European Union Risk Management Plan
IMAAVY (nipocalimab)

Details of this RMP Submission

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Rationale for Submitting an Updated RMP

Not applicable

Summary of Significant Changes in this RMP

Not applicable

Other RMP Versions Under Evaluation

Version number	Date submitted	Procedure number
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Version number: Not applicable
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QPPV Details

QPPV Name: Dr. Laurence Oster-Gozet, PharmD, PhD
QPPV Oversight Declaration: The QPPV has reviewed and approved this RMP (electronic signature on file, as applicable).

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ABBREVIATIONS

AChR	acetylcholine receptor
ADR	adverse drug reaction
AE	adverse event
AESI	adverse event of special interest
AI	artificial intelligence
ATC	anatomical therapeutic chemical
BMI	body mass index
C5	complement component 5 protein
CHMP	Committee for Medicinal Products for Human Use
CHO	Chinese hamster ovary
CI	confidence interval
CNS	central nervous system
COVID-19	coronavirus 2019
CV	cardiovascular
DNA	deoxyribonucleic acid
EEA	European Economic Area
EOS-HDFN	early onset severe hemolytic disease of the fetus and newborn
EU	European Union
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ePPND	enhanced pre- and postnatal development
Fc	fragment crystallizable
FcRn	neonatal Fc receptor
FOIA	Freedom of Information Act
GD	gestation days
gMG	generalized myasthenia gravis
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IgA	immunoglobulin A
IgE	immunoglobulin E
IgG	immunoglobulin G
IgM	immunoglobulin M
IRR	infusion-related reaction
IV	intravenous(ly)
IVIg	intravenous immune globulin
LCV	lymphocryptovirus
LDL	low-density lipoprotein
LPLV	last participant last visit
LRP4	low-density lipoprotein receptor 4
LTE	long-term extension
M281	nipocalimab
mAb	monoclonal antibody
MACE	major adverse cardiovascular event(s)
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
MuSK	muscle-specific tyrosine kinase
NK	natural killer

OLE	open-label extension
PASS	postauthorization safety study
PL	patient leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
QPPV	Qualified Person for Pharmacovigilance
q2w	every 2 weeks
q4w	every 4 weeks
RMP	risk management plan
SAE	serious adverse event
SmPC	summary of product characteristics
SMQ	standardized MedDRA queries
SOC	system organ class
TOIQ	topic of interest questionnaire
US	United States

PART I: PRODUCT(S) OVERVIEW

Active substance(s) (INN or common name)	Nipocalimab
Pharmacotherapeutic group(s) (ATC Code)	Immunosuppressants, monoclonal antibodies (L04AL03)
Marketing Authorization Applicant	Janssen-Cilag International, NV
Medicinal products to which the RMP refers	1
Invented name(s) in the EEA	IMAAVY
Marketing authorization procedure	Centralized
Brief description of the product	**Chemical class** Nipocalimab is a fully human IgG1 mAb. **Summary of mode of action** Nipocalimab specifically targets the IgG Fc binding site of FcRn with high specificity and high affinity at both neutral (extracellular) and acidic (intracellular) pH 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. Nipocalimab reduces the placental transfer of IgG from mother to fetus. **Important information about its composition** Nipocalimab is a fully human IgG1 mAb produced in CHO cells by recombinant DNA technology.
Reference to the Product Information	Module 1.3.1 Summary of Product Characteristics, Labelling and Package Leaflet
Indication(s) in the EEA	**Current** <u>Generalized Myasthenia Gravis</u> IMAAVY is indicated as an add-on to standard therapy for the treatment of gMG in adult and adolescent patients aged 12 years and older who are anti-AChR or anti-MuSK antibody positive.
	Proposed Not applicable
Dosage(s) in the EEA	**Current** <u>Generalized Myasthenia Gravis</u> The recommended dose regimen of IMAAVY is an initial dose of 30 mg/kg administered IV, followed by a maintenance dose of 15 mg/kg administered q2w thereafter.
	Proposed Not applicable
Pharmaceutical form(s) and strength(s)	**Current** Sterile concentrate for solution for infusion containing 185 mg/mL nipocalimab. One vial of 1.62 mL contains 300 mg of nipocalimab, and one vial of 6.5 mL contains 1,200 mg of nipocalimab.

	Proposed Not applicable	
Is/will the product be subject to additional monitoring in the EU?	☒Yes	☐No

PART II: SAFETY SPECIFICATION

Module SI: Epidemiology of the Indication(s) and Target Population(s)

Indication: Generalized Myasthenia Gravis

MG is a rare, heterogeneous, IgG autoantibody-mediated neuromuscular disease characterized by fluctuating muscle weakness and fatigability due to pathogenic IgG-mediated disruption of cholinergic transmission at the neuromuscular junction (Gilhus 2015). Patients are grouped according to the presence of antibodies, symptoms, age at onset, and thymus pathology (Gilhus 2019). The majority of MG cases (85%) present as gMG (Gilhus 2019), which affects ocular, bulbar, proximal extremity, neck, and respiratory muscles, fluctuates during the day, and worsens with fatigue, repetitive activities, heat, infection, and stress (Grob 2008; Scherer 2005). The remaining MG cases (15%) present as ocular MG, which affects only oculomotor muscles (Gilhus 2019). Of those, 53% to 80% progress to gMG within 2 years of diagnosis (Kerty 2014; Kupersmith 2003).

Incidence

The annual incidence rate of MG ranges from 0.8 to 1 case per 100,000 individuals (Gilhus 2016). In Europe, studies have reported incidence rates between 0.63 and 4.6 cases per 100,000 person-years (Andersen 2014a; Carey 2021; Maddison 2019; Martinka 2018; Mevius 2023; Santos 2016; Westerberg 2020; Zieda 2018). Approximately 10% to 15% of new cases of MG are diagnosed in the adolescent population (12 to <18 years of age) (Evoli 1998; Evoli 2010; Finnis 2011).

Prevalence

The global prevalence of MG is 15 to 25 cases per 100,000 individuals (Gilhus 2019). A meta-analysis of 63 studies reported an estimated global prevalence of 12.4 (95% CI: 10.6-14.5) cases per 100,000 individuals (Salari 2021). Prevalence varies by geographical location, with the prevalence in Europe estimated at 10 (95% CI: 8.2-12.2) cases per 100,000 individuals (Salari 2021). Studies in Europe have reported prevalence rates between 11.2 and 36.1 cases per 100,000 individuals (Santos 2016; Westerberg 2020).

Demographics of the Population in Generalized Myasthenia Gravis and Risk Factors for the Disease

Women tend to have an earlier age of onset of MG than men (Bubuioc 2021) and a greater incidence overall (Ye 2024). Early-onset MG disproportionately impacts women of reproductive age (Grob 2008; Rodrigues 2024). There is a bimodal age distribution in the incidence of MG in women, with one peak at about 30 years of age and another peak around 50 years of age (Dresser 2021). Conversely, for men, there is a steady increase in incidence with age, with the highest incidence between the ages of 60 and 89 years (Dresser 2021). A similar pattern of incidence by age and sex has been reported in several European countries (Carr 2010). The highest prevalence of all age groups is in males aged 65 years and older (Ye 2024). Juvenile (children <18 years old) MG has been reported at an incidence rate of 0.1 to 0.5 cases per

100,000 person-years in Europe (McGrogan 2010). Similar to adults, among pediatric MG patients, girls are affected more often than boys (Parr 2014).

MG occurs in people of all races and ethnicities (Dresser 2021). The age of onset is higher in the white population than in non-white populations (Bubuioc 2021). In the US, the incidence is highest in the non-Hispanic white population and lowest in the Hispanic population, although the prevalence is highest in the black population (Ye 2024). There is currently no race-specific information from Europe. Early-onset MG is reported more often in Asian populations than in other ethnicities (Huang 2013).

Viral infection has been suggested as a precipitating event for MG (Gilhus 2018; Gilhus 2019), as have asthma, cancer, immunotherapy, rheumatic disease, and other autoimmune diseases (Gilhus 2019; Yingchoncharoen 2021). There are also genetic risk factors, with human leukocyte antigen genes having the strongest association with MG (Gilhus 2018). Considering the differential sex ratio in early- and late-onset MG and that young females are disproportionately affected, it has been hypothesized that sex hormones play a role in MG etiology (Gilhus 2018; Gilhus 2019).

Main Existing Treatment Options

There is no cure for gMG, and most patients require lifelong treatment (Barnett 2019; Dalakas 2019; Farmakidis 2018; Gilhus 2019; Mantegazza 2018; Morren 2020). Given the similar pathophysiology between pediatric and adult patients with gMG, pediatric MG treatment modalities have largely been extrapolated from experience with adult patients (Finnis 2011).

Treatments used to manage gMG include the following:

- Symptomatic treatment: Acetylcholinesterase inhibitors may provide some relief in mild cases of gMG (Sanders 2016).
- Surgical intervention and immunosuppressive agents: Most patients with moderate to severe gMG require thymectomy (most effective in anti-AChR positive patients) and/or treatment with standard-of-care therapies (corticosteroids, azathioprine, mycophenolate, cyclosporine, and tacrolimus) (Barnett 2019).
- Other therapeutic modalities: Both plasma exchange and immunoadsorption, aimed at removing autoantibodies, and IVIg, which produces immunomodulatory effects, are typically used for patients with a myasthenic crisis.
- Newer agents: C5 complement inhibitors (eculizumab, ravulizumab, zilucoplan) prevent the formation of the membrane attack complex and reduce damage caused by complement-fixing AChR antibodies (Dhillon 2018). FcRn blockers (efgartigimod, and rozanolixizumab) reduce circulating IgG, including pathogenic IgG autoantibodies.

As early-onset gMG in adults disproportionately impacts women of reproductive age (Grob 2008; Rodrigues 2024) and most long-term immunosuppressants have stringent requirements regarding contraceptive use, therapies compatible with pregnancy are lacking.

Natural History of Generalized Myasthenia Gravis in the Untreated Population, Including Mortality and Morbidity

MG predominantly manifests as muscle weakness that typically worsens with repeated muscle use such that function is usually the best in the morning, with more pronounced weakness later in the day (Gilhus 2019). Patients with MG are classified based on the type of autoantibodies measured in serum (ie, AChR, MuSK, and LRP4). Those without measurable autoantibodies are classified as having seronegative MG. Antibody classification is important, as patients may have different clinical courses and responses to treatment depending on the type of antibody involved (Hehir 2022).

Typical symptoms of MG are drooping of the upper eyelid, double vision, reduced facial expression, and speech and swallowing weakness (Gilhus 2019). Among patients who initially present with ocular MG, 53% to 80% progress to gMG within 2 years (Kerty 2014; Kupersmith 2003). Many patients experience at least 1 exacerbation of the disease, which involves the development of a major physical disability that can involve respiratory failure. Exacerbations can be triggered by infection, changes in treatments, use of aggravating medications, and emotional distress (Gelinas 2022). Approximately 15% to 20% of patients experience a myasthenic crisis, defined by respiratory insufficiency that requires the use of invasive or noninvasive ventilation, usually within the first 2 to 3 years of the disease course (Claytor 2023). In over 90% of patients with MG, the distribution and severity of weakness and the general course of the disease are determined within the first 1 or 2 years after onset; subsequent improvement typically occurs in most patients (Grob 2008). With adequate treatment, most patients can obtain a stable condition with only mild muscle weakness, although symptoms can fluctuate over time. In 10% to 30% of patients, MG is refractory to conventional immunosuppression, with persistent and disabling weakness despite treatment (Gilhus 2019).

Mortality from MG ranges from 5% to 9% (Bubuioc 2021). Estimates of annual all-cause mortality for patients with MG in various European countries range from 2.6% to 5.7% (Mevius 2023; Santos 2016; Sobieszczuk 2022). A study in Portugal provided an MG-specific mortality rate of 0.5% (Santos 2016). The mortality rate is greater in males than in females (Bubuioc 2021). A study in Poland reported all-cause mortality rates for MG as 3.9% to 4.8% for men and 2.4% to 3.0% for women (Sobieszczuk 2022).

Important Comorbidities

Common comorbidities in patients with MG include thymic abnormalities; other autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, Hashimoto thyroiditis, Graves' disease, and pernicious anemia; respiratory diseases; osteoporosis; cardiomyositis; diabetes; dyslipidemia; depression; infection; and hypertension (Andersen 2014b; Gilhus 2015; Klimiec-Moskal 2022; Tanovska 2018; Yingchoncharoen 2021).

PART II: SAFETY SPECIFICATION

Module SII: Nonclinical Part of the Safety Specification

Key Safety Findings From Nonclinical Studies	Relevance to Human Usage
Toxicity	
Single and repeat-dose toxicity	
Nipocalimab was tested in cynomolgus monkeys for 2, 4, and 26 weeks at weekly doses up to 300 mg/kg IV (up to 44-fold higher than the exposure in humans dosed at 15 mg/kg q2w). Nipocalimab was well tolerated, with no target organ toxicity. There were treatment-related, dose-dependent, reversible, and non-adverse decreases in serum albumin and increases in cholesterol concentrations for which the mechanism is unclear.	Small magnitude of changes in albumin and cholesterol observed nonclinically, even at the highest dose tested, would be monitorable, and expected to be reversible in humans.
Reproductive and developmental toxicity	
In a 26-week study in male and female cynomolgus monkeys, no effects of nipocalimab on reproductive organs were noted upon histopathological assessment following weekly doses up to 300 mg/kg IV (up to 44-fold higher than the exposure in humans dosed at 15 mg/kg q2w).	Nonclinical findings do not suggest that nipocalimab adversely affects fertility, fetal development, or infant development. Animal immunogenicity is not predictive in humans.
In an ePPND study, cynomolgus monkeys received nipocalimab from the end of organogenesis (GD45) through parturition (approximately GD160) at weekly doses of 100 or 300 mg/kg. Nipocalimab showed no effect on fetal or infant losses or on fetal or infant development. Of 25 placentas available for evaluation from nipocalimab-exposed pregnancies assigned to delivery (Phase 2), 4 showed large, central placental infarctions and thrombosis of maternal spiral arteries; pregnancy outcomes included 1 healthy infant and 3 abortions/stillbirths. The placental infarctions may be related to animal immunogenicity against human biological drugs (Chellman 2025).	
Genotoxicity	
Genotoxicity studies are not applicable for biotechnology-derived pharmaceuticals such as nipocalimab because their large molecular size precludes them from diffusing into cells and interacting with DNA and other chromosomal material (ICH guideline S6 [R1]: Preclinical safety evaluation of biotechnology-derived pharmaceuticals).	Nipocalimab is not expected to be genotoxic in humans.

Key Safety Findings From Nonclinical Studies	Relevance to Human Usage
Carcinogenicity	
Carcinogenicity studies were not conducted due to the lack of cross-reactivity of nipocalimab with rodent FcRn. Consistent with ICH guideline S6 (R1), a weight-of-evidence approach was taken to assess the carcinogenic potential of nipocalimab. Nipocalimab does not affect the biosynthesis of IgG, nor does it selectively remove any specific IgGs. FcRn is not a signaling receptor and does not affect other immune cells, including T cells and NK cells. The potential antigen or immune complex presentation function of FcRn does not appear to play a major role in immune surveillance, as inhibition or ablation of FcRn does not abolish T-cell-dependent antibody responses. The overall nipocalimab toxicology program lacked any proliferative signals, and the completed nipocalimab clinical trials to date have not identified any malignancies linked to nipocalimab. No evidence was found in the literature to indicate a direct relationship between FcRn inhibition and an increased risk for carcinogenicity, and approved FcRn inhibitors have not shown a carcinogenic risk potential.	Nipocalimab is not expected to be carcinogenic in humans.
Safety pharmacology	
Cardiovascular system (including potential effect on the QT interval)	
In the repeat-dose toxicity studies in cynomolgus monkeys, no effects on CV safety were observed.	Nonclinical findings do not suggest that nipocalimab adversely affects the CV system.
Nervous system	
In the repeat-dose toxicity studies in cynomolgus monkeys, no effects on the CNS were observed.	Nonclinical findings do not suggest that nipocalimab adversely affects the CNS.

Key Safety Findings From Nonclinical Studies	Relevance to Human Usage
Other toxicity-related information or data	
Immunotoxicology Nipocalimab was evaluated in an 8-week IV immunotoxicity study in cynomolgus monkeys at doses up to 300 mg/kg/wk. Other than expected decreases in serum IgG, no infections and no effects on immune cell population, T-cell-dependent antibody responses (except the decrease in magnitude of IgG), or overall innate or adaptive immunity were noted. In a 26-week study in cynomolgus monkeys, self-limited and recoverable maximal reductions in serum IgG concentrations of approximately 60% were observed. No increases in infections or neoplasms compared with controls occurred, except for a single case of possible LCV recrudescence involving a male monkey that received high-dose nipocalimab (ie, 300 mg/kg/week) and was terminated on Study Day 20 after 2 doses due to possible LCV recrudescence and secondary inflammation. This isolated incident, which was considered unlikely to be related to nipocalimab, occurred relatively early in the 26-week study. No similar incident was observed in any of the other cynomolgus monkey toxicology studies with the same dose levels and 4-week or longer treatment periods.	Nonclinical findings do not suggest an increased risk of infection.

PART II: SAFETY SPECIFICATION

Module SIII: Clinical Trial Exposure

SIII.1. Overview of Clinical Trials in the RMP

Data from the following clinical trials are included in this RMP:

Generalized Myasthenia Gravis

- **MOM-M281-011:** A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of nipocalimab administered to adults with generalized myasthenia gravis. The trial included adult participants with gMG who were inadequately controlled with standard-of-care therapy. Participants received an initial nipocalimab dose of 30 mg/kg IV, followed by 15 mg/kg q2w IV. Participants who completed the double-blind phase could enter an OLE phase, which evaluated long-term safety and efficacy at a dose of 15 mg/kg q2w IV. Initially, there was a 30 mg/kg q4w option after Week 24. However, Protocol Amendment 2 streamlined the visit schedule and treatment administration to allow only q2w dosing in the OLE. The option to receive 30 mg/kg q4w was therefore removed for operational considerations and was not related to any safety or efficacy considerations. Twenty-four participants who switched to 30 mg/kg q4w dosing in the OLE were transitioned back to the 15 mg/kg q2w regimen following implementation of Protocol Amendment 2. The LPLV of the double-blind phase of the trial was 09 November 2023. The OLE phase of the trial is ongoing.
- **MOM-M281-004:** A Phase 2, multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of nipocalimab administered to adults with generalized myasthenia gravis. The trial compared nipocalimab to placebo in adult participants with gMG who had an insufficient clinical response to ongoing, stable, standard-of-care therapy. Participants were randomized to receive nipocalimab 5 mg/kg q4w IV, 30 mg/kg q4w IV, a single dose of 60 mg/kg IV, or 60 mg/kg q2w IV. Participants who completed the double-blind trial could enroll in an OLE trial, MOM-M281-005.
- **MOM-M281-005:** An OLE study of MOM-M281-004 to evaluate the safety, tolerability, and efficacy of nipocalimab administered to adults with generalized myasthenia gravis. Participants received an initial nipocalimab dose of 30 mg/kg q4w IV. Thereafter, the dose and/or frequency of administration could be individually adjusted. All participants received either 30 mg/kg or 60 mg/kg nipocalimab on a q2w or q4w basis. The trial was paused in April 2020 and subsequently terminated in December 2020 due to the COVID-19 pandemic, after which participants were given the option to enroll in the OLE phase of the Phase 3 gMG trial MOM-M281-011.
- **80202135MYG2001:** An open-label, uncontrolled, multicenter study to evaluate the pharmacokinetics, pharmacodynamics, safety, and activity of nipocalimab in children aged 2 to less than 18 years with generalized myasthenia gravis. In the active treatment phase, Cohort 1 participants (children aged 12 to <18 years) receive an initial nipocalimab dose of 30 mg/kg IV, followed by 15 mg/kg q2w IV. After completion of the active treatment phase, all participants have the option to enroll in an LTE phase at a dose of either 15 mg/kg q2w IV or 30 mg/kg q4w IV. At the time of the data lock point (23 August 2024), Cohort 2 participants (children aged 2 to <12 years) had not yet been enrolled. The trial is ongoing.

SIII.2. Clinical Trial Exposure

Clinical trial exposure to nipocalimab is presented in the following tables by duration of exposure, by age group and sex, by dose, and by race.

Exposure in Randomized, Blinded Clinical Trials

The tables below present nipocalimab exposure from the following randomized, blinded clinical trial:

- gMG: MOM-M281-011 (double-blind period only)

Note: Trial MOM-M281-004 is not included in the randomized, blinded clinical trials population because participants enrolled in this trial were not treated with the same dose regimen as was used in the Phase 3 gMG trial MOM-M281-011, which is the recommended dose regimen (ie, an initial single nipocalimab dose of 30 mg/kg IV, followed by 15 mg/kg q2w IV). This recommended dose regimen was not yet determined at the time the Phase 2 trial was conducted.

Table SIII.1: Nipocalimab Exposure in Randomized, Blinded Clinical Trials by Duration of Exposure

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Duration of Exposure		
≤3 months	10 (10.2%)	0.9
>3 to <6 months	88 (89.8%)	37.3
Total	98	38.2

The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trial MOM-M281-011 (double-blind period only).
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Table SIII.2: Nipocalimab Exposure in Randomized, Blinded Clinical Trials by Age Group and Sex

	Male		Female	
	Subjects, n (%)	Subject-Years	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]				
Age Group				
≥18 to <45 Years	8 (25.0%)	3.4	19 (28.8%)	7.3
≥45 to <65 Years	14 (43.8%)	5.9	32 (48.5%)	12.5
≥65 to <75 Years	7 (21.9%)	2.7	10 (15.2%)	3.5
≥75 Years	3 (9.4%)	1.0	5 (7.6%)	1.8
Total	32	13.0	66	25.1

The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trial MOM-M281-011 (double-blind period only).
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Table SIII.3: Nipocalimab Exposure in Randomized, Blinded Clinical Trials by Dose

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Dose		
30 mg/kg at Week 0 and 15 mg/kg q2w	98 (100.0%)	38.2
Total	98	38.2

The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trial MOM-M281-011 (double-blind period only).
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Table SIII.4: Nipocalimab Exposure in Randomized, Blinded Clinical Trials by Race

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Race		
White	66 (67.3%)	25.6
Black or African American	1 (1.0%)	0.4
Asian	28 (28.6%)	10.9
Other	3 (3.1%)	1.3
Total	98	38.2

The duration of exposure includes days on which subjects did not actually take study treatment.
Note: 'Other' includes American Indian or Alaska Native, Multiple, Not Reported, Other, and Unknown.
[a] Includes Trial MOM-M281-011 (double-blind period only).

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Exposure in All Clinical Trials

The tables below present nipocalimab exposure from all clinical trials:

- gMG: MOM-M281-011, MOM-M281-004, and MOM-M281-005 in the adult population and 80202135MYG2001 (Cohort 1) in the pediatric population.

Table SIII.5: Nipocalimab Exposure in All Clinical Trials by Duration of Exposure

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Duration of Exposure		
≤3 months	40 (16.0%)	5.3
>3 to <6 months	26 (10.4%)	10.6
≥6 to <12 months	51 (20.4%)	36.9
≥12 to <18 months	55 (22.0%)	64.6
≥18 to <24 months	41 (16.4%)	67.7
≥24 months	37 (14.8%)	84.4
Total	250	269.6
gMG Pediatric Trials[b]		
Duration of Exposure		
≤3 months	0	-
>3 to <6 months	2 (25.0%)	0.8
≥6 to <12 months	2 (25.0%)	1.4
≥12 to <18 months	2 (25.0%)	2.6
≥18 to <24 months	2 (25.0%)	3.8
≥24 months	0	-
Total	8	8.5

The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.
[b] Includes Trial 80202135MYG2001 (Cohort 1).

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Table SIII.6: Nipocalimab Exposure in All Clinical Trials by Age Group and Sex

	Male		Female	
	Subjects, n (%)	Subject-Years	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]				
Age Group				
≥18 to <45 Years	21 (22.1%)	25.8	56 (36.8%)	61.2
≥45 to <65 Years	40 (42.1%)	44.2	61 (40.1%)	72.8
≥65 to <75 Years	21 (22.1%)	21.8	23 (15.1%)	20.7
≥75 Years	13 (13.7%)	12.2	12 (7.9%)	10.6
Total	95	104.1	152	165.2
gMG Pediatric Trials[b]				
Age Group				
≥12 to <18 Years	1 (100.0%)	1.8	7 (100.0%)	6.7
Total	1	1.8	7	6.7

The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.
[b] Includes Trial 80202135MYG2001 (Cohort 1).
Note: If subjects participated in more than 1 trial, the first available age information is presented.
Note: 3 subjects with missing age information from Trial MOM-M281-004 were excluded from this table.

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Table SIII.7: Nipocalimab Exposure in All Clinical Trials by Dose

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Dose		
30 mg/kg at Week 0 and 15 mg/kg q2w	98 (39.2%)	124.0
5 mg/kg/q4w	14 (5.6%)	2.1
30 mg/kg/q4w	42 (16.8%)	11.2
60 mg/kg/q2w	14 (5.6%)	2.1
60 mg/kg single dose	13 (5.2%)	1.8
15 mg/kg/q2w	107 (42.8%)	96.7
Flex dose in OLE	29 (11.6%)	31.6
Total[b]	250	269.6
gMG Pediatric Trials[c]		
Dose		
30 mg/kg at Week 0 and 15 mg/kg q2w	8 (100.0%)	5.0
Flex dose in LTE	4 (50.0%)	3.5
Total[b]	8	8.5

Flex dose level includes 15 mg/kg/q2w, 30 mg/kg/q4w and 60 mg/kg/q2w.
The duration of exposure includes days on which subjects did not actually take study treatment.
[a] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.
[b] Each subject is only counted once for Total.
[c] Includes Trial 80202135MYG2001 (Cohort 1).

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Table SIII.8: Nipocalimab Exposure in All Clinical Trials by Race

	Subjects, n (%)	Subject-Years
gMG Adult Trials[a]		
Race		
White	184 (73.6%)	204.2
Black or African American	4 (1.6%)	3.3
Asian	53 (21.2%)	55.0
Other	9 (3.6%)	7.1
Total	250	269.6
gMG Pediatric Trials[b]		
Race		
White	0	-
Black or African American	1 (12.5%)	1.5
Asian	5 (62.5%)	6.0
Other	2 (25.0%)	1.1
Total	8	8.5

The duration of exposure includes days on which subjects did not actually take study treatment.
Note: 'Other' includes American Indian or Alaska Native, Multiple, Not Reported, Other, and Unknown.
[a] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.
[b] Includes Trial 80202135MYG2001 (Cohort 1).

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PART II: SAFETY SPECIFICATION

Module SIV: Populations Not Studied in Clinical Trials

SIV.1. Exclusion Criteria in Pivotal Clinical Trials Across the Development Program

Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program	
Criterion 1	**Confirmed or suspected clinical immunodeficiency syndrome not related to treatment of gMG or a family history of congenital or hereditary immunodeficiency.**
Reason for being an exclusion criterion	Nipocalimab causes a reduction in IgG, which may increase the risk of infection if used in patients with underlying primary immune deficiencies.
Included as missing information?	No
Rationale if not included as missing information	Serious infections is an important potential risk for nipocalimab.
Criterion 2	**Actively undergoing radiation or chemotherapy for an unresected malignant thymoma.**
Reason for being an exclusion criterion	MG may present as a thymoma-associated paraneoplastic neurological disease. The standard-of-care for patients with MG and unresected malignant thymoma is surgical resection, followed by radiation and/or chemotherapy. Inclusion of MG patients with an unresected malignant thymoma could confound the safety and efficacy evaluations of nipocalimab.
Included as missing information?	No
Rationale if not included as missing information	Patients with unresected malignant thymoma with paraneoplastic MG are not candidates for nipocalimab therapy.
Criterion 3	**Current malignancy or a history of malignancy within 3 years before screening, with the exception of localized basal cell carcinoma and/or squamous cell carcinoma that has been adequately treated with no evidence of recurrence for at least 3 months before the first study intervention administration or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first study intervention administration.**
Reason for being an exclusion criterion	Because mutagenesis and carcinogenicity studies have not been conducted with nipocalimab, patients with malignancy or a recent history of malignancy were excluded from nipocalimab clinical trials as a precautionary measure.
Included as missing information?	No
Rationale if not included as missing information	The weight of evidence suggests that nipocalimab is not expected to be carcinogenic in humans (see Module SII: Nonclinical Part of the Safety Specification - Carcinogenicity).

Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program	
Criterion 4	**Known allergies, hypersensitivity, or intolerance to nipocalimab or its excipients.**
Reason for being an exclusion criterion	These patients were excluded from nipocalimab clinical trials to avoid potentially life-threatening hypersensitivity reactions.
Included as missing information?	No
Rationale if not included as missing information	Nipocalimab is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients (SmPC Section 4.3).
Criterion 5	**Has shown a previous severe immediate hypersensitivity reaction, such as anaphylaxis to therapeutic proteins (eg, mAbs)**
Reason for being an exclusion criterion	These patients were excluded from nipocalimab clinical trials to avoid potentially life-threatening hypersensitivity reactions and to avoid confounding the safety evaluation of nipocalimab.
Included as missing information?	No
Rationale if not included as missing information	Hypersensitivity is a known risk for therapeutic proteins, including mAbs. It is not possible to predict which patients may develop a hypersensitivity reaction to a therapeutic protein.
Criterion 6	**Experienced myocardial infarction, unstable ischemic heart disease, or stroke within 12 weeks of screening.**
Reason for being an exclusion criterion	Inclusion of patients who experienced myocardial infarction, unstable ischemic heart disease, or stroke within 12 weeks of screening could confound the safety evaluation of nipocalimab.
Included as missing information?	No
Rationale if not included as missing information	This exclusion criterion was implemented for the purpose of the clinical trials and not for a specific safety concern.
Criterion 7	**Currently breastfeeding or pregnant or intends to become pregnant during the study or within 30 days after the last dose of study intervention.**
Reason for being an exclusion criterion	Pregnant and breastfeeding women are generally excluded from clinical trials.
Included as missing information?	Yes: Use during pregnancy
Rationale if not included as missing information	Although limited data show that nipocalimab is excreted in colostrum and human milk at low levels for up to 8 days post-partum, the risk to infants is low considering that nipocalimab, like other IgG antibodies, is expected to be degraded in the gastrointestinal tract (Hurley 2011, Anderson 2021). Treatment of breastfeeding women with IMAAVY could be considered if the clinical benefit outweighs the risks (SmPC Section 4.6).

Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program	
Criterion 8	**Currently taking eculizumab or other novel immune agents, IgG Fc-related protein therapeutics, or Fc-conjugated therapeutic agents, including factor or enzyme replacement.**
Reason for being an exclusion criterion	Nipocalimab is expected to increase catabolism and thus reduce exposure of therapeutic agents that incorporate the Fc region of IgG; this includes IVIg and most therapeutic antibodies and Fc fusion proteins. Consequently, nipocalimab should not be administered if a patient requires concomitant use of IgG therapeutic antibodies, IVIg, or other Fc-containing biologic therapies for any indication.
Included as missing information?	No
Rationale if not included as missing information	SmPC Section 4.5 includes information on treatment with medicinal products that bind to the IgG binding site of the human FcRn.
Criterion 9	**Received rituximab within 6 months prior to the first administration of study intervention. (This criterion does not apply to returning Phase 2 participants.)**
Reason for being an exclusion criterion	Rituximab can cause immune suppression. Nipocalimab causes a reduction in IgG, which may increase the risk of infection if used in patients previously treated with rituximab.
Included as missing information?	No
Rationale if not included as missing information	Serious infections is an important potential risk for nipocalimab.
Criterion 10	**Received or is expected to receive a live vaccine within 4 weeks prior to screening or has a known need to receive a live vaccine during the study or within 8 weeks after the last administration of study intervention.**
Reason for being an exclusion criterion	Because nipocalimab causes a reduction in IgG, the risk of infection following live vaccine administration may be increased.
Included as missing information?	No
Rationale if not included as missing information	Vaccination with live or live-attenuated vaccines is not recommended in patients treated with nipocalimab. 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 (SmPC Section 4.4).

Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program	

Criterion 11	• **Severe infection, including opportunistic infection (eg, pneumonia, biliary tract infection, diverticulitis, Clostridium difficile infection, cytomegalovirus, pneumocystosis, aspergillosis), requiring parenteral anti-infectives and/or hospitalization and/or assessed as serious/clinically significant by the investigator within 8 weeks prior to screening.**
	• **Chronic infection (eg, bronchiectasis, chronic osteomyelitis, chronic pyelonephritis) or chronic treatment with anti-infectives (eg, antibiotics, antivirals).**
	• **Positive test result for HBV infection.**
	• **Seropositive for antibodies to HCV unless**
	  ○ **successfully treated for HCV infection, defined as a negative test result for HCV RNA at least 24 weeks after completing antiviral treatment and a negative HCV RNA test result at screening or**
	  ○ **negative HCV RNA test result while seropositive at least 24 weeks prior to screening and a negative HCV RNA test result at screening.**
	• **COVID-19 infection.**
	• **History of active granulomatous infection, including histoplasmosis or coccidioidomycosis, before screening.**

Reason for being an exclusion criterion	Because nipocalimab causes a reduction in IgG, the risk of infection or worsening an existing infection may be increased.
Included as missing information?	No
Rationale if not included as missing information	Serious infections is an important potential risk for nipocalimab.
Criterion 12	**History of being HIV1 or HIV2 antibody-positive or tests positive for HIV at screening.**
Reason for being an exclusion criterion	HIV infection can cause immunosuppression. Because nipocalimab causes reduction in IgG, the risk of infection may be increased.
Included as missing information?	No
Rationale if not included as missing information	Serious infections is an important potential risk for nipocalimab.
Criterion 13	**Has had a Bacille Calmette-Guérin vaccination within 1 year of first administration of study intervention.**
Reason for being an exclusion criterion	Administration of live or live-attenuated vaccines during immunomodulatory therapy may increase the risk of active infection following vaccination.
Included as missing information?	No

Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program	
Rationale if not included as missing information	Vaccination with live or live-attenuated vaccines is not recommended in patients treated with nipocalimab. 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 (SmPC Section 4.4).

SIV.2. Limitations to Detecting Adverse Reactions in the Clinical Development Program

The clinical development program is unlikely to detect certain types of adverse reactions such as rare adverse reactions, adverse reactions with a long latency, and adverse reactions caused by prolonged or cumulative exposure.

SIV.3. Limitations With Respect to Populations Typically Under-represented in Clinical Development Programs

Table SIV.2: Exposure of Special Populations Included or Not in the Clinical Development Program

Type of Special Population	Exposure
Pregnant women	Not included in the gMG clinical development program. Up to the data lock point of 23 August 2024, no pregnancy cases were reported in the gMG clinical trials.
Breastfeeding women	Not included in the gMG clinical development program.
Population of relevant different ethnic origin	Of the 250 participants in the gMG adult all clinical trials population, 184 (73.6%) participants were white, 53 (21.2%) were Asian, 4 (1.6%) were black or African American, and 9 (3.6%) were of other racial origin. Of the 8 participants in the gMG pediatric all clinical trials population, 5 (62.5%) were Asian, 1 (12.5%) was black or African American, and 2 (25.0%) were of other racial origin.
Subpopulations carrying relevant genetic polymorphisms	Not included in the gMG clinical development program.

Type of Special Population	Exposure
Patients with relevant comorbidities	
• Patients with hepatic impairment • Patients with renal impairment • Patients with CV impairment • Immunocompromised patients • Patients with a disease severity different from inclusion criteria in clinical trials	Although participants with these comorbidities may have been included in the gMG clinical development program at the discretion of the investigator, no exposure data are available.

PART II: SAFETY SPECIFICATION

Module SV: Postauthorization Experience

SV.1. Postauthorization Exposure

SV.1.1. Method Used to Calculate Exposure

Not applicable.

SV.1.2. Exposure

No postmarketing exposure data are available as IMAAVY is not currently marketed.

PART II: SAFETY SPECIFICATION

Module SVI: Additional EU Requirements for the Safety Specification

Potential for Misuse for Illegal Purposes

The pharmacokinetic and pharmacodynamic properties of nipocalimab are not characteristic of drugs with abuse potential. The potential for the misuse of IMAAVY for illegal purposes is unlikely.

PART II: SAFETY SPECIFICATION

Module SVII: Identified and Potential Risks and Missing Information

SVII.1. Identification of Safety Concerns in the Initial RMP Submission

SVII.1.1. Risks Not Considered Important for Inclusion in the List of Safety Concerns

Reasons for Not Including an Identified or Potential Risk in the List of Safety Concerns

Risks with minimal clinical impact on patients in relation to the severity of the indication treated:

- Abdominal pain
- Decreased serum albumin
- Diarrhea
- Dizziness
- Insomnia
- Lipid increases
- Muscle spasms
- Nausea
- Peripheral edema
- Pyrexia

Risks which are well-known to health professionals and do not require additional pharmacovigilance activities or additional risk minimization measures:

- Hypersensitivity reactions
- Infusion-related reactions

SVII.1.2. Important Risks and Missing Information for Inclusion in the List of Safety Concerns

Safety Concerns	Risk-Benefit Impact
Important potential risks	
Serious infections	As nipocalimab causes reduction in IgG levels, treatment with nipocalimab could theoretically increase the risk of serious infections that require medical intervention, including hospitalization, or increase the severity of infections. Although serious infections have been reported in nipocalimab adult gMG clinical trials, the impact of this risk on the overall risk-benefit balance of nipocalimab is considered low. Serious infections is considered an important potential risk for nipocalimab because the impact on an individual patient may be significant, as patients who develop infections may have a more severe course due to their use of nipocalimab.

Safety Concerns	Risk-Benefit Impact
Long-term cardiovascular risk	Treatment-related increases in plasma lipids occurred in adult and adolescent participants who received nipocalimab in the gMG clinical trials. The mean change from baseline for fasting total cholesterol, HDL, and LDL peaked at Week 4, then decreased and plateaued by Week 24. Lipids increased was identified as an ADR. Although there was no evidence of an increased risk of MACE, considering the impact of nipocalimab on plasma lipids, long-term cardiovascular risk is considered an important potential risk for nipocalimab.
Missing information	
Use during pregnancy	No data on the use of nipocalimab in pregnant women with gMG are available. Although limited data from animal studies and a completed clinical trial for a non-gMG indication (ie, an open-label Phase 2 trial in pregnant women at high-risk for EOS-HDFN in which nipocalimab was administered during the second and third trimesters of pregnancy) did not identify any safety concerns related to nipocalimab, the effect of nipocalimab exposure during pregnancy in women with gMG is unknown. Therefore, use during pregnancy is considered missing information for nipocalimab.

SVII.2. New, Reclassified, and Removed Safety Concerns with Submission of an Updated RMP

Not applicable.

SVII.3. Details of Important Identified Risks, Important Potential Risks, and Missing Information

Important Identified Risks

None

Important Potential Risks

1. Serious infections
2. Long-term cardiovascular risk

Missing Information

1. Use during pregnancy

SVII.3.1. Presentation of Important Identified Risks and Important Potential Risks

Important Potential Risk: Serious Infections

Potential Mechanisms

By targeting the IgG binding site on FcRn, nipocalimab is expected to block the binding and hence inhibit recycling of native IgG, resulting in a decrease in circulating IgG antibodies, including pathogenic IgG antibodies. A decrease in serum IgG concentrations could theoretically increase the risk for serious infections that require medical intervention, including hospitalization, or increase the severity of infections.

Evidence Source(s) and Strength of Evidence

Serious infections have been reported in nipocalimab clinical trials. However, because these events were confounded, a causal relationship between nipocalimab and serious infections has not been confirmed.

Characterization of the Risk

All AEs identified by the SOC Infections and infestations are presented in the following tables, along with the number of AEs considered serious.

Adult Population

Important Potential Risk – Serious Infections; Nipocalimab Clinical Trials – Adult Population

	gMG Adult Trials		
	Randomized, Blinded Trials[f]		All Clinical Trials[g]
	Nipocalimab (N=98) n (%)	Placebo (N=98) n (%)	Nipocalimab (N=250) n (%)
Frequency of any infection[a]	42 (42.9%)	42 (42.9%)	163 (65.2%)
Odds Ratio	1.0		
95% CI[b]	0.5 to 1.8		
Seriousness[c]			
Was serious	3 (3.1%)	4 (4.1%)	15 (6.0%)
Outcomes[c,d]			
Fatal	0	0	0
Recovered/Resolved	38 (38.8%)	36 (36.7%)	138 (55.2%)
Recovered/Resolved with sequelae	1 (1.0%)	1 (1.0%)	3 (1.2%)
Recovering/Resolving	1 (1.0%)	0	10 (4.0%)
Not recovered/Not resolved	2 (2.0%)	5 (5.1%)	11 (4.4%)
Unknown	0	0	1 (0.4%)
Severity[c,e]			
Mild	29 (29.6%)	27 (27.6%)	77 (30.8%)
Moderate	10 (10.2%)	12 (12.2%)	75 (30.0%)
Severe	3 (3.1%)	3 (3.1%)	11 (4.4%)
Unknown	0	0	0

AEs relevant to the risk were coded using MedDRA version 26.1.
[a] Includes all subjects who experienced at least 1 occurrence of any AE identified by the SOC Infections and infestations (ie, serious and non-serious).
[b] 2-sided exact 95% CI.
[c] Subjects are included only once regardless of the number of AEs or the number of occurrences of an AE.
[d] The event experienced by the subject with the worst outcome is used.
[e] The event experienced by the subject with the worst severity is used.
[f] Includes Trial MOM-M281-011 (double-blind period only).
[g] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.

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Pediatric Population

Important Potential Risk – Serious Infections; Nipocalimab Clinical Trials – Pediatric Population

	gMG Pediatric Trials
	All Clinical Trials[e]
	Nipocalimab (N=8) n (%)
Frequency of any infection[a]	6 (75.0%)
Seriousness[b]	
Was serious	0
Outcomes[b,c]	
Fatal	0
Recovered/Resolved	5 (62.5%)
Recovered/Resolved with sequelae	0
Recovering/Resolving	0
Not recovered/Not resolved	1 (12.5%)
Unknown	0
Severity[b,d]	
Mild	6 (75.0%)
Moderate	0
Severe	0
Unknown	0

AEs relevant to the risk were coded using MedDRA version 26.1.
[a] Includes all subjects who experienced at least 1 occurrence of any AE identified by the SOC Infections and infestations (ie, serious and non-serious).
[b] Subjects are included only once regardless of the number of AEs or the number of occurrences of an AE.
[c] The event experienced by the subject with the worst outcome is used.
[d] The event experienced by the subject with the worst severity is used.
[e] Includes Trial 80202135MYG2001 (Cohort 1).

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Risk Factors and Risk Groups

Risk factors for the development of serious infections in patients with MG include muscle weakness and immunosuppressive treatment. Thymus disorders, specifically thymoma, may predispose patients to severe infections (Gilhus 2018). Rurality, chronic obstructive pulmonary disease, hypertension, prior infection, frailty, and comorbidity burden have also been identified as risk factors for serious infections in patients with MG (Kassardjian 2020).

Risk factors for recurrent serious infections in patients with MG include deep vein thrombosis, thymic cancer, diabetes mellitus, electrolyte imbalances (ie, hypokalemia, hypomagnesemia), and hypoalbuminemia (Chien 2023).

Preventability

The risk of serious infections is mitigated through appropriate warnings and precautions in the SmPC and PL, including guidance for monitoring patients during treatment with IMAAVY and managing patients who develop clinical signs and symptoms of infection.

Impact on the Risk-benefit Balance of the Product

Although serious infections have been reported in nipocalimab adult gMG clinical trials, the impact of this risk on the overall risk-benefit balance of nipocalimab is considered low. The impact on an individual patient may be significant, as patients who develop infections may have a more severe course due to their use of nipocalimab. Further characterization of the risk is conducted through routine and additional pharmacovigilance activities. Routine risk minimization activities are sufficient to manage the risk.

Public Health Impact

No public health impact is anticipated.

Important Potential Risk: Long-term Cardiovascular Risk

Potential Mechanisms

Increased plasma lipid levels and other factors may contribute to long-term cardiovascular risk. Following nipocalimab administration, increases in fasting total cholesterol, HDL, and LDL were observed in some participants exposed to nipocalimab. While the mechanism by which nipocalimab may be associated with hyperlipidemia has not been established, such lipid increases may be secondary to albumin lowering or decreases in oncotic pressure due to combined decreases in IgG and albumin, which, in some individuals, may be compensated for by hyperlipidemia (Appel 1985; Minchiotti 2019). These observed changes are similar to, but less marked than the hyperlipidemia observed in primary hypoalbuminemia due to the genetic absence of albumin (ie, familial analbuminemia) (Del Ben 2013; Caridi 2016, 2018; Suppressa 2019).

Evidence Source(s) and Strength of Evidence

Increases in plasma lipid levels occurred during nipocalimab clinical trials. The mean change from baseline for fasting total cholesterol, HDL, and LDL peaked at Week 4, then decreased and plateaued by Week 24. Lipids increased was identified as an ADR and this ADR is described in the SmPC for IMAAVY. No MACE were reported in participants treated with nipocalimab during the placebo-controlled portions of the clinical trials. In the OLE of Trial MOM-M281-011, MACE was reported infrequently. These events were not associated with increased lipid levels and the incidence proportion for MACE was lower for nipocalimab compared with placebo. A 10-year cardiovascular risk analysis using the European Academy of Cardiology Systematic Coronary Risk Evaluation system showed that up to 72 weeks of nipocalimab exposure in the adult gMG population did not increase the 10-year composite cardiovascular risk.

The available data do not suggest that nipocalimab increases the risk of MACE. However, because the long-term safety profile of nipocalimab has not yet been established, the long-term impact of increased lipid levels remains to be elucidated.

Characterization of the Risk

Adult Population

Important Potential Risk – Long-term Cardiovascular Risk; Nipocalimab Clinical Trials – Adult Population

	gMG Adult Trials		
	Randomized, Blinded Trials[f]		All Clinical Trials[g]
	Nipocalimab (N=98) n (%)	Placebo (N=98) n (%)	Nipocalimab (N=250) n (%)
Frequency of any long-term cardiovascular risk[a]	0	3 (3.1%)	3 (1.2%)
Odds Ratio	0.0		
95% CI[b]	-		
Seriousness[c]			
Was serious	0	2 (2.0%)	2 (0.8%)
Outcomes[c,d]			
Fatal	0	1 (1.0%)	1 (0.4%)
Recovered/Resolved	0	1 (1.0%)	1 (0.4%)
Recovered/Resolved with sequelae	0	0	0
Recovering/Resolving	0	0	0
Not recovered/Not resolved	0	0	1 (0.4%)
Unknown	0	1 (1.0%)	0
Severity[c,e]			
Mild	0	0	1 (0.4%)
Moderate	0	1 (1.0%)	1 (0.4%)
Severe	0	2 (2.0%)	1 (0.4%)
Unknown	0	0	0

AEs relevant to the risk were coded using MedDRA version 26.1.
[a] Includes all subjects who experienced at least 1 occurrence of any AE identified by the SMQ Myocardial infarction (narrow), Ischaemic central nervous system vascular conditions (narrow), Haemorrhagic central nervous system vascular conditions (narrow), or Preferred Term Sudden Death.
[b] 2-sided exact 95% CI.
[c] Subjects are included only once regardless of the number of AEs or the number of occurrences of an AE.
[d] The event experienced by the subject with the worst outcome is used.
[e] The event experienced by the subject with the worst severity is used.
[f] Includes Trial MOM-M281-011 (double-blind period only).
[g] Includes Trials MOM-M281-004, MOM-M281-005, and MOM-M281-011.

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Pediatric Population

No AEs relevant to long-term cardiovascular risk were reported in the pediatric population (Trial 80202135MYG2001 [Cohort 1]).

Risk Factors and Risk Groups

Risk factors for cardiovascular events include hypertension, hypercholesterolemia, obesity, diabetes, smoking, chronic corticosteroid use, age, male sex, and family history of cardiovascular disease.

Preventability

The risk of long-term cardiovascular risk is mitigated through appropriate warnings and precautions in the SmPC and PL, including guidance for measuring plasma lipid levels, monitoring of plasma lipid levels, and closer periodic monitoring in adolescents and patients with a high body weight or BMI.

Impact on the Risk-benefit Balance of the Product

Lipid increases have been reported in nipocalimab clinical trials; however, a direct correlation of nipocalimab exposure with long-term cardiovascular risk has not been established. The impact of long-term cardiovascular risk on the overall risk-benefit balance of nipocalimab is considered low. However, the effect of increased lipids and subsequent cardiovascular risk for an individual patient over time may be significant if there is no intervention. Further characterization of the risk is conducted through routine and additional pharmacovigilance activities. Routine risk minimization activities are sufficient to manage the risk.

Public Health Impact

No public health impact is anticipated.

SVII.3.2. Presentation of the Missing Information

Missing Information: Use During Pregnancy

Evidence Source

Pregnant women were excluded from nipocalimab gMG clinical trials.

No data on the use of nipocalimab in pregnant women with gMG are available.

Although limited data from animal studies and a completed clinical trial for a non-gMG indication (ie, an open-label Phase 2 trial [MOM-M281-003] in pregnant women at high-risk for EOS-HDFN in which nipocalimab was administered during the second and third trimesters of pregnancy) did not identify any safety concerns related to nipocalimab, the effect of nipocalimab exposure during pregnancy in women with gMG is unknown.

Population in Need of Further Characterization

Pregnant women with gMG who are treated with nipocalimab during pregnancy.

PART II: SAFETY SPECIFICATION

Module SVIII: Summary of the Safety Concerns

Table SVIII.1: Summary of Safety Concerns

Important Identified Risks	None
Important Potential Risks	Serious infections
	Long-term cardiovascular risk
Missing Information	Use during pregnancy

PART III: PHARMACOVIGILANCE PLAN (Including Postauthorization Safety Studies)

III.1. Routine Pharmacovigilance Activities Beyond Adverse Reaction Reporting and Signal Detection

Specific Adverse Reaction Follow-up Questionnaires

Safety Concern	Purpose/Description
Not applicable	

Other Forms of Routine Pharmacovigilance Activities

Activity	Objective(s)	Milestones
Not applicable		

III.2. Additional Pharmacovigilance Activities

Study name and title	**OLE of Trial MOM-M281-011** (A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of nipocalimab administered to adults with generalized myasthenia gravis).
Rationale and study objectives	To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in adults with gMG.
Safety concern(s) addressed	Serious infections Long-term cardiovascular risk
Study design	OLE of a multicenter, randomized, double-blind, placebo-controlled trial .
Study population	Adults aged ≥18 years with gMG who are inadequately controlled with standard-of-care therapy.
Milestones	Final study report submission: 31 May 2028

Study name and title	**LTE of Trial 80202135MYG2001** (An open-label, uncontrolled, multicenter study to evaluate the pharmacokinetics, pharmacodynamics, safety, and activity of nipocalimab in children aged 2 to less than 18 years with generalized myasthenia gravis)
Rationale and study objectives	To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in children aged 2 to less than 18 years with gMG.
Safety concern(s) addressed	Serious infections Long-term cardiovascular risk
Study design	LTE of an open-label, uncontrolled, multicenter trial.
Study population	Children aged 2 to less than 18 years with gMG who are inadequately controlled with standard-of-care therapy.
Milestones	Final study report submission: 30 April 2029

Study name and title	**Retrospective cohort study in pregnancy:** A retrospective cohort study using US administrative health insurance claims databases to assess pregnancy, maternal, and infant outcomes in women with myasthenia gravis who were exposed to nipocalimab during pregnancy
Rationale and study objectives	To assess the use of nipocalimab among MG patients in pregnancy and to estimate the incidence proportions of pregnancy, maternal, and infant outcomes among women with MG exposed to nipocalimab or comparator treatments during pregnancy.
Safety concern(s) addressed	Use during pregnancy
Study design	Observational, retrospective cohort study.
Study population	Pregnant females aged 12 years and older at pregnancy start who have been diagnosed with MG, have a completed pregnancy, and were exposed to nipocalimab or a comparator drug shortly before or during pregnancy.
Milestones	Protocol submission: Q2 2026 Start of data collection[1]: Q4 2029 First interim report submission: Q4 2030 Second interim report submission: Q4 2033 End of data collection[1]: Q4 2035 Final study report submission: Q4 2036

[1] Start of data collection refers to the start of data extraction for the purpose of the first interim report. End of data collection refers to the date on which the analytical dataset will be completely available.

Study name and title	**PASS 1 (United States):** A non-interventional, postauthorization safety study (PASS) of patients treated with nipocalimab for generalized myasthenia gravis (gMG) in routine clinical practice in the United States
Rationale and study objectives	To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.
Safety concern(s) addressed	Serious infections Long-term cardiovascular risk
Study design	Non-interventional, new user, active comparator study.
Study population	Patients with gMG aged 12 years and older.
Milestones	Protocol submission: Q2 2026 Start of data collection[2]: Q1 2028 First interim report submission: Q3 2028 Second interim report submission: Q3 2031 End of data collection[2]: Q3 2033 Final study report submission: Q3 2034

Study name and title	**PASS 2 (France):** A non-interventional, postauthorization safety study (PASS) of patients treated with nipocalimab for generalized myasthenia gravis (gMG) in routine clinical practice in France
Rationale and study objectives	To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.
Safety concern(s) addressed	Serious infections Long-term cardiovascular risk
Study design	Non-interventional, new user, active comparator study.
Study population	Patients with gMG aged 12 years and older.
Milestones	Protocol submission: Q2 2026 Start of data collection[2]: Q1 2030 First interim report submission: Q3 2030 Second interim report submission: Q3 2033 End of data collection[2]: Q1 2036 Final study report submission: Q4 2036

[2] Start of data collection refers to the start of data extraction for the purpose of the first interim report. End of data collection refers to the date on which the analytical dataset will be completely available.

III.3. Summary Table of Additional Pharmacovigilance Activities

Table Part III.3: Ongoing and Planned Additional Pharmacovigilance Activities

Study and Status	Summary of Objectives	Safety Concern(s) Addressed	Milestones	Due Dates
Category 1: Imposed mandatory additional pharmacovigilance activities which are conditions of the marketing authorization				
Not applicable				
Category 2: Imposed mandatory additional pharmacovigilance activities which are specific obligations in the context of a conditional marketing authorization or a marketing authorization under exceptional circumstances				
Not applicable				
Category 3: Required additional pharmacovigilance activities				
OLE of Trial MOM-M281-011 Ongoing	To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in adults with gMG.	• Serious infections • Long-term cardiovascular risk	Final study report submission	31 May 2028
LTE of Trial 80202135MYG2001 Ongoing	To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in children aged 2 to less than 18 years with gMG.	• Serious infections • Long-term cardiovascular risk	Final study report submission	30 April 2029
Retrospective cohort study in pregnancy Planned	To assess the use of nipocalimab among MG patients in pregnancy and to estimate the incidence proportions of pregnancy, maternal, and infant outcomes among women with MG exposed to nipocalimab or comparator treatments during pregnancy.	• Use during pregnancy	Protocol submission First interim report submission Second interim report submission Final study report submission	Q2 2026 Q4 2030 Q4 2033 Q4 2036
PASS 1 (United States) Planned	To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.	• Serious infections • Long-term cardiovascular risk	Protocol submission First interim report submission Second interim	Q2 2026 Q3 2028 Q3 2031

Study and Status	Summary of Objectives	Safety Concern(s) Addressed	Milestones	Due Dates
			report submission Final study report submission	 Q3 2034
PASS 2 (France) Planned	To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.	• Serious infections • Long-term cardiovascular risk	Protocol submission First interim report submission Second interim report submission Final study report submission	Q2 2026 Q3 2030 Q3 2033 Q4 2036

PART IV: PLANS FOR POSTAUTHORIZATION EFFICACY STUDIES

Table Part IV: Planned and Ongoing Postauthorization Efficacy Studies That Are Conditions of the Marketing Authorization or Specific Obligations

Study and Status	Summary of Objectives	Efficacy Uncertainties Addressed	Milestones	Due Dates
Efficacy studies which are conditions of the marketing authorization				
Not applicable				
Efficacy studies which are specific obligations in the context of a conditional marketing authorization or a marketing authorization under exceptional circumstances				
Not applicable				

PART V: RISK MINIMIZATION MEASURES (Including Evaluation of the Effectiveness of Risk Minimization Measures)

Risk Minimization Plan

V.1. Routine Risk Minimization Measures

Table Part V.1: Description of Routine Risk Minimization Measures by Safety Concern

Serious infections
Routine risk communication • SmPC Section 4.4 • PL Section 2 **Routine risk minimization activities recommending specific clinical measures to address the risk** • Advice to delay initiation of IMAAVY treatment in patients with active infection until the infection resolves and to monitor patients for clinical signs and symptoms of infection during treatment with IMAAVY is included in SmPC Section 4.4. • Advice on the management of clinically important active infection is included in SmPC Section 4.4. • Advice for patients to report any signs and symptoms of infection before starting treatment with IMAAVY or during treatment to their doctor is included in PL Section 2. **Other routine risk minimization activities beyond the Product Information** • Legal status: Restricted medical prescription
Long-term cardiovascular risk
Routine risk communication • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 4 **Routine risk minimization activities recommending specific clinical measures to address the risk** • A recommendation to measure plasma lipid levels is included in SmPC Section 4.4. • Advice on monitoring in adolescents and patients with high body weight or BMI is included in SmPC Section 4.4. • Advice on the continued monitoring of plasma lipid levels and alternative treatment options is included in SmPC Section 4.4. • Information on the measurement of blood fat (cholesterol) levels is included in PL Section 2. **Other routine risk minimization activities beyond the Product Information** • Legal status: Restricted medical prescription

Use during pregnancy
Routine risk communication • SmPC Section 4.6 • PL Section 2 **Routine risk minimization activities recommending specific clinical measures to address the risk** • None **Other routine risk minimization activities beyond the Product Information** • Legal status: Restricted medical prescription

V.2. Additional Risk Minimization Measures

Not applicable. Routine risk minimization activities as described in Part V.1 are sufficient to manage the safety concerns of IMAAVY.

V.2.1. Removal of Additional Risk Minimization Measures

Not applicable.

V.3. Summary of Risk Minimization Measures

Table Part V.3: Summary of Risk Minimization Measures and Pharmacovigilance Activities by Safety Concern

Safety Concern	Risk Minimization Measures	Pharmacovigilance Activities
Serious infections	**Routine risk communication** • SmPC Section 4.4 • PL Section 2 **Specific clinical measures** • Advice to delay initiation of IMAAVY treatment in patients with active infection until the infection resolves and to monitor patients for clinical signs and symptoms of infection during treatment with IMAAVY: SmPC Section 4.4. • Advice on the management of clinically important active infection: SmPC Section 4.4. • Advice for patients report any signs and symptoms of infection before starting treatment with IMAAVY or during treatment to their doctor: PL Section 2. **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection** • None **Additional pharmacovigilance activities** • OLE of Trial MOM-M281-011 Final study report due date: 31 May 2028 • LTE of Trial 80202135MYG2001 Final study report due date: 30 April 2029 • PASS 1 (United States) Final study report due date: Q3 2034 • PASS 2 (France) Final study report due date: Q4 2036

Safety Concern	Risk Minimization Measures	Pharmacovigilance Activities
Long-term cardiovascular risk	**Routine risk communication** • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 4 **Specific clinical measures** • Recommendation to measure plasma lipid levels: SmPC Section 4.4. • Advice on monitoring in adolescents and patients with high body weight or BMI: SmPC Section 4.4. • Advice on the continued monitoring of plasma lipid levels and alternative treatment options: SmPC Section 4.4. • Information on the measurement of blood fat (cholesterol) levels: PL Section 2. **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection** • None **Additional pharmacovigilance activities** • OLE of Trial MOM-M281-011 Final study report due date: 31 May 2028 • LTE of Trial 80202135MYG2001 Final study report due date: 30 April 2029 • PASS 1 (United States) Final study report due date: Q3 2034 • PASS 2 (France) Final study report due date: Q4 2036
Use during pregnancy	**Routine risk communication** • SmPC Section 4.6 • PL Section 2 **Specific clinical measures** • None **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection** • None **Additional pharmacovigilance activities** • Retrospective cohort study in pregnancy Final study report due date: Q4 2036

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for IMAAVY (Nipocalimab)

This is a summary of the risk management plan (RMP) for IMAAVY. The RMP details important risks of IMAAVY, how these risks can be minimized, and how more information will be obtained about IMAAVY's risks and uncertainties (missing information).

IMAAVY's Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how IMAAVY should be used.

This summary of the RMP for IMAAVY should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of IMAAVY's RMP.

I. The Medicine and What it is Used For

IMAAVY is authorized as an add-on to standard therapy for the treatment of generalized myasthenia gravis (gMG) in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive (see SmPC for the full indication). It contains nipocalimab as the active substance and it is given by intravenous infusion.

Further information about the evaluation of IMAAVY’s benefits can be found in IMAAVY’s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website under the medicine’s webpage: link to the EPAR summary landing page.

II. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of IMAAVY, together with measures to minimize such risks and the studies for learning more about IMAAVY's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals.
- Important advice on the medicine’s packaging.
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly.
- The medicine’s legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization measures*.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed including periodic safety update report assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of IMAAVY is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of IMAAVY are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of IMAAVY. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	Serious infections Long-term cardiovascular risk
Missing information	Use during pregnancy

II.B. Summary of Important Risks

Serious Infections	
Evidence for linking the risk to the medicine	Serious infections have been reported in IMAAVY clinical trials. However, because these events were confounded, a causal relationship between IMAAVY and serious infections has not been confirmed.
Risk factors and risk groups	Risk factors for the development of serious infections in patients with myasthenia gravis (MG) include muscle weakness and immunosuppressive treatment. Thymus disorders, specifically thymoma, may predispose patients to severe infections. Rurality, chronic obstructive pulmonary disease, hypertension, prior infection, frailty, and comorbidity burden have also been identified as risk factors for serious infections in patients with MG. Risk factors for recurrent serious infections in patients with MG include deep vein thrombosis, thymic cancer, diabetes mellitus, electrolyte imbalances (ie, hypokalemia, hypomagnesemia), and hypoalbuminemia.
Risk minimization measures	**Routine risk communication** • SmPC Section 4.4 • PL Section 2 **Specific clinical measures** • Advice to delay initiation of IMAAVY treatment in patients with active infection until the infection resolves and to monitor patients for clinical signs and symptoms of infection during treatment with IMAAVY: SmPC Section 4.4. • Advice on the management of clinically important active infection: SmPC Section 4.4. • Advice for patients to report any signs and symptoms of infection before starting treatment with IMAAVY or during treatment to their doctor: PL Section 2. **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None
Additional pharmacovigilance activities	• Open-label extension (OLE) of Trial MOM-M281-011 • Long-term extension (LTE) of Trial 80202135MYG2001 • Postauthorization safety study (PASS) 1 (United States) • PASS 2 (France) See Section II.C of this summary for an overview of the postauthorization development plan.

Long-term Cardiovascular Risk	
Evidence for linking the risk to the medicine	Increases in plasma lipid levels occurred during nipocalimab clinical trials. The mean change from baseline for fasting total cholesterol, high-density lipoprotein, and low-density lipoprotein peaked at Week 4, then decreased and plateaued by Week 24. Lipids increased was identified as an adverse drug reaction (ADR) and this ADR is described in the SmPC for IMAAVY. No major adverse cardiovascular events (MACE) were reported in participants treated with nipocalimab during the placebo-controlled portions of the clinical trials. In the OLE of Trial MOM-M281-011, MACE was reported infrequently. These events were not associated with increased lipid levels and the incidence proportion for MACE was lower for nipocalimab compared with placebo. A 10-year cardiovascular risk analysis using the European Academy of Cardiology Systematic Coronary Risk Evaluation system showed that up to 72 weeks of nipocalimab exposure in the adult gMG population did not increase the 10-year composite cardiovascular risk. The available data do not suggest that nipocalimab increases the risk of MACE. However, because the long-term safety profile of nipocalimab has not yet been established, the long-term impact of increased lipid levels remains to be elucidated.
Risk factors and risk groups	Risk factors for cardiovascular events include hypertension, hypercholesterolemia, obesity, diabetes, smoking, chronic corticosteroid use, age, male sex, and family history of cardiovascular disease.
Risk minimization measures	**Routine risk communication** • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 4 **Specific clinical measures** • Recommendation to measure plasma lipid levels: SmPC Section 4.4. • Advice on monitoring in adolescents and patients with high body weight or body mass index: SmPC Section 4.4. • Advice on the continued monitoring of plasma lipid levels and alternative treatment options: SmPC Section 4.4. • Information on the measurement of blood fat (cholesterol) levels: PL Section 2. **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None
Additional pharmacovigilance activities	• OLE of Trial MOM-M281-011 • LTE of Trial 80202135MYG2001 • PASS 1 (United States)

Long-term Cardiovascular Risk	
	• PASS 2 (France) See Section II.C of this summary for an overview of the postauthorization development plan.

Use During Pregnancy	
Risk minimization measures	**Routine risk communication** • SmPC Section 4.6 • PL Section 2 **Specific clinical measures** • None **Other routine risk minimization activities** • Restricted medical prescription **Additional risk minimization activities** • None
Additional pharmacovigilance activities	• Retrospective cohort study in pregnancy See Section II.C of this summary for an overview of the postauthorization development plan.

II.C. Postauthorization Development Plan

II.C.1. Studies That are Conditions of the Marketing Authorization

No studies are conditions of the marketing authorization or specific obligations of IMAAVY.

II.C.2. Other Studies in Postauthorization Development Plan

1. **OLE of Trial MOM-M281-011**: A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of nipocalimab administered to adults with generalized myasthenia gravis.

   Purpose of the trial (OLE phase): To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in adults with gMG.

2. **LTE of Trial 80202135MYG2001**: An open-label, uncontrolled, multicenter study to evaluate the pharmacokinetics, pharmacodynamics, safety, and activity of nipocalimab in children aged 2 to less than 18 years with generalized myasthenia gravis.

   Purpose of the trial (LTE phase): To evaluate the maintenance of nipocalimab's effect and the long-term safety of nipocalimab in children aged 2 to less than 18 years with gMG.

3. **Retrospective cohort study in pregnancy**: A retrospective cohort study using US administrative health insurance claims databases to assess pregnancy, maternal, and infant

outcomes in women with myasthenia gravis who were exposed to nipocalimab during pregnancy.

Purpose of the trial: To assess the use of nipocalimab among MG patients in pregnancy and to estimate the incidence proportions of pregnancy, maternal, and infant outcomes among women with MG exposed to nipocalimab or comparator treatments during pregnancy.

4. **PASS 1 (United States)**: A non-interventional, postauthorization safety study (PASS) of patients treated with nipocalimab for generalized myasthenia gravis (gMG) in routine clinical practice in the United States.

   Purpose of the trial: To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.

5. **PASS 2 (France)**: A non-interventional, postauthorization safety study (PASS) of patients treated with nipocalimab for generalized myasthenia gravis (gMG) in routine clinical practice in France.

   Purpose of the trial: To assess the long-term safety of nipocalimab among cohorts of patients with gMG treated with nipocalimab and those treated with other gMG medications.

PART VII: ANNEXES

Table of Contents

Annex 4: Specific Adverse Reaction Follow-up Questionnaires

Not applicable.

Annex 6: Details of Additional Risk Minimization Activities

Key Messages of Additional Risk Minimization Activities

Not applicable.