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

Imaavy 185 mg/mL concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of concentrate for solution for infusion contains 185 mg nipocalimab.

One vial of 1.62 mL contains 300 mg of nipocalimab.

One vial of 6.5 mL contains 1200 mg of nipocalimab.

Nipocalimab is a fully human immunoglobulin G1 monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

Excipient with known effect

Each vial contains 0.97 mg (300 mg vial) or 3.9 mg (1200 mg vial) of polysorbate 80 which is equivalent to 0.60 mg/mL.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate)

Colourless to slightly brownish, clear to slightly opalescent, pH 6.0.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Imaavy is indicated as an add-on to standard therapy for the treatment of generalised Myasthenia Gravis (gMG) in adult and adolescent patients aged 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

4.2 Posology and method of administration

Treatment should be supervised by a physician experienced in the management of patients with neuromuscular disorders and must be administered by a healthcare professional.

Posology

The recommended dose regimen is shown in Table 1.

Table 1: Recommended dose regimen

Population	Recommended dose (IV)	
	Initial single dose	**Maintenance dose (every 2 weeks)**
Adults and adolescents (12 years and older)	30 mg/kg	15 mg/kg

Missed dose(s)
If a scheduled infusion appointment is missed, the maintenance dose should be administered as soon as possible. Dosing should be resumed every 2 weeks thereafter.

Special populations

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

Renal impairment
No dose adjustment is required for patients with renal impairment (see section 5.2).

Hepatic impairment
No dose adjustment is required for patients with hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of nipocalimab in children below 12 years of age have not been established. No data are available.

Method of administration

This medicinal product should only be administered via intravenous infusion with in-line or add-on filtration as described in section 6.6. Do not administer as an intravenous push or bolus injection.

The initial single dose of medicinal product should be administered over approximately 30 minutes and the maintenance dose should be administered over approximately 15 minutes.

Patients should be monitored for 30 minutes after each infusion for signs or symptoms of an infusion-related or hypersensitivity reaction. If an adverse reaction occurs during administration of treatment, the infusion may be slowed or discontinued (see section 4.4).

Prior to administration, this medicinal product requires dilution in sodium chloride 9 mg/mL (0.9%) solution for infusion. 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 nipocalimab 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 nipocalimab, and their potential interactions, should be considered (see section 4.5).

Infusion-related and hypersensitivity reactions

Administration of nipocalimab may result in infusion-related and hypersensitivity reactions. The most commonly reported infusion-related reactions were headache, rash, nausea, fatigue, dizziness, chills, and erythema. The most commonly reported hypersensitivity reactions were rash, urticaria and eczema. Most infusion-related and hypersensitivity reactions were non-serious, mild or moderate and did not lead to treatment discontinuation. A case of anaphylaxis has been reported that led to the discontinuation of treatment.

The patient should be monitored for 30 minutes after each infusion for clinical signs and symptoms of infusion-related or hypersensitivity reactions. If a serious infusion-related or hypersensitivity reaction occurs during administration, the infusion should be discontinued and appropriate supportive measures should be instituted, if needed. Once resolved, administration may be resumed (see section 4.2).

Increased plasma lipid levels

Increased plasma lipid levels are very common during treatment with Imaavy, both in adolescent and adult patients of all ages (see section 4.8). Plasma lipid levels should therefore be measured approximately 12 weeks following treatment initiation. In adolescents (12 to <18 years) and in patients with high body weight/BMI (e.g. ≥125 kg or BMI >35 kg/m²), consider closer periodic monitoring thereafter. The evaluation whether to continue treatment with Imaavy should consider the potential negative impact on long-term cardiovascular risk, considering also other risk factors, and weigh this against the expected gMG treatment benefit. Continued monitoring of plasma lipid levels and alternative treatment options should be considered.

Infections

As nipocalimab causes reduction in IgG levels, the risk of infections, including the activation of latent viral infections such as herpes zoster, may increase (see section 4.8). Initiation of treatment administration should be delayed in patients with an active infection until the infection is resolved. During treatment, patients should be monitored for clinical signs and symptoms of infection. In patients with a clinically important active infection, appropriate treatment should be administered and nipocalimab treatment should be withheld until the infection has resolved.

Immunisations

The safety of immunisation with live or live-attenuated vaccines and the response to immunisation with these vaccines during treatment are unknown.

For patients that are being treated with nipocalimab, vaccination with live or live-attenuated vaccines is 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 nipocalimab.

Non-live vaccines may be administered as needed at any time during treatment (see sections 4.5 and 5.1). All vaccines should be administered according to immunisation guidelines.

Excipient with known effect

This medicinal product contains 0.97 mg (300 mg vial) or 3.9 mg (1200 mg vial) of polysorbate 80 in each single-use vial which is equivalent to 0.60 mg/mL. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of nipocalimab on other medicinal products

Concomitant use of nipocalimab is likely to reduce systemic exposure of medicinal products that bind to the immunoglobulin G (IgG) binding site of the human neonatal Fc receptor (FcRn) (e.g., IgG products, IgG-based monoclonal antibodies, antibody derivates containing the human Fc domain of the IgG subclass, or Fc fusion proteins).

In a dedicated clinical interaction study in healthy participants, nipocalimab (single dose 30 mg/kg intravenously) reduced the systemic C_{max} and AUC of fremanezumab (a full IgG-based monoclonal antibody), co-administered on the same day, by 42% and 66%, respectively. When, in this study, the same dose of nipocalimab was administered 14 days after the fremanezumab dose, C_{max} of fremanezumab was not altered while its AUC was reduced by 53%.

In another dedicated clinical interaction study in healthy participants, concomitant dosing of nipocalimab (15 mg/kg intravenously every 2 weeks) and etanercept, an Fc-fusion protein, reduced etanercept systemic exposure (C_{max} by ~9% and AUC by ~28%).

If patients on nipocalimab need treatment with medicinal products that bind to the IgG binding site of FcRn, it is recommended these medicinal products are started 2 weeks after the previous dose of nipocalimab.

When concomitant long-term use of such medicinal products is essential for patient care, closely monitor for reduced effectiveness of such medicinal products and consider discontinuing nipocalimab or using alternative therapies.

Effects of other medicinal products on nipocalimab

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

Vaccines

The impact of nipocalimab on a T-cell dependent (Tdap) or a T-cell independent (PPSV23) vaccine response was assessed in healthy volunteers (n=16). Participants were able to mount a specific IgG response to these vaccines, but vaccine-specific IgG antibody levels were reduced during nipocalimab treatment with recovery to levels similar to the control group after treatment cessation (see sections 4.4 and 5.1).

For patients that are being treated with nipocalimab, vaccination with live or live-attenuated vaccines is 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 nipocalimab (see section 4.4).

Paediatric population

Paediatric patients 12 years and older with gMG
The same interactions as observed in the adult population may occur in adolescent patients aged 12 years and older.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data from the use of nipocalimab in pregnant women. There is no available data with nipocalimab use in pregnant women with gMG, and limited data from an open-label Phase 2 clinical study in 13 pregnant women at high-risk for Haemolytic Disease of the Foetus and Newborn, in which nipocalimab was studied in the second and third trimesters of pregnancy. In this study, maternal administration of nipocalimab did not result in pharmacologically active concentrations in neonates or infants, due to nipocalimab's high affinity at neutral (extracellular) pH (see section 5.1).

In an animal study where pregnant cynomolgus monkeys were dosed with nipocalimab during the late first, second and third trimesters of pregnancy, large, central placental infarctions and thrombosis of maternal spiral arteries were observed. In some cases, the findings were associated with foetal loss. However, this study does not indicate maternal toxicity or direct or indirect harmful effects on pre- or postnatal development. Reversible nipocalimab-induced reductions in infant monkey IgG levels were demonstrated (see section 5.3).

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

As nipocalimab is expected to reduce maternal IgG antibody levels, reduction in passive protection to the newborn is anticipated. Risks and benefits should be considered prior to administering live or live-attenuated vaccines to infants exposed to nipocalimab *in utero*.

Breast-feeding

There are limited data showing that nipocalimab administered during pregnancy is excreted in colostrum and human milk at low levels for up to 8 days post-partum.

Maternal IgG is known to be present in breastmilk during the first days after birth, which decreases to low levels soon thereafter: consequently, a risk to breast-fed infants cannot be excluded during this short period. Afterwards, treatment of breast-feeding women with Imaavy could be considered if the clinical benefit outweighs the risks.

Fertility

There are no data on the effects of nipocalimab on fertility in humans. Animal studies do not indicate harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions were muscle spasms (12%) and peripheral oedema (12%).

Tabulated list of adverse reactions

A total of 250 adult gMG patients were treated with nipocalimab in Phase 2 and Phase 3 studies. Of these, 205 patients were treated in the Phase 3 study, including 98 in the double-blind phase. In total, 178 were exposed to the recommended maintenance dose (15 mg/kg every 2 weeks, see section 4.2) for at least 6 months, and 132 were exposed for at least 12 months.

Adverse reactions are listed in Table 2 below, classified by MedDRA System Organ Class (SOC). Within each SOC, the adverse reactions are ranked by frequency, with the most frequent reactions first.

Frequency categories are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100) or rare (≥ 1/10 000 to < 1/1 000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse reactions

System organ class	Adverse reaction	Frequency category
Infections and infestations	Herpes zoster[1]	Common
	Urinary tract infection*	Common
	Lower respiratory tract infection*[2]	Common
Metabolism and nutrition disorders	Lipids increased*[3]	Very common
	Decreased serum albumin*	Very common
Psychiatric disorders	Insomnia	Common
Nervous system disorders	Dizziness	Common
Gastrointestinal disorders	Diarrhoea	Common
	Abdominal pain[4]	Common
	Nausea	Common
Musculoskeletal and connective tissue disorders	Muscle spasms	Very Common
General disorders and administration site conditions	Peripheral oedema[5]	Very Common
	Pyrexia	Common

* See paragraph Description of selected adverse reactions

1 Includes Herpes zoster and Herpes zoster oticus; evaluation and frequency based on completed placebo-controlled Phase 2 and Phase 3 studies across several indications under study

2 Includes pneumonia and bronchitis

3 Includes hypercholesterolaemia, low density lipoproteins increased, blood cholesterol increased and hyperlipidaemia.

4 Includes abdominal pain and abdominal pain upper

5 Includes peripheral oedema, oedema, and peripheral swelling

Description of selected adverse reactions

Infections

In the Phase 3 double-blind placebo-controlled clinical study in gMG, the overall rate of infections was the same between patients in the nipocalimab group and patients in the placebo group (42 [42.9%] in each group). Most cases were mild to moderate in severity and did not lead to discontinuation of nipocalimab treatment. Urinary tract infection was reported in 5 patients (5.1%) in the nipocalimab group compared to 0 patients (0%) in the placebo group. The events of urinary tract infection were mild (3 [3.1%]) and

moderate (2 [2.0%]) in severity. Pneumonia or bronchitis was reported in 5 patients (5.1%) in the nipocalimab group compared to 2 patients (2.0%) in the placebo group.

Lipids increased

In adult and adolescent patients with gMG who received nipocalimab, increases in lipids were observed in most patients. In adults, 30% had treatment-emergent markedly abnormal total cholesterol (≥6.2 mmol/L), compared to 4% in the placebo group. The mean change from baseline for fasting total cholesterol, HDL, and LDL peaked at Week 4, then decreased and plateaued by Week 24 to a mean increase of 0.37 mmol/L, 0.12 mmol/L, and 0.19 mmol/L, respectively. Of the patients with LDL values <4.1 mmol/L prior to starting treatment, 11.3% of patients treated with nipocalimab had LDL values ≥4.1 mmol/L at Week 24 relative to 4.6% of patients on placebo. See section 4.4.

Decreased serum albumin levels

In the Phase 3 double-blind placebo-controlled clinical study in gMG, the mean (SD) percent change from baseline in serum albumin levels during the double-blind phase was -8.4% (5.27%) at Week 2 and -7.2% (5.37%) at Week 24 in patients treated with nipocalimab relative to -0.5% (6.29%) at Week 2 and -2.1% (7.08%) at Week 24 in patients on placebo. No patients had serum albumin levels below the laboratory lower limit of normal (LLN=33 g/L) in the double-blind phase or markedly low serum albumin levels (≤ 20 g/L) in the double-blind or open-label phase.

Paediatric population

The safety of nipocalimab was assessed in an open-label study including adolescent gMG patients aged 12 years and older (n=8) for up to 24 weeks (see section 5.1). No major differences in the safety profile were identified between adult and adolescent patients. Increased lipid levels in adolescents followed a similar trend to that observed in adults.

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

Single doses up to 60 mg/kg have been administered intravenously in clinical studies without dose-limiting toxicity. There are no known specific signs and symptoms of overdose with nipocalimab. In case of overdose, it is recommended that patients are monitored closely for any adverse reactions, and appropriate symptomatic and supportive treatment should be initiated immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, monoclonal antibodies, ATC code: L04AL03.

Mechanism of action

Nipocalimab is a human IgG1 monoclonal antibody specifically targeting the IgG Fc binding site of FcRn with high specificity and high affinity at both neutral (extracellular) and acidic pH (intracellular) resulting

in the reduction of circulating IgG, including IgG autoantibodies, without affecting other immunoglobulins (IgA, IgE or IgM). Nipocalimab did not demonstrate any clinically relevant impact on circulating levels of albumin, which binds at a different site on FcRn.

IgG autoantibodies are the underlying cause of the pathogenesis of MG. IgG autoantibodies impair neuromuscular transmission by binding to AChR, MuSK or LRP4.

Nipocalimab reduces the placental transfer of IgG from mother to foetus (see section 4.6).

Pharmacodynamic effects

In a double-blind placebo-controlled study in gMG patients, intravenous administration of nipocalimab at the recommended dose regimen (see section 4.2) resulted in a significant rapid reduction in total IgG serum concentrations of 75% compared to baseline within 2 weeks of treatment initiation, followed by a sustained reduction of approximately 70% compared to baseline from Week 4 through to Week 24. Similar dose-dependent reductions in all IgG subclasses (IgG1, IgG2, IgG3, and IgG4) were observed.

Immunisations (vaccinations)

The impact of nipocalimab on a T-cell dependent (Tdap) and a T-cell independent (PPSV23) vaccine response was assessed in a randomised, open-label study in healthy participants (n=15 for control, n=16 for nipocalimab). In the nipocalimab group, participants received nipocalimab at Week 0 (30 mg/kg IV), Week 2 (15 mg/kg IV) and Week 4 (15 mg/kg IV), and Tdap and PPSV23 were administered subcutaneously 3 days after the first nipocalimab dose.

Participants were able to mount a specific IgG response to these vaccines, but vaccine-specific IgG antibody levels were reduced during nipocalimab treatment with recovery to levels similar to the control group after treatment cessation.The anti-TT (tetanus toxoid) specific IgG levels are shown in Table 3. In participants who received nipocalimab, the anti-TT specific IgG levels achieved the peak response at Week 2, decreased at Week 4 and then increased through Week 16, 12 weeks after the last dose of nipocalimab at Week 4. Anti-PCP (pneumococcal capsular polysaccharide) specific IgG levels followed a similar pattern over time. See sections 4.4 and 4.5.

Table 3: Anti-TT IgG levels (mean±SE) over time

Time Point	**Nipocalimab (n=16) IU/mL**	**Control (n=15) IU/mL**
Baseline	1.97±0.612	2.38±0.538
Week 2	3.38±0.325	4.92±0.619
Week 4	1.63±0.269	4.56±0.591
Week 8 (4 weeks post last dose)	2.39±0.491	3.87±0.538
Week 16 (12 weeks post last dose)	2.53±0.223	3.20±0.474

Immunogenicity

Anti-drug antibodies (ADA) were very commonly detected at low titre. However, no evidence of ADA impact on pharmacokinetics, pharmacodynamics, efficacy or safety was observed.

Clinical efficacy and safety

Study MOM-M281-011 (adults)

The safety and efficacy of nipocalimab for the treatment of adults with gMG was studied in a 24-week, randomised, double-blind, placebo-controlled study. Patients participating in this study were subsequently allowed to enter an open-label extension phase during which all patients received nipocalimab.

The study enrolled patients who met the following main criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- MG-Activities of Daily Living (MG-ADL) total score of ≥ 6
- On stable dose of standard of care (SoC) therapy prior to baseline, including acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone.

A total of 196 patients (with or without autoantibodies) were randomised and received either nipocalimab plus SoC (n=98) or placebo plus SoC (n=98). Of these, 153 patients were antibody positive (n=77 for nipocalimab, n=76 for placebo). Patients were treated with nipocalimab at the recommended dose regimen (see section 4.2).

Of the 153 antibody positive patients, 88% were antibody positive for AChR, 10% were antibody positive for MuSK, and 2% were antibody positive for LRP4. Baseline characteristics were similar between treatment groups, including median age at screening (52 [20-81] years, 24% patients ≥65 years of age), median time since diagnosis (6 [0-38] years), gender (60% female), and race (63% white, 32% Asian). Mean MG-ADL total score was 9.2, and mean Quantitative Myasthenia Gravis total score was 15.4.

At baseline, over 97% in each treatment group were on stable background SoC therapy. During treatment, 85% were on AChE inhibitors, 66% were on steroids, and 54% were on non-steroidal immunosuppressive therapies (NSISTs) at stable doses.

The efficacy of nipocalimab was measured using the Myasthenia Gravis 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 response was defined as a ≥2-point reduction in the total MG-ADL score compared to baseline. The efficacy of nipocalimab was also measured using the Quantitative Myasthenia Gravis (QMG) total score which measures muscle weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment. A QMG response was defined as a ≥3-point reduction in the total QMG score compared to baseline.

The key efficacy results for the primary and major secondary study endpoints are shown in Table 4. A statistically significant difference favouring nipocalimab was observed on MG-ADL and QMG changes from baseline.

Table 4: Summary of the primary and key secondary clinical responses

	Nipocalimab (n=77) LS mean (SE)	Placebo (n=76) LS mean (SE)	Nipocalimab change relative to placebo LS mean difference (95% CI)	P-value
MG-ADL[1]	-4.68 (0.324)	-3.29 (0.333)	-1.39 (-2.31, -0.47)	0.003
QMG[2]	-4.77 (0.488)	-1.90 (0.491)	-2.87 (-4.23, -1.50)	<0.001
MG-ADL responder based on average change over Weeks 22, 23, and 24[3]	68.8%	52.6%	16.2 (0.9, 31.5)	0.021
MG-ADL responder from Week 4 through Week 24[4]	55.8%	26.3%	29.5 (14.7, 44.4)	-
≥50% improvement on MG-ADL based on average change over Weeks 22, 23 and 24[5]	46.8%	25.0%	21.8 (7.0, 36.6)	-

[1] Mean change from baseline over Weeks 22, 23, and 24.

[2] Mean change from baseline over Weeks 22 and 24.

[3] Average change over Weeks 22, 23, and 24 is at least a 2-point improvement from baseline.

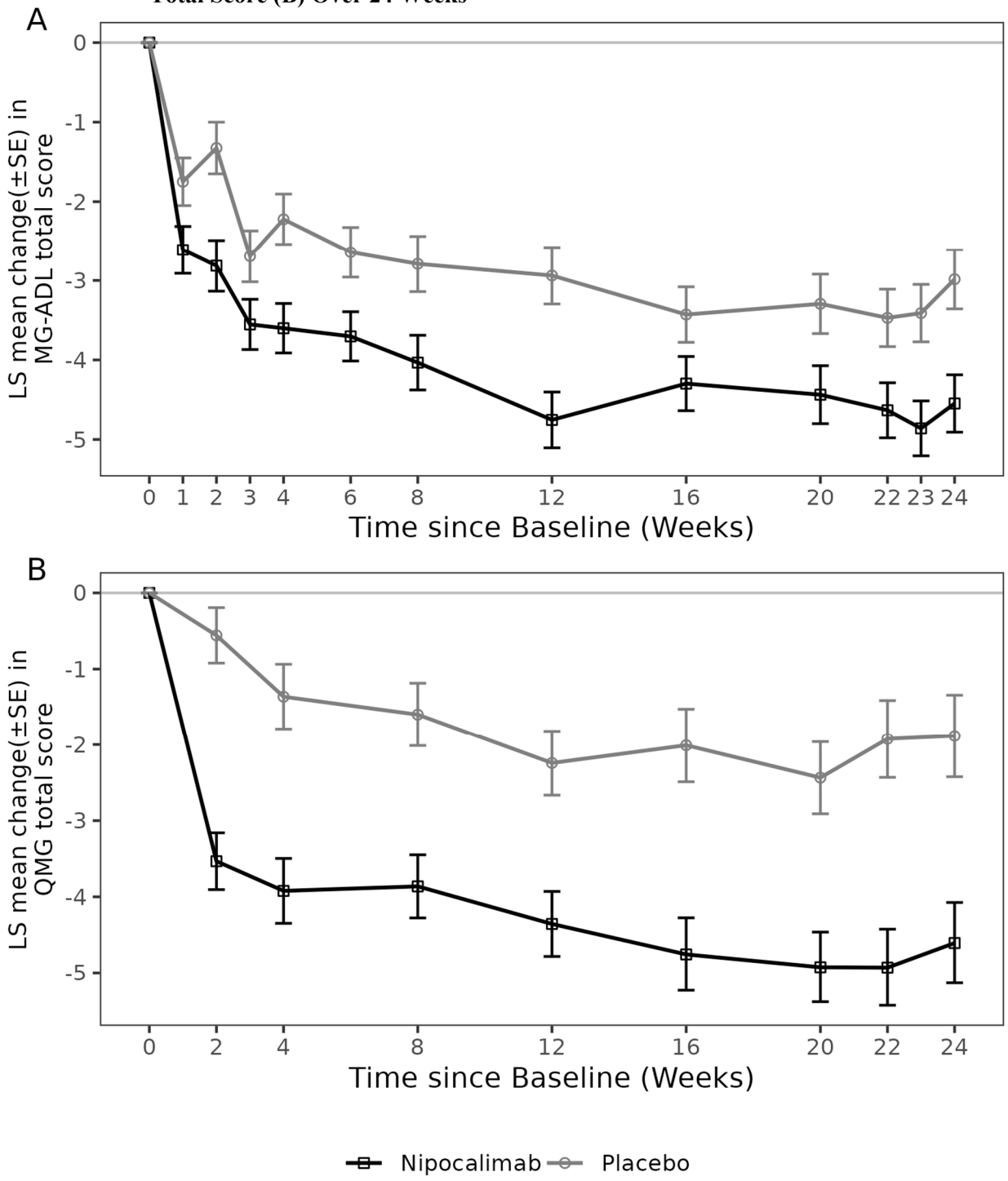
[4] At least 2-point improvement in MG-ADL total score at Week 4 and Week 24, and at least 2 point improvement at Week 6 through Week 23 with no more than 2 non-consecutive excursions (improvement less than 2 points) allowed.

[5] Average change over Weeks 22, 23, and 24 is at least a 50% improvement from baseline.

Response over time (double-blind phase)
Improvements with nipocalimab compared to placebo were observed through Week 24.

The time course of response for the primary efficacy endpoint (MG-ADL) and key secondary efficacy endpoint (QMG) is shown in Figure 1.

Figure 1: Least Squares Mean Change from Baseline in MG-ADL Total Score (A) and QMG Total Score (B) Over 24 Weeks



Over time, a higher proportion of patients achieved sustained MG-ADL (improvement $\geq$ 2 points from Week 2 through Week 24) and QMG (improvement $\geq$ 3 points from Week 2 through Week 24) responses in the nipocalimab group (45.5% and 33.8%, respectively) compared to the placebo group (21.1% and 7.9%, respectively).

Response over time (open-label extension phase)
Of the 153 antibody positive patients in the double-blind placebo-controlled phase, 137 entered into the open-label extension phase to receive nipocalimab. At the time of the analysis, in patients who initially received nipocalimab during the double-blind phase and continued to receive nipocalimab during the first 48 weeks (n=52) and 84 weeks (n=20) of the open-label extension phase, the mean improvements in MG-ADL and QMG total scores were maintained.

Paediatric population

Study 80202135MYG2001 (adolescent cohort)

The pharmacodynamics, pharmacokinetics, and efficacy of nipocalimab for the treatment of gMG in adolescent patients are evaluated at Week 24 in an ongoing open-label study.

Main study inclusion criteria are as follows:
- MGFA clinical classification class II to IV
- Positive for autoantibodies to AChR or MuSK
- On stable dose of SoC therapy prior to screening, including AChE inhibitors, steroids or NSISTs, either in combination or alone.

Eight patients had a median age of 13.5 years at screening (range 12 to 16 years) and a median time since diagnosis of 3.6 years (range 0.8 to 11.5). Seven patients were female; 5 were Asian, 1 was Black and 2 were of unknown race. Mean (SD) MG-ADL total score at baseline was 4.4 (2.26), and mean (SD) QMG total score was 13.3 (4.13). All patients were AChR antibody positive. At baseline, 4 patients were on AChE inhibitors, 6 were on steroids, and 7 were on NSISTs at stable doses.

Seven of the 8 adolescent patients were evaluated through Week 24 and received nipocalimab at the recommended dose regimen (see section 4.2). The primary endpoint was the effect of nipocalimab on total serum IgG. At Week 24, the median pre-dose percent reduction in total IgG from baseline (n=7) was 73.3%, consistent with the IgG reduction seen in the adult gMG study. The mean (SD) change at Week 24 in MG-ADL was -2.57 (0.535) and the mean change at Week 24 in QMG was -4.93 (3.81).

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

5.2 Pharmacokinetic properties

Distribution

The mean (SD) volume of distribution is 2.84 (0.63) L or 0.0359 (0.0087) L/kg.

Biotransformation

Nipocalimab is expected to be degraded by proteolytic enzymes into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

Nipocalimab exhibits concentration-dependent pharmacokinetics. Following a single intravenous administration of 15 mg/kg of nipocalimab, the mean clearance is 0.0627 L/h and half-life is 29.3 hours. After stopping administration, serum IgG concentrations recover towards baseline levels within approximately 8 weeks.

Linearity/non-linearity

Nipocalimab exhibits non-linear, dose-dependent pharmacokinetics. Following a single intravenous infusion of nipocalimab at doses ranging from 0.3 to 60 mg/kg in healthy participants, C_{max} increased in a dose-proportional manner while AUC increased in a greater than dose proportional manner.

Due to the relatively short half-life of nipocalimab, repeated dosing administered in accordance with the recommended maintenance dose (see section 4.2) results in no drug accumulation over time.

Special populations

Paediatric population
Pharmacokinetics of nipocalimab were evaluated in adolescent patients 12 to 17 years of age with gMG (n=8). Following treatment with nipocalimab at the recommended dose regimen (see section 4.2), the observed serum nipocalimab concentrations were comparable between adult and adolescent patients with gMG (Table 5).

Table 5: Serum nipocalimab concentrations in adult and adolescent patients with gMG

Timepoint	**Exposure Parameter**	**Adolescents (n=8) Median (IQ Range)**	**Adults (n=97) Median (IQ Range)**
Initial dose	$C_{eoi,ld}$ (µg/mL)	701 (673, 922)	864 (774, 1000)
	$C_{trough,ld}$ (µg/mL)	0.01 (BQL, 0.02)	0.02 (BQL, 0.03)
Maintenance doses	$C_{eoi,ss}$ (µg/mL)	394 (335, 491)	424 (392, 479)
	$C_{trough,ss}$ (µg/mL)	BQL	BQL

BQL = Below Quantification Limit (i.e., <0.01 µg/mL); $C_{eoi,ld}$ = end of infusion concentration after 30 mg/kg initial dose; $C_{trough,ld}$ = pre-dose concentration at Week 2 after 30 mg/kg initial dose; $C_{eoi,ss}$ = end of infusion concentrations at steady state after 15 mg/kg every two weeks maintenance doses; $C_{trough,ss}$ = pre-dose concentration at steady state after 15 mg/kg every two weeks maintenance doses; IQ = interquartile.

Elderly
Clinical studies with nipocalimab did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger adult patients. No apparent differences in clearance and volume of distribution were observed in patients ≥ 65 years of age compared to patients < 65 years of age, suggesting no dose adjustment is needed for elderly patients (see section 4.2).

Age, gender, and ethnicity
A population pharmacokinetics analysis assessing the effects of age, sex, and race did not suggest any clinically relevant impact of these covariates on nipocalimab exposures.

Body weight
Body weight has an impact on systemic exposure to nipocalimab. The recommended weight-based dosing (in mg/kg) accounts for the differences in patient body weight.

Renal impairment
No formal studies have been performed in patients with renal impairment. Renal impairment is not expected to affect the pharmacokinetics of nipocalimab. Based on a population pharmacokinetic analysis, which included patients with mild to moderate renal impairment, renal function had no clinically relevant effect on nipocalimab apparent clearance. No dose adjustment is required in patients with renal impairment (see section 4.2).

Hepatic impairment
No formal studies have been performed in patients with hepatic impairment. Nipocalimab is not metabolised by cytochrome P450 enzymes, and therefore, hepatic impairment is not expected to affect the pharmacokinetics of nipocalimab. Based on a population pharmacokinetic analysis, which included participants with mild and a limited number of participants with moderate hepatic impairment, there was no clinically relevant effect on nipocalimab apparent clearance. No dose adjustment is required in patients with hepatic impairment (see section 4.2).

5.3 Preclinical safety data

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

There were no nipocalimab-related adverse effects on male and female fertility in non-pregnant cynomolgus monkeys in a 6-month repeat-dose study when evaluated by changes in the reproductive organs (organ weights and histopathology). All females and 80% of males, at the highest dose tested, became sexually mature during the 6-month treatment period in which exposure levels up to 44 times the expected exposure level in patients on the recommended maintenance dose (see section 4.2) were evaluated.

In an enhanced pre- and postnatal development study, where pregnant cynomolgus monkeys were intravenously exposed to nipocalimab during the late first, second and third trimesters of pregnancy, 16% (4/25) of placentas showed large, central placental infarctions and thrombosis of maternal spiral arteries. Three of the 4 cases of placental infarction were associated with second or third trimester foetal losses. The placental infarctions may be related to maternal immunogenicity in pregnant cynomolgus monkeys. The clinical relevance of these findings is unknown. Nipocalimab exposure levels (AUC) in pregnant cynomolgus monkeys reached at least 5 to 24 times the expected exposure level in non-pregnant women based on the recommended maintenance dose regimen (see section 4.2). No pre- or postnatal development concerns were raised. Foetuses and infants from treated dams showed negligible exposure to maternal nipocalimab but had low levels of IgG at birth. The infant IgG levels recovered within 6 months. There was no adverse impact on immune function of the infants of treated dams as assessed by a T-cell Dependent Antibody Response assay.

The mutagenic potential of nipocalimab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

Carcinogenicity studies have not been conducted with nipocalimab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Arginine hydrochloride
Histidine
Histidine monohydrochloride monohydrate
Methionine
Polysorbate 80 (E433)
Sucrose
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

Unopened vial

2 years.

After dilution

From a microbiological point of view, unless the method of dilution precludes the risks of microbial contaminations, the prepared diluted solution (see section 6.6) should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. If immediate administration is not possible, the diluted solution can be refrigerated for up to 24 hours at 2 °C to 8 °C, with an additional 12 hours of storage at room temperature, including infusion time, at 15 °C to 30 °C. Do not freeze.

6.4 Special precautions for storage

Store in a refrigerator (2 °C to 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

1.62 mL concentrate for solution for infusion in a single-use Type 1 glass vial with an elastomeric stopper with an aluminium seal with a flip-off cap containing 300 mg of nipocalimab. Pack size of 1 vial.

6.5 mL concentrate for solution for infusion in a single-use Type 1 glass vial with elastomeric stopper with an aluminium seal with a flip-off cap containing 1200 mg of nipocalimab. Pack size of 1 vial.

6.6 Special precautions for disposal and other handling

Prior to administration, Imaavy single-dose vials require dilution in sodium chloride 9 mg/mL (0.9%) solution for infusion.

Preparation
Prepare the solution for infusion using aseptic technique as follows:

- Calculate the dose (mg), total volume (mL) of concentrate required, and the number of vials needed based on the patient's current weight for the recommended initial single dose of 30 mg/kg or 15 mg/kg for subsequent doses every 2 weeks. Each vial is at a concentration of 185 mg/mL.
- Check that the solution in each vial is colourless to slightly brownish, clear to slightly opalescent, and free of visible particles. Do not use if visible particles are present or if the solution is discoloured (other than colourless to slightly brownish). Do not shake.
- Gently withdraw the calculated volume of concentrate from the vial(s). Discard any unused portion of the vials.

- Dilute the total volume of the withdrawn concentrate by adding it to an infusion bag containing 250 mL sodium chloride 9 mg/mL (0.9%) solution for infusion for patients who weigh 40 kg or more, or 100 mL sodium chloride 9 mg/mL (0.9%) solution for infusion for patients who weigh less than 40 kg. Only use infusion bags made of polyolefin, polypropylene, or polyvinylchloride.
- Gently invert the infusion bag at least ten times to mix the solution. Do not shake.
- Verify that a uniform solution has been achieved by visual inspection. Do not use if particulate matter or discolouration are present.

Administration
- Administer the diluted solution by intravenous infusion using an infusion set with an in-line or add-on, sterile, non-pyrogenic, low protein-binding filter made of polyethersulfone or polysulfone (pore size 0.2 micrometre or less). Administration sets must be made of either polybutadiene, polyethylene, polyurethane, polypropylene, or polyvinylchloride.
- Do not infuse the diluted concentrate concomitantly in the same intravenous line with other agents.
- Administer the infusion intravenously over approximately 30 minutes for the initial dose (30 mg/kg) and approximately 15 minutes for subsequent doses (15 mg/kg).
- If an adverse reaction occurs during administration, the infusion may be slowed or stopped at the discretion of the heatlthcare professional.

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

7. MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1989/001
EU/1/25/1989/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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/en.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER 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. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

WuXi Biologics Co., Ltd.
108 Meiliang Road
Mashan, Binhu District, Wuxi, Jiangsu, 214092, China

Janssen Sciences Ireland UC (JSI)
Barnahely, Ringaskiddy
Co. Cork, P43 FA46, Ireland

Name and address of the manufacturer responsible for batch release

Janssen Biologics B.V.
Einsteinweg 101
Leiden, 2333 CB, The Netherlands

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 (300 mg)

1. NAME OF THE MEDICINAL PRODUCT

Imaavy 185 mg/mL concentrate for solution for infusion
nipocalimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial of 1.62 mL contains 300 mg of nipocalimab (185 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: arginine hydrochloride, histidine, histidine monohydrochloride monohydrate, methionine, E433, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

concentrate for solution for infusion
300 mg/1.62 mL
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use after dilution.

Read the package leaflet before use.

For single use only.

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

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1989/001

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 (300 mg)

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

Imaavy 185 mg/mL sterile concentrate
nipocalimab
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

300 mg/1.62 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (1200 mg)

1. NAME OF THE MEDICINAL PRODUCT

Imaavy 185 mg/mL concentrate for solution for infusion
nipocalimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial of 6.5 mL contains 1200 mg of nipocalimab (185 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: arginine hydrochloride, histidine, histidine monohydrochloride monohydrate, methionine, E433, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

concentrate for solution for infusion
1200 mg/6.5 mL
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use after dilution.

Read the package leaflet before use.

For single use only.

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

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1989/002

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 (1200 mg)

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

Imaavy 185 mg/mL sterile concentrate
nipocalimab
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

1200 mg/6.5 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Imaavy 185 mg/mL concentrate for solution for infusion
nipocalimab

▼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 Imaavy is and what it is used for

What Imaavy is
Imaavy contains the active substance nipocalimab. Nipocalimab binds to a protein in the body called FcRn. By binding to FcRn, nipocalimab decreases the level of IgG autoantibodies. IgG autoantibodies are proteins of the immune system that attack parts of the person's own body by mistake.

What Imaavy is used for
Imaavy is used together with standard therapy to treat adult and adolescent patients aged 12 years and older 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 certain proteins on the 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, Imaavy 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 Imaavy

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

Warnings and precautions

Infusion reactions and allergic reactions

Imaavy contains a protein that can cause reactions such as headache, nausea, rash, tiredness, chills, reddening of the skin and dizziness in some people. You will be monitored for signs of an infusion or serious allergic (anaphylactic) reaction during and for at least 30 minutes after treatment. Signs of a serious allergic reaction include: 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. If you experience any of these symptoms tell your doctor immediately.

Infections

Imaavy treatment may reduce your natural resistance to infections. Before starting or during treatment with this medicine, inform your doctor if you have any symptoms of infection (such as fever, chills or shivering, cough or sore throat).

Imaavy treatment may allow herpes zoster infection (shingles) to come back. Tell your doctor if you get a painful skin rash with blisters as these can be signs of shingles.

Additional monitoring tests

Your doctor will carry out blood tests to check your blood fat (cholesterol) levels after Imaavy treatment (see section 4).

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 (within a couple of weeks).

Children
Imaavy is not for use in children less than 12 years of age, because it has not been studied in these patients.

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

Taking Imaavy with other medicines such as therapeutic antibodies or immunoglobulins may decrease their effectiveness. Other interventions such as plasma exchange (plasmapheresis), may impair the effect of Imaavy.

Pregnancy, breast-feeding and fertility
There is limited information about the use of Imaavy in pregnancy or while breast-feeding. 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
Imaavy is not expected to influence the ability to drive or use machines.

Imaavy contains polysorbate
This medicine contains 0.97 mg (300 mg vial) or 3.9 mg (1200 mg vial) of polysorbate 80 in each single-use vial which is equivalent to 0.60 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Imaavy

The treatment will be given by your doctor or other healthcare provider.

What dose of Imaavy you will receive and how often
The dose you receive will depend on your bodyweight and will be given directly into your blood as an infusion (drip) given into a vein every 2 weeks.

If you receive more Imaavy than you should
The dose of this medicine will be carefully calculated by your doctor. If you suspect that you have accidentally been given a higher dose of Imaavy than prescribed, please contact your doctor for advice.

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

If you stop using Imaavy
Interrupting or stopping treatment with Imaavy may cause your gMG symptoms to come back. Please speak to your doctor before stopping Imaavy. Your doctor will discuss the possible side effects and risks with you. Your doctor may 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 Imaavy with you prior to treatment.

Very common (may affect more than 1 in 10 people)
- high level of lipids (fats) or cholesterol in the blood
- decreases in the level of 'albumin' (a protein) in the blood
- muscle spasms
- swollen hands, ankles or feet (peripheral oedema)

Common (may affect up to 1 in 10 people)
- urinary tract infection (may cause pain or a burning sensation during urination)
- chest infection (such as pneumonia or bronchitis)
- shingles (herpes zoster virus infection)
- difficulty sleeping (insomnia)
- feeling dizzy
- diarrhoea
- belly (abdominal) pain
- nausea
- fever

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 Imaavy

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 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 Imaavy contains
- The active substance is nipocalimab.
  - Each vial of 1.62 mL contains 300 mg of nipocalimab (185 mg/mL).
  - Each vial of 6.5 mL contains 1200 mg of nipocalimab (185 mg/mL).

- The other ingredients are: arginine hydrochloride, histidine, histidine monohydrochloride monohydrate, methionine, polysorbate 80 (E433), sucrose, and water for injections.

What Imaavy looks like and contents of the pack
Imaavy is presented as a sterile concentrate for solution for infusion (300 mg or 1200 mg in a vial – pack size of 1).

Imaavy is a liquid. It is colourless to slightly brownish, clear to slightly opalescent.

Marketing Authorisation Holder
Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Manufacturer
Janssen Biologics B.V.
Einsteinweg 101
Leiden, 2333 CB
The Netherlands

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

België/Belgique/Belgien
Janssen-Cilag NV
Tel/Tél: +32 14 64 94 11
janssen@jacbe.jnj.com

България
„Джонсън & Джонсън България” ЕООД
Тел.: +359 2 489 94 00
jjsafety@its.jnj.com

Česká republika
Janssen-Cilag s.r.o.
Tel: +420 227 012 227

Danmark
Janssen-Cilag A/S
Tlf.: +45 4594 8282
jacdk@its.jnj.com

Deutschland
Janssen-Cilag GmbH
Tel: 0800 086 9247 / +49 2137 955 6955
jancil@its.jnj.com

Eesti
UAB "JOHNSON & JOHNSON" Eesti filiaal
Tel: +372 617 7410
ee@its.jnj.com

Ελλάδα
Janssen-Cilag Φαρμακευτική Μονοπρόσωπη A.E.B.E.
Τηλ: +30 210 80 90 000

España
Janssen-Cilag, S.A.
Tel: +34 91 722 81 00
contacto@its.jnj.com

France
Janssen-Cilag
Tél: 0 800 25 50 75 / +33 1 55 00 40 03
medisource@its.jnj.com

Hrvatska
Johnson & Johnson S.E. d.o.o.
Tel: +385 1 6610 700
jjsafety@JNJCR.JNJ.com

Ireland

Lietuva
UAB "JOHNSON & JOHNSON"
Tel: +370 5 278 68 88
lt@its.jnj.com

Luxembourg/Luxemburg
Janssen-Cilag NV
Tél/Tel: +32 14 64 94 11
janssen@jacbe.jnj.com

Magyarország
Janssen-Cilag Kft.
Tel.: +36 1 884 2858
janssenhu@its.jnj.com

Malta
AM MANGION LTD
Tel: +356 2397 6000

Nederland
Janssen-Cilag B.V.
Tel: +31 76 711 1111
janssen@jacnl.jnj.com

Norge
Janssen-Cilag AS
Tlf: +47 24 12 65 00
jacno@its.jnj.com

Österreich
Janssen-Cilag Pharma GmbH
Tel: +43 1 610 300

Polska
Janssen-Cilag Polska Sp. z o.o.
Tel.: +48 22 237 60 00

Portugal
Janssen-Cilag Farmacêutica, Lda.
Tel: +351 214 368 600

România
Johnson & Johnson România SRL
Tel: +40 21 207 1800

Slovenija

Janssen Sciences Ireland UC
Tel: 1 800 709 122
medinfo@its.jnj.com

Ísland
Janssen-Cilag AB
c/o Vistor ehf.
Sími: +354 535 7000
janssen@vistor.is

Italia
Janssen-Cilag SpA
Tel: 800.688.777 / +39 02 2510 1
janssenita@its.jnj.com

Κύπρος
Βαρνάβας Χατζηπαναγής Λτδ
Τηλ: +357 22 207 700

Latvija
UAB "JOHNSON & JOHNSON" filiāle Latvijā
Tel: +371 678 93561
lv@its.jnj.com

Johnson & Johnson d.o.o.
Tel: +386 1 401 18 00
JNJ-SI-safety@its.jnj.com

Slovenská republika
Johnson & Johnson, s.r.o.
Tel: +421 232 408 400

Suomi/Finland
Janssen-Cilag Oy
Puh/Tel: +358 207 531 300
jacfi@its.jnj.com

Sverige
Janssen-Cilag AB
Tfn: +46 8 626 50 00
jacse@its.jnj.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/en.

The following information is intended for healthcare professionals only:

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

1. How is Imaavy supplied?

The vials contain:

- 300 mg of nipocalimab in 1.62 mL concentrate for solution for infusion OR
- 1200 mg of nipocalimab in 6.5 mL concentrate for solution for infusion.

The concentration is 185 mg nipocalimab/mL in all vials.

2. Before administration

Imaavy 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 Imaavy required is based on the patient's bodyweight at the recommended initial single dose of 30 mg/kg or maintenance dose of 15 mg/kg.
- The volume of concentrate required is calculated from the concentration of 185 mg/mL. Each vial contains 300 mg or 1200 mg of nipocalimab.
- The number of vials needed is calculated from the volume of concentrate.

Table 1. Formula

Step 1 – Calculate the dose (mg)	30 mg/kg (initial single dose) or 15 mg/kg (maintenance dose) x weight (kg)
Step 2 – Calculate the volume of concentrate (mL)	dose (mg) ÷ 185 mg/mL
Step 3 – Calculate the number vials	volume of concentrate (mL) ÷ 1.62 or 6.5 mL

3. Preparation and administration

- Do not administer as an intravenous push or bolus injection.
- Only administer via intravenous infusion as described below.

Preparation

- Check that the solution in each vial is colourless to slightly brownish, clear to slightly opalescent, and free of visible particles. Do not use if visible particles are present or if the solution is discoloured (other than colourless to slightly brownish). Do not shake the vials.
- Gently withdraw the calculated volume of concentrate from the vial(s). Discard any unused portion of the vials.
- Dilute the total volume of the withdrawn concentrate by adding it to an infusion bag containing 250 mL sodium chloride 9 mg/mL (0.9%) solution for infusion for patients who weigh 40 kg or more, or 100 mL sodium chloride 9 mg/mL (0.9%) solution for infusion for patients who weigh less than 40 kg. Only use infusion bags made of polyolefin, polypropylene, or polyvinylchloride.
- Gently invert the infusion bag at least 10 times to mix the solution. Do not shake.
- Verify that a uniform solution has been achieved by visual inspection. Do not use if particulate matter or discolouration are present.

Administration

- Administer the diluted solution by intravenous infusion using an infusion set with an in-line or add-on, sterile, non-pyrogenic, low protein-binding filter made of polyethersulfone or polysulfone (pore size

0.2 micrometre or less). Administration sets must be made of either polybutadiene, polyethylene, polyurethane, polypropylene, or polyvinylchloride.

- Do not infuse the diluted concentrate concomitantly in the same intravenous line with other agents.
- Administer the infusion intravenously over approximately 30 minutes for the initial dose (30 mg/kg) and approximately 15 minutes for subsequent doses (15 mg/kg).
- If an adverse reaction occurs during administration, the infusion may be slowed or stopped at the discretion of the heatlthcare professional.
- From a microbiological point of view, unless the method of dilution precludes the risks of microbial contamination, the prepared diluted solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. If immediate administration is not possible, the diluted solution can be refrigerated for up to 24 hours at 2 °C to 8 °C, with an additional 12 hours of storage at room temperature, including infusion time, at 15 °C to 30 °C. Do not freeze.

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.