swissmedic

Date: 24 June 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report
Extension of therapeutic indication

Vyvgart

International non-proprietary name: efgartigimod alfa

Pharmaceutical form:	solution for injection
Dosage strength:	1000 mg/ 5.6 ml
Route of administration:	subcutaneous use
Marketing authorisation holder:	argenx Switzerland SA
Marketing authorisation no.:	69725
Decision and decision date:	extension of therapeutic indication approved on 12 May 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, definitions, abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension of the therapeutic indication
The applicant requested the addition of a new therapeutic indication in accordance with Article 23 TPO.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA. Orphan drug status was granted on 23 April 2025.

Authorisation of a new indication in accordance with Article 13 TPA
The applicant requested a reduced assessment procedure in accordance with Article 13 TPA.

2.2 Indication and dosage

2.2.1 Requested indication

Vyvgart is indicated as monotherapy for the treatment of adult patients with progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) after prior treatment with corticosteroids or immunoglobulins.

2.2.2 Approved indication

Vyvgart is indicated as monotherapy for the treatment of adult patients with progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) after prior treatment with corticosteroids or immunoglobulins.

2.2.3 Requested dosage

Summary of the requested standard dosage:

The recommended dose is 1000 mg administered subcutaneously as a once-weekly injection. Treatment is initiated with a weekly dose regimen and may be adjusted to every other week based on clinical evaluation. If symptoms worsen, administration of once-weekly injections should be resumed.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	22 August.2025
Formal control completed	19 September 2025
Preliminary decision	22 January 2026
Response to preliminary decision	23 March 2026
Final decision	12.May.2026
Decision	approval

Based on Art. 13 TPA, Swissmedic has only assessed parts of the primary data submitted with this application. As regards the remaining data, Swissmedic relies for its decision on the assessment of the foreign reference authority European Medicines Agency (EMA). This SwissPAR relates to the assessment report Vyvgart, EMA procedure EMEA/H/C/005849/II/0020 (25 April 2025) issued by EMA.

3 Medical context

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated disease which affects peripheral nerves. Typical CIDP is characterised by proximal and distal muscle weakness and sensory loss. The reported prevalence of CIDP ranges from 0.7 to 10.3 cases per 100,000 people and is predominant in males. It affects primarily adults, and incidence rises with age. Pathogenetic hypotheses describe the involvement of both cellular and humoral components via T cell activation and Ig and complement deposition on myelinated nerve fibres.

Current therapeutic options include intravenous immune globulin (IVIG), glucocorticoids or plasma exchange.

Vyvgart corresponds to efgartigimod alfa (ARGX-113) coformulated with recombinant human hyaluronidase PH20 (rHuPH20). Efgartigimod alfa is a human IgG1 antibody Fc (fragment crystallisable region), which is a natural FcRn (neonatal Fc receptor) ligand. By blocking FcRn, efgartigimod prevents FcRn-mediated IgG recycling and increases IgG degradation, thereby reducing the levels of circulating disease-causing IgG antibodies.

4 Nonclinical aspects

Swissmedic has not assessed the primary data relating to nonclinical aspects submitted with this application and relies on the assessment of the foreign reference authority EMA (EMEA/H/C/005849/II/0020).

5 Clinical aspects

The clinical and clinical pharmacology assessment has been carried out in reliance on the results of the assessment of the foreign reference authority EMA (EMEA/H/C/005849/II/0020). The available assessment reports and respective product information from this procedure were used as a basis for the clinical and clinical pharmacology evaluation.

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Vyvgart, solution for injection was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ 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 new or serious adverse reactions. See «Undesirable effects» for advice on the reporting of adverse reactions.

Vyvgart®, solution for injection

Composition

Active substances

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

Excipients

Recombinant human hyaluronidase (rHuPH20) (genetically modified using CHO cells), l-histidine, l-histidine hydrochloride monohydrate, l-methionine, polysorbate 20 (E 432), sodium chloride, sucrose, water for injections.
Each vial contains 12,9 mg sodium.

Pharmaceutical form and active substance quantity per unit

Solution for injection.
Each vial contains 1000 mg of efgartigimod alfa in 5.6 ml (180 mg/ml).
Yellowish, clear to opalescent, pH 6.0.

Indications/Uses

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.

Dosage/Administration

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

Usual dosage

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 1000 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 «Properties/Effects»).
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.
No experience is available regarding efficacy in patients with generalized myasthenia gravis who have not previously responded to plasma exchange (PLEX) treatment.

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 1000 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.
To ensure traceability of biotechnological medicinal products, it is recommended that the trade name and the batch number should be documented for each treatment.

Special dosage instructions

Patients with hepatic disorders

No data in patients with hepatic impairment are available. No dose adjustment is required in patients with hepatic impairment (see «Pharmacokinetics»).

Patients with renal disorders

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 «Pharmacokinetics»).

Elderly patients

No dose adjustment is required in patients aged 65 years and older (see «Pharmacokinetics»).

Children and adolescents

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

Delayed administration

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.

Mode of administration

This medicinal product should only be administered via subcutaneous injection. The solution for injection must not be administered intravenously.
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 (see section «Instructions for handling»).
During the initial administrations of efgartigimod alfa (see «Dosage/Administration»), appropriate treatment for injection and hypersensitivity-related reactions should be readily available (see «Warnings and precautions»). 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.
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 handling in the package leaflet.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in «Composition».

Warnings and precautions

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 «Interactions»).

Infections

As efgartigimod alfa causes transient reduction in IgG levels the risk of infections may increase (see «Undesirable effects» and «Properties/Effects»). The most common infections observed in clinical trials were upper respiratory tract infections and urinary tract infections (see «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.

Injection reactions and hypersensitivity reactions

Injection reactions such as rash or pruritus were reported in the clinical trials (see «Undesirable effects»). 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 «Dosage/Administration»). 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 must be informed of the possible occurrence and 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 «Properties/Effects»).
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.

Sodium content

Vyvgart, solution for injection contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially «sodium-free».

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 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.
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 further information to vaccines see «Warnings and precautions»).

Pregnancy, 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 «Warnings and Precautions»).
Treatment of pregnant women with Vyvgart should only be considered if the clinical benefit outweighs the risks.

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. No studies are available on possible changes in maternal IgG in human milk and passive protection of the newborn during treatment with Vyvgart.
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 «Preclinical data»).

Effects on ability to drive and use machines

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

Undesirable effects

Summary of the safety profile

The most frequently observed adverse reactions were injection site reactions (38.2%, subcutaneous only), headache (12.7%), upper respiratory tract infections (10.7%) and urinary tract infections (9.5%). The overall safety data indicate that the safety profile is consistent for both routes of administration (for both cyclic and continuous dose regimens), with the exception of injection site reactions for Vyvgart (subcutaneous), which are due to the route of administration.

List of adverse reactions

The safety of Vyvgart (intravenous) was evaluated in 167 patients (84 patients treated with efgartigimod alfa and 83 patients treated with placebo) with gMG in the 26-week Phase 3 double-blind placebo-controlled clinical study (ARGX-113-1704).
Additional long-term safety data were collected in 145 patients with generalized myasthenia gravis who were treated with up to 19 cycles of Vyvgart intravenously following ARGX-113-1704 in the open-label Phase III extension study ARGX-113-1705.
In addition, the safety of Vyvgart subcutaneous and intravenous was comparatively evaluated in 110 patients with gMG in a 10-week Phase 3 open-label, randomized, parallel group clinical study (ARGX-113-2001): 55 patients received the intravenous and 55 patients the subcutaneous formulation.
Adverse reactions described in this section were based upon clinical studies and from post-marketing reports.
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 frequency.

Table 1. Adverse reactions

System organ class	*Adverse reaction*	*Frequency category*
Infections and infestations[*]	Upper respiratory tract infections (10.7%)	Very common
	Urinary tract infections	Common
	Bronchitis	Common
Immune system disorders	Rash	Common
	Infusion related reaction[c]	Common
	Anaphylactic reaction [a]	Not known
Nervous system disorders	Headache (12.7%)	Very common
Gastrointestinal disorders	Nausea	Common

Musculoskeletal and connective tissue disorders	Myalgia	Common
General disorders and administration site conditions	Injection site reactions (38.2%)[b]	Very common
	Fatigue	Common
Injury, poisoning and procedural complications[*]	Procedural headache[c]	Common

[*] See paragraph «Description of specific adverse reactions and additional information»

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

[b] Subcutaneous administration only (see also «Description of specific adverse reactions and additional information»)

[c] Intravenous administration only.

Description of specific adverse reactions and additional information

Injection site reactions (only with subcutaneous use)

In the open label phase 3 study in gMG (ARGX-113-2001) totally 55 subjects with subcutaneous efgartigimod alfa have been treated. All injection site reactions (e.g. injection site rash, injection site erythema, injection site pruritus, injection site pain) were mild to moderate in severity and did not lead to treatment discontinuation. 38.2% (n = 21)) of patients treated with efgartigimod alfa subcutaneous experienced an injection site reaction. If injection site reactions occurred, these resolved without treatment in 81.0% (17/21) of the patients.
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 (IV), the most frequently reported adverse reactions were infections. Overall, in the 26-week controlled phase 3 study treatment emergent infections were reported in 46.4% (n = 39) of patients treated with efgartigimod alfa IV and 37.3% (n = 31) of patients treated with placebo. The median time from treatment initiation to emergence of infections was 6 weeks. 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). In the 10 week open-label study (ARGX-113-2001) with efgartigimod alfa IV and subcutaneous (SC), treatment emergent infections were reported in 16.4% (n=9) of patients treated with efgartigimod alfa IV and in 18.2% (n=10) of patients treated with efgartigimod alfa SC. The most reported infection was urinary

tract infection (5.5% [n = 3] of patients treated with efgartigimod alfa IV and 1.8% [n = 1] in patients treated with efgartigimod alfa SC). Infections were mostly mild to moderate in severity in patients who received efgartigimod alfa IV and SC (≤ Grade 2 according to the Common Terminology Criteria for Adverse Events).
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 «Properties/Effects»).

Procedural headache (intravenous administration only)

Procedural headache was reported in the 26-week placebo controlled phase 3 study in 4.8% of the patients treated with efgartigimod alfa intravenous and 1.2% of patients treated with placebo, while this did not occur in any of the patients in the 10-week open-label study (ARGX-113-2001) with intravenous (i.v.) and subcutaneous (s.c.) efgartigimod alfa. 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).

Anaphylaxis

In blinded and open-label clinical studies (with both intravenous and subcutaneous formulations) there were no anaphylactic reactions reported. Cases of anaphylactic reaction have been reported with efgartigimod alfa intravenous in the post-marketing setting. To date, no anaphylactic reactions were reported since market launch of efgartigimod alfa subcutaneous.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the EIViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

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.

Properties/Effects

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 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.

Pharmacodynamics

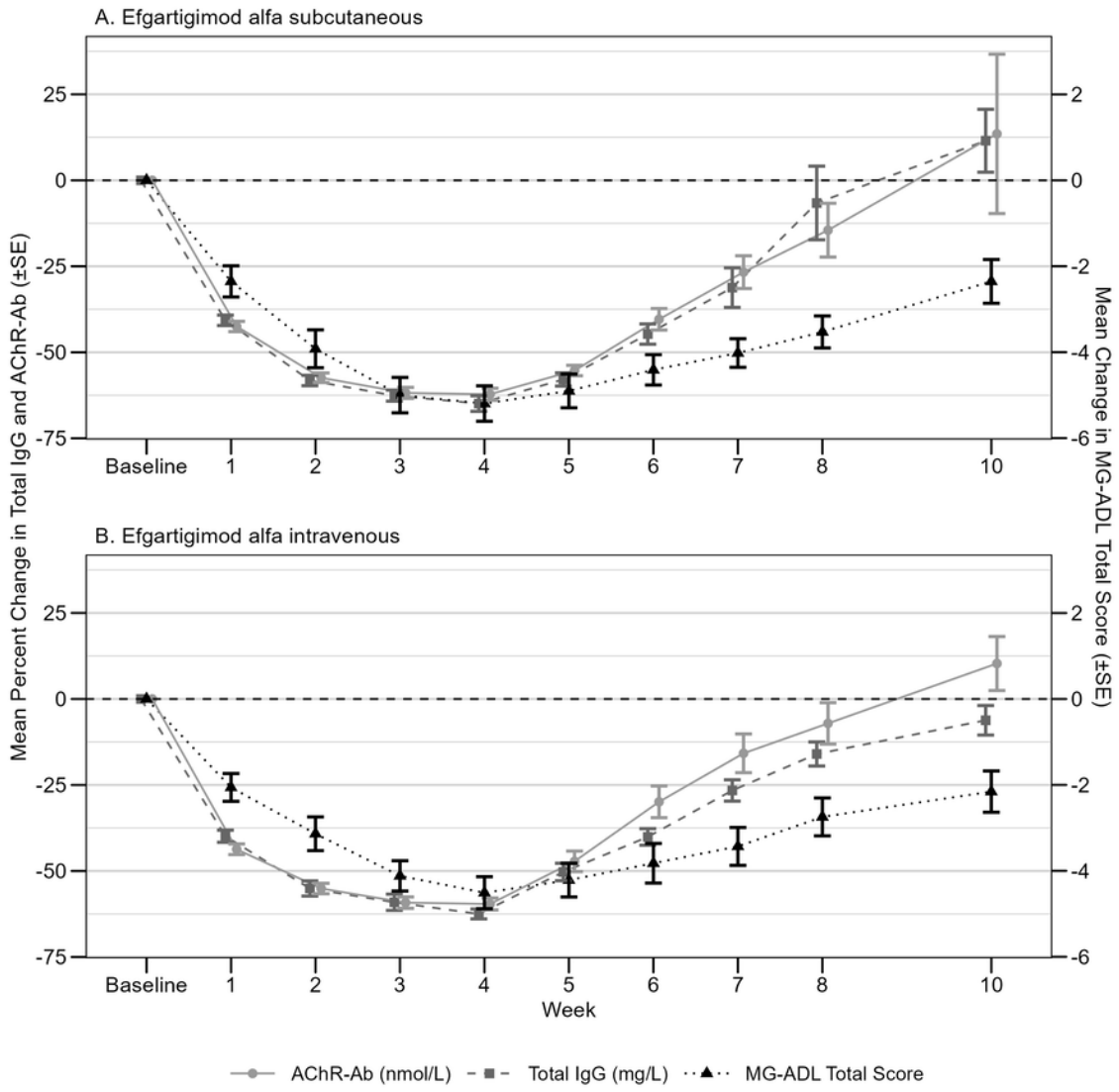
Intravenous formulation

In the ARGX-113-1704 double-blind placebo-controlled study in gMG patients, efgartigimod alfa administered at the recommended dose of 10 mg/kg and schedule (once weekly for 4 weeks) decreased serum IgG levels and AChR autoantibody (AChR-Ab) levels
(see «Dosage/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.

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 1000 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%).

Clinical efficacy

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 plasma exchange (PLEX); patients treated with PLEX, intravenous Immunoglobulin (IVIg) one month and monoclonal antibodies six months prior to starting treatment; patients who had undergone thymectomy in the three months prior to study entry and patients with active (acute or chronic) hepatitis B infection, hepatitis C seropositivity, diagnosis of AIDS, and a severe infection in the last 8 weeks or an underlying malignant disease that has not been successfully treated in the last three years including malignant thymoma, 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 at the recommended dose regimen of 10 mg/kg administered once weekly for 4 weeks and received a maximum of 3 treatment cycles (see «Dosage/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.

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.

In patients with a history of thymectomy, 27 (60%) patients were MG-ADL responders in the efgartigimod alfa group compared to 8 (27%) patients in the placebo group.
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) according to the clinical study protocol, a subsequent treatment cycle could only be initiated if all of the following criteria were met:
(1) the minimum time between treatment cycles was 8 weeks from the first infusion of the previous cycle;
(2) the patient had a total MG-ADL score of ≥ 5 points with > 50% of the total score due to non-ocular symptoms; and
(3) only for patients who achieved responder status (see definition above) in the previous treatment cycle and now show a loss of response (defined as a reduction in the MG-ADL total score < 2 points compared to the corresponding initial cycle value).
In the overall population, the median 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 in the first treatment cycle.
In patients that responded to treatment (≥ a 2-point reduction in MG-ADL total score within the respective cycle versus baseline), 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 1000 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 1000 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

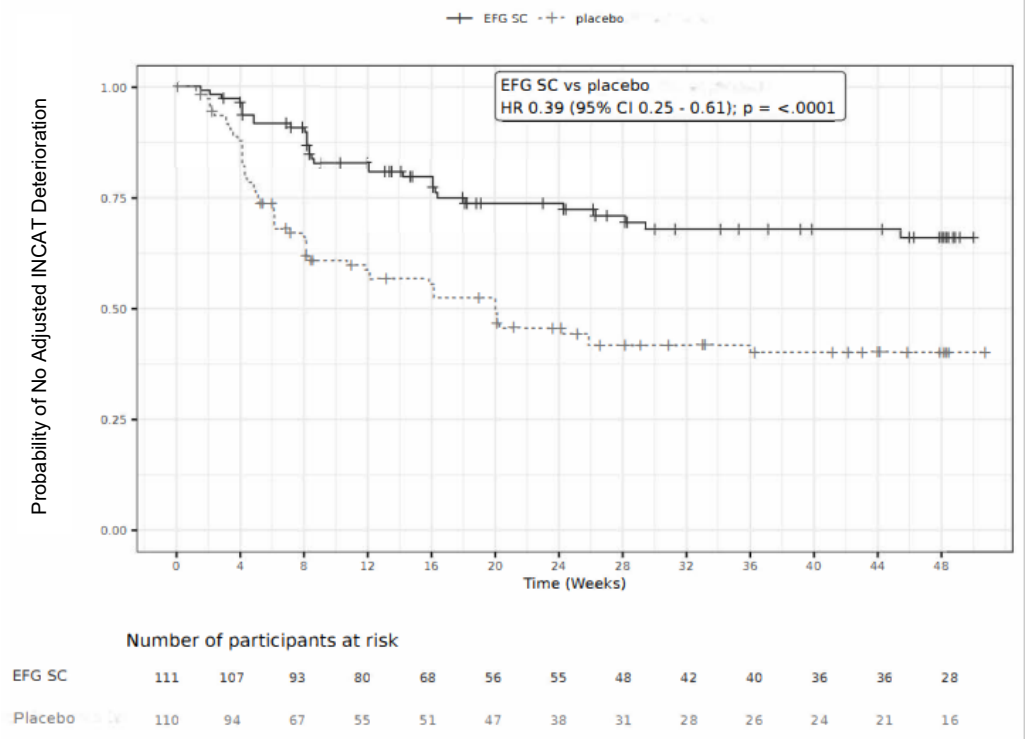
In Stage B, the primary endpoint was defined as the time to the occurrence of the first evidence of clinical deterioration (a 1-point increase in aINCAT compared to Stage B baseline, which was confirmed at a consecutive visit after the first 1-point increase in aINCAT or, a ≥ 2-point increase in aINCAT 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



Pharmacokinetics

Absorption

Based upon population PK data analysis, the estimated bioavailability with efgartigimod alfa 1000 mg subcutaneous is 77%.

The mean C_{trough} after 4 once weekly administrations with efgartigimod alfa 1000 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 1000 mg subcutaneous and 10 mg/kg intravenous were comparable.

In patients receiving continuous subcutaneous administration of efgartigimod alfa 1000 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.

Metabolism

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.

Kinetics in specific patient groups

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.

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.

Age, gender, race and bodyweight

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

Preclinical 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 (10 mg/kg).

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 recombinant human hyaluronidase revealed embryofoetal toxicity in mice at high systemic exposure, but did not show teratogenic potential.

Other information

Incompatibilities

In the absence of compatibility studies, Vyvgart, solution for injection must not be mixed with other medicinal products.

Shelf life

Do not use this medicine after the expiry date «EXP» stated on the pack.
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.
For microbiological reasons, unless the method of preparation of the syringe 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.

Special precautions for storage

Store in a refrigerator (2 - 8 °C).
Do not freeze.
Store in the original packaging in order to protect the contents from light. Do not shake.
Keep out of the reach of children.

Instructions for handling

Vyvgart comes as a ready-to-use solution in single-use vial. The medicinal product does not need to be diluted.
Visually inspect that the vial content is a yellowish, clear to opalescent solution, and devoid of particulate matter. If visible particles are observed the vial must not be used.
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 «Shelf life»).

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.

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

Authorisation number

69725 (Swissmedic)

Packs

Vyvgart, 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. (A)

Marketing authorisation holder

argenx Switzerland SA, 1214 Vernier

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