markers as covariates in a population pharmacokinetic analysis did not show any impact on the pharmacokinetics of efgartigimod alfa.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeated dose toxicity.

In reproduction studies in rats and rabbits, intravenous administration of efgartigimod alfa did not result in adverse effects on fertility and pregnancy nor were teratogenic effects observed up to dose levels corresponding to 11-fold (rats) and 56-fold (rabbits) to the exposure (AUC) at the maximum recommended therapeutic dose.

Carcinogenicity and genotoxicity

No studies have been conducted to assess the carcinogenic and genotoxic potential of efgartigimod alfa.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

L-histidine
L-histidine hydrochloride monohydrate
L-methionine
Sodium chloride
Sucrose
L-arginine hydrochloride
Polysorbate 80 (E433)
Water for injections

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

### 6.3 Shelf life

3 years

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C to 8 °C.
From a microbiological point of view, unless the method of dilution precludes the risks of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

### 6.4 Special precautions for storage

Store in a refrigerator (2 °C - 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

For storage conditions after dilution of the medicinal product, see section 6.3.

### 6.5 Nature and contents of container

Concentrate in single-dose 20 mL glass vials (Type I) with rubber stopper (butyl, siliconised), aluminium seal and polypropylene flip-off cap.

Pack size of 1 vial.

### 6.6 Special precautions for disposal and other handling

The efgartigimod alfa solution diluted in sodium chloride 9 mg/mL (0.9%) solution for injection can be administered using polyethylene (PE), polyvinyl chloride (PVC), ethylene vinyl acetate (EVA) and ethylene/polypropylene copolymer bags (polyolefins bags), as well as with PE, PVC and polyurethane/polypropylene infusion lines, together with polyurethane (PUR) or PVC filters with polyethersulfone (PES) or polyvinylidene fluoride (PVDF) filter membrane.

Using the formula in the table below, calculate the following:

- The dose of Vyvgart required based on the patient's bodyweight at the recommended dose of 10 mg/kg. For patients weighing over 120 kg use a bodyweight of 120 kg to calculate the dose. The maximum total dose per infusion is 1 200 mg. Each vial contains 400 mg of efgartigimod alfa at a concentration of 20 mg/mL.
- The number of vials needed.
- The volume of sodium chloride 9 mg/mL (0.9%) solution for injection. The total volume of diluted medicinal product is 125 mL.

**Table 4. Formula**

| | |
|---|---|
| Step 1 – Calculate the dose (mg) | 10 mg/kg x weight (kg) |
| Step 2 – Calculate the volume of concentrate (mL) | dose (mg) ÷ 20 mg/mL |
| Step 3 – Calculate the number vials | volume of concentrate (mL) ÷ 20 mL |
| Step 4 – Calculate the volume of sodium chloride 9 mg/mL (0.9%) solution for injection (mL) | 125 mL – concentrate volume (mL) |

*Dilution*

- Visually inspect that the vial content is clear to slightly opalescent, colourless to slightly yellow, and devoid of particulate matter. If visible particles are observed and/or the liquid in the vial is discoloured, the vial must not be used. Do not shake the vials.
- Using aseptic technique throughout the preparation of the diluted solution:
  - Gently withdraw the required amount of Vyvgart from the appropriate number of vials with a sterile syringe and needle (see Table 4). Discard any unused portion of the vials.
  - Transfer the calculated dose of the product into an infusion bag.
  - Dilute the withdrawn product by adding the calculated amount of sodium chloride 9 mg/mL (0.9%) solution for injection to make a total volume of 125 mL.
  - Gently invert the infusion bag containing the diluted product **without shaking** to ensure thorough mixing of the product and the diluent.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1674/001

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 August 2022

## 10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 1 000 mg solution for injection
Vyvgart 1 000 mg solution for injection in pre-filled syringe

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Vyvgart 1 000 mg solution for injection
Each vial contains 1 000 mg of efgartigimod alfa in 5.6 mL (180 mg/mL).

Vyvgart 1 000 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 1 000 mg of efgartigimod alfa in 5 mL (200 mg/mL).

Efgartigimod alfa is a human recombinant immunoglobulin G1 (IgG1)-derived Fc fragment produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection

Yellowish, clear to opalescent, pH 6.0.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Vyvgart is indicated as
- an add-on to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
- monotherapy for the treatment of adult patients with progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) after prior treatment with corticosteroids or immunoglobulins.

### 4.2 Posology and method of administration

Treatment must be initiated and supervised by a physician experienced in the management of patients with neuromuscular disorders.

Posology

*Generalised myasthenia gravis*

The first treatment cycle and first administration of the second treatment cycle must be administered either by or under the supervision of a healthcare professional. Subsequent treatment should be administered by a healthcare professional or may be administered at home by a patient or caregiver after adequate training in the subcutaneous injection technique.

The recommended dose is 1 000 mg to be administered subcutaneously in cycles of once weekly injections for 4 weeks. Subsequent treatment cycles should be administered according to clinical evaluation. The frequency of treatment cycles may vary by patient (see section 5.1).

In the clinical development program, the earliest time to initiate a subsequent treatment cycle was 7 weeks from the initial infusion of the previous cycle.

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 first 4 injections must be administered either by or under the supervision of a healthcare professional. Subsequent injections should be administered by a healthcare professional or may be administered at home by a patient or caregiver after adequate training in the subcutaneous injection technique.

The recommended dose is 1 000 mg administered subcutaneously as once-weekly injections.

Treatment is initiated with a weekly dose regimen and may be adjusted to every other week based on clinical evaluation. In case of worsening of symptoms, administration of once-weekly injections should be resumed.

For those patients transitioning from their current CIDP therapies, Vyvgart 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 efgartigimod alfa subcutaneous. Clinical evaluation should be considered 3 to 6 months after treatment initiation to assess the treatment effect and at regular intervals thereafter.

*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.

<u>Special populations</u>

*Elderly*
No dose adjustment is required in patients aged 65 years and older (see section 5.2).

*Renal impairment*
Limited safety and efficacy data in patients with mild renal impairment is available, no dose adjustment is required for patients with mild renal impairment. There is very limited safety and efficacy data in patients with moderate or severe renal impairment (see section 5.2).

*Hepatic impairment*
No data in patients with hepatic impairment are available. No dose adjustment is required in patients with hepatic impairment (see section 5.2).

*Paediatric population*
The safety and efficacy of efgartigimod alfa in paediatric population have not yet been established. No data are available.

Method of administration

This medicinal product should only be administered via subcutaneous injection. Do not administer intravenously.

*Vyvgart 1 000 mg solution for injection*
After removing the vial from the refrigerator, wait for at least 15 minutes before injecting to allow the solution to reach room temperature. Use aseptic technique when preparing and administering the medicinal product solution. Do not shake the vial.

The solution for injection can be administered using a polypropylene syringe, stainless steel transfer needles and polyvinyl chloride winged infusion set, with a maximum priming volume of 0.4 mL.

- Withdraw the entire content of the efgartigimod alfa solution from the vial using a transfer needle.
- Change the needle on the syringe to the winged infusion set.
- Prior to administration, the volume in the syringe should be adjusted to 5.6 mL.

During the initial administrations of efgartigimod alfa (see section 4.2), appropriate treatment for injection and hypersensitivity-related reactions should be readily available (see section 4.4). The recommended injection sites (abdomen) should be rotated and injections should never be given into moles, scars, or areas where the skin is tender, bruised, red or hard. The volume of 5.6 mL should be injected over 30 to 90 seconds. The injection may be slowed if the patient experiences discomfort.

*Vyvgart 1 000 mg solution for injection in pre-filled syringe*
After removing the pre-filled syringe from the refrigerator, wait for at least 30 minutes before injecting to allow the solution to reach room temperature. A safety needle, which is not included in the carton, should be connected to the pre-filled syringe. Use aseptic technique when handling the pre-filled syringe and during administration. Do not shake the pre-filled syringe.

During the initial administrations of efgartigimod alfa (see section 4.2), appropriate treatment for injection and hypersensitivity-related reactions should be readily available (see section 4.4). The recommended injection sites (abdomen) should be rotated and injections should never be given into moles, scars, or areas where the skin is tender, bruised, red or hard. The medicinal product should be injected for approximately 20 to 30 seconds. The injection may be slowed if the patient experiences discomfort.

The first self-administration must always be conducted under the supervision of a healthcare professional. After adequate training in subcutaneous injection technique, patients or caregivers may inject the medicinal product at home if a healthcare professional determines that it is appropriate. Patients or caregivers should be instructed to inject Vyvgart according to the directions provided in the package leaflet.
For comprehensive instructions for the administration of the medicinal product, please refer to the Instructions for Use in the package leaflet.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Myasthenia Gravis Foundation of America (MGFA) Class V patients

Treatment with efgartigimod alfa in patients with MGFA Class V (i.e. myasthenic crisis), defined as intubation with or without mechanical ventilation except in the setting of routine postoperative care, has not been studied. The sequence of therapy initiation between established therapies for MG crisis and efgartigimod alfa, and their potential interactions, should be considered (see section 4.5).

Infections

As efgartigimod alfa causes transient reduction in IgG levels the risk of infections may increase (see sections 4.8 and 5.1). The most common infections observed in clinical trials were upper respiratory tract infections and urinary tract infections (see section 4.8). Patients should be monitored for clinical signs and symptoms of infections during treatment with Vyvgart. In patients with an active infection, the benefit-risk of maintaining or withholding treatment with efgartigimod alfa should be considered until the infection has resolved. If serious infections occur, delaying treatment with efgartigimod alfa should be considered until the infection has resolved.

Injection reactions and hypersensitivity reactions

Injection reactions such as rash or pruritus were reported in the clinical trials (see section 4.8). These were mild to moderate. Cases of anaphylactic reaction have been reported with efgartigimod alfa intravenous in the post-marketing setting. The first administrations of Vyvgart must be performed under the supervision of a healthcare professional (see section 4.2). Patients should be monitored for 30 minutes after administration for clinical signs and symptoms of injection reactions. Should a reaction occur and based on the severity of the reaction, appropriate supportive measures should be initiated. Subsequent injections may be cautiously administered, based on clinical evaluation.
If an anaphylactic reaction is suspected, administration of Vyvgart should be immediately discontinued and appropriate medical treatment initiated. Patients should be informed of the signs and symptoms of hypersensitivity and anaphylactic reactions and advised to contact their healthcare professional immediately should they occur.

Immunisations

All vaccines should be administered according to immunisation guidelines.

The safety of immunisation with live or live-attenuated vaccines and the response to immunisation with these vaccines during treatment with efgartigimod alfa are unknown. For patients that are being treated with efgartigimod alfa, vaccination with live or live-attenuated vaccines is generally not recommended. If vaccination with live or live-attenuated vaccines is required, these vaccines should be administered at least 4 weeks before treatment and at least 2 weeks after the last dose of efgartigimod alfa.
Other vaccines may be administered as needed at any time during treatment with efgartigimod alfa.

Immunogenicity

In the active-controlled study ARGX-113-2001, pre-existing antibodies that bind to efgartigimod alfa were detected in 12/110 (11%) patients with gMG. Anti-efgartigimod alfa antibodies were detected in 19/55 (35%) patients treated with efgartigimod alfa subcutaneous compared to 11/55 (20%) patients treated with the intravenous formulation. Neutralising antibodies were detected in 2 (4%) patients treated with efgartigimod alfa subcutaneous and 2 (4%) patients treated with efgartigimod alfa intravenous.

In study ARGX-113-1802, pre-existing antibodies that bind to efgartigimod alfa were detected in 13/317 (4.1%) patients with CIDP. Anti-efgartigimod alfa antibodies were detected in 20/317 (6.3%) of patients treated in the open-label part of the study (Stage A), and in 2/111 (1.8%) of patients treated in the placebo-controlled part (Stage B). Neutralising antibodies were detected in 1 (0.3%) patient in the open-label part of the study only (see section 5.1).

The impact of antibodies to efgartigimod alfa on clinical efficacy or safety, pharmacokinetics and pharmacodynamic cannot be assessed given the low incidence of neutralizing antibodies.

Immunosuppressant and anticholinesterase therapies

When non-steroidal immunosuppressants, corticosteroids and anticholinesterase therapies are decreased or discontinued, patients should be monitored closely for signs of disease exacerbation.

Excipients with known effect

*Sodium*
This medicinal product contains less than 1 mmol sodium (23 mg) per vial/pre-filled syringe, that is to say essentially 'sodium-free'.

*Polysorbates*
*Vyvgart 1 000 mg solution for injection*
This medicinal product contains 2.7 mg of polysorbate 80 in each vial which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions.

*Vyvgart 1 000 mg solution for injection in pre-filled syringe*
This medicinal product contains 2.1 mg of polysorbate 80 in each syringe which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions.

## 4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Efgartigimod alfa may decrease concentrations of compounds that bind to the human neonatal Fc Receptor (FcRn), i.e., immunoglobulin products, monoclonal antibodies, or antibody derivatives containing the human Fc domain of the IgG subclass. If possible, it is recommended to postpone the initiation of treatment with these products to 2 weeks after the last dose of Vyvgart. As a precaution, patients receiving Vyvgart while on treatment with these products should be closely monitored for the intended efficacy response of those products.

Plasma exchange, immunoadsorption, and plasmapheresis may reduce circulating levels of efgartigimod alfa.

All vaccines should be administered according to immunisation guidelines.
The potential interaction with vaccines was studied in a nonclinical model using Keyhole limpet hemocyanin (KLH) as the antigen. The weekly administration of 100 mg/kg to monkeys did not impact the immune response to KLH immunisation.
For patients that are being treated with efgartigimod alfa, vaccination with live or live-attenuated vaccines is generally not recommended. If vaccination with live or live-attenuated vaccines is required, these vaccines should be administered at least 4 weeks before treatment and at least 2 weeks after the last dose of efgartigimod alfa (see section 4.4).

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There is no available data on the use of efgartigimod alfa during pregnancy. Antibodies including therapeutic monoclonal antibodies are known to be actively transported across the placenta (after 30 weeks of gestation) by binding to FcRn.

Efgartigimod alfa may be transmitted from the mother to the developing foetus. As efgartigimod alfa is expected to reduce maternal antibody levels, and is also expected to inhibit the transfer of maternal

antibodies to the foetus, reduction in passive protection to the newborn is anticipated. Therefore, risks and benefits of administering live/live-attenuated vaccines to infants exposed to efgartigimod alfa *in utero* should be considered (see section 4.4).

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

Breast-feeding

There is no information regarding the presence of efgartigimod alfa in human milk, the effects on the breastfed child or the effects on milk production. Animal studies on the transfer of efgartigimod alfa into milk have not been conducted, and therefore, excretion into maternal milk cannot be excluded. Maternal IgG is known to be present in human milk. Treatment of lactating women with efgartigimod alfa should only be considered if the clinical benefit outweighs the risks.

Fertility

There is no available data on the effect of efgartigimod alfa on fertility in humans. Animal studies showed no impact of efgartigimod alfa on male and female fertility parameters (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Vyvgart has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

Summary of the safety profile

The most frequently observed adverse reactions were injection site reactions (33%), upper respiratory tract infections (10.7%) and urinary tract infections (9.5%).

The overall safety profile of Vyvgart subcutaneous for both cyclic and continuous dose regimens was consistent with the known safety profile of the intravenous formulation.

Tabulated list of adverse reactions

Adverse reactions described in this section were identified in clinical trials and from post-marketing reports. These reactions are presented by system organ class and preferred term. Frequency categories are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000) or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 1. Adverse reactions**

| System organ class | Adverse reaction | Frequency category |
|---|---|---|
| **Infections and infestations*** | Upper respiratory tract infections | Very common |
| | Urinary tract infections | Common |
| | Bronchitis | Common |
| **Immune system disorders** | Anaphylactic reaction [a] | Not known |
| **Gastrointestinal disorders** | Nausea [b] | Common |
| **Musculoskeletal and connective tissue disorders** | Myalgia | Common |
| **General disorders and administration site conditions*** | Injection site reactions [c, d] | Very common |
| **Injury, poisoning and procedural complications*** | Procedural headache [e] | Common |

* See paragraph "Description of selected adverse reactions"

[a] From spontaneous post-marketing reporting with intravenous route of administration

[b] From spontaneous post-marketing reporting.
[c] Subcutaneous administration only.
[d] (e.g. injection site rash, injection site erythema, injection site pruritus, injection site pain)
[e] Intravenous administration only.

Description of selected adverse reactions

*Injection site reactions*

In the pooled dataset from two clinical studies in gMG with efgartigimod alfa subcutaneous (n = 168), all injection site reactions were mild to moderate in severity and did not lead to treatment discontinuation. 44.0% (n = 74)) of patients experienced an injection site reaction. Injection site reactions occurred within 24 hours after administration in 78.4% (58/74) of patients and resolved without treatment in 85.1% (63/74) of the patients. The incidence of injection site reactions was the highest in the first treatment cycle, reported in 36.3% (61/168) of patients during the first treatment cycle and decreased to 20.1% (30/149), 15.4% (18/117) and 12.5% (10/80) of patients with the second, third and fourth treatment cycle. In a pooled dataset from 2 clinical studies in patients with CIDP who received continuous administration of efgartigimod alfa subcutaneous the incidence of injection site reactions was 26% (61/235). Analysis by 3-month intervals showed that the percentage of participants with injection-site reactions was highest in the first 3 months of treatment (73 [22.2%] participants) and decreased in subsequent 3-month intervals (range: 0 to 17 [6.8%] participants).

*Infections*

In the gMG ARGX-113-1704 placebo-controlled study with efgartigimod alfa intravenous, the most frequently reported adverse reactions were infections, and the most reported infections were upper respiratory tract infections, (10.7% [n = 9] of patients treated with efgartigimod alfa intravenous and 4.8% [n = 4] of patients treated with placebo) and urinary tract infections (9.5% [n = 8] of patients treated with efgartigimod alfa intravenous and 4.8% [n = 4] of patients treated with placebo). These infections were mild to moderate in severity in patients who received efgartigimod alfa intravenous (≤ Grade 2 according to the Common Terminology Criteria for Adverse Events). Overall, treatment emergent infections were reported in 46.4% (n = 39) of patients treated with efgartigimod alfa intravenous and 37.3% (n = 31) of patients treated with placebo. The median time from treatment initiation to emergence of infections was 6 weeks. Incidence of infections did not increase with subsequent treatment cycles. Treatment discontinuation or temporary interruption of treatment due to an infection occurred in less than 2% of patients. In the placebo-controlled part of the ARGX-113-1802 study in patients with CIDP, continuous administration of efgartigimod alfa subcutaneous was not associated with any increase in the incidence of infections (31.5% [35/111] in the efgartigimod alfa subcutaneous group and 33.6% [37/110] in the placebo group) (see section 5.1).

*Procedural headache*

Procedural headache was reported in 4.8% of the patients treated with efgartigimod alfa intravenous 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 efgartigimod alfa. All were mild or moderate except one event which was reported as severe (Grade 3).

All other adverse reactions were mild or moderate with the exception of one case of myalgia (Grade 3).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

## 4.9 Overdose

There are no known specific signs and symptoms of overdose with efgartigimod alfa. In the event of an overdose the adverse events that may occur are not expected to be different from those that may be 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 efgartigimod alfa.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, neonatal fragment crystallizable receptor (FcRn) inhibitors, ATC code: L04AL01

Mechanism of action

Efgartigimod alfa is a human IgG1 antibody fragment engineered for increased affinity to the neonatal Fc Receptor (FcRn). Efgartigimod alfa binds to FcRn, resulting in a reduction in the levels of circulating IgG including pathogenic IgG autoantibodies. Efgartigimod alfa does not affect the levels of other immunoglobulins (IgA, IgD, IgE or IgM), and does not reduce those of albumin.

IgG autoantibodies are the underlying cause of the pathogenesis of IgG mediated autoimmune diseases.

In MG these impair neuromuscular transmission by binding to acetylcholine receptors (AChR), muscle-specific tyrosine kinase (MuSK) or low density lipoprotein receptor-related protein 4 (LRP4).

In CIDP, several lines of evidence point to the key role of IgG autoantibodies in the pathogenesis of this disease. This includes the demonstration of autoreactive IgG antibodies against components of myelinated nerves, passive transfer of CIDP symptoms to animal models using sera or IgG's from patients with CIDP, and the therapeutic effect of plasma exchange and immunoadsorption for treating patients with CIDP.

Pharmacodynamic effects

*Intravenous formulation*

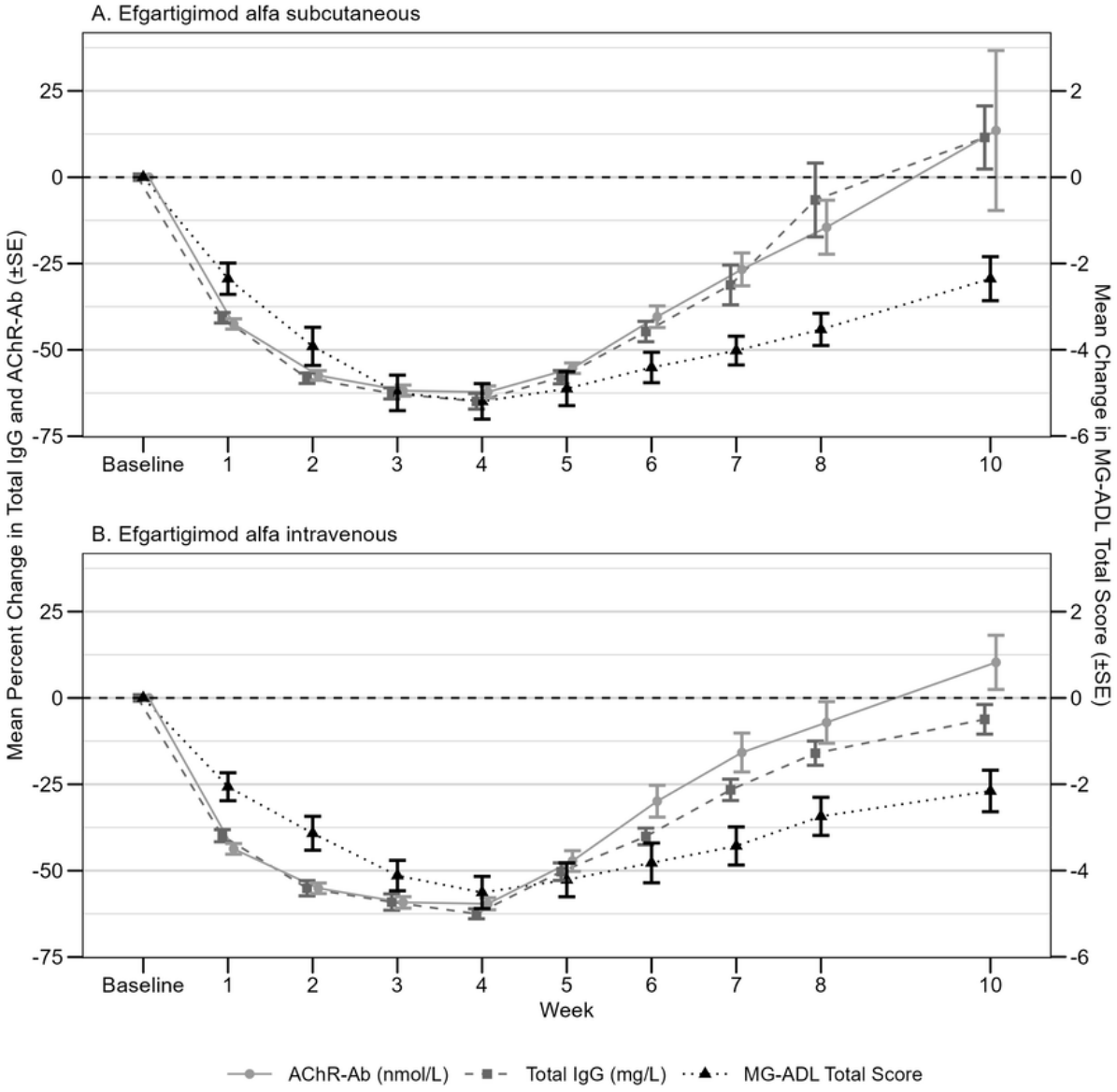
In the ARGX-113-1704 double-blind placebo-controlled study in gMG patients, efgartigimod alfa 10 mg/kg administered once weekly for 4 weeks decreased serum IgG levels and AChR autoantibody (AChR-Ab) levels. Maximum mean percentage decrease in total IgG levels compared to baseline reached 61% one week after the last infusion of the initial treatment cycle and returned to baseline levels 9 weeks after the last infusion. Similar effects were also observed for all subtypes of IgG. Decrease in AChR-Ab levels followed a similar time course with maximum mean percentage decrease of 58% one week after the last infusion and return to baseline levels 7 weeks after the last infusion. Similar changes were observed during the second cycle of the study.

*Subcutaneous formulation*

In the ARGX-113-2001 study, decreases in AChR-Ab levels followed a comparable time course as total IgG levels and were similar between the efgartigimod alfa subcutaneous and intravenous groups. Maximum mean percentage decreases in AChR-Ab levels of 62.2% and 59.6% were observed one week after the last administration in the efgartigimod alfa subcutaneous and intravenous groups, respectively. For both the efgartigimod alfa subcutaneous and intravenous groups, decrease in total

IgG and AChR-Ab levels were associated with a clinical response, as measured by the change from baseline in MG-ADL total score (see figure 1).

**Figure 1. Relationship between total IgG and AChR-Ab and MG-ADL total score in AChR-Ab seropositive population treated with efgartigimod alfa subcutaneous (1A) and efgartigimod alfa intravenous (1B) (study ARGX-113-2001)**




In the ARGX-113-1802 study in patients with CIDP receiving continuous once-weekly administration of efgartigimod alfa subcutaneous at 1 000 mg, the mean percent change from baseline in total IgG levels was sustained from Week 4 throughout the treatment period (mean percentage reduction from baseline ranging between 66.8 to 71.6%).

<u>Clinical efficacy and safety</u>

*Generalised Myasthenia Gravis*

*Intravenous formulation*

Efficacy of efgartigimod alfa for the treatment of adults with generalised Myasthenia Gravis (gMG) was studied in a 26-week, multicentre randomised double-blind placebo-controlled trial (ARGX-113-1704).

In this study, patients had to meet the following main criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II, III or IV;
- Patients with either positive or negative serologic tests for antibodies to AChR;
- MG-Activities of Daily Living (MG-ADL) total score of ≥ 5;
- On stable doses of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapy (NSIST), either in combination or alone [NSISTs included but were not limited to azathioprine, methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, and cyclophosphamide];
- IgG levels of at least 6 g/L.

Patients with MGFA Class V gMG; patients with documented lack of clinical response to PLEX; patients treated with PLEX, IVIg one month and monoclonal antibodies six months prior to starting treatment; and patients with active (acute or chronic) hepatitis B infection, hepatitis C seropositivity, and diagnosis of AIDS, were excluded from the trials.

A total of 167 patients were enrolled in the study and were randomised to either efgartigimod alfa intravenous (n = 84) or placebo (n = 83). Baseline characteristics were similar between treatment groups, including median age at diagnosis [45 (19-81) years], gender [most were female; 75% (efgartigimod alfa) versus 66% (placebo)], race [most patients were white; 84.4%] and median time since diagnosis [8.2 years (efgartigimod alfa) and 6.9 years (placebo)].

The majority of patients (77% in each group) tested positive for antibodies to AChR (AChR-Ab) and 23% of patients tested negative for AChR-Ab.

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.

Median MG-ADL total score was 9.0 in both treatment groups, and median Quantitative Myasthenia Gravis (QMG) total score was 17 and 16 in the efgartigimod alfa and placebo groups, respectively.

Patients were treated with efgartigimod alfa intravenous 10 mg/kg administered once weekly for 4 weeks and received a maximum of 3 treatment cycles.

The efficacy of efgartigimod alfa was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which assesses the impact of gMG on daily functions. A total score ranges from 0 to 24 with the higher scores indicating more impairment. In this study, an MG-ADL responder was a patient with ≥ 2-point 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 efgartigimod alfa was also measured using the QMG total score which is a grading system that assesses muscle weakness with a total possible score of 0 to 39 where higher scores indicate more severe impairment. In this study, a QMG responder was a patient who had a ≥ 3-point 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 (C1) between treatment groups in the AChR-Ab seropositive population.

A key secondary endpoint was the comparison of the percentage of QMG responders during C1 between both treatment groups in the AChR-Ab seropositive patients.

**Table 2. MG-ADL and QMG responders during cycle 1 in AChR-Ab seropositive population (mITT analysis set)**

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

AChR-Ab = acetylcholine receptor-antibody; MG-ADL = Myasthenia Gravis Activities of Daily Living; QMG = Quantitative Myasthenia Gravis; mITT = modified intent-to-treat; n = number of patients for whom the observation was reported; N = number of patients in the analysis set; CI = confidence interval;
Logistic regression stratified for AChR-Ab status (if applicable), Japanese/Non-Japanese and standard of care, with baseline MG-ADL as covariate/QMG as covariates
Two-sided exact p-value

Analyses show that during the second treatment cycle MG-ADL responder rates were similar to those during the first treatment cycle (see Table 3).

**Table 3. MG-ADL and QMG responders during cycle 2 in AChR-Ab seropositive population (mITT analysis set)**

| | Population | Efgartigimod alfa n/N (%) | Placebo n/N (%) |
|---|---|---|---|
| MG-ADL | AChR-Ab seropositive | 36/51 (70.6) | 11/43 (25.6) |
| QMG | AChR-Ab seropositive | 24/51 (47.1) | 5/43 (11.6) |

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

Exploratory data shows that onset of response was observed within 2 weeks of initial infusion in 37/44 (84%) patients treated with efgartigimod alfa intravenous in the AChR-Ab seropositive MG-ADL responders.

In the double-blind placebo-controlled study (ARGX-113-1704), the earliest possible time to initiating the subsequent treatment cycle was 8 weeks after the initial infusion of the first treatment cycle. In the overall population the mean time to the second treatment cycle in the efgartigimod alfa intravenous group was 13 weeks (SD 5.5 weeks) and the median time was 10 weeks (8-26 weeks) from the initial infusion of the first treatment cycle. In the open-label extension study (ARGX-113-1705) the earliest possible time of initiation of the subsequent treatment cycles was 7 weeks.

In patients that responded to treatment, the duration of clinical improvement was 5 weeks in 5/44 (11%) patients, 6-7 weeks in 14/44 (32%) of patients, 8-11 weeks in 10/44 (23%) patients and 12 weeks or more in 15/44 (34%) patients.

*Subcutaneous formulation*

A 10-week, randomised, open-label, parallel-group, multicentre study (ARGX-113-2001) was conducted in adult patients with gMG to evaluate the non-inferiority of the pharmacodynamic effect of efgartigimod alfa subcutaneous compared to efgartigimod alfa intravenous. The main inclusion and exclusion criteria were the same as in study ARGX-113-1704.

A total of 110 patients were randomised and received one cycle of once weekly administrations for 4 weeks, of either efgartigimod alfa subcutaneous 1 000 mg (n = 55) or efgartigimod alfa intravenous 10 mg/kg (n = 55). The majority of patients were positive for antibodies to AChR (AChR-Ab): 45 patients (82%) in efgartigimod alfa subcutaneous group and 46 patients (84%) in efgartigimod alfa intravenous group. All patients were on stable doses of MG therapy prior to screening, that included AChE inhibitors, steroids or NSISTs, either in combination or alone.

Baseline characteristics were similar between treatment groups.

During the study, over 80% of patients in each group received AChE inhibitors, over 60% of patients in each group received steroids and about 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 in total IgG levels from baseline at day 29 between treatment groups in the overall population. The results in the AChR-Ab seropositive population demonstrates non-inferiority of efgartigimod alfa subcutaneous compared to efgartigimod alfa intravenous (see Table 4).

**Table 4. ANCOVA analysis of percent change from baseline in total IgG level at day 29 in AChR-Ab seropositive population (mITT analysis set)**

| Efgartigimod alfa SC | | | Efgartigimod alfa IV | | | Difference Efgartigimod alfa SC-Efgartigimod alfa IV | | |
|---|---|---|---|---|---|---|---|---|
| **N** | **LS Mean** | **95% CI** | **N** | **LS Mean** | **95% CI** | **LS of Mean difference** | **95% CI** | **p-value** |
| 41 | -66.9 | -69.78, -64.02 | 43 | -62.4 | -65.22, -59.59 | -4.5 | -8.53, -0.46 | < 0.0001 |

AChR-Ab = acetylcholine receptor–antibody; ANCOVA = analysis of covariance; CI = confidence interval; SC = subcutaneous; IV = intravenous; LS = least squares; mITT = modified intent-to-treatment analysis set; N = number of patients per group that were included in the ANCOVA analysis

Efficacy secondary endpoints were comparisons of the percentage of MG-ADL and QMG responders, as defined in study ARGX-113-1704, between both treatment groups. The results in AChR-Ab seropositive population are presented in Table 5.

**Table 5. MG-ADL and QMG responders at day 29 in AChR-Ab seropositive population (mITT analysis set)**

| | Efgartigimod alfa SC n/N (%) | Efgartigimod alfa IV n/N (%) | Difference Efgartigimod alfa SC-Efgartigimod alfa IV (95% CI) |
|---|---|---|---|
| MG-ADL | 32/45 (71.1) | 33/46 (71.7) | -0.6 (-19.2 to 17.9) |
| QMG | 31/45 (68.9) | 24/45 (53.3) | 15.6 (-4.3 to 35.4) |

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

Exploratory data shows that onset of response was observed within 2 weeks of initial administration in 28/32 (88%) patients treated with efgartigimod alfa subcutaneous and 27/33 (82%) patients treated with efgartigimod alfa intravenous in the AChR-Ab seropositive MG-ADL responders.

*Chronic Inflammatory Demyelinating Polyneuropathy*

The efficacy of efgartigimod alfa subcutaneous for the treatment of adults with CIDP was studied in a prospective, multicentre study ARGX-113-1802 conducted in 2 treatment stages: an open-label Stage A and a randomized-withdrawal, double-blinded, placebo-controlled Stage B.

Patients had been either on or off CIDP treatment during the 6 months prior to study entry. 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 were enrolled in Stage A. Patients received up to 12 once weekly injections of efgartigimod alfa subcutaneous 1 000 mg 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 efgartigimod alfa subcutaneous (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.

In Stage A, patients had a median age of 54 years (range: 20 to 82 years), a median time since CIDP diagnosis of 2.8 years and median INCAT score of 4.0. Sixty-five percent were male and 66% were White. In Stage B, patients had a median age of 55 years (range: 20 to 82 years), a median time since CIDP diagnosis of 2.2 years and median INCAT score of 3.0. Sixty-four percent were male and 65% were White. Baseline characteristics of Stage B were similar between treatment groups.

In Stage A, the primary endpoint was the percentage of responders defined as patients achieving confirmed ECI. The primary endpoint was met in 66.5% of patients; further details are presented in Table 6.

A secondary endpoint in Stage A was the time to the first confirmed ECI. Week 4 was the earliest time point at which ECI criteria could be met. At that time point, up to 40% of patients achieved ECI. Based on an additional pre-specified analysis, 25% of patients showed clinically relevant improvement after 9 days in at least one of 3 parameters (aINCAT, I-RODS or Grip Strength).

The majority of patients achieved confirmed ECI across all prior CIDP medication groups.

**Table 6. Evidence of clinical improvement in patients with CIDP in ARGX-113-1802 Stage A**

| **ECI responders and time to initial confirmed ECI** | **Stage A** |
|---|---|
| | **Efgartigimod alfa 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

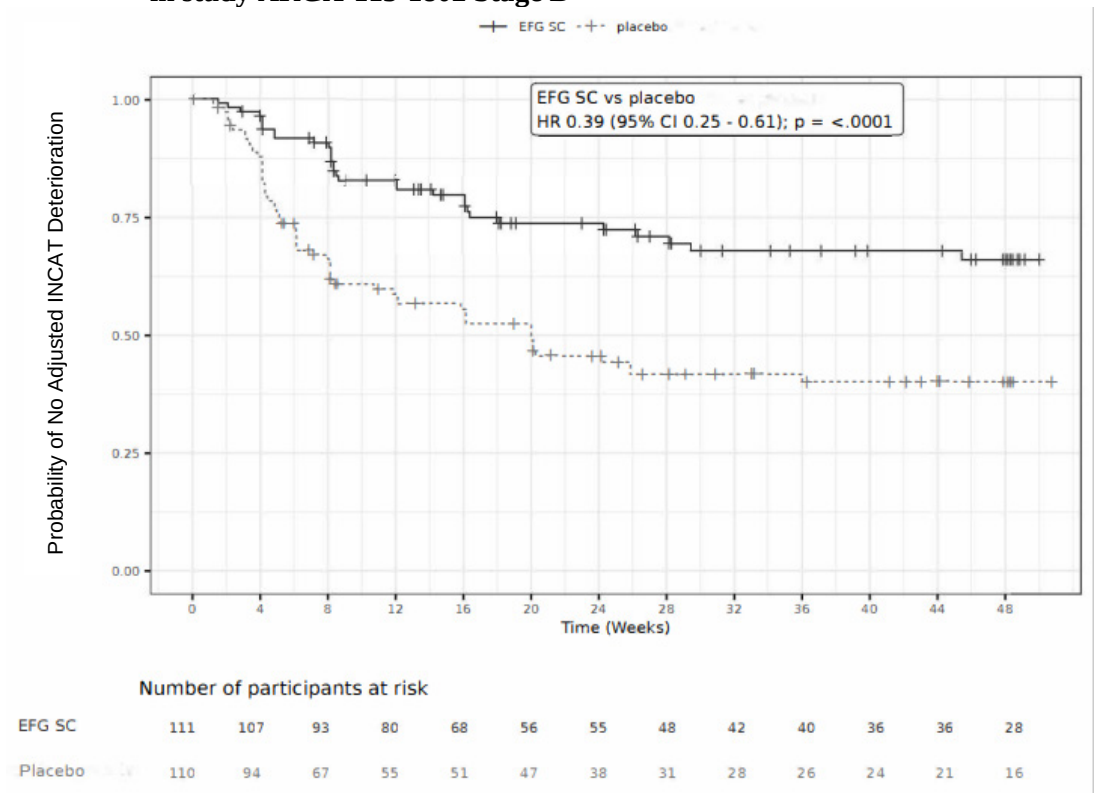
In Stage B, the primary endpoint was defined as the time to the occurrence of the first evidence of clinical deterioration (a 1-point increase in aINCAT compared to Stage B baseline, which was confirmed at a consecutive visit after the first 1-point increase in aINCAT or, a ≥ 2-point increase in aINCAT compared to Stage B baseline). Patients who received efgartigimod alfa subcutaneous 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)]. 31/111 (27.9%) of patients who received efgartigimod alfa subcutaneous during Stage B of the study relapsed compared to 59/110 (53.6%) of patients who received placebo. The results are presented in Table 7 and Figure 2.

**Table 7. First evidence of clinical deterioration in patients with CIDP in study ARGX-113-1802 Stage B**

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

NC = not calculated; N = number of patients in the analysis set; aINCAT = adjusted Inflammatory Neuropathy Cause and Treatment

**Figure 2. Time to the first aINCAT deterioration (Kaplan-Meier Curve) in patients with CIDP in study ARGX-113-1802 Stage B**




Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Vyvgart in one or more subsets of the paediatric population in treatment of myasthenia gravis (see section 4.2 for information on paediatric use).

The European Medicines Agency has waived the obligation to submit the results of studies with Vyvgart in all subsets of the paediatric population in CIDP (see section 4.2 for information on paediatric use).

## 5.2 Pharmacokinetic properties

Absorption

Based upon population PK data analysis, the estimated bioavailability with efgartigimod alfa 1 000 mg subcutaneous is 77%.

The mean $C_{trough}$ after 4 once weekly administrations with efgartigimod alfa 1 000 mg subcutaneous and efgartigimod alfa 10 mg/kg intravenous were 22.0 µg/mL (37% CV) and 14.9 µg/mL (43% CV), respectively. The $AUC_{0\text{-}168h}$ of efgartigimod alfa after administration of one treatment cycle with 1 000 mg subcutaneous and 10 mg/kg intravenous were comparable.

In patients receiving continuous subcutaneous administration of efgartigimod alfa 1 000 mg once weekly, mean $C_{trough}$ ranged from 14.9 to 20.1 µg/mL.

Distribution

Based upon population PK data analysis in healthy subjects and patients the volume of distribution is 18 L.

Biotransformation

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

Elimination

The terminal half-life is 80 to 120 hours (3 to 5 days). Based upon population PK data analysis, the clearance is 0.128 L/h. The molecular weight of efgartigimod alfa is approximately 54 kDa, which is at the boundary of molecules that are renally filtered.

Linearity/non-linearity

The pharmacokinetics profile of efgartigimod alfa is linear, independent of dose or time, with minimal accumulation.

Special populations

*Age, gender, race and bodyweight*
The pharmacokinetics of efgartigimod alfa were not affected by age (19-84 years), gender, race and bodyweight.

*Renal impairment*
No dedicated pharmacokinetic studies have been performed in patients with renal impairment.

The effect of renal function marker estimated glomerular filtration rate [eGFR] as a covariate in a population pharmacokinetic analysis showed an increase in exposure (11% to 21%) in patients with mild renal impairment (eGFR 60-89 mL/min/1.73 $m^2$). No specific dose adjustment is recommended in patients with mild renal impairment.

There is insufficient data on the impact of moderate renal impairment (eGFR 30-59 mL/min/1.73 $m^2$) and severe renal impairment (eGFR < 30 mL/min/1.73 $m^2$) on efgartigimod alfa pharmacokinetic parameters.

*Hepatic impairment*
No dedicated pharmacokinetic study has been performed in patients with hepatic impairment.

The effect of hepatic function markers as covariates in a population pharmacokinetic analysis did not show any impact on the pharmacokinetics of efgartigimod alfa.

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeated dose toxicity.

In reproduction studies in rats and rabbits, intravenous administration of efgartigimod alfa did not result in adverse effects on fertility and pregnancy nor were teratogenic effects observed up to dose levels corresponding to 11-fold (rats) and 56-fold (rabbits) a human 10 mg/kg exposure based on AUC.

Carcinogenicity and genotoxicity

No studies have been conducted to assess the carcinogenic and genotoxic potential of efgartigimod alfa.

Hyaluronidase is found in most tissues of the human body. Non-clinical data for recombinant human hyaluronidase reveal no special hazard for humans based on conventional studies of repeated dose toxicity including safety pharmacology endpoints. Reproductive toxicology studies with rHuPH20 revealed embryofoetal toxicity in mice at high systemic exposure, but did not show teratogenic potential.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Recombinant human hyaluronidase (rHuPH20)
L-arginine hydrochloride
L-histidine
L-histidine hydrochloride monohydrate
L-methionine
Polysorbate 80 (E433)
Sodium chloride
Sucrose
Water for injections

### 6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### 6.3 Shelf life

Vyvgart 1 000 mg solution for injection
18 months

If needed, unopened vials may be stored at room temperature (up to 30 °C) for up to 3 days. After storage at room temperature, unopened vials may be returned to the refrigerator. If stored out of and then returned to refrigeration, the total combined time out of refrigeration should not exceed 3 days.

From a microbial point of view, unless the method of preparation of the syringe precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Vyvgart 1 000 mg solution for injection in pre-filled syringe
2 years

Patients may store the unopened pre-filled syringe at room temperature in the original carton up to 30 °C for a single period of up to 1 month after removing it from the refrigerator or by the expiry date, whichever occurs first.

From a microbial point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

### 6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

### 6.5 Nature and contents of container

Vyvgart 1 000 mg solution for injection
5.6 mL solution in a 6 mL Type I glass vial with rubber stopper, aluminium seal and polypropylene flip-off cap.

Pack size of 1 vial.

Vyvgart 1 000 mg solution for injection in pre-filled syringe
5 mL solution in a single-use pre-filled syringe (type I glass) with a rubber stopper and a rubber tip cap.

Pack size:
1 pre-filled syringe.
4 pre-filled syringes.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

Vyvgart comes as a ready-to-use solution in single-use vial or pre-filled syringe. The medicinal product does not need to be diluted.

Visually inspect that the vial/pre-filled syringe content has a yellowish, clear to opalescent solution/colour, and devoid of particulate matter. If visible particles are observed the vial/pre-filled syringe must not be used.

Vyvgart 1 000 mg solution for injection
After removing the vial from the refrigerator, wait for at least 15 minutes before injecting to allow the solution to reach room temperature (see section 6.3).

Vyvgart 1 000 mg solution for injection in pre-filled syringe
After removing the pre-filled syringe from the refrigerator, wait for at least 30 minutes before injecting to allow the solution to reach room temperature (see section 4.2). After preparation for injection, it should be administered immediately.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1674/002
EU/1/22/1674/003
EU/1/22/1674/004

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 August 2022

## 10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

# ANNEX II

**A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

## A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Lonza Biologics Inc.
101 International Drive
Portsmouth NH 03801
United States of America

Name and address of the manufacturer(s) responsible for batch release

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

## C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

## D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

# ANNEX III

# LABELLING AND PACKAGE LEAFLET

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 20 mg/mL concentrate for solution for infusion
efgartigimod alfa

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

400 mg/20 mL
Each 20 ml vial contains 400 mg of efgartigimod alfa.

## 3. LIST OF EXCIPIENTS

Excipients: L-histidine; L-histidine hydrochloride monohydrate, L-methionine; sodium chloride; sucrose, L-arginine hydrochloride; polysorbate 80; water for injections.

See the package leaflet for further information

## 4. PHARMACEUTICAL FORM AND CONTENTS

concentrate for solution for infusion
1 vial

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use after dilution.
Do not shake.
Read the package leaflet before use.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1674/001

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

## 17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

## 18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**VIAL LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vyvgart 20 mg/mL sterile concentrate
efgartigimod alfa
For IV use after dilution

## 2. METHOD OF ADMINISTRATION

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Lot

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

400 mg/20 mL

## 6. OTHER

Store in a refrigerator.
Do not freeze.
Do not shake.

Store in the original package.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 1 000 mg solution for injection
efgartigimod alfa

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 1 000 mg/5.6 mL of efgartigimod alfa.

## 3. LIST OF EXCIPIENTS

Excipients: Recombinant human hyaluronidase, L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, sodium chloride, sucrose, water for injections.

See the package leaflet for further information

## 4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 vial

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Do not shake.
Read the package leaflet before use.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1674/002

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

vyvgart 1000 mg

## 17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

## 18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**VIAL LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vyvgart 1 000 mg injection
efgartigimod alfa
Subcutaneous

## 2. METHOD OF ADMINISTRATION

Do not shake.

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Lot

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5.6 mL

## 6. OTHER

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 1 000 mg solution for injection in pre-filled syringe
efgartigimod alfa

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 1 000 mg of efgartigimod alfa.

## 3. LIST OF EXCIPIENTS

Excipients: Recombinant human hyaluronidase, L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, sodium chloride, sucrose, water for injections.

See the package leaflet for further information

## 4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pre-filled syringe
4 pre-filled syringes

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Do not shake.
Read the package leaflet before use.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1674/003 1 pre-filled syringe
EU/1/22/1674/004 4 pre-filled syringes

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

vyvgart 1000 mg

## 17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

## 18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**TRAY BACKING TEXT**

## 1. NAME OF THE MEDICINAL PRODUCT

Vyvgart 1 000 mg solution for injection in pre-filled syringe
efgartigimod alfa

## 2. NAME OF THE MARKETING AUTHORISATION HOLDER

argenx (as logo)

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Lot

## 5. OTHER

For storage information, see package leaflet.
Do not shake.
For single use only.

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**SYRINGE LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vyvgart 1 000 mg injection
efgartigimod alfa
SC

## 2. METHOD OF ADMINISTRATION

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Lot

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 mL

## 6. OTHER

# B. PACKAGE LEAFLET

**Package leaflet: Information for the patient**

**Vyvgart 20 mg/ml concentrate for solution for infusion**
efgartigimod alfa

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**


1. What Vyvgart is and what it is used for
2. What you need to know before you use Vyvgart
3. How to use Vyvgart
4. Possible side effects
5. How to store Vyvgart
6. Contents of the pack and other information


## 1. What Vyvgart is and what it is used for

**What Vyvgart is**
Vyvgart contains the active substance efgartigimod alfa. Efgartigimod alfa binds to and blocks a protein in the body called neonatal Fc receptor (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 Vyvgart is used for**
Vyvgart is used together with standard therapy 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 on nerves called acetylcholine receptors. 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 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.

## 2. What you need to know before you use Vyvgart

**Do not use Vyvgart**
- if you are allergic to efgartigimod alfa or any of the other ingredients of this medicine (listed in section 6).

**Warnings and precautions**
Talk to your doctor before using Vyvgart.

MGFA class V
Your doctor may not prescribe this medicine if you are on a ventilator due to gMG muscle weakness (myasthenic crisis).

Infections
Vyvgart treatment may reduce your natural resistance to infections. Therefore, before starting Vyvgart, inform your doctor if you have any infections.

Infusion reactions and allergic reactions
Vyvgart contains a protein that can cause reactions such as rash or itching in some people. Vyvgart may cause anaphylactic reaction (a serious allergic reaction). If you experience allergic reactions such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, or shortness of breath, feeling of losing consciousness, or skin rash during or after the infusion, then tell your doctor immediately.
You will be monitored for signs of an infusion reaction or allergic reaction during and for 1 hour after treatment.

Immunisations (vaccinations)
Please inform your doctor if you have received a vaccine in the last 4 weeks, or if you plan to be vaccinated in the near future.

**Children and adolescents**
Do not give this medicine to children below 18 years of age because the safety and efficacy of Vyvgart have not been established in this population.

**Elderly**
There are no special precautions needed for the treatment of patients who are older than 65 years of age.

**Other medicines and Vyvgart**
Tell your doctor if you are using, have recently used or might use any other medicines.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

**Driving and using machines**
Vyvgart is not expected to influence the ability to drive or use machines.

**Vyvgart contains sodium**
This medicine contains 33.2 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.7% of the recommended maximum daily dietary intake of sodium for an adult. This medicinal product will be further prepared for administration with sodium-containing solution and this should be considered in relation to the total sodium intake to the patient from all sources per day.

**Vyvgart contains polysorbate**
This medicine contains 8.2 mg of polysorbate 80 in each vial which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

## 3. How to use Vyvgart

The treatment will be given by your doctor or other health care provider. Your healthcare provider will first dilute the product. The dilution will be administered from a drip bag through a tube directly into one of your veins over the course of 1 hour.

**What dose of Vyvgart you will receive and how often**
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. Instructions for the healthcare provider on the proper use of this medicine are provided at the end of this document.

**If you receive more Vyvgart than you should**
If you suspect that you have been accidentally administered a higher dose of Vyvgart than prescribed, please contact your doctor for advice.

**If you forget an appointment to receive Vyvgart**
If you forget an appointment, please contact your doctor immediately for advice and see section below "If you stop using Vyvgart".

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

If you have any further questions on the use of this medicine, ask your doctor.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Your doctor will discuss the possible side effects with you and explain the risks and benefits of Vyvgart with you prior to treatment.

**Tell your doctor straight away if you notice:**
Signs of a serious allergic reaction (anaphylactic reaction) such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, shortness of breath, feeling of loss of consciousness, or skin rash during or after the infusion.
If you are not sure what the side effects below are, ask your doctor to explain them to you.

**Very common** (may affect more than 1 in 10 people)
- nose and throat (upper respiratory tract) infections.

**Common** (may affect up to 1 in 10 people)
- pain or a burning sensation during urination, which may be a sign of a urinary tract infection
- inflammation of the airways in the lungs (bronchitis)
- muscle pain (myalgia)
- headache during or after the administration of Vyvgart
- nausea.

**Not known** (frequency cannot be estimated from the available data)
- Allergic reactions during or after infusion
  - swelling of the face, lips, throat, or tongue which makes it difficult to swallow or breathe, shortness of breath
  - pale skin, a weak and rapid pulse, or a feeling of loss of consciousness
  - sudden rash, itching, or hives.

**Reporting of side effects**
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Vyvgart

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C - 8 °C).

Do not freeze.

Store in the original package in order to protect from light.

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

After dilution the product should be used immediately and the infusion (drip) should be completed within 4 hours of dilution. Allow the diluted medicinal product to reach room temperature before administration. The infusion should be completed within 4 hours of removal from the refrigerator.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Vyvgart contains**
The active substance is efgartigimod alfa.
- Each 20 mL vial contains 400 mg efgartigimod alfa (20 mg/mL).

The other ingredients are:
- L-histidine
- L-histidine hydrochloride monohydrate
- L-methionine
- sodium chloride
- sucrose
- L-arginine hydrochloride
- polysorbate 80 (E433)
- water for injections

**What Vyvgart looks like and contents of the pack**
Vyvgart is presented as a sterile concentrate for intravenous (IV) infusion (20 mL in a vial – pack size of 1).
Vyvgart is a liquid. It is colourless to slightly yellow, clear to almost clear.

**Marketing Authorisation Holder and Manufacturer**
argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**
argenx BV
Tél/Tel: +32 (0)9 39 69 394/+32 (0)800 54 477
medinfobe@argenx.com

**България**
argenx BV
Тел.: +359 (0)800 46 273
medinfobg@argenx.com

**Česká republika**
argenx BV
Tel: +420 800 040 854
medinfocz@argenx.com

**Danmark**
argenx BV
Tlf.: +45 80 25 41 88
medinfodk@argenx.com

**Deutschland**
argenx Germany GmbH
Tel: +49 (0)800 180 3963
medinfode@argenx.com

**Eesti**
argenx BV
Tel: +372 800 010 0919
medinfoee@argenx.com

**Ελλάδα**
Medison Pharma Greece Single Member Societe Anonyme
Τηλ: +30 210 0100 188
medinfogr@argenx.com

**España**
argenx Spain S.L.
Tel: +34 900 876 188
medinfoes@argenx.com

**France**
argenx France SAS
Tél: +33 (0)1 88 89 89 92
medinfofr@argenx.com

**Hrvatska**
argenx BV
Tel: +385 (0)800 806 524
medinfohr@argenx.com

**Lietuva**
argenx BV
Tel: +370 (0)800 80 052
medinfolt@argenx.com

**Luxembourg/Luxemburg**
argenx BV
Tél/Tel: +352 800 25 233
medinfolu@argenx.com

**Magyarország**
argenx BV
Tel.: +36 800 88 578
medinfohu@argenx.com

**Malta**
argenx BV
Tel: +356 800 65 101
medinfomt@argenx.com

**Nederland**
argenx BV
Tel: +31 (0)800 023 2882
medinfonl@argenx.com

**Norge**
argenx BV
Tlf: +47 800 62 225
medinfono@argenx.com

**Österreich**
argenx BV
Tel: +43 (0)800 017936
medinfoat@argenx.com

**Polska**
argenx BV
Tel.: +48 800 005 155
medinfopl@argenx.com

**Portugal**
argenx Spain S.L. Sucursal Em Portugal
Tel: +351 800 180 844
medinfopt@argenx.com

**România**
argenx BV
Tel: +40 (0)800 360 912
medinforo@argenx.com

**Ireland**
argenx BV
Tel: +353 1800 851 868
medinfoie@argenx.com

**Ísland**
argenx BV
Sími: +354 800 4422
medinfois@argenx.com

**Italia**
argenx Italia s.r.l
Tel: +39 800 729 052
medinfoit@argenx.com

**Κύπρος**
argenx BV
Τηλ: +357 800 77 122
medinfocy@argenx.com

**Latvija**
argenx BV
Tel: +371 80 205 267
medinfolv@argenx.com

**Slovenija**
argenx BV
Tel: +386 (0)80 688 955
medinfosi@argenx.com

**Slovenská republika**
argenx BV
Tel: +421 (0)800 002 646
medinfosk@argenx.com

**Suomi/Finland**
argenx BV
Puh/Tel: +358 (0)800 412 838
medinfofi@argenx.com

**Sverige**
argenx BV
Tel: +46 (0)20 12 74 56
medinfose@argenx.com

**This leaflet was last revised in.**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

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The following information is intended for healthcare professionals only:

## Instructions for use for healthcare professionals handling Vyvgart

### 1. How is Vyvgart supplied?

Each vial contains 400 mg efgartigimod alfa at a concentration of 20 mg/mL, to be diluted in sodium chloride 9 mg/mL (0.9%) solution for injection.

### 2. Before administration

Reconstitution and dilution should be performed in accordance with good practices rules, particularly for the respect of asepsis.

Vyvgart should be prepared for administration by a qualified healthcare professional using aseptic technique.

Using the formula in the table below, calculate the following:

- The dose of Vyvgart required based on the patient's bodyweight at the recommended dose of 10 mg/kg. For patients weighing over 120 kg use a bodyweight of 120 kg to calculate the dose. The maximum total dose per infusion is 1 200 mg. Each vial contains 400 mg of efgartigimod alfa at a concentration of 20 mg/mL.
- The number of vials needed.
- The volume of sodium chloride 9 mg/mL (0.9%) solution for injection. The total volume of diluted medicinal product is 125 mL.

**Table 1. Formula**

| | |
|---|---|
| Step 1 – Calculate the dose (mg) | 10 mg/kg x weight (kg) |
| Step 2 – Calculate the volume of concentrate (mL) | dose (mg) ÷ 20 mg/mL |
| Step 3 – Calculate the number vials | volume of concentrate (mL) ÷ 20 mL |
| Step 4 – Calculate the volume of sodium chloride 9 mg/mL (0.9%) solution for injection (mL) | 125 mL – concentrate volume (mL) |

### 3. Preparation and Administration

- Do not administer Vyvgart as an intravenous push or bolus injection.
- Vyvgart should only be administered via intravenous infusion as described below.

**Preparation**

- Visually inspect that the vial content is clear to slightly opalescent, colourless to slightly yellow, and devoid of particulate matter. If visible particles are observed and/or the liquid in the vial is discoloured, the vial must be discarded. Do not shake the vials.
- Using aseptic technique throughout the preparation of the diluted solution:
  - Gently withdraw the required amount of Vyvgart from the appropriate number of vials with a sterile syringe and needle. Discard any partially used or empty vials.
  - Transfer the calculated dose of the product into an infusion bag.
  - Dilute the withdrawn product by adding the calculated amount of sodium chloride 9 mg/mL (0.9%) solution for injection to make a total volume of 125 mL.
  - Gently invert the infusion bag containing the diluted product **without shaking** to ensure thorough mixing of the product and the diluent.

- The efgartigimod alfa solution diluted in sodium chloride 9 mg/mL (0.9%) solution for injection can be administered using polyethylene (PE), polyvinyl chloride (PVC), ethylene vinyl acetate (EVA) and ethylene/polypropylene copolymer bags (polyolefins bags), as well as with PE, PVC and polyurethane/polypropylene infusion lines, together with polyurethane (PUR) or PVC filters with polyethersulfone (PES) or polyvinylidene fluoride (PVDF) filter membrane.

**Administration**

- Vyvgart should be administered via intravenous infusion by a healthcare professional. Do not administer as a push or bolus injection.
- Inspect the solution visually for particulate matter prior to administration.
- Infuse the total 125 mL of diluted medicine over 1 hour using a 0.2 µm filter. Administer the full amount of solution. After administration of the product, the line should be flushed with sodium chloride 9 mg/mL (0.9%) solution for injection.
- Administer immediately after dilution and complete the infusion of diluted solution within 4 hours of dilution.
- Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C. From a microbiological point of view, unless the method of dilution precludes the risks of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Do not freeze. Allow the diluted medicine to reach room temperature before administration. Complete the infusion within 4 hours of removal from the refrigerator. The diluted medicine should not be heated in any other manner than via ambient air.
- Should infusion reactions occur, the infusion should be administered at a slower rate, interrupted or discontinued.
- Other medicines should not be injected into infusion side ports or mixed with Vyvgart.

## 4. Special Handling and Storage

Store the vials in a refrigerator (2 °C - 8 °C) until the time of use. Do not freeze. Store in the original package in order to protect from light.

Do not use this medicine after the expiry date which is stated on the carton after ‘EXP’. The expiry date refers to the last day of that month.

**Package leaflet: Information for the patient**

**Vyvgart 1 000 mg solution for injection**
efgartigimod alfa

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**


1. What Vyvgart is and what it is used for
2. What you need to know before you use Vyvgart
3. How to use Vyvgart
4. Possible side effects
5. How to store Vyvgart
6. Contents of the pack and other information


## 1. What Vyvgart is and what it is used for

**What Vyvgart is**
Vyvgart contains the active substance efgartigimod alfa. Efgartigimod alfa binds to and blocks a protein in the body called neonatal Fc receptor (FcRn). By blocking FcRn, efgartigimod alfa decreases the level of immunoglobulin G (IgG) autoantibodies which are proteins of the immune system that attack parts of a person’s own body by mistake.

**What Vyvgart is used for**
Vyvgart is used together with standard therapy 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 on nerves called acetylcholine receptors. 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 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.

Vyvgart 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 can protect the nerves from being attacked and reduce the symptoms of the disease and their impact on daily activities.

## 2. What you need to know before you use Vyvgart

**Do not use Vyvgart**
- if you are allergic to efgartigimod alfa or any of the other ingredients of this medicine (listed in section 6).

**Warnings and precautions**
Talk to your doctor before using Vyvgart.

MGFA class V
Your doctor may not prescribe this medicine if you are on a ventilator due to gMG muscle weakness (myasthenic crisis).

Infections
Vyvgart treatment may reduce your natural resistance to infections. Therefore, before starting Vyvgart, inform your doctor if you have any infections.

Injection reactions and allergic reactions
Vyvgart contains a protein that can cause reactions such as rash or itching in some people. Vyvgart may cause anaphylactic reaction (a serious allergic reaction). If you experience allergic reactions such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, shortness of breath, feeling of loss of consciousness, or skin rash during or after the injection, then tell your doctor immediately.

Immunisations (vaccinations)
Please inform your doctor if you have received a vaccine in the last 4 weeks, or if you plan to be vaccinated in the near future.

**Children and adolescents**
Do not give this medicine to children below 18 years of age because the safety and efficacy of Vyvgart have not been established in this population.

**Elderly**
There are no special precautions needed for the treatment of patients who are older than 65 years of age.

**Other medicines and Vyvgart**
Tell your doctor if you are using, have recently used or might use any other medicines.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

**Driving and using machines**
Vyvgart is not expected to influence the ability to drive or use machines.

**Vyvgart contains sodium**
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially “sodium-free”.

**Vyvgart contains polysorbate**
This medicine contains 2.7 mg of polysorbate 80 in each vial which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

## 3. How to use Vyvgart

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

**What dose of Vyvgart you will receive and how often**

*Generalized myasthenia gravis*

The recommended dose is 1 000 mg given in cycles of one injection per week for 4 weeks. Your doctor will determine when further treatment cycles are needed.

If you are already on intravenous Vyvgart treatment and wish to transition to Vyvgart subcutaneous, you should receive the subcutaneous injection instead of your intravenous infusion at the start of the next treatment cycle.

*Chronic inflammatory demyelinating polyneuropathy*

The recommended dose is 1 000 mg, one injection per week. Depending on how you respond to treatment, your doctor may change this to 1 injection every 2 weeks.

**Injecting Vyvgart**
Vyvgart is given by injection under the skin (*subcutaneously*). You and your doctor should decide if, after adequate training, you or your caregiver may inject Vyvgart. The first self-injection should be carried out in front of your healthcare provider. It is important not to try to inject Vyvgart before being trained by a healthcare professional.

If you or your caregiver inject Vyvgart, you or your caregiver must carefully read and follow the Instructions for administration at the end of this leaflet (see **"Important instructions for use"**). Talk to your doctor, pharmacist or nurse if you have any questions about giving yourself an injection.

**If you use more Vyvgart than you should**
Because Vyvgart is given in one single-use vial, it is unlikely that you will receive too much. However, if you are worried, please contact your doctor, pharmacist or nurse for advice.

**If you miss a dose of or forget an appointment to receive Vyvgart**
Keep track of your next dose. It is important to use Vyvgart exactly as prescribed by your doctor.

- If you miss your dose within three days of when you are supposed to take it, take your dose as soon as you remember and then follow your original dosing schedule.
- If you miss your dose by more than three days, ask your doctor when to take your next dose.
- If you forget an appointment, please contact your doctor immediately for advice.

Do not take a double dose to make up for a forgotten dose.

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

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Your doctor will discuss the possible side effects with you and explain the risks and benefits of Vyvgart with you prior to treatment.

**Tell your doctor straight away if you notice:**
Signs of a serious allergic reaction (anaphylactic reaction) such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, shortness of breath, feeling of loss of consciousness, or skin rash during or after the injection.

If you are not sure what the side effects below are, ask your doctor to explain them to you.

**Very common** (may affect more than 1 in 10 people)
- nose and throat (upper respiratory tract) infections
- reactions where the injection was given, which may include redness, itching, pain. These injection site reactions are usually mild to moderate and usually occur within a day after the injection.

**Common** (may affect up to 1 in 10 people)
- pain or a burning sensation during urination, which may be a sign of a urinary tract infection
- inflammation of the airways in the lungs (bronchitis)
- muscle pain (myalgia)
- nausea.

**Not known** (frequency cannot be estimated from the available data)
- allergic reactions during or after injection
  - swelling of the face, lips, throat, or tongue which makes it difficult to swallow or breathe, shortness of breath
  - pale skin, a weak and rapid pulse, or a feeling of loss of consciousness
  - sudden rash, itching, or hives.

**Reporting of side effects**
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Vyvgart

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C - 8 °C). Do not freeze.
If needed, unopened vials may be stored at room temperature (up to 30 °C) for up to 3 days. After storage at room temperature unopened vials may be returned to the refrigerator. The total amount of time outside cold storage and at room temperature should not exceed 3 days.

Store in the original package in order to protect from light.

Do not use this medicine if you notice visible particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Vyvgart contains**

- The active substance is efgartigimod alfa. Each vial contains 1 000 mg efgartigimod alfa in 5.6 mL. Each mL contains 180 mg of efgartigimod alfa.
- The other ingredients are: Recombinant human hyaluronidase (rHuPH20), L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, Polysorbate 80 (E433), Sodium chloride, sucrose, Water for injections. See section 2 “Vyvgart contains sodium”.

**What Vyvgart looks like and contents of the pack**

Vyvgart is a ready to use, slightly yellow, clear to slightly cloudy solution, supplied as a solution for subcutaneous injection.

**Marketing Authorisation Holder and Manufacturer**

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**
argenx BV
Tél/Tel: +32 (0)9 39 69 394/+32 (0)800 54 477
medinfobe@argenx.com

**България**
argenx BV
Тел.: +359 (0)800 46 273
medinfobg@argenx.com

**Česká republika**
argenx BV
Tel: +420 800 040 854
medinfocz@argenx.com

**Danmark**
argenx BV
Tlf.: +45 80 25 41 88
medinfodk@argenx.com

**Deutschland**
argenx Germany GmbH
Tel: +49 (0)800 180 3963
medinfode@argenx.com

**Eesti**
argenx BV
Tel: +372 800 010 0919
medinfoee@argenx.com

**Lietuva**
argenx BV
Tel: +370 (0)800 80 052
medinfolt@argenx.com

**Luxembourg/Luxemburg**
argenx BV
Tél/Tel: +352 800 25 233
medinfolu@argenx.com

**Magyarország**
argenx BV
Tel.: +36 800 88 578
medinfohu@argenx.com

**Malta**
argenx BV
Tel: +356 800 65 101
medinfomt@argenx.com

**Nederland**
argenx BV
Tel: +31 (0)800 023 2882
medinfonl@argenx.com

**Norge**
argenx BV
Tlf: +47 800 62 225
medinfono@argenx.com

**Ελλάδα**
Medison Pharma Greece Single Member Societe Anonyme
Τηλ: +30 210 0100 188
medinfogr@argenx.com

**España**
argenx Spain S.L.
Tel: +34 900 876 188
medinfoes@argenx.com

**France**
argenx France SAS
Tél: +33 (0)1 88 89 89 92
medinfofr@argenx.com

**Hrvatska**
argenx BV
Tel: +385 (0)800 806 524
medinfohr@argenx.com

**Ireland**
argenx BV
Tel: +353 1800 851 868
medinfoie@argenx.com

**Ísland**
argenx BV
Sími: +354 800 4422
medinfois@argenx.com

**Italia**
argenx Italia s.r.l
Tel: +39 800 729 052
medinfoit@argenx.com

**Κύπρος**
argenx BV
Τηλ: +357 800 77 122
medinfocy@argenx.com

**Latvija**
argenx BV
Tel: +371 80 205 267
medinfolv@argenx.com

**Österreich**
argenx BV
Tel: +43 (0)800 017936
medinfoat@argenx.com

**Polska**
argenx BV
Tel.: +48 800 005 155
medinfopl@argenx.com

**Portugal**
argenx Spain S.L. Sucursal Em Portugal
Tel: +351 800 180 844
medinfopt@argenx.com

**România**
argenx BV
Tel: +40 (0)800 360 912
medinforo@argenx.com

**Slovenija**
argenx BV
Tel: +386 (0)80 688 955
medinfosi@argenx.com

**Slovenská republika**
argenx BV
Tel: +421 (0)800 002 646
medinfosk@argenx.com

**Suomi/Finland**
argenx BV
Puh/Tel: +358 (0)800 412 838
medinfofi@argenx.com

**Sverige**
argenx BV
Tel: +46 (0)20 12 74 56
medinfose@argenx.com

**This leaflet was last revised in.**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

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**Important instructions for use**
Vyvgart 1 000 mg solution for injection
efgartigimod alfa
Subcutaneous use

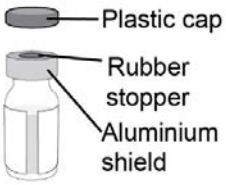
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Be sure to read and understand these instructions for use before injecting Vyvgart.
If you or your caregiver are willing to administer Vyvgart, you will get training on how to inject Vyvgart by your healthcare professional. Your healthcare professional should show you or your caregiver how to prepare and inject Vyvgart properly before using it for the first time. A demonstration of proper self-administration under supervision of healthcare professional is considered necessary. It is important that you do not try to inject the medicinal product until you have been trained and you or your caregiver are sure that you understand how to use Vyvgart. Ask your healthcare professional if you have any questions.

**Important information you need to know before injecting Vyvgart subcutaneous**
- **For subcutaneous use only.**
- The vial is for single use only. **Do not** save vials, even if they are not empty.
- **Do not** use a vial if you see unusual cloudiness or visible particles. The medicine should appear slightly yellow, clear to slightly cloudy.
- **Do not** shake the vial during handling.
- **Do not** use damaged vials or vials missing a protective cap. Report and return damaged or uncapped vials to the pharmacy.

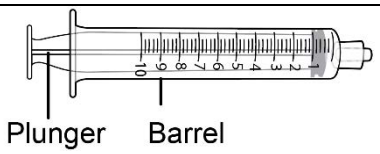
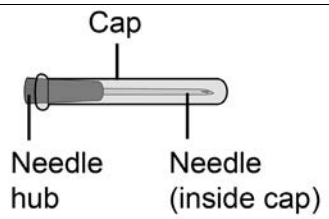
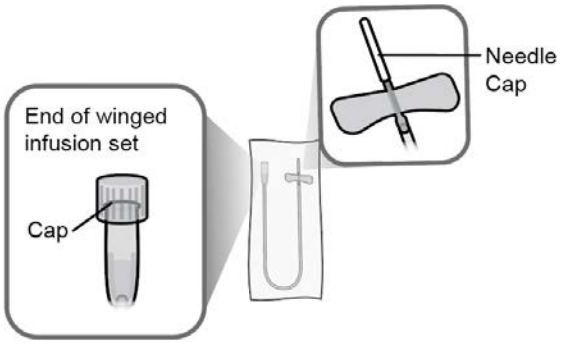
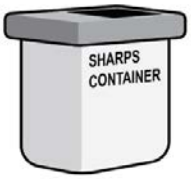
**Storing Vyvgart**
- Store in a refrigerator (2 °C - 8 °C).
- **Do not** freeze.
- If needed, unopened vials may be stored at room temperature (up to 30 °C) for up to 3 days. After storage at room temperature unopened vials may be returned to the refrigerator. The total amount of time outside cold storage and at room temperature should not exceed 3 days.
- Store in the original package in order to protect from light.
- Keep this medicine out of the sight and reach of children.

**Package contents**

| | |
|---|---|
| 1 vial containing Vyvgart |   |
| Vyvgart package leaflet and instructions for use | |

**Additional supplies not included**
Store additional supplies at room temperature in a dry location

| | |
|---|---|
| Alcohol swabs | |

| | |
|---|---|
| Syringe 10 mL |  |
| Transfer needle 18-gauge, ≥ 38 mm length |  |
| Winged infusion set 25-gauge, 30 cm tubing, maximum priming volume of 0.4 mL |  |
| Sterile gauze | |
| Adhesive bandage | |
| Sharps container |  |

**Preparing the supplies**

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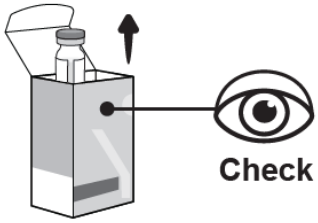
|---|---|
| **Step 1**<br>Remove vial carton from the refrigerator. | |
| **Step 2**<br>Remove the vial from the carton and check:<br>• the vial is not cracked, broken, missing the protective cap, or shows any signs of damage.<br>• the expiry date has not passed.<br><br>If any of the conditions above are not met, **do not** inject, and report this information to the pharmacy. |  |

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| **Step 3**<br>Wait at least 15 minutes for the vial to naturally warm-up to room temperature.<br><br>Check if the medicine in the vial is slightly yellow, clear to slightly cloudy, and has no visible particles.<br><br>• **Do not** attempt to warm the vial in any way other than letting it sit at room temperature.<br>• **Do not** shake the vial. | |
| **Step 4**<br>Collect all of the following additional supplies:<br>• 2 alcohol swabs<br>• 1 syringe 10 mL<br>• 1 transfer needle 18-gauge<br>• 1 winged infusion set 25-gauge x 30 cm<br>• 1 sterile gauze<br>• 1 adhesive bandage<br>• 1 sharps container (see Step 28) | |
| **Step 5**<br>**5a.** Clean the work area.<br>**5b.** Wash your hands with soap and thoroughly dry them. | |

**Preparing the syringe**

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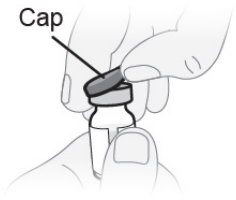
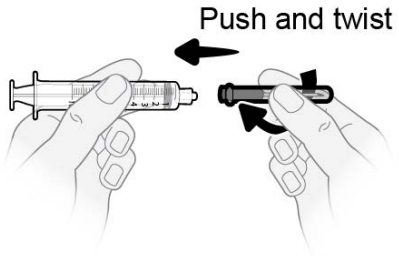
| **Step 6**<br>Remove the plastic flip-off protective cap from the vial.<br><br>The aluminium shield should remain in place. |  |
| **Step 7**<br>Clean the rubber stopper with a new alcohol swab.<br><br>Allow to air dry naturally for at least 30 seconds. **Do not** blow on the rubber stopper. | |
| **Step 8**<br>Unwrap the syringe and transfer needle. Push the transfer needle onto the syringe and twist it clockwise until the needle is firmly connected to the syringe.<br><br>**Do not** touch the tip of the syringe or the bottom of the needle to avoid germs and infection risk. |  |

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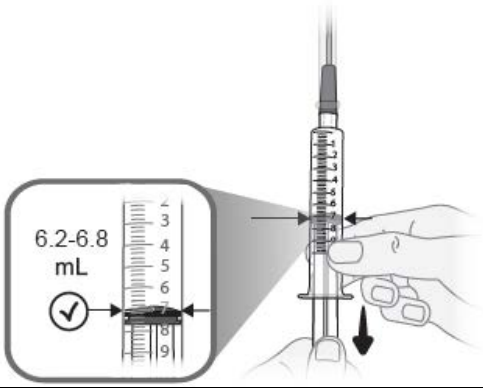
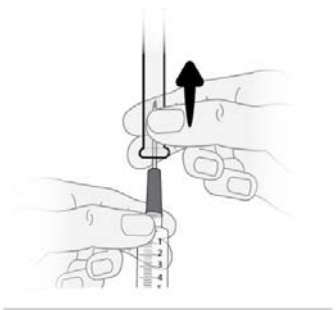
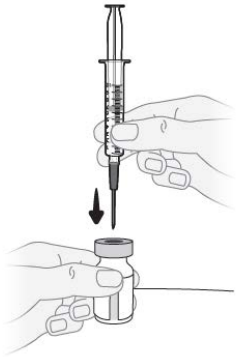
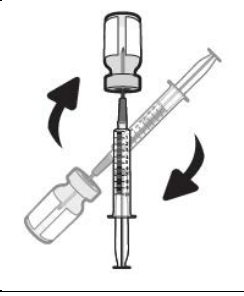
| **Step 9**<br>Slowly pull back on the plunger and draw between 6.2 to 6.8 mL air into the syringe. |  |
| **Step 10**<br>**10a.** Hold the syringe at the needle hub where the syringe is connected to the needle.<br>**10b.** Grip the transfer needle cap and carefully pull the needle cap straight off, away from your body.<br>**10c.** Place the transfer needle cap down on a clean, flat surface.<br><br>• **Do not** throw the cap away. You will need to recap and remove the transfer needle after use.<br>Keep the needle sterile:<br>• **Do not** touch the needle or needle tip.<br>• **Do not** place it on a surface after the needle cap has been removed. | 10b)<br>  <br>10c)<br> |
| **Step 11**<br>Keep the vial upright on a flat surface and insert the transfer needle through the centre of the disinfected rubber stopper.<br><br>**Do not** puncture the vial's rubber stopper more than one time to avoid leaking. |  |
| **Step 12**<br>Turn the vial upside down while keeping transfer needle in the vial. |  |

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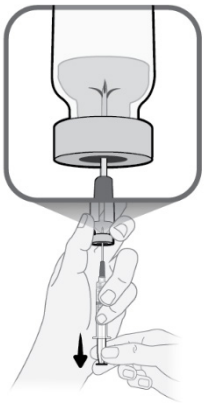
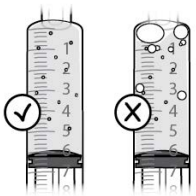
| **Step 13**<br>**13a.** Make sure the transfer needle in the vial points upwards with the needle tip above the medicine solution.<br>**13b.** Gently push the plunger to inject all the air from the syringe into the empty space above the medicine solution in the vial.<br>**13c.** Keep your finger pressed down on the syringe plunger.<br><br>**Do not** inject air into the medicine solution as this could create air bubbles or foam. | |
| **Step 14**<br>Fill the syringe, as follows:<br>**14a.** Keep your finger pressed on the syringe plunger and slide the transfer needle tip into the medicine solution in the neck of the vial (close to the vial cap) so that the needle tip remains completely covered in the solution.<br>**14b.** Slowly pull back the plunger, keeping the transfer needle tip in the solution to avoid air bubbles and foam in the syringe.<br><br>**Fill the syringe with the entire content of the vial.** | 14a) <br>14b)  |
| **Step 15**<br>Remove large air bubbles, if present.<br>**15a.** Keep the transfer needle in the vial and check the syringe for large air bubbles.<br>**15b.** Remove the large air bubbles by gently tapping the syringe barrel with your fingers until the air bubbles rise to the top of the syringe.<br>**15c.** Move the transfer needle tip above the medicine solution and slowly push the plunger up to push the air bubbles out of the syringe.<br>**15d.** To remove any remaining medicine solution from the vial, move the tip of the transfer needle into the solution again and slowly pull back the plunger until you have the full contents of the vial in the syringe.<br>**15e.** Repeat the steps above until you have removed the large air bubbles.<br>If you cannot remove all of the liquid from the vial, turn the vial upright to reach the remaining amount. | 15c) <br>15e)  |

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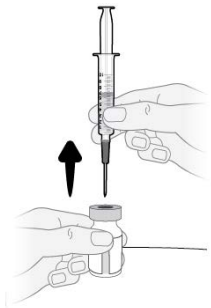
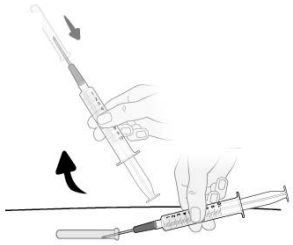
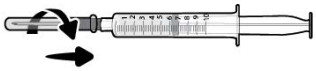
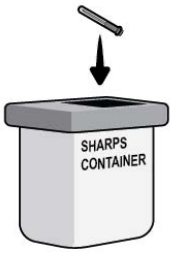
| **Step 16**<br>**16a.** Turn the vial upright and remove the syringe and transfer needle from the vial.<br>**16b.** Using one hand, slide the transfer needle into the cap and scoop upwards to cover the needle.<br>**16c.** After the transfer needle is covered, twist the transfer needle cap onto the syringe to fully attach it. | 16a)<br>  <br>16b)<br>  <br>16c)<br>  |
| **Step 17**<br>**17a.** Gently pull and twist the transfer needle counter-clockwise to remove it from the syringe.<br>**17b.** Throw away (dispose of) the transfer needle in the sharps container. | 17a)<br> <br>17b)<br>  |

**Preparing to inject Vyvgart**

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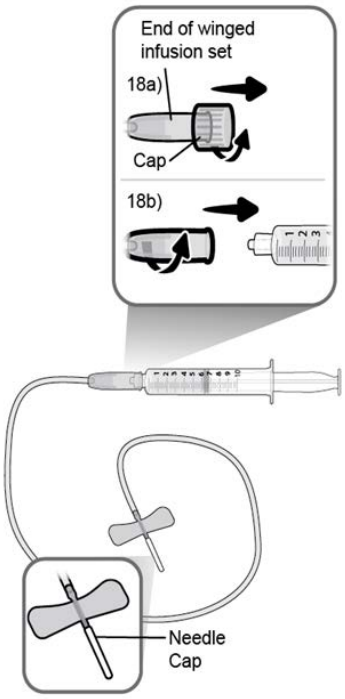
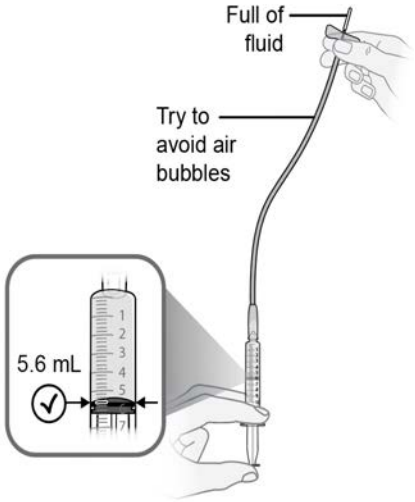
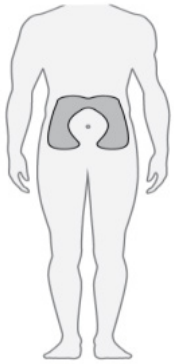
| **Step 18**<br>**18a.** Remove the cap from the end of the winged infusion set.<br><br>**18b.** Gently push and twist the end of the winged infusion set clockwise onto the syringe until firmly connected.<br><br>The final syringe setup should look like the figure to the right.<br><br>• **Do not** touch the tip of the syringe.<br>• **Do not** remove the needle cap. |  |
| **Step 19**<br>**19a.** Fill the tubing of the winged infusion set by gently pressing the syringe plunger until the plunger is at the 5.6 mL mark. You should see some liquid at the end of the needle.<br>**19b.** Place the syringe and attached winged infusion set down on the clean, flat surface.<br><br>**Do not** wipe off any excess medicine solution expelled from the infusion set while filling the tubing. |  |
| **Step 20**<br>Choose an injection site<br>• on the abdomen (belly area) that is at least 5 cm away from the belly button<br><br>Choose a different injection site each time you inject (rotate the site) to decrease discomfort.<br><br>Note:<br>**Do not** inject into areas where the skin is red, bruised, tender, hard, or into areas where there are moles or scars. |  |

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| **Step 21**<br>Disinfect the injection site with a new alcohol swab. Use a circular motion and wipe from inside to outside.<br><br>Allow the site to air dry for at least 30 seconds.<br><br>**Do not** touch the injection site after disinfecting. | |

**Injecting Vyvgart**

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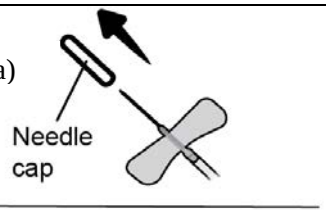
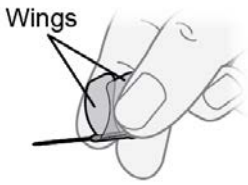
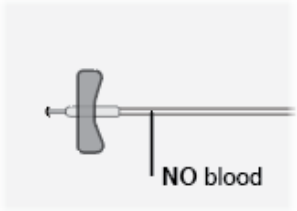
| **Step 22**<br>**22a.** Remove the needle cap carefully from the winged infusion set.<br>**22b.** Fold the wings of the infusion set upwards and hold the wings between your thumb and index finger, with the needle below the wings.<br><br>Note:<br>To avoid infection, make sure the needle does not come into contact with anything prior to skin insertion. | 22a)<br>  <br><br>22b)<br>  <br> |
| **Step 23**<br>With your free hand, pinch a fold of skin around the disinfected injection site and lift upwards. Grab enough skin to create a "tent" for the needle to insert into.<br><br>**Do not** hold the skin too tight to avoid bruising. | |
| **Step 24**<br>Insert the needle into the middle of the pinched skin area at an angle of about 45 degrees.<br><br>Note:<br>The needle should smoothly insert into the skin. If you feel resistance, you can pull the needle back slightly. | |
| **Step 25**<br>Check the infusion set. Make sure there is no blood.<br><br>Important:<br>If you see blood, slightly pull back on the needle without removing the needle from the skin. |  <br> |

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| **Step 26**<br>Inject by pushing the plunger of the syringe with steady pressure until no medicine remains in the syringe. This corresponds to the injection of the recommended dose of 5.6 mL. The injection usually takes 30 to 90 seconds.<br><br>Note:<br>• If you experience discomfort, or if any of the medicine flows back into the infusion tubing, you can inject more slowly.<br>• There will be some fluid left in the infusion tubing that is not injected. This is normal and the remaining medicine can be thrown away. | |
| **Step 27**<br>**27a.** After all solution is injected, remove the needle from the skin.<br>**27b.** Cover the injection site with a sterile dressing, like an adhesive bandage.<br><br>Note:<br>If there is a small drop of blood after removing the needle, **do not** worry. This can happen if the needle nicks the skin during removal. Dab the blood with a sterile piece of gauze and apply gentle pressure. Further bleeding should not occur. Apply a sterile dressing to cover the site. | |

**Disposing of Vyvgart**

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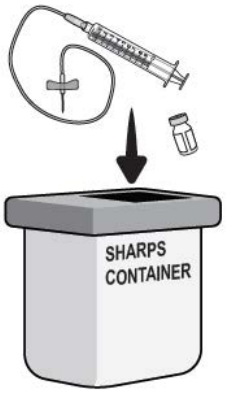
| **Step 28**<br>Throw away (dispose of) the winged infusion set (with the attached needle and syringe) and the vial into the sharps container.<br><br>If you **do not** have an sharps disposal container, a household container can be used if it is:<br>• Made of heavy-duty plastic;<br>• Can be closed with a tight-fitting, puncture-resistant lid, without sharps spilling out;<br>• Upright and stable;<br>• Leak-resistant;<br>• Appropriately labeled with a warning that hazardous waste is inside the container.<br><br>Dispose of the full container as instructed by your healthcare provider or pharmacist.<br><br>Note:<br>Always keep the sharps container out of the sight and reach of children. |  |

**Package leaflet: Information for the patient**

**Vyvgart 1 000 mg solution for injection in pre-filled syringe**
efgartigimod alfa

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**


1. What Vyvgart is and what it is used for
2. What you need to know before you use Vyvgart
3. How to use Vyvgart
4. Possible side effects
5. How to store Vyvgart
6. Contents of the pack and other information


## 1. What Vyvgart is and what it is used for

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

**What Vyvgart is used for**
Vyvgart is used together with standard therapy 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 on nerves called acetylcholine receptors. 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 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.

Vyvgart 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 can protect the nerves from being attacked and reduce the symptoms of the disease and their impact on daily activities.

## 2. What you need to know before you use Vyvgart

**Do not use Vyvgart**
- if you are allergic to efgartigimod alfa or any of the other ingredients of this medicine (listed in section 6).

**Warnings and precautions**
Talk to your doctor before using Vyvgart.

MGFA class V
Your doctor may not prescribe this medicine if you are on a ventilator due to gMG muscle weakness (myasthenic crisis).

Infections
Vyvgart treatment may reduce your natural resistance to infections. Therefore, before starting Vyvgart, inform your doctor if you have any infections.

Injection reactions and allergic reactions
Vyvgart contains a protein that can cause reactions such as rash or itching in some people. Vyvgart may cause anaphylactic reaction (a serious allergic reaction). If you experience allergic reactions such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, shortness of breath, feeling of loss of consciousness, or skin rash during or after the injection, then tell your doctor immediately.

Immunisations (vaccinations)
Please inform your doctor if you have received a vaccine in the last 4 weeks, or if you plan to be vaccinated in the near future.

**Children and adolescents**
Do not give this medicine to children below 18 years of age because the safety and efficacy of Vyvgart have not been established in this population.

**Elderly**
There are no special precautions needed for the treatment of patients who are older than 65 years of age.

**Other medicines and Vyvgart**
Tell your doctor if you are using, have recently used or might use any other medicines.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

**Driving and using machines**
Vyvgart is not expected to influence the ability to drive or use machines.

**Vyvgart contains sodium**
This medicinal product contains less than 1 mmol sodium (23 mg) per syringe, that is to say essentially “sodium-free”.

**Vyvgart contains polysorbate**
This medicine contains 2.1 mg of polysorbate 80 in each syringe which is equivalent to 0.4 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

## 3. How to use Vyvgart

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

**What dose of Vyvgart you will receive and how often**

*Generalized myasthenia gravis*

The recommended dose is 1 000 mg given in cycles of one injection per week for 4 weeks. Your doctor will determine when further treatment cycles are needed.

If you are already on intravenous Vyvgart treatment and wish to transition to Vyvgart subcutaneous, you should receive the subcutaneous injection instead of your intravenous infusion at the start of the next treatment cycle.

*Chronic inflammatory demyelinating polyneuropathy*

The recommended dose is 1 000 mg, one injection per week. Depending on how you respond to treatment, your doctor may change this to 1 injection every 2 weeks.

**Injecting Vyvgart**
Vyvgart is given by injection under the skin (*subcutaneously*). You and your doctor should decide if, after adequate training, you or your caregiver may inject Vyvgart. The first self-injection should be carried out in front of your healthcare provider. It is important not to try to inject Vyvgart before being trained by a healthcare professional.

If you or your caregiver inject Vyvgart, you or your caregiver must carefully read and follow the Instructions for administration at the end of this leaflet (see **"Important instructions for use"**). Talk to your doctor, pharmacist or nurse if you have any questions about giving yourself an injection.

**If you use more Vyvgart than you should**
Because Vyvgart is given in one single-use pre-filled syringe, it is unlikely that you will receive too much. However, if you are worried, please contact your doctor, pharmacist or nurse for advice.

**If you miss a dose of or forget an appointment to receive Vyvgart**
Keep track of your next dose. It is important to use Vyvgart exactly as prescribed by your doctor.

- If you miss your dose within three days of when you are supposed to take it, take your dose as soon as you remember and then follow your original dosing schedule.
- If you miss your dose by more than three days, ask your doctor when to take your next dose.
- If you forget an appointment, please contact your doctor immediately for advice.

Do not take a double dose to make up for a forgotten dose.

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

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Your doctor will discuss the possible side effects with you and explain the risks and benefits of Vyvgart with you prior to treatment.

**Tell your doctor straight away if you notice:**
Signs of a serious allergic reaction (anaphylactic reaction) such as swelling of the face, lips, throat or tongue which makes it difficult to swallow or breathe, shortness of breath, feeling of loss of consciousness, or skin rash during or after the injection.

If you are not sure what the side effects below are, ask your doctor to explain them to you.

**Very common** (may affect more than 1 in 10 people)
- nose and throat (upper respiratory tract) infections
- reactions where the injection was given, which may include redness, itching, pain. These injection site reactions are usually mild to moderate and usually occur within a day after the injection.

**Common** (may affect up to 1 in 10 people)
- pain or a burning sensation during urination, which may be a sign of a urinary tract infection
- inflammation of the airways in the lungs (bronchitis)
- muscle pain (myalgia)
- nausea.

**Not known** (frequency cannot be estimated from the available data)
- allergic reactions during or after injection
  - swelling of the face, lips, throat, or tongue which makes it difficult to swallow or breathe, shortness of breath
  - pale skin, a weak and rapid pulse, or a feeling of loss of consciousness
  - sudden rash, itching, or hives.

**Reporting of side effects**
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Vyvgart

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C - 8 °C). Do not freeze.
You can also store the unopened pre-filled syringe at room temperature in the original carton up to 30 °C for a single period of up 1 month after removing it from the refrigerator. Discard it if it has not been used within the 1 month period or by the expiry date, whichever happens first.

Store in the original package in order to protect from light.

Do not use this medicine if you notice visible particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Vyvgart contains**

- The active substance is efgartigimod alfa. Each pre-filled syringe contains 1 000 mg efgartigimod alfa in 5.0 mL. Each mL contains 200 mg of efgartigimod alfa.
- The other ingredients are: Recombinant human hyaluronidase (rHuPH20), L-arginine hydrochloride, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, Polysorbate 80 (E433), Sodium chloride, sucrose, Water for injections. See section 2 “Vyvgart contains sodium”.

**What Vyvgart looks like and contents of the pack**

Vyvgart is a ready to use, slightly yellow, clear to slightly cloudy solution, supplied as a solution for subcutaneous injection in a pre-filled syringe.

**Marketing Authorisation Holder and Manufacturer**

argenx BV
Industriepark-Zwijnaarde 7
9052 Gent
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**
argenx BV
Tél/Tel: +32 (0)9 39 69 394/+32 (0)800 54 477
medinfobe@argenx.com

**България**
argenx BV
Тел.: +359 (0)800 46 273
medinfobg@argenx.com

**Česká republika**
argenx BV
Tel: +420 800 040 854
medinfocz@argenx.com

**Danmark**
argenx BV
Tlf.: +45 80 25 41 88
medinfodk@argenx.com

**Deutschland**
argenx Germany GmbH
Tel: +49 (0)800 180 3963
medinfode@argenx.com

**Eesti**
argenx BV
Tel: +372 800 010 0919
medinfoee@argenx.com

**Lietuva**
argenx BV
Tel: +370 (0)800 80 052
medinfolt@argenx.com

**Luxembourg/Luxemburg**
argenx BV
Tél/Tel: +352 800 25 233
medinfolu@argenx.com

**Magyarország**
argenx BV
Tel.: +36 800 88 578
medinfohu@argenx.com

**Malta**
argenx BV
Tel: +356 800 65 101
medinfomt@argenx.com

**Nederland**
argenx BV
Tel: +31 (0)800 023 2882
medinfonl@argenx.com

**Norge**
argenx BV
Tlf: +47 800 62 225
medinfono@argenx.com

**Ελλάδα**
Medison Pharma Greece Single Member Societe Anonyme
Τηλ: +30 210 0100 188
medinfogr@argenx.com

**España**
argenx Spain S.L.
Tel: +34 900 876 188
medinfoes@argenx.com

**France**
argenx France SAS
Tél: +33 (0)1 88 89 89 92
medinfofr@argenx.com

**Hrvatska**
argenx BV
Tel: +385 (0)800 806 524
medinfohr@argenx.com

**Ireland**
argenx BV
Tel: +353 1800 851 868
medinfoie@argenx.com

**Ísland**
argenx BV
Sími: +354 800 4422
medinfois@argenx.com

**Italia**
argenx Italia s.r.l
Tel: +39 800 729 052
medinfoit@argenx.com

**Κύπρος**
argenx BV
Τηλ: +357 800 77 122
medinfocy@argenx.com

**Latvija**
argenx BV
Tel: +371 80 205 267
medinfolv@argenx.com

**Österreich**
argenx BV
Tel: +43 (0)800 017936
medinfoat@argenx.com

**Polska**
argenx BV
Tel.: +48 800 005 155
medinfopl@argenx.com

**Portugal**
argenx Spain S.L. Sucursal Em Portugal
Tel: +351 800 180 844
medinfopt@argenx.com

**România**
argenx BV
Tel: +40 (0)800 360 912
medinforo@argenx.com

**Slovenija**
argenx BV
Tel: +386 (0)80 688 955
medinfosi@argenx.com

**Slovenská republika**
argenx BV
Tel: +421 (0)800 002 646
medinfosk@argenx.com

**Suomi/Finland**
argenx BV
Puh/Tel: +358 (0)800 412 838
medinfofi@argenx.com

**Sverige**
argenx BV
Tel: +46 (0)20 12 74 56
medinfose@argenx.com

**This leaflet was last revised in.**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

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**Important instructions for use**
Vyvgart 1 000 mg solution for injection in pre-filled syringe
efgartigimod alfa
Subcutaneous use

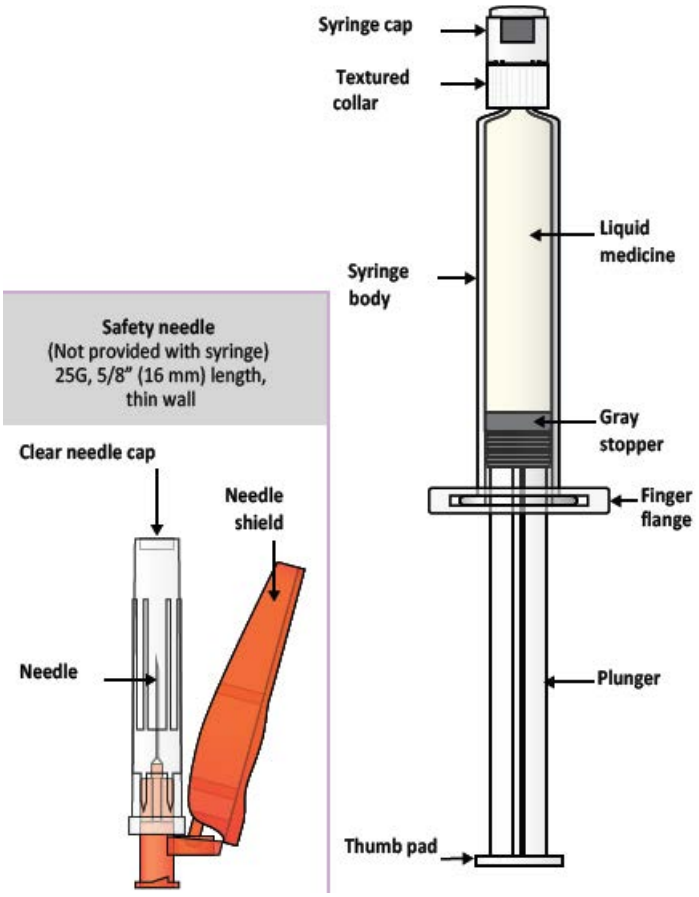
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Be sure to read and understand these instructions for use before injecting Vyvgart.
If you or your caregiver are willing to administer Vyvgart, you will get training on how to inject Vyvgart by your healthcare professional. Your healthcare professional should show you or your caregiver how to prepare and inject Vyvgart properly before using it for the first time. A demonstration of proper self-administration under supervision of healthcare professional is considered necessary. It is important that you do not try to inject the medicinal product until you have been trained and you or your caregiver are sure that you understand how to use Vyvgart. Ask your healthcare professional if you have any questions.

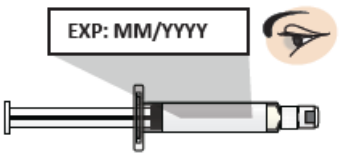
**Important information you need to know before injecting Vyvgart subcutaneous**
- **For subcutaneous use only.**
- The pre-filled syringe is for single use only and cannot be reused.
- **Do not** use the pre-filled syringe if it has been at room temperature for longer than 1 month.
- **Do not** use the pre-filled syringe if the expiry date has passed.
- **Do not** use the pre-filled syringe if it is cracked, broken, damaged or if the cap is missing. Report and return these damaged pre-filled syringes to the pharmacy.
- **Do not** use the pre-filled syringe if the medicine is discoloured or contains particles. The medicine should appear clear to light yellow. A little cloudiness is normal.
- **Do not** shake the pre-filled syringe.

**Storing Vyvgart pre-filled syringe**
- Store in a refrigerator (2 °C - 8 °C).
- **Do not** freeze.
- You can also store the unopened pre-filled syringe at room temperature in the original carton up to 30 °C for a single period of up 1 month after removing it from the refrigerator. Discard it if it has not been used within the 1 month period or by the expiry date, whichever happens first.
- Store in the original package in order to protect from light.
- Keep this medicine out of the sight and reach of children.

## Pre-filled syringe parts

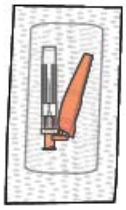
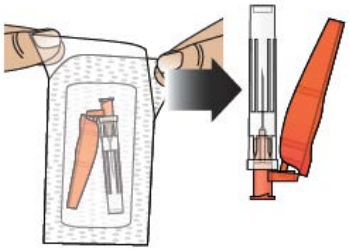



## Gathering and checking the supplies

| | |
|---|---|
| **1 Removing the carton from the refrigerator**<br>**1.1** Remove the pre-filled syringe carton from the refrigerator<br>**1.2** Remove 1 pre-filled syringe from the carton and place any remaining pre-filled syringes back into the refrigerator for later use.<br>**1.3** Remove the pre-filled syringe from the tray. | |
| **2 Checking the pre-filled syringe before use**<br>**2.1** Check the expiry date on the pre-filled syringe.<br>**Do not** use the pre-filled syringe if the expiry date has passed.<br>**2.2** Check the condition of the pre-filled syringe and the pre-filled syringe cap.<br>**Do not** use the pre-filled syringe if it is cracked, broken, damaged, or if the cap is missing. |  |

| | |
|---|---|
| **2.3** Check the appearance of the medicine in the pre-filled syringe. The medicine should look clear to light yellow in colour. A little cloudiness is normal.<br><br>**Do not** use the pre-filled syringe if the medicine is discoloured or contains particles. | |

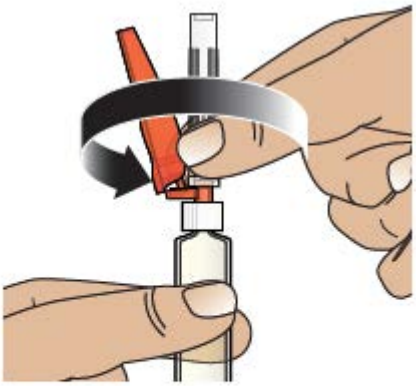
**Preparing for the injection**

| | |
|---|---|
| **3. Allowing the pre-filled syringe to warm to room temperature**<br>Place the pre-filled syringe on a clean flat surface and let it sit for at least 30 minutes, to allow it to warm to room temperature.<br><br>**Do not** attempt to warm the pre-filled syringe in any other way.<br>**Do not** use the pre-filled syringe if it has been at room temperature for longer than 1 month. | |
| **4. Gathering supplies and wash hands**<br>**4.1** Gather the following supplies that are **not** provided with the pre-filled syringe.<br><br>**4.2** Wash hands with soap and water. | • Safety needle<br>  <br>• Alcohol swab<br> <br>• Sharps container<br> <br>• Sterile gauze and/ or bandage (As needed)<br> |
| **5. Snap off the pre-filled syringe cap and attach the needle**<br>**5.1** Carefully open the needle package, remove the needle. Throw away the packaging via the household waste. | Peel and remove<br>  |

**5.2** Bend the pre-filled syringe cap to one side to snap it off and remove it from the pre-filled syringe.
Throw away the syringe cap in the household waste, and set the pre-filled syringe on a clean and flat surface.

> **Do not** touch the tip of the pre-filled syringe after the cap has been removed.

**5.3** Hold the pre-filled syringe in one hand and attach the needle to the pre-filled syringe by twisting it on (clockwise/to the right) until you feel resistance.

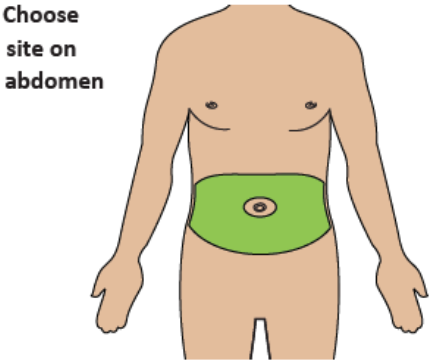


The needle is now attached to the pre-filled syringe.

**6. Choosing and cleaning the injection site on abdomen**

**6.1** Choose an injection site on the abdomen (belly area) at least 5 cm away from the belly button (navel). 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. The pre-filled syringe is for injection (under the skin) only.




**6.2** Clean the chosen injection site with an alcohol swab and let it air dry.

> **Do not** blow on or touch the injection site after it has been cleaned.

**Injecting Vyvgart**

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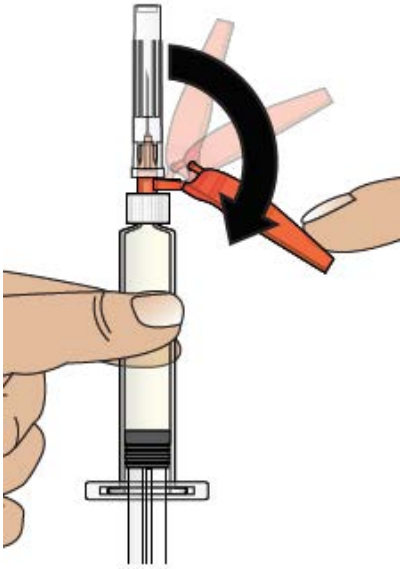
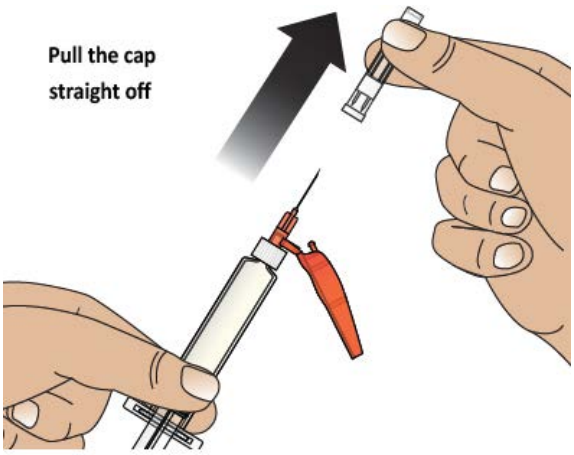
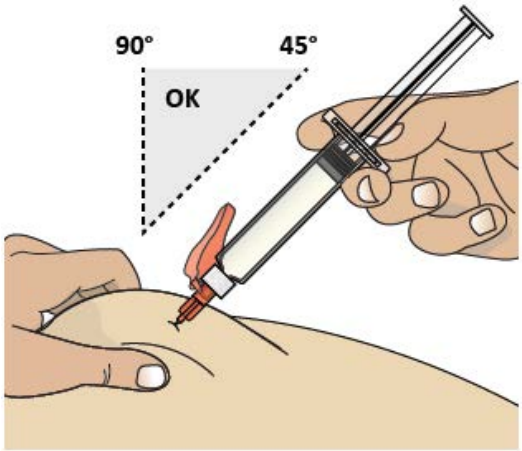
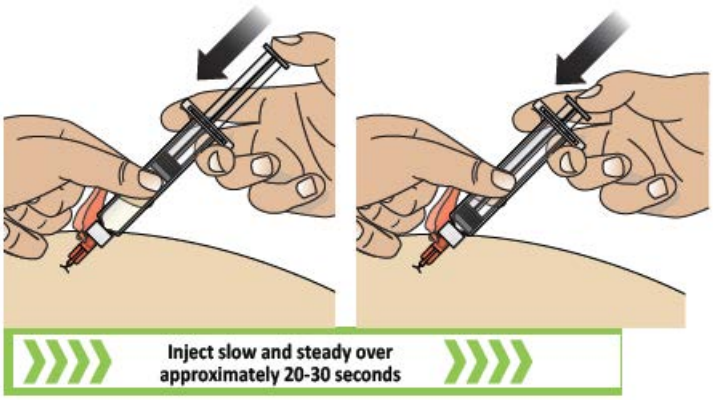
| **7. Pulling back the needle shield and removing the needle cap**<br>**7.1** Pull the needle shield back.<br><br>**Note:** The needle shield will be used after the injection to cover the needle and protect from needle-stick injuries. |  |
| **7.2** Hold the pre-filled syringe body and remove the clear needle cap by pulling it straight off of the needle. Throw away the needle cap into the household waste.<br><br>**Do not** put the needle cap back on the needle. |  |
| **8. Giving the injection**<br>**8.1** Pinch the cleaned injection site. While pinching the skin, insert the needle at a 45 to 90 degree angle into the pinched skin.<br>Then release the pinched skin.<br><br>**Do not** pinch the skin too tightly as this can cause bruising. |  |

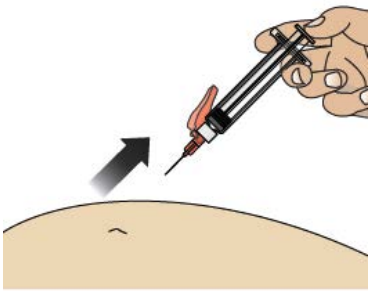
**8.2** Slowly press the plunger down all the way until it stops in order to inject the medicine. It will take approximately 20-30 seconds to inject all of the medicine.
You will feel resistance as you press down. In case of discomfort inject more slowly.

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.

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

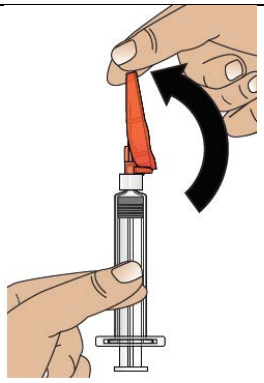


**Disposing of the used syringe**

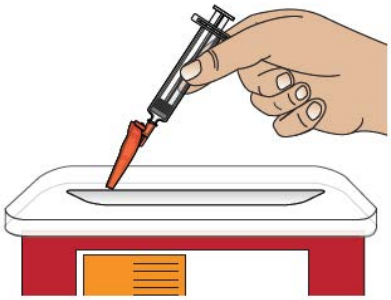
**9 Covering the needle and throwing away the used syringe**
**9.1** Carefully push the needle shield over the needle until it snaps into place and covers the needle.
This helps to prevent needle-stick injuries.

> **Do not** put the needle cap back on; only use the needle shield to cover the needle.



**9.2** Throw away the used syringe, with the needle still attached, into the sharps container immediately after use.

> **Do not** throw away (dispose of) loose needles and syringes in your household waste.



If you **do not** have a sharps container, a household container can be used if it:

- Is made of heavy-duty plastic;
- Can be closed with a tight-fitting, puncture-resistant lid, without sharps spilling out;
- Is upright and stable;

| | |
|---|---|
| • Is leak-resistant;<br>• Is appropriately labelled with a warning that hazardous waste is inside the container.<br><br>Dispose of the full container as instructed by your doctor, nurse or pharmacist. | |
| **10 Treating the injection site**<br>If there is a small amount of blood or liquid at the injection site, press a gauze on it until the bleedings stops.<br>If needed, you may apply a small adhesive bandage. | |