

NAME OF THE MEDICINAL PRODUCT

IMAAVY

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.

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 15.1.

PHARMACEUTICAL FORM

Concentrate for solution for infusion

Colourless to slightly brownish, clear to slightly opalescent solution

1 INDICATIONS AND USAGE

IMAAVY is indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti- muscle-specific tyrosine kinase (MuSK) antibody positive.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Vaccination

Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of IMAAVY. Because IMAAVY causes transient reduction in IgG levels, vaccination with live vaccines is not recommended during treatment with IMAAVY [*see Warnings and Precautions (5.1)*].

2.2 Recommended Dosage

Dilute IMAAVY prior to administration. Administer via intravenous infusion only [*see Dosage and Administration (2.3)*].

The recommended initial dosage of IMAAVY is 30 mg/kg administered once via intravenous infusion over at least 30 minutes. Two weeks after the initial dosage administer a maintenance dosage of 15 mg/kg via intravenous infusion over at least 15 minutes. Continue the maintenance dosage every two weeks thereafter.

If a scheduled infusion appointment is missed, the maintenance dosage of IMAAVY should be administered as soon as possible. Resume dosing every two weeks thereafter.

2.3 Preparation and Administration Instructions

Prior to administration, dilute IMAAVY single-dose vials with only 0.9% sodium chloride injection using the instructions below. For patients who weigh 40 kg or more, the total volume to be administered is 250 mL; for patients who are 12 years or older and weigh less than 40 kg, the total volume to be administered is 100 mL (*see Preparation*).

Preparation

Prepare the solution for infusion using aseptic technique as follows:

- Calculate the dosage (mg), total drug volume (mL) of IMAAVY solution required, and the number of IMAAVY vials needed, based on the patient's current weight [*see Dosage and Administration (2.2)*]. Each single-dose vial of IMAAVY is at a concentration of 185 mg/mL.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Check that the solution in each vial is colorless 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 discolored (other than colorless to slightly brownish).
- Gently withdraw the calculated volume of IMAAVY from the vial(s). Discard any unused portion of the vials.
- Dilute total volume withdrawn of IMAAVY by adding to an infusion container containing 0.9% sodium chloride injection to a final volume of:
 - 250 mL for patients who weigh 40 kg or more, or
 - 100 mL for patients who weigh less than 40 kg.Only use infusion containers made of polyolefin, polypropylene, or polyvinylchloride.
- Gently invert the infusion container 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 discoloration is present.

Storage Conditions of the Diluted Solution

- Administer the diluted IMAAVY solution immediately after preparation.
- If the diluted IMAAVY solution is not used immediately:
 - Protect from light.
 - Store refrigerated at 2°C to 8°C for no more than 24 hours.
 - Do not freeze.
 - After preparation or removal from the refrigerator, use or discard the IMAAVY diluted solution within 12 hours, including infusion time. During these 12 hours, store under ambient light at 15°C to 30°C.

Administration

- If the diluted solution is refrigerated prior to administration, allow to warm to room temperature. Do not use external heat sources to warm IMAAVY.
- Administer the diluted solution by intravenous infusion only 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 micrometer or less). Administration sets must be made of either polybutadiene, polyethylene, polyurethane, polypropylene, or polyvinylchloride.
- Do not infuse IMAAVY concomitantly in the same intravenous line with other agents.
- Administer IMAAVY infusion intravenously over at least 30 minutes for the initial dose (30 mg/kg) and at least 15 minutes for subsequent doses (15 mg/kg).
- If an adverse reaction occurs during administration of IMAAVY, the infusion may be slowed or stopped at the discretion of the healthcare professional.
- Monitor the patient for 30 minutes after each infusion for signs or symptoms of an infusion-related or hypersensitivity reaction [*see Warnings and Precautions (5.2, 5.3)*].

3 DOSAGE FORMS AND STRENGTHS

colorless to slightly brownish, clear to slightly opalescent solution available as:

- 300 mg/1.62 mL (185 mg/mL) in a single-dose vial
- 1,200 mg/6.5 mL (185 mg/mL) in a single-dose vial

4 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section 15.1. Reactions have included anaphylaxis and angioedema [*see Warnings and Precautions (5.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Infections

IMAAVY may increase the risk of infection [*see Adverse Reactions (6.1)*]. In Study 1 [*see Clinical Studies (14)*], 42 (43%) out of 98 patients treated with IMAAVY reported 71 events of infection. Across Study 1 (double blind period) and its extension study (open label-period), out of 186 patients treated with IMAAVY, 132 (71%) patients reported 360 events of infection. Serious infections were reported in 7% of patients treated with IMAAVY. Delay IMAAVY administration in patients with an active infection until the infection is resolved. During treatment with IMAAVY, monitor for clinical signs and symptoms of infection. If serious infection occurs, administer appropriate treatment and consider withholding IMAAVY until the infection has resolved.

Latent Viral Infections

Patients treated with IMAAVY may be at an increased risk of activation of latent viral infections,

such as herpes zoster [see *Adverse Reactions* (6.1)]. In the extension period of Study 1, there were 2 patients with serious adverse reactions related to Epstein-Barr virus (EBV) infection, and 1 of these patients had fatal complications. Patients who screened positive for hepatitis were excluded from Study 1. Follow standard vaccination guidelines [see *Dosage and Administration* (2.1)].

Immunization

The safety of immunization with live vaccines and the immune response to vaccination during treatment with IMAAVY are unknown. Because IMAAVY causes a reduction in IgG levels, vaccination with live vaccines is not recommended during treatment with IMAAVY.

Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of treatment with IMAAVY.

5.2 Hypersensitivity Reactions

In clinical trials, hypersensitivity reactions, including angioedema, anaphylaxis, rash, urticaria, and eczema were observed in patients treated with IMAAVY. In Study 1, hypersensitivity reactions were mild or moderate, occurred within one hour to 2 weeks of administration [see *Adverse Reactions* (6.1)]. One patient experienced a hypersensitivity reaction (urticaria) that led to treatment discontinuation.

Management of hypersensitivity reactions depends on the type and severity of the reaction. Monitor the patient during treatment with IMAAVY and for 30 minutes after the administration is complete for clinical signs and symptoms of hypersensitivity reactions [see *Dosage and Administration* (2.3)]. If a hypersensitivity reaction occurs during administration, discontinue IMAAVY infusion and institute appropriate supportive measures if needed. IMAAVY is contraindicated in patients with a history of hypersensitivity to nipocalimab or any of the excipients of IMAAVY [see *Contraindications* (4)].

5.3 Infusion-Related Reactions

In clinical trials, infusion-related reactions, including headache, influenza-like illness, rash, nausea, fatigue, dizziness, chills, and erythema were observed in patients treated with IMAAVY. In Study 1, infusion-related reactions were mild to moderate in severity and occurred within one hour to 2 days of administration [see *Adverse Reactions* (6.1)].

Monitor patients during treatment with IMAAVY and for 30 minutes after each infusion [see *Dosage and Administration* (2.3)]. If a severe infusion-related reaction occurs, discontinue IMAAVY infusion and initiate appropriate therapy. Consider the risks and benefits of readministering IMAAVY following a severe infusion-related reaction. If a mild to moderate infusion related reaction occurs, patients may be rechallenged with close clinical observation, slower infusion rates, and pre-medication.

5.4 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 6.1). 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.

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.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling

- Infections [see *Warnings and Precautions (5.1)*]
- Hypersensitivity Reactions [see *Warnings and Precautions (5.2)*]
- Infusion-related Reactions [see *Warnings and Precautions (5.3)*]
- Increased plasma lipid levels [see *Warnings and Precautions (5.4)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults

In Study 1 and its extension study the safety of IMAAVY was evaluated in 186 patients with gMG who received at least one dose of IMAAVY. Of those patients, 168 patients were exposed to IMAAVY every 2 weeks for at least 6 months, and 140 patients were exposed for at least 12 months.

In Study 1, 98 adult patients with gMG received IMAAVY 15 mg/kg every two weeks (after 30 mg/kg initial dose) [see *Clinical Studies (14)*]. Of these 98 patients, approximately 67% were female, 67% were White, 29% were Asian, and 10% were of Hispanic or Latino ethnicity. The mean age at study entry was 53 years (range 20 to 81).

Adverse reactions reported in at least 5% of patients treated with IMAAVY and more frequently than placebo, are summarized in Table 1. The most common adverse reactions (reported in at least 10% of patients treated with IMAAVY) were respiratory tract infection, peripheral edema, and muscle spasms.

Table 1: Adverse Reactions (≥ 5%) of Patients Treated with IMAAVY and More Frequently than in Placebo in Study 1

Adverse Reaction	IMAAVY N=98 %	Placebo N=98 %
Infection		
Respiratory tract infection ^a	18	13
Urinary tract infection ^b	6	3
Herpes zoster and Herpes simplex	6	2

Oral infection ^c	5	3
Peripheral edema	12	2
Muscle spasm	12	3
Hypersensitivity reaction ^d	8	7
Abdominal pain	8	3
Back pain	8	5
Pyrexia	7	1
Diarrhea	7	3
Cough	7	3
Anemia ^b	6	4
Dizziness	5	1
Nausea	5	2
Hypertension	5	2
Insomnia	5	2

Includes the following reported in patients treated with IMAAVY:

^a COVID-19 (and other related terms), pneumonia, bronchitis, pneumonia bacteria

^b other related terms

^c glossitis, oral candidiasis, pericoronitis, pulpitis dental, tooth abscess, tooth infection

^d angioedema, dermatitis atopic, eczema, gingival swelling, rash (and other related terms), urticaria

Infections

In Study 1 and its extension study, infections that occurred in patients treated with IMAAVY (n=186) included upper respiratory tract infection (46%), respiratory tract infection (28%; including pneumonia, bronchitis, COVID-19), urinary tract infection (15%), herpes (8%; including herpes simplex, herpes zoster, herpes zoster ophthalmicus), influenza (8%), oral infection (8%; including candidiasis and dental infections), and skin infection (7%; including cellulitis). Two (1%) cases of infections (cellulitis and urinary tract infection) led to discontinuation of IMAAVY [see *Warnings and Precautions (5.1)*].

Hypersensitivity Reactions

In Study 1 and its extension study, out of 186 patients treated with IMAAVY, 30 (16%) patients experienced hypersensitivity reactions, which occurred within one hour to two weeks of administration. One patient experienced hypersensitivity reaction (urticaria) that required discontinuation of IMAAVY [see *Warnings and Precautions (5.2)*].

Infusion-Related Reactions

In Study 1 and its extension study, out of 186 patients treated with IMAAVY, 20 (11%) patients experienced infusion-related reactions, which occurred within one hour to 2 days of administration. No patients experienced infusion-related reaction that required discontinuation of IMAAVY [see *Warnings and Precautions (5.3)*].

Laboratory Findings

Lipids

In Study 1 (N=98), patients treated with IMAAVY had elevations from normal to high of fasting total cholesterol (≥ 240 mg/dL) and LDL cholesterol (≥ 160 mg/dL) (24% and 11% of patients, respectively). In Study 1, these changes from baseline peaked at Week 4, then decreased and plateaued by Week 24 to mean increases of 14 mg/dL and 7 mg/dL, respectively. Five percent of patients treated with IMAAVY had decreases from normal to low of fasting HDL cholesterol (< 40 mg/dL).

Pediatric Patients 12 Years of Age and Older

In a 24-week, single arm study evaluating the safety of IMAAVY in 7 pediatric patients age 12 to 16 years with gMG who were AChR positive, adverse reactions were consistent with those observed in adult patients with gMG [*see Use in Specific Populations (8.4)*].

6.2 Effects on ability to drive and use machines

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <http://sideeffects.health.gov.il>

7 DRUG INTERACTIONS

7.1 Effect of IMAAVY on Other Drugs

Concomitant use of IMAAVY with medications that bind to the human neonatal Fc receptor (FcRn) (e.g., immunoglobulin products, monoclonal antibodies, or antibody derivatives containing the human Fc domain of the IgG subclass) may lower systemic exposures and reduce effectiveness of such medications. Closely monitor for reduced effectiveness of medications that bind to the human neonatal Fc receptor. When concomitant long-term use of such medications is essential for patient care, consider discontinuing IMAAVY, and using alternative therapies [*see Clinical Pharmacology (12.3)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are limited data on the use of IMAAVY in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

There was no evidence of direct adverse effects on fetal development following administration of nipocalimab to pregnant monkeys; however, adverse effects on the placenta were associated with fetal loss at both doses tested.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Monoclonal antibodies are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third trimester. Because IMAAVY reduces maternal serum IgG concentration and impedes placental IgG transfer to the fetus, passive immunity in the infant may be reduced for 6 months or more; therefore:

- Monitor for the development of serious infection.
- Effectiveness of vaccines may be reduced.
- Consider the risks and benefits prior to administering live vaccines to infants exposed to IMAAVY *in utero*.

Animal Data

Intravenous administration of nipocalimab (0, 100, or 300 mg/kg) to pregnant monkeys weekly from the end of organogenesis (gestation day 45) through parturition resulted in placental ischemia, associated with fetal loss and decreased levels of IgG in the offspring at both doses tested. IgG levels in offspring returned to normal levels and no adverse effects on immune function were evident by 6 months after birth. The doses tested are 6 and 20 times the recommended human maintenance dose (15 mg/kg) on a mg/kg basis.

8.2 Lactation

Risk Summary

Nipocalimab is excreted in human colostrum and breastmilk based on limited data from an investigational study of 13 pregnant women administered nipocalimab during pregnancy where colostrum and breastmilk was assessed in the first 8 days after birth. There are insufficient data on the effect of IMAAVY in the breastfed infant. There are no data on the effect of nipocalimab on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IMAAVY, and any potential adverse effects on the breastfed infant from IMAAVY, or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of IMAAVY for the treatment of gMG have been established in pediatric patients 12 years of age and older. Use of IMAAVY in pediatric patients for this indication is supported by evidence from an adequate and well-controlled trial in adults with additional pharmacokinetic and safety data in pediatric patients who are 12 years of age and older [see *Adverse Reactions* (6.1), *Clinical Pharmacology* (12.3), and *Clinical Studies* (14)].

Safety and effectiveness of IMAAVY for the treatment of gMG in pediatric patients below the age of 12 years have not been established.

8.5 Geriatric Use

Clinical studies of IMAAVY did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger adult patients.

11 DESCRIPTION

Nipocalimab, a neonatal Fc receptor blocker, is a recombinant human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody, expressed in a genetically engineered Chinese hamster ovary cell line. Nipocalimab has an aglycosylated Fc region, therefore it lacks effector functions. Nipocalimab has an approximate molecular weight of 142 kilodaltons (kDa).

IMAAVY is a sterile, preservative-free, colorless to slightly brownish, clear to slightly opalescent solution, supplied in a single-dose vial for intravenous infusion after dilution.

Each single-dose vial contains either 300 mg/1.62 mL or 1,200 mg/6.5 mL of nipocalimab at a concentration of 185 mg/mL.

12 CLINICAL PHARMACOLOGY

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

12.1 Mechanism of Action

Nipocalimab is a human IgG1 monoclonal antibody that binds to neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG levels.

12.2 Pharmacodynamics

In Study 1 [see *Clinical Studies (14)*], the pharmacological effect of nipocalimab was assessed by measuring the decrease in serum IgG levels and anti-AChR and anti-MuSK autoantibody levels. In patients positive for AChR and MuSK autoantibodies who were treated with IMAAVY, there was a reduction in AChR and MuSK autoantibodies relative to baseline. Decreases in total IgG levels followed a similar pattern. A similar reduction in AChR autoantibodies was observed in adolescent patients with gMG compared to adults.

12.3 Pharmacokinetics

Nipocalimab exhibits nonlinear pharmacokinetics. Following a single intravenous infusion of IMAAVY at doses ranging from 0.3 to 60 mg/kg (4 times the recommended maintenance dosage) in healthy participants, C_{max} of nipocalimab increased in a dose-proportional manner while AUC increased in a greater than dose-proportional manner.

Distribution

Mean volume of distribution of nipocalimab is 2.67 L.

Metabolism

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

Elimination

Nipocalimab exhibits concentration-dependent pharmacokinetics. After a single intravenous administration of 15 mg/kg nipocalimab, the mean clearance is 0.0627 L/h and half-life is 29.3 hours.

Specific Populations

Age, Sex, and Race

The pharmacokinetics of nipocalimab were not affected by age, sex, or race based on a population pharmacokinetics analysis.

Pediatric Patients

Following the recommended intravenous doses of IMAAVY in adolescent patients 12 to 16 years of age with gMG (N=7), the observed steady-state serum nipocalimab concentrations were within the range of those observed for adult patients with gMG [see *Use in Specific Populations* (8.4)].

Patients with Renal Impairment

No dedicated pharmacokinetic study has been conducted in patients with renal impairment. Renal impairment is not expected to affect the pharmacokinetics of nipocalimab. Based on a population pharmacokinetic analysis, which included healthy volunteers and patients with gMG with mild to moderate renal impairment, renal function (estimated glomerular filtration rate [eGFR] 30-89 mL/min/1.73 m²) had no clinically significant effect on nipocalimab clearance. No dose adjustment is required in patients with renal impairment.

Patients with Hepatic Impairment

No dedicated pharmacokinetic study has been performed in patients with hepatic impairment. Nipocalimab is not metabolized by cytochrome P450 enzymes, and hepatic impairment is not expected to affect the pharmacokinetics of nipocalimab. Based on a population pharmacokinetic analysis, which included healthy volunteers and patients with gMG with mild to moderate hepatic impairment, there was no clinically significant effect on nipocalimab clearance. No dose adjustment is required in patients with hepatic impairment.

Drug Interactions with Other Drugs or Biological Products

IgG-Based Monoclonal Antibodies

Nipocalimab decreases concentrations of compounds that bind to the human FcRn, including IgG based monoclonal antibodies.

Cytochrome P450 Enzymes

Nipocalimab is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of nipocalimab or of other nipocalimab products.

In clinical trials, antibodies to nipocalimab were detected in 49/102 (48%) adult and pediatric patients 12 years of age and older during 24-week treatment period.

Out of the 49 patients who were positive for antibodies to nipocalimab, 19 (38.8%) patients had neutralizing antibodies to nipocalimab. There was no identified clinically relevant effect of antibodies, including neutralizing antibodies, to nipocalimab on the pharmacokinetics, pharmacodynamics, safety, or effectiveness of IMAAVY.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Studies to assess the carcinogenic potential of nipocalimab have not been conducted.

Mutagenesis

Studies to assess the genotoxic potential of nipocalimab have not been conducted. As an antibody, nipocalimab is not expected to interact directly with DNA.

Impairment of Fertility

Once or twice weekly intravenous administration of nipocalimab (0, 20, 50, 100, or 300 mg/kg) to male and female monkeys for 26 weeks resulted in no adverse effects on reproductive organs upon histopathological examination. The highest dose tested was 20 times the recommended human maintenance dose (15 mg/kg) on a mg/kg basis.

14 CLINICAL STUDIES

The efficacy of IMAAVY for the treatment of gMG in adults who are anti-AChR or anti-MuSK antibody positive was established in a 24-week, multicenter, randomized, double-blind, placebo-controlled study (Study 1; NCT04951622). Patients were treated with IMAAVY with the recommended dosage regimen [*see Dosage and Administration (2.1)*].

Study 1 enrolled patients with gMG who met the following criteria:

- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 6
- On stable dose of standard of care MG therapy prior to baseline that included acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone.

In Study 1, a total of 196 patients were randomized 1:1 to receive IMAAVY (n=98) or placebo (n=98). Baseline characteristics were similar between treatment groups. For the primary efficacy analysis population (n=153), patients had a median age of 52 years at screening (range 20 to 81 years) and a median time since diagnosis of 6 years. Sixty percent of patients were female; 63% were White; 32% were Asian; 1% were Black or African-American; and <1% were American Indian or Alaskan Native. At baseline, median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis (QMG) total score was 15. Eighty-eight percent (n=134) of patients were positive for AChR antibodies and 10% (n=16) were positive for MuSK antibodies.

At baseline, in each group, 85% of patients received AChE inhibitors, 66% of patients received steroids, and 54% of patients received NSISTs at stable doses

The efficacy of IMAAVY was measured using the MG-ADL scale, which assesses the impact of gMG on daily functions of 8 signs and symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment.

The primary efficacy endpoint was the comparison of the mean change from baseline to Weeks

22, 23, and 24 between treatment groups in the MG-ADL total score. A statistically significant difference favoring IMAAVY was observed in MG-ADL total score change from baseline ($p=0.002$; see Table 2 and Figure 1).

The efficacy of IMAAVY was also measured using the QMG total score, which is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4 -point scale, where a score of 0 represents no weakness, and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.

The secondary endpoint was the comparison of the mean change from baseline to Weeks 22 and 24 between treatment groups in the QMG total score. A statistically significant difference favoring IMAAVY was observed in the QMG total score change from baseline ($p<0.001$; see Table 2).

The results are presented shown in Table 2.

Table 2: Least Squares Mean Change from Baseline to Week 24 in MG-ADL and QMG Total Scores in Study 1

Efficacy Endpoints	IMAAVY N = 77 LS Mean (SE)	Placebo N = 76 LS Mean (SE)	IMAAVY Change Relative to Placebo LS Mean Difference (95% CI)	p-value
Primary Endpoint				
MG-ADL Total Score ¹	-4.7 (0.33)	-3.3 (0.34)	-1.5 (-2.4, -0.5)	0.002
Secondary Endpoint				
QMG Total Score ²	-4.9 (0.5)	-2.1 (0.5)	-2.8 (-4.2, -1.4)	<0.001

Key: CI=confidence interval; MG-ADL = Myasthenia Gravis – Activities of Daily Living; QMG = Quantitative Myasthenia Gravis; LS mean = Least squares mean; SE = standard error

¹ Mean change from baseline over weeks 22, 23, and 24

² Mean change from baseline over weeks 22 and 24

Figure 1 shows the mean change from baseline to Week 24 in MG-ADL total score in Study 1, and Figure 2 shows the mean change from baseline to Week 24 in QMG total score in Study 1

Figure 1: Least Squares Mean Change from Baseline in MG-ADL Total Score Over 24 Weeks in Study 1

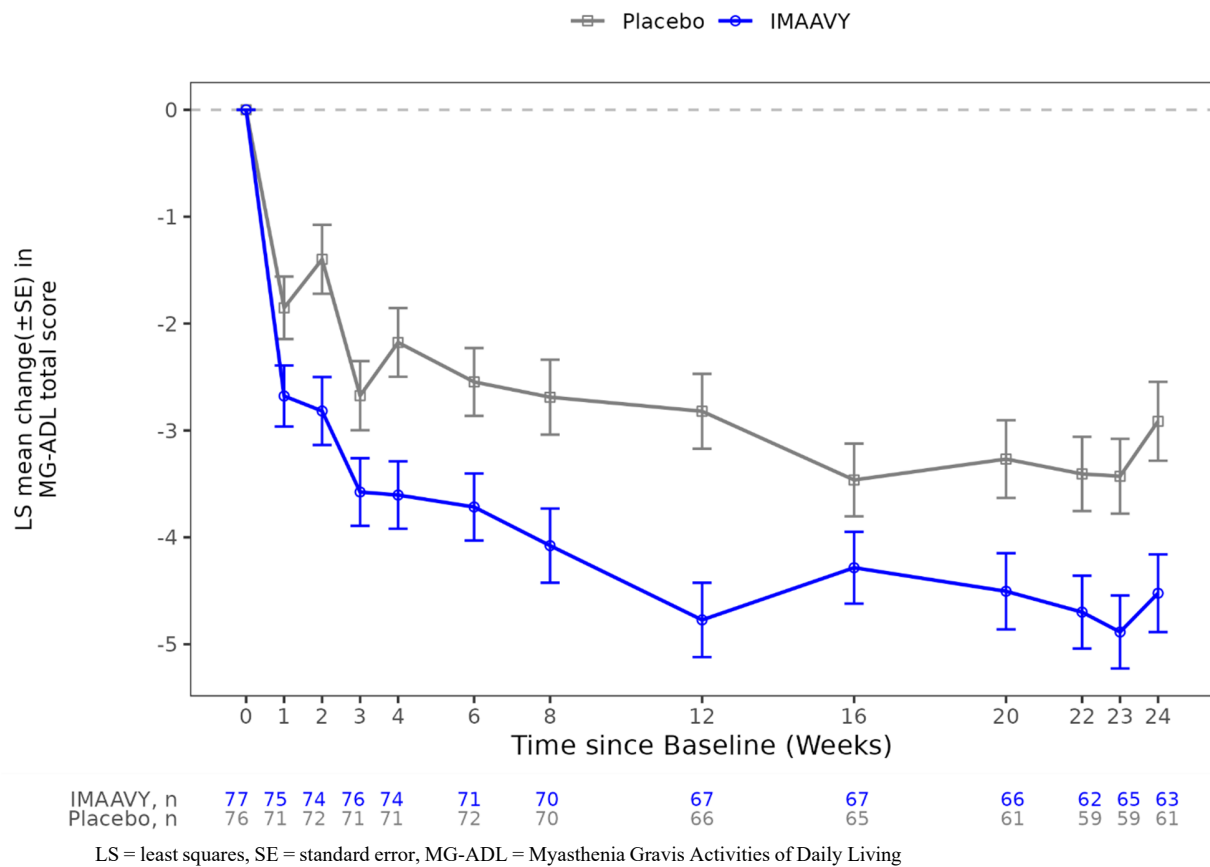
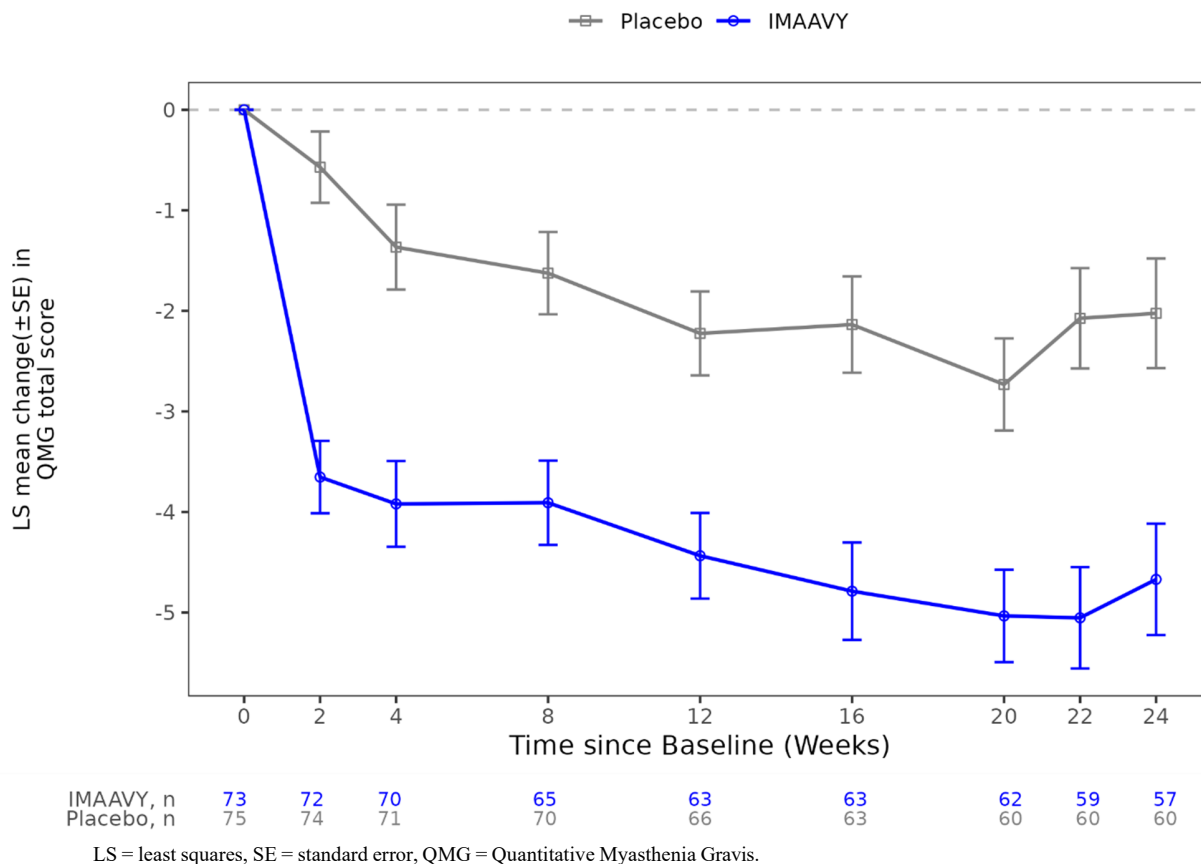


Figure 2: Least Squares Mean Change from Baseline in QMG Total Score Over 24 Weeks in Study 1



15. PHARMACEUTICAL PARTICULARS

15.1 List of excipients

Sucrose

L-arginine hydrochloride

L-histidine monohydrochloride monohydrate

L- methionine

L- histidine

Polysorbate 80

Water for injection

15.2 Shelf life

The expiry date of the product is indicated on the packaging materials

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

IMAAVY concentrate for solution for infusion is a sterile, preservative-free, colorless to slightly brownish, clear to slightly opalescent solution.

IMAAVY is supplied in cartons containing a single-dose vial per carton as:

- 300 mg/1.62 mL (185 mg/mL)
- 1,200 mg/6.5 mL (185 mg/mL)

Storage and Handling

Unopened Vials

Store vials refrigerated at 2°C to 8°C in the original carton to protect from light until the time of use. Do not freeze. Do not shake.

Diluted Solution

For storage of the diluted IMAAVY solution, *see Dosage and Administration (2.3)*.

17. MARKETING AUTHORISATION HOLDER

J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel

18. MANUFACTURER

Janssen Biotech Inc.
800/850 Ridgeview Drive,
Horsham, PA, 19044,
USA.

19. MARKETING AUTHORISATION NUMBER

181-37-38466-00

Approved in February 2026