 This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

# AUSTRALIAN PRODUCT INFORMATION – VYVGART (EFGARTIGIMOD ALFA) CONCENTRATED INJECTION FOR INTRAVENOUS INFUSION

## 1 NAME OF THE MEDICINE

Efgartigimod alfa 20 mg/mL Concentrated Injection for Intravenous 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 67.2 mg sodium.

## 3 PHARMACEUTICAL FORM

Concentrated Injection for Intravenous Infusion.

Colourless to slightly yellow, clear to slightly opalescent, pH 6.7.

## 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 DOSE 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.

Dosage

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 Pharmacodynamic Properties*).

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. The safety of initiating subsequent cycles sooner than 7 weeks from the start of the previous treatment cycle has not been established.

In patients weighing 120 kg or more, the recommended dose is 1,200 mg (3 vials) per infusion (see *Instructions for Dilution below*).

*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.

Instructions for dilution

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 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) |

*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 1). 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.

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 above.

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 Special Warnings and Precautions for Use*).

*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 sterilising 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, the product should be used immediately. 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.
- 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 discontinued (see *section 4.4 Special Warnings and Precautions for Use*).
- Other medicinal products should not be injected into infusion side ports or mixed with Vyvgart.

### 4.3 CONTRAINDICATIONS

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

### 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 Interaction with other medicinal products and other forms of interaction*).

Infections

As efgartigimod alfa causes transient reduction in IgG levels the risk of infections may increase (see *sections 4.8 Adverse effects (Undesirable effects)* and *5.1 Pharmacodynamic properties, Clinical Efficacy and Safety*). The most common infections observed in clinical trials were upper respiratory tract infections and urinary tract infections (see *section 4.8 Adverse effects (Undesirable effects)*). 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 antidrug 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.

Sodium content

This medicinal product contains 67.2 mg sodium per vial, equivalent to 3.4% 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 4.2) and this should be considered in relation to the total sodium intake to the patient from all sources per day.

**Special populations**

**Use in 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 Pharmacokinetic Properties*).

**Use in 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 Pharmacokinetic Properties*).

**Use in the elderly**

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

**Paediatric use**

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

### 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 Special Warnings and Precautions for Use*).

### 4.6 FERTILITY, PREGNANCY AND LACTATION

**Effects on fertility**

There are no available data on the effect of efgartigimod alfa on fertility in humans. In reproduction studies in rats, intravenous administration of efgartigimod alfa did not adversely affect male and female fertility or pregnancy at dose levels corresponding to 9-fold to the exposure (AUC) at the maximum recommended therapeutic dose.

**Use in pregnancy – Pregnancy Category C**

There are 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 Special Warnings and Precautions for Use*).

In animal studies, intravenous administration of efgartigimod alfa did not adversely affect embryofetal development nor was it embryotoxic or teratogenic at dose levels corresponding to 9-fold (rats) and 42-fold (rabbits) to the exposure (AUC) at the maximum recommended therapeutic dose.

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

**Use in lactation**

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.

### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of Vyvgart on a person's ability to drive and use machines have not been assessed.

### 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Summary of the safety profile

In the clinical study ARGX-113-1704, 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 events

The safety of Vyvgart was evaluated in 167 patients with gMG treated with efgartigimod alfa (n=84) or placebo (n=83) in the Phase 3 double-blind placebo-controlled clinical study ARGX-113-1704. Adverse events occurring with a frequency of ≥ 5% (where the frequency of AEs reported with efgartigimod alfa was greater than reported in the placebo group) are listed in Table 2 by system organ class (SOC) and preferred term (PT).

**Table 2. Adverse events (≥ 5% and at greater frequency than placebo) by SOC and PT for the Overall Population treated with efgartigimod alfa or placebo (Safety Analysis Set) Study ARGX-113-1704**

| Adverse Events by System Organ Class (SOC) | Efgartigimod (n=84) | Placebo (n=83) |
|---|---|---|
| | n (%) | n (%) |
| **Infections and Infestations** | | |
| Bronchitis | 5 (6.0) | 2 (2.4) |
| Upper Respiratory Tract Infection | 9 (10.7) | 4 (4.8) |
| Urinary Tract Infection | 8 (9.5) | 4 (4.8) |
| **Injury, poisoning and procedural complications** | | |
| Procedural headache | 4 (4.8) | 1 (1.2) |
| **Musculoskeletal and connective tissue disorders** | | |
| Myalgia | 5 (6.0) | 1 (1.2) |

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

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).

Post-marketing reports

Cases of anaphylactic reactions have been reported in the post-marketing setting. For further information, refer to *Section 4.4: Special Warnings and Precaution for Use.*

**Reporting suspected adverse effects**

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

### 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. For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Immunosuppressants, selective immunosuppressants, ATC code: L04AA58.

**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 Dose and Method of administration*). 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 trials**

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 Dose and method of administration*).

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 (see Table 3).

**Table 3. 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.*

** Two-sided exact p-value of the 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.*

Analyses show that during the second treatment cycle MG-ADL responder rates were similar to those during the first treatment cycle (see Table 4).

**Table 4. 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) |

*AChRAb = acetylcholine receptor antibody; MGADL = 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*.

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

### Absorption

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.

### Distribution

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

### Metabolism

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

**Excretion**

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.

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

**Genotoxicity**

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

**Carcinogenicity**

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

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 LIST OF EXCIPIENTS

Monobasic sodium phosphate monohydrate
Dibasic sodium phosphate
Sodium chloride
Arginine hydrochloride
Polysorbate 80
Water for injections

### 6.2 INCOMPATIBILITIES

This medicinal product must not be mixed with other medicinal products except those mentioned in *section 4.2 Dose and method of Administration*.

### 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C.

From a microbiological point of view, the product should be used immediately.

### 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 Shelf Life*.

### 6.5 NATURE AND CONTENTS OF CONTAINER

Vyvgart Concentrated Injection for Intravenous Infusion 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

For use in one patient on one occasion only. Contains no antimicrobial preservative. Discard any residue.

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

### 6.7 PHYSICOCHEMICAL PROPERTIES

**CAS number**

1821402-21-4

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

## 8 SPONSOR

argenx Australia Pty Ltd
Level 14, 2 Riverside Quay
Southbank VIC 3006

## 9 DATE OF FIRST APPROVAL

24/02/2025

## 10 DATE OF REVISION

DD/MM/YYYY

**SUMMARY TABLE OF CHANGES**

| Section | Summary of changes |
|---|---|
| | |