

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

Pr**EMGALITY**[®]

Galcanezumab Injection

100 mg/mL solution for subcutaneous injection

120 mg/mL solution for subcutaneous injection

CGRP binding antibody

Eli Lilly Canada Inc.
Exchange Tower
130 King Street West, Suite 900
P.O. Box 73
Toronto, Ontario
M5X 1B1
1-888-545-5972
www.lilly.ca

Date of Initial Approval:
July 30, 2019

Date of Revision:
September 17, 2020

Submission Control No: 232324

EMGALITY is a registered trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

RECENT MAJOR LABEL CHANGES

Indications (1)	09/2020
Dosage and Administration, Dosing Considerations (3.1)	09/2020
Dosage and Administration, Recommended Dose and Dosage Adjustment (3.2)	09/2020
Dosage and Administration, Administration (3.3)	09/2020
Dosage and Administration, Missed Dose (3.4)	09/2020
Warnings and Precautions (7)	09/2020
Warnings and Precautions, Pregnant Women (7.1.1)	09/2020

TABLE OF CONTENTS

PART I: HEALTH PROFESSIONAL INFORMATION	4
1 INDICATIONS	4
1.1 Pediatrics	4
1.2 Geriatrics	4
2 CONTRAINDICATIONS	4
3 DOSAGE AND ADMINISTRATION	4
3.1 Dosing Considerations	4
3.2 Recommended Dose and Dosage Adjustment	4
3.3 Administration	5
3.4 Missed Dose	6
4 OVERDOSAGE	6
5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING	6
6 DESCRIPTION	7
7 WARNINGS AND PRECAUTIONS	7
7.1 Special Populations	7
7.1.1 Pregnant Women	7
7.1.2 Breast-feeding	8
7.1.3 Pediatrics	8
7.1.4 Geriatrics	8
8 ADVERSE REACTIONS	8
8.1 Adverse Reaction Overview	8
8.2 Clinical Trial Adverse Reactions	9
8.3 Less Common Clinical Trial Adverse Reactions	14
8.4 Immunogenicity	14
8.5 Post-Market Adverse Reactions	15
9 DRUG INTERACTIONS	15
9.1 Drug-Drug Interactions	15
9.2 Drug-Food Interactions	15
9.3 Drug-Herb Interactions	15
9.4 Drug-Laboratory Test Interactions	15
10 ACTION AND CLINICAL PHARMACOLOGY	16

10.1	Mechanism of Action	16
10.2	Pharmacodynamics	16
10.3	Pharmacokinetics	16
11	STORAGE, STABILITY AND DISPOSAL	17
PART II: SCIENTIFIC INFORMATION		18
12	PHARMACEUTICAL INFORMATION	18
13	CLINICAL TRIALS	18
13.1	Migraine Trial Design and Study Demographics	18
13.2	Migraine Study Results	19
13.3	Episodic Cluster Headache Trial Design and Study Demographics	22
13.4	Episodic Cluster Headache Study Results	24
14	NON-CLINICAL TOXICOLOGY	24
PATIENT MEDICATION INFORMATION		27

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

EMGALITY® (galcanezumab) is indicated for:

- the prevention of migraine in adults who have at least 4 migraine days per month.
- the reduction in the frequency of attacks throughout a cluster period in adults with episodic cluster headache with prior cluster headache periods lasting at least 6 weeks and who have had an inadequate response to, or tolerated poorly, or had contraindications to conventional preventive therapies established by Canadian practice guidelines.

For patients with episodic cluster headache, the treatment benefit should be assessed within 3 weeks after initiation of the treatment. In patients with no improvement within this time period, continuation of the treatment should be carefully considered based on individual patient basis and clinical judgement (see PART I: DOSAGE AND ADMINISTRATION and PART II: CLINICAL TRIALS).

EMGALITY should be initiated by physicians experienced in the diagnosis and treatment of migraine or episodic cluster headache.

1.1 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): The safety and efficacy of EMGALITY has not been studied in patients aged 65 or older.

2 CONTRAINDICATIONS

EMGALITY is contraindicated in patients with known serious hypersensitivity to galcanezumab or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see DOSAGE FORMS, STRENGTHS, COMPOSITION and PACKAGING.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

EMGALITY is administered subcutaneously through a single-use prefilled syringe or prefilled pen. EMGALITY is intended for patient self-administration. Administration should be performed by an individual who has been trained to administer the product (see ADMINISTRATION and INSTRUCTIONS FOR USE).

3.2 Recommended Dose and Dosage Adjustment

Migraine

The recommended dose is an initial (loading) dose of 240 mg (administered as two consecutive subcutaneous injections of 120 mg), followed by once monthly doses of 120 mg (one injection).

Episodic Cluster Headache

The recommended dose is 300 mg once a month (administered as three consecutive subcutaneous injections of 100 mg each) at the onset of the cluster period. The dose regimen must be followed as prescribed.

The treatment benefit should be assessed within 3 weeks after initiation of the treatment. In patients with no improvement within this time period, any further decisions for continuation of the treatment during the current cluster period or initiation of the treatment for subsequent cluster periods should be carefully considered based on individual patient basis and clinical judgement (see PART II: CLINICAL TRIALS).

If further dosing is warranted, EMGALITY **should not** be administered more than once a month during a cluster period.

EMGALITY **should not** be used after the end of a cluster period and during the remission time.

Health Canada has not authorized an indication for pediatric use (see INDICATIONS).

3.3 Administration

EMGALITY is for subcutaneous use only.

EMGALITY may be administered by healthcare professionals, patients, and/or caregivers. Prior to use, provide proper training to patients and/or caregivers on the preparation and administration of EMGALITY prefilled syringe or prefilled pen, including aseptic technique (see INSTRUCTIONS FOR USE).

- Remove EMGALITY from the refrigerator. Prior to use, allow EMGALITY to sit at room temperature for 30 minutes protected from direct sunlight. Do not warm by using a heat source such as hot water or a microwave.
- Follow aseptic injection technique every time EMGALITY is administered.
- Inspect EMGALITY visually for particles or discolouration prior to administration. Do not use if the solution is cloudy, discoloured, or contains particles (see DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).
- Do not shake the product.
- Administer EMGALITY by subcutaneous injection into areas of the abdomen, thigh, upper arm, or buttocks that are not tender, bruised, red, or indurated.
- For multiple injections, you may use the same body site, but not the exact location of the previous injection.
- Do not co-administer EMGALITY with other injectable drugs at the same injection site.

Migraine

EMGALITY for migraine is available both as a 120 mg/mL prefilled syringe and 120 mg/mL prefilled pen.

Two prefilled syringes or pens will deliver the initial 240 mg loading dose. One prefilled syringe or pen will deliver the monthly 120 mg dose. Deliver the entire contents of the prefilled syringe or pen.

Episodic Cluster Headache

EMGALITY for episodic cluster headache is only available as a 100 mg/mL prefilled syringe. Patients should be advised that one dose consists of three consecutive injections of 100 mg.

Three prefilled syringes will deliver the 300 mg dose. Deliver the entire contents of each prefilled syringe.

3.4 Missed Dose

Migraine

Instruct patients to inject a missed dose as soon as possible. Thereafter, resume monthly dosing.

Episodic Cluster Headache

The treatment benefit should be assessed within 3 weeks after initiation of the treatment. In patients with no improvement within this time period, any further decisions for continuation of the treatment during the current cluster period or initiation of the treatment for subsequent cluster periods should be carefully considered based on individual patient basis and clinical judgement (see PART II: CLINICAL TRIALS).

If patients administer a partial dose (inject only 1 or 2 of the three syringes), they should be instructed to inject the missed injection(s) as soon as possible.

If further dosing is warranted and required, inject the next complete dose one month from the date of administering the missed injection(s).

4 OVERDOSAGE

Doses up to 600 mg subcutaneously have been administered to healthy subjects (N = 7) in clinical trials with no evidence of dose limiting toxicity. In case of an overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

For management of a suspected drug overdose, contact your regional poison control centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
By subcutaneous injection	120 mg/mL solution in a 1 mL single-use prefilled syringe or pen	L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride, and water for injection
By subcutaneous injection	100 mg/mL solution in a 1 mL single-use prefilled syringe	

EMGALITY is a sterile, preservative-free, clear and colourless to slightly yellow solution.

For migraine, each single-use prefilled syringe or pen contains 120 mg EMGALITY in 1 mL (120 mg/mL) (see 3.2 RECOMMENDED DOSE and DOSAGE ADJUSTMENT).

For episodic cluster headache, each single-use prefilled syringe contains 100 mg EMGALITY in 1 mL (100 mg/mL) (see 3.2 RECOMMENDED DOSE and DOSAGE ADJUSTMENT).

6 DESCRIPTION

EMGALITY (galcanezumab) is a humanized IgG4 monoclonal antibody that binds calcitonin gene-related peptide (CGRP).

7 WARNINGS AND PRECAUTIONS

Sensitivity

Serious Hypersensitivity

Serious hypersensitivity reactions, including cases of anaphylaxis, angioedema and urticaria, have been reported with CGRP-class products, including EMGALITY, in clinical trials and in post-market experience.

These reactions may occur within minutes, although some may occur up to one month after administration.

If a serious hypersensitivity reaction occurs, administration of EMGALITY should be discontinued immediately and appropriate therapy initiated.

Patients with Cardiovascular Diseases

No safety data are available in these populations. In the migraine and episodic cluster headache studies, patients who had myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, stroke, certain ECG abnormalities or deep vein thrombosis/pulmonary embolism within 6 months of screening, or had planned cardiovascular surgery or percutaneous coronary angioplasty were excluded (see PART II: CLINICAL TRIALS).

Vascular Disorders

No safety data are available in these populations. In the episodic cluster headache study only, patients who had uncontrolled high blood pressure, characterized by systolic blood pressure > 160 mmHg or diastolic blood pressure > 100 mmHg, and evidence of peripheral vascular disease or a diagnosis of Raynaud's phenomenon were excluded (see PART II: CLINICAL TRIALS).

7.1 Special Populations

7.1.1 Pregnant Women

There are very limited human data to establish the safety of EMGALITY during pregnancy. Human IgG is known to cross the placental barrier; therefore, EMGALITY may be transmitted from the mother to the developing fetus.

EMGALITY has a half-life of approximately 27 days (see CLINICAL PHARMACOLOGY). This should be taken into consideration for women who are pregnant or plan to become pregnant while using EMGALITY (see NON-CLINICAL TOXICOLOGY).

EMGALITY should not be used by pregnant women unless the expected benefit to the mother justifies the potential risk to the fetus.

7.1.2 Breast-feeding

There are no data on the presence of EMGALITY in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EMGALITY and any potential effects on the breastfed infant. Human IgG is known to be excreted in breast milk; therefore, EMGALITY may be transmitted from the mother to the breastfed infant. Precaution should be exercised.

7.1.3 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (≥ 65 years of age): The safety and efficacy of EMGALITY has not been studied in patients aged 65 or older.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

A total of 3459 patients and healthy volunteers were exposed to EMGALITY, representing more than 1807 patient years of exposure. Of these, 2129 patients were exposed to EMGALITY once monthly for at least 6 months and 750 patients were exposed for 12 months.

In the migraine and cluster headache studies, patients who had myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, stroke, certain ECG abnormalities or deep vein thrombosis/pulmonary embolism within 6 months of screening, or had planned cardiovascular surgery or percutaneous coronary angioplasty, and BMI ≥ 40 kg/m² were excluded.

In the cluster headache studies only, patients who had uncontrolled high blood pressure, characterized by systolic blood pressure > 160 mmHg or diastolic blood pressure > 100 mmHg, and evidence of peripheral vascular disease or a diagnosis of Raynaud's phenomenon were also excluded.

In three controlled migraine trials, 705 patients received at least one dose of EMGALITY (120 mg) once monthly. Of those patients, 1.8% of patients treated with EMGALITY discontinued double-blind treatment because of adverse events.

In the two controlled cluster headache trials, 166 patients received at least one dose of EMGALITY (300 mg) once monthly. Of those patients, 1.8% treated with EMGALITY discontinued double-blind treatment because of adverse events.

Adverse drug reactions (ADRs) were identified based on findings across Phase 3 efficacy and safety clinical studies in migraine and cluster headache.

The most common adverse reaction reported in ≥ 10% of patients in any study receiving galcanezumab were injection site reactions, and less frequent (≤ 2%) adverse reactions

included constipation, vertigo, pruritus and urticaria. Injection site reactions included multiple preferred terms, such as injection site pain, injection site erythema, injection site pruritus, injection site bruising, injection site swelling, and injection site induration.

8.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Migraine

The data described below reflect exposure to EMGALITY in 1435 patients. In the pivotal studies, the following adverse events listed in Tables 2 and 3 were observed to occur at or above 1% during the double-blind treatment phase.

Table 2: Incidence of Treatment-emergent Adverse Events in \geq 1% of Patients with Episodic Migraine in either EMGALITY Group (120 mg or 240 mg) in Studies EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH)

System Organ Class Preferred Term	EMGALITY 120 mg N = 432 n (%)	EMGALITY 240 mg N = 448 n (%)	Placebo N = 893 n (%)
Ear and labyrinth disorders			
Vertigo	4 (0.9)	7 (1.6)	3 (0.3)
Gastrointestinal disorders			
Nausea	9 (2.1)	11 (2.5)	30 (3.4)
Diarrhea	11 (2.6)	5 (1.1)	21 (2.4)
Constipation	5 (1.2)	8 (1.8)	5 (0.6)
Abdominal pain upper	6 (1.4)	5 (1.1)	4 (0.5)
Dyspepsia	4 (0.9)	6 (1.3)	6 (0.7)
Abdominal pain	7 (1.6)	2 (0.5)	15 (1.7)
Vomiting	1 (0.2)	5 (1.1)	9 (1.0)
General disorders and administration site conditions			
Injection site pain	54 (12.5)	65 (14.5)	114 (12.8)
Injection site reaction	14 (3.2)	30 (6.7)	4 (0.5)
Injection site erythema	16 (3.7)	16 (3.6)	15 (1.7)
Injection site pruritus	15 (3.5)	17 (3.8)	1 (0.1)
Fatigue	11 (2.6)	10 (2.2)	24 (2.7)
Injection site bruising	4 (0.9)	6 (1.3)	7 (0.8)
Injection site swelling	8 (1.9)	2 (0.5)	1 (0.1)
Infections and infestations			
Nasopharyngitis	35 (8.1)	22 (4.9)	68 (7.6)
Upper respiratory tract infection	22 (5.1)	27 (6.0)	47 (5.3)
Sinusitis	16 (3.7)	11 (2.5)	26 (2.9)
Urinary tract infection	13 (3.0)	14 (3.1)	26 (2.9)
Influenza	8 (1.9)	14 (3.1)	19 (2.1)
Bronchitis	5 (1.2)	10 (2.2)	14 (1.6)

Viral infection	8 (1.9)	2 (0.5)	8 (0.9)
Tonsillitis	1 (0.2)	5 (1.1)	6 (0.7)
Injury, poisoning and procedural complications			
Contusion	6 (1.4)	2 (0.5)	8 (0.9)
Investigations			
Weight increased	5 (1.2)	3 (0.7)	11 (1.2)
Musculoskeletal and connective tissue disorders			
Back pain	7 (1.6)	12 (2.7)	26 (2.9)
Arthralgia	8 (1.9)	6 (1.3)	18 (2.0)
Neck pain	8 (1.9)	6 (1.3)	13 (1.5)
Pain in extremity	6 (1.4)	5 (1.1)	14 (1.6)
Musculoskeletal pain	6 (1.4)	3 (0.7)	11 (1.2)
Myalgia	3 (0.7)	6 (1.3)	8 (0.9)
Nervous system disorders			
Dizziness	14 (3.2)	12 (2.7)	21 (2.4)
Headache	4 (0.9)	7 (1.6)	11 (1.2)
Migraine	2 (0.5)	8 (1.8)	9 (1.0)
Psychiatric disorders			
Anxiety	8 (1.9)	2 (0.5)	9 (1.0)
Reproductive system and breast disorders			
Dysmenorrhea ^a	1 (0.3)	5 (1.3)	3 (0.4)
Menorrhagia ^a	2 (0.5)	4 (1.1)	0 (0.0)
Respiratory, thoracic and mediastinal disorders			
Cough	8 (1.9)	9 (2.0)	16 (1.8)
Oropharyngeal pain	8 (1.9)	7 (1.6)	10 (1.1)
Nasal congestion	3 (0.7)	6 (1.3)	6 (0.7)
Skin and subcutaneous tissue disorders			
Rash	6 (1.4)	7 (1.6)	14 (1.6)
Pruritus	5 (1.2)	7 (1.6)	2 (0.2)
Vascular disorders			
Hypertension	6 (1.4)	4 (0.9)	11 (1.2)

^a Denominator adjusted for female-specific event.

Table 3: Incidence of Treatment-emergent Adverse Events in $\geq 1\%$ of Patients with Chronic Migraine in either EMGALITY Group (120 mg or 240 mg) in Study REGAIN (CGAI)

System Organ Class Preferred Term	EMGALITY 120 mg N = 273 n (%)	EMGALITY 240 mg N = 282 n (%)	Placebo N = 558 n (%)
Gastrointestinal disorders			
Nausea	9 (3.3)	8 (2.8)	23 (4.1)
Abdominal pain	6 (2.2)	4 (1.4)	9 (1.6)
Diarrhea	3 (1.1)	6 (2.1)	9 (1.6)
Constipation	2 (0.7)	3 (1.1)	3 (0.5)
Toothache	1 (0.4)	3 (1.1)	3 (0.5)
General disorders and administration site conditions			
Injection site pain	17 (6.2)	20 (7.1)	24 (4.3)
Injection site reaction	8 (2.9)	15 (5.3)	10 (1.8)

Injection site erythema	4 (1.5)	13 (4.6)	5 (0.9)
Fatigue	6 (2.2)	6 (2.1)	10 (1.8)
Influenza like illness	5 (1.8)	4 (1.4)	3 (0.54)
Injection site pruritus	0 (0.0)	7 (2.5)	1 (0.2)
Pyrexia	5 (1.8)	1 (0.4)	2 (0.4)
Injection site bruising	0 (0.0)	4 (1.4)	2 (0.4)
Injection site swelling	0 (0.0)	3 (1.1)	6 (1.1)
Infections and infestations			
Nasopharyngitis	17 (6.2)	9 (3.2)	26 (4.7)
Upper respiratory tract infection	9 (3.3)	9 (3.2)	13 (2.3)
Sinusitis	4 (1.5)	8 (2.8)	5 (0.9)
Urinary tract infection	6 (2.2)	4 (1.4)	7 (1.3)
Influenza	0 (0.0)	6 (2.1)	15 (2.7)
Bronchitis	4 (1.5)	1 (0.4)	3 (0.5)
Gastrointestinal viral	1 (0.4)	4 (1.4)	1 (0.2)
Pneumonia	1 (0.4)	3 (1.1)	1 (0.2)
Pharyngitis streptococcal	0 (0.0)	3 (1.1)	1 (0.2)
Tooth infection	0 (0.0)	3 (1.1)	4 (0.7)
Injury, poisoning and procedural complications			
Arthropod bite	0 (0.0)	3 (1.1)	0 (0.0)
Fall	0 (0.0)	3 (1.1)	3 (0.5)
Investigations			
Weight increased	4 (1.5)	3 (1.1)	1 (0.2)
Musculoskeletal and connective tissue disorders			
Back pain	9 (3.3)	2 (0.7)	14 (2.5)
Neck pain	7 (2.6)	0 (0.0)	8 (1.4)
Arthralgia	1 (0.4)	5 (1.8)	5 (0.9)
Pain in extremity	3 (1.1)	2 (0.7)	6 (1.1)
Nervous system disorders			
Dizziness	6 (2.2)	8 (2.8)	20 (3.6)
Migraine	5 (1.8)	4 (1.4)	5 (0.9)
Headache	4 (1.5)	1 (0.4)	10 (1.8)
Somnolence	4 (1.5)	1 (0.4)	3 (0.5)
Lethargy	3 (1.1)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders			
Cough	4 (1.5)	4 (1.4)	3 (0.5)
Oropharyngeal pain	2 (0.7)	5 (1.8)	3 (0.5)
Sinus congestion	3 (1.1)	3 (1.1)	2 (0.4)
Rhinitis allergic	2 (0.7)	3 (1.1)	2 (0.4)
Skin and subcutaneous tissue disorders			
Rash	2 (0.7)	3 (1.1)	3 (0.5)
Acne	3 (1.1)	1 (0.4)	0 (0.0)

Injection site reactions

In the 3 integrated pivotal migraine placebo-controlled study periods, injection site pain was the most frequently ($\geq 10\%$) reported event. In most patients, reported injection site pain occurred

within 1 hour of injection and resolved the same day. The majority of injection site reactions were reported within 1 day and most resolved within a few days. Most events were mild to moderate and did not lead to discontinuation of galcanezumab.

Constipation

In the 3 integrated pivotal migraine placebo-controlled study periods, all constipation events were mild or moderate in severity. There were no serious events.

Vertigo

In the 3 integrated pivotal migraine placebo-controlled study periods, the majority of vertigo events were mild or moderate in severity. There were no serious events.

Pruritus

In the 3 integrated pivotal migraine placebo-controlled study periods, the majority of pruritus events were mild or moderate in severity. There were no serious events.

Urticaria

In the 3 integrated pivotal migraine placebo-controlled study periods, cases of urticaria were uncommon. However, serious cases of urticaria have been reported in galcanezumab clinical studies.

Episodic Cluster Headache

The safety of EMGALITY (300 mg once a month) is based on the assessment of data from 2 placebo-controlled clinical studies: CGAL and CGAM. The efficacy assessment of EMGALITY 300 mg once a month is based on Study CGAL (episodic cluster headache). Study CGAM was performed in patients with chronic cluster headache and used for the safety assessment only.

The data described below reflect exposure to EMGALITY in 166 patients. In the placebo-controlled studies, the following adverse events listed in Table 4 were observed to occur in $\geq 1\%$ of patients during the double-blind treatment phase.

Table 4: Incidence of Treatment-emergent Adverse Events in $\geq 1\%$ of Patients in the EMGALITY Safety Population Group (300 mg) (Studies CGAL and CGAM)

System Organ Class Preferred Term	EMGALITY 300 mg N = 166 n (%)	Placebo N = 177 n (%)
Ear and labyrinth disorders		
Tinnitus	3 (1.8)	2 (1.1)
Vertigo	2 (1.2)	3 (1.7)
Gastrointestinal disorders		
Nausea	6 (3.6)	6 (3.4)
Constipation	3 (1.8)	2 (1.1)
Vomiting	3 (1.8)	3 (1.7)
Abdominal pain	2 (1.2)	3 (1.7)
Gastrointestinal disorder	2 (1.2)	0 (0.0)
Toothache	2 (1.2)	2 (1.1)
General disorders and administration site conditions		

Injection site pain	17 (10.2)	11 (6.2)
Injection site erythema	9 (5.4)	1 (0.6)
Fatigue	6 (3.6)	7 (4.0)
Influenza like illness	5 (3.0)	2 (1.1)
Injection site pruritis	5 (3.0)	2 (1.1)
Pyrexia	5 (3.0)	2 (1.1)
Injection site swelling	3 (1.8)	1 (0.6)
Non-cardiac chest pain	3 (1.8)	1 (0.6)
Chills	2 (1.2)	1 (0.6)
Injection site bruising	2 (1.2)	0 (0.0)
Injection site induration	2 (1.2)	0 (0.0)
Infections and infestations		
Nasopharyngitis	15 (9.0)	16 (9.0)
Gastroenteritis	3 (1.8)	1 (0.6)
Influenza	3 (1.8)	3 (1.7)
Bronchitis	2 (1.2)	1 (0.6)
Rhinitis	2 (1.2)	1 (0.6)
Tooth abscess	2 (1.2)	0 (0.0)
Urinary tract infection	2 (1.2)	0 (0.0)
Metabolism and nutrition disorders		
Decreased appetite	2 (1.2)	1 (0.6)
Musculoskeletal and connective tissue disorders		
Back pain	5 (3.0)	4 (2.3)
Myalgia	4 (2.4)	3 (1.7)
Pain in extremity	4 (2.4)	1 (0.6)
Nervous system disorders		
Dizziness	5 (3.0)	5 (2.8)
Headache	3 (1.8)	4 (2.3)
Memory impairment	2 (1.2)	0 (0.0)
Migraine	2 (1.2)	1 (0.6)
Psychiatric disorders		
Irritability	2 (1.2)	0 (0.0)
Reproductive system and breast disorders		
Dysmenorrhoea ^a	1 (2.6)	0 (0.0)
Menstrual disorder ^a	1 (2.6)	0 (0.0)
Prostatitis ^b	2 (1.6)	0 (0.0)
Respiratory, thoracic and mediastinal disorders		
Asthma	2 (1.2)	0 (0.0)
Cough	2 (1.2)	1 (0.6)
Skin and subcutaneous tissue disorders		
Pruritis	3 (1.8)	0 (0.0)
Erythema	2 (1.2)	1 (0.6)

Vascular disorders		
Hot flush	3 (1.8)	0 (0.0)
Hypertension	2 (1.2)	3 (1.7)

^a Denominator adjusted for female-specific event.

^b Denominator adjusted for male-specific event.

Injection site reactions

In two integrated cluster headache placebo-controlled study periods, injection site pain was the most frequently reported event (10.2%). The majority of injection site reactions, including pain, were reported within 1 day and most resolved within a few days. Most events were mild to moderate and did not lead to discontinuation of galcanezumab. There were no serious adverse events.

Constipation

In two integrated cluster headache placebo-controlled study periods, three patients reported constipation. None led to discontinuation. One event was reported as serious, which resolved.

Vertigo

In two integrated cluster headache placebo-controlled study periods, two patients reported vertigo both of mild severity, one led to discontinuation. There were no serious adverse events.

Pruritus

In two integrated cluster headache placebo-controlled study periods, three patients reported pruritus of mild to moderate severity and did not lead to discontinuation. There were no serious adverse events.

Urticaria

In two integrated cluster headache placebo-controlled study periods, no patients reported urticaria.

8.3 Less Common Clinical Trial Adverse Reactions

From all clinical trials with EMGALITY in adult patients with episodic and chronic migraine, and episodic and chronic cluster headache, the following less common adverse events of < 1% have been observed. The causality to EMGALITY has not been established.

Cardiac disorders: palpitations, angina pectoris, acute myocardial infarction

Eye disorders: amaurosis

Hepatobiliary disorders: cholelithiasis, cholecystitis

Psychiatric disorders: anxiety, confusion state, disorientation

Skin and subcutaneous tissue disorders: swelling face

8.4 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The immunogenicity of EMGALITY has been evaluated using an immunoassay for the detection of binding anti-galcanezumab antibodies. For patients whose sera tested positive in the screening immunoassay, an in vitro ligand-binding immunoassay was performed to detect neutralizing antibodies.

In placebo-controlled clinical studies [EVOLVE -1 (CGAG), EVOLVE-2 (CGAH), and REGAIN (CGAI)] with EMGALITY administration up to 6 months, the incidence of anti-galcanezumab antibody development was 4.8% (33/688) in patients receiving EMGALITY once monthly (32 of whom had in vitro neutralizing activity). With 12 months of treatment in an open-label study, 12.5% (16/128) of EMGALITY-treated patients developed anti-galcanezumab antibodies (all 16 of whom had in vitro neutralizing activity). With up to 3 months of double-blind treatment, up to 0.9% of galcanezumab treated patients with cluster headache developed antidrug antibodies of low titer with neutralizing activity in vitro.

The incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to galcanezumab with the incidence of antibodies to other products may be misleading.

In clinical trials, the presence of anti-drug antibodies did not affect the efficacy or safety of EMGALITY.

8.5 Post-Market Adverse Reactions

The following adverse reactions are based on post-marketing spontaneous reports. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate the frequency.

Immune System disorders: Anaphylaxis, Angioedema

Skin and subcutaneous tissue disorders: Rash

9 DRUG INTERACTIONS

9.1 Drug-Drug Interactions

Interactions with other drugs have not been studied.

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

9.2 Drug-Food Interactions

Interactions with food have not been studied.

9.3 Drug-Herb Interactions

Interactions with herbal products have not been studied.

9.4 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been studied.

10 ACTION AND CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Galcanezumab is a humanized IgG4 monoclonal antibody that binds calcitonin gene-related peptide (CGRP) and prevents its biological activity.

Galcanezumab targets CGRP with high affinity ($K_D = 31$ pM) and does not bind to the CGRP receptor or related peptides adrenomedullin, amylin, calcitonin and intermedin.

10.2 Pharmacodynamics

There are no relevant data on the pharmacodynamic effects of galcanezumab.

10.3 Pharmacokinetics

Galcanezumab exhibits linear pharmacokinetics (PK) and exposure increases proportionally across the dose range of 5-300 mg.

Steady-state galcanezumab concentrations at 120 mg monthly are achieved with an initial loading dose of 240 mg. Steady-state PK parameters after a 240 mg loading dose followed by 5 consecutive monthly doses of 120 mg are shown in Table 5.

A dose of 300 mg monthly achieves steady-state concentration after the fourth dose administration. Table 5 shows steady-state PK parameters at 300 mg monthly.

Based upon population PK modelling, there were no significant differences in PK parameters between healthy volunteers, patients with episodic or chronic migraine, and patients with episodic cluster headache.

Table 5: Steady-State Pharmacokinetic Parameters of EMGALITY at 120 mg Monthly (Migraine) and 300 mg Monthly (Episodic Cluster Headache)^{a, b}

Parameter	120 mg Monthly	300 mg Monthly
C _{max} mean (%CV)	28 mcg/mL (35)	62 mcg/mL (24)
AUC _{tau} mean (%CV)	15,900 mcg x hour/mL (42)	34,700 mcg x hour/mL (28)
C _{min} mean (% CV)	15 mcg/mL (53)	33 mcg/mL (35)

^a Based on population PK analysis.

^b PK parameters reported as geometric mean (percent coefficient of variation).

Absorption: Following administration of galcanezumab at steady-state, the median time to maximum concentration was 5 days (range: 3 to 14 days).

Injection site location did not significantly influence the absorption of galcanezumab.

Distribution: Based on a population PK analysis, the apparent volume of distribution (V/F) of galcanezumab was estimated to be 7.3 L (34% Inter Individual Variability [IIV]).

Metabolism: As a humanized IgG4 monoclonal antibody, galcanezumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination: Based on a population PK analysis, the apparent clearance (CL/F) of galcanezumab was estimated to be 0.008 L/h and the half-life of galcanezumab was approximately 27 days.

Special Populations and Conditions

Based on a population PK analysis, age (18-65), sex, race, injection site, anti-drug antibodies, or ethnicity had no clinically meaningful effects on the PK of galcanezumab.

Hepatic Insufficiency: No clinical studies have been conducted to evaluate the effect of hepatic impairment on the PK of galcanezumab. Based on a population PK analysis, bilirubin concentration did not significantly influence the CL/F of galcanezumab.

Renal Insufficiency: No clinical studies have been conducted to evaluate the effect of renal impairment on the PK of galcanezumab. Population PK analysis of integrated data from the galcanezumab clinical studies revealed that creatinine clearance did not affect the CL/F of galcanezumab in patients with mild or moderate renal impairment. Patients with severe renal impairment (creatinine clearance <30 mL/min) have not been studied.

11 STORAGE, STABILITY AND DISPOSAL

The prefilled syringes or pens should be stored under refrigeration at 2°C to 8°C until time of use. Keep the syringe or pen in the carton in order to protect from exposure to light. **DO NOT FREEZE OR SHAKE** the syringe or pen. The shelf life is 24 months when the syringes or pens are stored at 2°C to 8°C.

The chemical and physical stability for the EMGALITY solution was demonstrated for up to 7 days outside of refrigeration when stored at temperatures up to 30°C. If these conditions are exceeded, EMGALITY must be discarded.

Discard the EMGALITY single-use prefilled syringe or pen in a puncture-resistant container.

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: galcanezumab

Chemical name: Immunoglobulin G4, anti-(human calcitonin gene-related peptide) (human-*Mus musculus* clone III heavy side chain), disulfide with human-*Mus musculus* clone III κ -chain, dimer

Molecular mass: The observed molecular weight of the non-glycosylated, disulfide linked form of galcanezumab is 144,084 Da

Structural formula: Galcanezumab is a humanized immunoglobulin G4 (IgG4) isotype monoclonal antibody composed of two identical immunoglobulin light (κ) chains consisting of 214 amino acids each of relative molecular weight 23,330 Da, and two identical immunoglobulin heavy (γ) chains consisting of 445 amino acids each of molecular weight 48,728 Da. The heavy chain subunit contains an N-linked glycosylation, which is modified with oligosaccharides.

Physicochemical properties: Clear to colourless to slightly yellow solution. The solution pH is 5.3 to 6.3. The osmolality is 255 to 345 mOsm/kg.

13 CLINICAL TRIALS

13.1 Migraine Trial Design and Study Demographics

EMGALITY was evaluated as a preventive treatment (a treatment expected to decrease migraine headache frequency) of episodic or chronic migraine in three Phase 3 randomized, multicenter, double-blind, placebo-controlled studies in adult patients. Studies enrolled patients with a history of migraine according to the International Classification of Headache Disorders (ICHD-3). Patients who had myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, stroke, certain ECG abnormalities or deep vein thrombosis/pulmonary embolism within 6 months of screening, or had planned cardiovascular surgery or percutaneous coronary angioplasty were excluded. Patients with a persistent daily headache, history of headache other than migraine and BMI ≥ 40 kg/m² were also excluded.

Demographics for these studies are outlined in Table 6.

Table 6: Summary of patient demographics for clinical trials in Migraine

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
EVOLVE-1 (CGAG)	Randomized, multicenter, double-blind, placebo-controlled study in episodic migraine patients.	subcutaneous injection	EMGALITY (120 mg) (n=213) EMGALITY (240 mg) (n=212) Placebo (n=433)	40.7 (18-65)	Female: 84% Male: 16%
EVOLVE-2 (CGAH)	Randomized, multicenter, double-blind, placebo-controlled study in episodic migraine patients.	subcutaneous injection	EMGALITY (120 mg) (n=231) EMGALITY (240 mg) (n=223) Placebo (n=461)	41.9 (18-65)	Female: 85% Male: 15%
REGAIN (CGAI)	Randomized, multicenter, double-blind, placebo-controlled study in chronic migraine patients.	subcutaneous injection	EMGALITY (120 mg) (n=278) EMGALITY (240 mg) (n=277) Placebo (n=558)	41.0 (18-65)	Female: 83% Male: 17%

13.2 Migraine Study Results

Episodic Migraine

EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH) were identically designed, randomized, 6-month, double-blind, placebo-controlled studies. In EVOLVE-1 (CGAG), a total of 858 patients with a history of episodic migraine (4 to 14 migraine days per month) were randomized to receive either galcanezumab 120 mg (EMGALITY, N = 213), galcanezumab 240 mg (N = 212), or placebo (N = 433) by subcutaneous injection once monthly (QM). In EVOLVE-2 (CGAH), a total of 915 patients with a history of episodic migraine were randomized to receive either galcanezumab 120 mg (EMGALITY, N = 231), galcanezumab 240 mg (N = 223), or placebo (N = 461) by subcutaneous injection once monthly (QM). All patients in the 120 mg dose group received an initial loading dose of 240 mg.

The primary efficacy endpoint for EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH) was the mean change from baseline in the number of monthly migraine headache days over months 1 to 6. Key secondary endpoints included response rates (the mean percentages of patients with $\geq 50\%$ reduction) and mean change from baseline in the number of monthly migraine headache days that acute medication was taken over months 1 to 6.

Patients were 18 to 65 years of age (mean age of 40.7 in EVOLVE-1 and 41.9 in EVOLVE-2) with a history of migraine for at least 1 year (mean 20 years in EVOLVE-1 and 2 trials) and migraine onset prior to age 50. The mean number of monthly migraine headache days at baseline was 9.1 in each study. Most patients were female (84% EVOLVE-1, 85% EVOLVE-2), white (80% EVOLVE-1, 70% EVOLVE-2) and had failed one or more migraine preventive therapies in the past. Patients were allowed to use acute headache treatments including migraine-specific medications (i.e., triptans, ergotamine derivatives), NSAIDs, and acetaminophen. Patients were not allowed any treatments for the prevention of migraine. Both studies excluded patients with medication overuse headache. A total of 60% and 65% of patients in EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH), respectively, had taken preventive treatments for migraine prior to baseline. A total of 177 (83%) patients in the EMGALITY 120 mg dose group and 351 (81%) patients on placebo completed the double-blind phase in EVOLVE-1 (CGAG), and a total of 203 (88%) patients in the EMGALITY 120 mg dose arm and 387 (84%) patients on placebo completed the double-blind phase in EVOLVE-2 (CGAH).

The results of the studies are presented in Table 7.

Table 7: Efficacy Results in Studies EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH)

	EVOLVE-1 (CGAG)		EVOLVE-2 (CGAH)	
	EMGALITY 120 mg N = 210	Placebo N = 425	EMGALITY 120 mg N = 226	Placebo N = 450
Primary Endpoint				
Mean Reduction in Monthly Migraine Headache Days (over Months 1 to 6)^a				
Mean change from baseline	-4.7	-2.8	-4.3	-2.3
Difference from placebo	-1.9		-2.0	
p-value ^b	<0.001		<0.001	
Key Secondary Endpoints				
$\geq 50\%$ Migraine Headache Days Responders (over Months 1 to 6)				
% Responders	62.3%	38.6%	59.3%	36.0%
Difference from placebo	23.7%		23.3%	
p-value ^b	<0.001		<0.001	
Mean Reduction in Monthly Migraine Headache Days that Acute Medication was Taken (over Months 1 to 6)^{a, c}				
Mean change from baseline (days)	-4.0	-2.2	-3.7	-1.9
Difference from placebo	-1.8		-1.8	
p-value ^b	<0.001		<0.001	

^a LS mean change from baseline, difference from placebo, and p-value are based on a mixed effects repeated measures model including treatment group, region or country (North America, Europe, or Other), month, interaction of treatment and month, baseline value, and interaction of baseline value and month. For the key secondary endpoints, the model also includes mean reduction in baseline migraine headache day category (<8 vs. ≥ 8).

- ^b A superchain procedure adjusting for multiple testing was used to maintain the 2-sided type I error at 0.05 for the primary and key secondary endpoints.
- ^c Monthly migraine headache days that acute medication was taken was calculated as the number of calendar days in a 30-day period on which migraine or probable migraine occurred and acute medication was used

A treatment effect was observed in a prespecified monthly analysis as early as month one.

Data from EVOLVE-1 (CGAG) and EVOLVE-2 (CGAH) studies were pooled and in 453 (26%) patients who failed one or more preventive treatments for efficacy reasons, the difference in the reduction of mean monthly migraine headache days observed between EMGALITY and placebo was -2.7 days. In 173 (10%) patients who failed two or more preventive treatments for efficacy reasons, the difference in the reduction of mean monthly migraine headache days observed between EMGALITY and placebo was -2.6 days.

Chronic Migraine

REGAIN (CGAI) was a randomized, 3-month, double-blind, placebo-controlled study. A total of 1113 patients with a history of chronic migraine (≥ 15 headache days per month with ≥ 8 migraine days per month) were randomized to receive either galcanezumab 120 mg (EMGALITY, N = 278), galcanezumab 240 mg (N = 277), or placebo (N = 558) by subcutaneous injection once monthly (QM). All patients in the 120 mg dose group received an initial loading dose of 240 mg.

The primary endpoint was the mean change from baseline in the number of monthly migraine headache days over months 1 to 3. Key secondary endpoints included response rates (the mean percentages of patients with $\geq 50\%$ reduction) and mean change from baseline in the number of monthly migraine headache days that acute medication was taken over months 1 to 3.

Patients were 18 to 65 years of age (mean age of 41.0 in REGAIN) with a history of migraine for at least 1 year (mean duration 21.1 years). The mean number of monthly migraine headache days at baseline was 19.4. Patients were allowed to use acute headache treatments including migraine-specific medications (i.e., triptans, ergotamine derivatives), NSAIDs, and acetaminophen. A total of 78% of patients had taken preventive treatments for migraine prior to baseline, 15% of patients were taking concomitant stable doses of topiramate or propranolol for prevention of migraine. Patients with medication overuse headache were not excluded.

A total of 263 (95%) patients in the EMGALITY 120 mg dose group and 508 (91%) patients on placebo completed the double-blind phase in REGAIN (CGAI).

The results of this study are shown in Table 8.

Table 8: Efficacy Results in REGAIN (CGAI)

	EMGALITY 120 mg N = 273	Placebo N = 538
Primary Endpoint		
Mean Reduction in Monthly Migraine Headache Days (over Months 1 to 3)^a		
Mean change from baseline	-4.8	-2.7
Difference from placebo	-2.1	

p-value ^b	<0.001	
Key Secondary Endpoints		
≥50% Migraine Headache Days Responders (over Months 1 to 3)		
% Responders	27.6%	15.4%
Difference from placebo	12.2%	
p-value ^b	<0.001	
Mean Reduction in Monthly Migraine Headache Days that Acute Medication was Taken (over Months 1 to 3)^{a, c}		
Mean change from baseline (days)	-4.7	-2.2
Difference from placebo	-2.5	
p-value ^d	<0.001 ^d	

^a LS mean change from baseline, difference from placebo, and p-value are based on a mixed effects repeated measures model including treatment group, baseline medication overuse [yes vs. no], use of concurrent migraine prophylaxis [yes vs. no], and country, month, interaction of treatment and month, baseline value, and interaction of baseline value and month.

^b A superchain procedure adjusting for multiple testing was used to maintain the 2-sided type I error at 0.05 for the primary and key secondary endpoints.

^c Monthly migraine headache days that acute medication was taken was calculated as the number of calendar days in a 30-day period on which migraine or probable migraine occurred and acute medication was used.

^d Not statistically significant versus placebo after multiplicity adjustment.

A treatment effect was observed in a prespecified monthly analysis as early as month one.

In the 355 (64%) patients from the REGAIN (CGAI) Study who had acute headache medication overuse at baseline, the difference in the reduction of mean monthly migraine headache days observed between EMGALITY and placebo was -2.53 days.

In the 549 (49%) patients from the REGAIN (CGAI) Study who failed one or more preventive treatment for efficacy reasons, the difference in the reduction of mean monthly migraine headache days observed between EMGALITY and placebo was -3.5. In 328 (30%) patients who failed two or more preventive treatments, the difference in the reduction of mean monthly migraine headache days observed between EMGALITY and placebo was -4.5 days.

13.3 Episodic Cluster Headache Trial Design and Study Demographics

The safety of EMGALITY (300 mg once a month) is based on the assessment of data from 2 placebo-controlled clinical studies: CGAL and CGAM.

Study CGAM was conducted in patients with chronic cluster headache and used for the safety assessment only.

The efficacy assessment of EMGALITY 300 mg once a month is based on Study CGAL (episodic cluster headache).

EMGALITY was evaluated as a preventive treatment (a treatment expected to decrease the frequency of cluster headache attacks throughout a cluster period) in adult patients with episodic cluster headache. Study CGAL included adults who met the International Classification of Headache Disorders 3rd edition (ICHD-3-beta version) diagnostic criteria for episodic cluster headache and had a prior history of a cluster period lasting 6 weeks or longer.

Study CGAL excluded patients on other preventive treatments; patients with medication overuse headache; patients with a history of myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft, certain ECG abnormalities or deep vein thrombosis/pulmonary embolism within 6 months of screening; and patients who had planned cardiovascular surgery or percutaneous coronary angioplasty. Patients with any history of stroke, intracranial or carotid aneurysm, intracranial hemorrhage, or vasospastic angina; clinical evidence of peripheral vascular disease; diagnosis of Raynaud's disease or BMI \geq 40 kg/m² were also excluded.

Table 9: Summary of patient demographics for clinical trials in Episodic Cluster Headache (CGAL)

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
CGAL	Randomized, multicenter, 8 week, double-blind, placebo-controlled study in adult patients with episodic cluster headache, and a prior history of a cluster period lasting 6 weeks or longer.	Once a month: EMGALITY 300 mg or placebo administered via subcutaneous injection	EMGALITY (300 mg) (n = 49) Placebo (n = 57)	46 (19 – 65)	Male: 88/106 (83%) Female: 18/106 (17%)

The study was composed of: I) screening/washout phase; II) a prospective baseline phase; III) 8-week double-blind treatment phase; IV) post-treatment follow up. Patients who entered phase I in an active cluster period and did not need to wash out any excluded medications moved directly to phase II. Patients could enter screening in an active cluster period, or in remission, but were required to be an active cluster period to enter the prospective baseline phase which was used to establish baseline attack frequency. During the prospective 7-day baseline assessment, patients were required to have a maximum of 8 attacks per day, a minimum of one attack every other day, and at least 4 attacks.

All patients were randomized at the initiation of phase III (1:1) to receive subcutaneous injections of either EMGALITY 300 mg once a month or placebo once a month, over an 8-week treatment period. Patients were allowed to use pre-specified acute/abortive cluster headache treatments, including triptans, oxygen, acetaminophen, and NSAIDs during the study.

No preventive medications were allowed during the double-blind 8-week treatment period.

Randomization was stratified based on sex, average daily attack frequency (\leq 4 attacks per day, $>$ 4 attacks per day), and investigative site.

Headache information was captured daily using the electronic patient-reported outcome (ePRO) diary device during study phases II and III.

A total of 106 (18 females, 88 males), ranging age 19 to 65 years of age (mean age of 46) patients were randomized and treated with either EMGALITY (galcanezumab) 300 mg (N = 49)

or placebo (N = 57) by subcutaneous injection once a month (QM). In the prospective baseline phase, a majority of patients had ≤ 4 cluster headache attacks per day at baseline (85.9%) and the mean number of weekly cluster headache attacks was 17.3 for placebo group and 17.8 for galcanezumab group, with an average severity of pain of moderate to severe. A total of 90 (84.9%) patients completed the 8-week double-blind treatment phase.

The primary efficacy endpoint was the mean change from baseline (defined as 7 consecutive days from the daily ePRO diary during the prospective baseline assessment) in weekly cluster headache attack frequency across Weeks 1 to 3. The key secondary endpoint was the proportion of patients achieving response (defined as a reduction from baseline of 50% or greater in the weekly cluster headache attack frequency) at Week 3. The primary endpoint (Weeks 1-3) and gated secondary endpoint (at Week 3) of Study CGAL measured the effect of only one dose of galcanezumab. Results are summarized in Table 10.

13.4 Episodic Cluster Headache Study Results

Table 10: Efficacy Results in Episodic Cluster Headache Study CGAL

	EMGALITY 300 mg N = 49	Placebo N = 57
Primary Endpoint		
Mean Reduction in Weekly Cluster Headache Attack Frequency (over Weeks 1 to 3)^a		
Prospective Baseline Cluster Headache Attack Frequency	17.8	17.3
Mean change from prospective baseline	-8.7	-5.2
Difference from placebo	-3.5	
p-value	0.036	
Key Secondary Endpoint		
$\geq 50\%$ Weekly Cluster Headache Attack Frequency Responders (at Week 3)		
% Responders	71.4%	52.6%
Difference from placebo	18.8%	
p-value ^b	0.046	

^a LS mean change from baseline, difference from placebo, and p-value are based on a mixed effects repeated measures model including treatment group, sex, pooled investigative site, week, interaction of treatment and week, and baseline value. The key secondary analysis is based on an ANCOVA model including treatment group, sex, baseline value, and stratified by pooled investigative site.

^b A sequential testing procedure adjusting for multiple testing was used to maintain the 2-sided type I error at 0.05 for the primary and key secondary endpoints.

Important baseline characteristics such as time from cluster onset before randomization, the historical length of cluster periods, and historical number of cluster headache attacks per day were not collected in pivotal Study CGAL. More patients in the EMGALITY treatment group had attacks in last 7 days prior to screening (visit 1) than in the placebo treatment group. No differences between the treatment groups have been observed in pain severity, attack duration, use of acute medication through week 1 to 8. The statistical significance for the primary and gated secondary endpoints was observed only up to week 3.

When interpreting the efficacy results of the trial, these observations should be taken into consideration.

14 NON-CLINICAL TOXICOLOGY

General Toxicology

Galcanezumab was well tolerated in cynomolgus monkeys and Sprague Dawley rats at weekly subcutaneous doses of up to 100 mg/kg and 20 mg/kg (72 and 3.7 times greater than the human exposure at the 300 mg once monthly dose based on AUC), respectively, for up to 6 months. There was no evidence of galcanezumab-related systemic toxicity in cynomolgus monkeys; however, in rats, two male deaths were observed at a dose of 250 mg/kg (8.7 times greater than the human exposure at 300 mg once monthly dose based on AUC) for which a drug-related effect could not be ruled out. In both rats and monkeys, galcanezumab-related non-adverse macroscopic and microscopic changes were limited to the injection sites and were consistent with inflammation. There were no galcanezumab-related effects on cardiovascular, respiratory, or central nervous systems as assessed in cynomolgus monkeys.

Carcinogenesis

Non-clinical studies have not been conducted to evaluate the carcinogenic potential of galcanezumab.

Genotoxicity

Non-clinical studies have not been conducted to evaluate the genotoxic potential of galcanezumab.

Reproductive and Developmental Toxicity

Male fertility and female fertility were assessed in separate studies in Sprague Dawley rats. In the male fertility study, males were administered subcutaneous doses up to 250 mg/kg once weekly prior to and during mating. In combined female fertility and embryo-fetal development studies, females were administered subcutaneous doses up to 250 mg/kg once every three days prior to and during mating and continuing throughout organogenesis. No galcanezumab-related adverse effects on male or female fertility parameters, including adverse effects on reproductive organs, estrous cycle, sperm motility and concentration, and mating and fertility indices, were observed at a dose of 250 mg/kg (3.6 and 18 times greater than the human exposure at the 300 mg once monthly dose based on AUC in males and females, respectively).

No galcanezumab-related malformations or embryo-fetal toxicity were observed in the combined female fertility and embryo-fetal development studies conducted in Sprague Dawley rats at maternal doses up to 250 mg/kg or in an embryo-fetal development study conducted in New Zealand White Rabbits at maternal doses up to 100 mg/kg administered on gestation day 7, 12, 16, and 20. Exposures (AUC) were 18 and 29 times higher than the human exposure at the 300 mg once monthly dose in rats and rabbits, respectively. While galcanezumab-related increases in the number of fetuses and litters with skeletal variations, consisting of short ribs and a decrease in the mean number of ossified caudal vertebrae, occurred at 250 mg/kg in the rat embryo-fetal development study, these deviations were considered non-adverse.

In a pre- and post-natal development study conducted in Sprague Dawley rats, there were no effects on survival, growth, sexual maturation, behaviour or reproduction in offspring exposed to galcanezumab in utero and through lactation at maternal doses up to 250 mg/kg administered once every three days (16 times greater than the human exposure at the 300 mg once monthly dose based on AUC).

Juvenile Toxicity

In a juvenile toxicology study, Sprague Dawley rats were administered galcanezumab at doses of 30 and 250 mg/kg twice weekly from Postnatal Day 21 through 90. There were no galcanezumab-related adverse effects on survival, clinical observations, body weight, food consumption, sexual maturation, behavioral assessments, reproduction, bone length, clinical pathology and histopathology. Decreases in metaphysis total bone mineral content associated with decreases in trabecular bone mineral content and bone mineral density occurred at 250 mg/kg. In males only, decreases in metaphysis and diaphysis total surface area and diaphysis periosteal circumference were also observed at 250 mg/kg. No galcanezumab-related findings were observed upon histopathological examination of bone.

Galcanezumab-related microscopic changes were limited to the injection sites and consisted of an increased incidence and severity of mononuclear inflammatory cell infiltrates in the subcutaneous tissue at the administration site in males and females given 30 and 250 mg/kg. Minimal to mild increases in fibrinogen and minimal increases in globulins occurred in males at 250 mg/kg and in females at 30 and 250 mg/kg. These changes were supportive of a minimal to mild inflammatory process and correlated with the injection site histopathology findings. At the end of the recovery period, the incidence of the injection site histopathology findings as well as the correlating clinical pathology changes were decreased, suggesting partial recovery.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

PrEMGALITY®
(pronounced em-GAL-it-ē)
galcanezumab injection

www.lilly.ca

Lilly

Read this carefully before you start taking **EMGALITY** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **EMGALITY**.

What is EMGALITY used for?

EMGALITY is a medicine used in adults:

- to prevent migraine in patients who have at least 4 migraine days per month
- to reduce the number of attacks throughout a cluster period in patients with episodic cluster headache

How does EMGALITY work?

EMGALITY contains the active substance galcanezumab, which belongs to a group of substances called monoclonal antibodies. Galcanezumab binds to a protein called calcitonin gene-related peptide (CGRP). Increased CGRP levels in the blood have been linked to migraine and episodic cluster headache.

What are the ingredients in EMGALITY?

Medicinal ingredients: galcanezumab

Non-medicinal ingredients: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride, water for injection

EMGALITY comes in the following dosage forms:

- 120 mg solution for injection in a 1 mL prefilled syringe for migraine
- 120 mg solution for injection in a 1 mL prefilled pen for migraine
- 100 mg solution for injection in a 1 mL prefilled syringe for episodic cluster headache

Do not use EMGALITY if:

- **You have an allergy to galcanezumab or any of the other ingredients of this medicine** (see **What are the ingredients in EMGALITY?** above).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take EMGALITY. Talk about any health conditions or problems you may have, including if you:

- have had an allergic reaction to EMGALITY.
- have any chronic medical disease or need to take medication regularly.

Other warnings you should know about:

- Allergic reactions with EMGALITY are usually mild to moderate (such as rash or itching). Rarely patients taking EMGALITY have experienced a serious allergic reaction and the signs

may include:

- Difficulty breathing or swallowing,
- Low blood pressure, which can cause dizziness or light-headedness,
- Swelling of the neck, face, mouth, lips, tongue or throat, which may develop rapidly,
- Severe itching of the skin with a red rash or raised bumps.

If you experience any of the signs of a serious allergic reaction, stop taking EMGALITY immediately and contact your healthcare professional immediately.

Reactions may occur within minutes but may occur up to one month after taking EMGALITY.

- Tell your healthcare professional if you are pregnant, think you are pregnant, or are planning to have a baby while receiving this medicine.
- Tell your healthcare professional if you are breastfeeding or plan to breastfeed. It is not known whether EMGALITY passes into breast milk.
- EMGALITY should not be given to patients under the age of 18 years.

How to take EMGALITY:

- **See the detailed Instructions for Use that comes with this Patient Medication Information for instructions about the right way to give yourself EMGALITY injections**
- EMGALITY is given as an injection under the skin (subcutaneous injection).
- EMGALITY comes as a single-use (1 time) prefilled syringe or pen.
- If your healthcare professional decides that you or your caregiver can give the injections of EMGALITY, you or your caregiver should receive training on the right way to inject EMGALITY. Do not try to inject EMGALITY until you have been shown the right way to give the injections by a healthcare professional.
- Your healthcare professional may help you decide where on your body to inject your dose. You can also read the “**Choose your injection site**” section of the **Instructions for Use** to help you choose which area can work best for you.
- If you have vision problems, **do not** use EMGALITY prefilled syringe or pen without help from a caregiver.

Usual dose:

For migraine: The recommended dose of EMGALITY is a first dose of 240 mg (2 injections of the 120 mg/mL strength) followed by 120 mg (1 injection of the 120 mg/mL strength) every month thereafter.

EMGALITY is not intended for the acute treatment of migraine; patients should not exceed the monthly dose prescribed by the healthcare professional.

For episodic cluster headache: The recommended dose of EMGALITY is 300 mg (3 injections of the 100 mg/mL strength) at the start of a cluster period. After 3 weeks your healthcare provider will decide if you should continue treatment. If you continue treatment, EMGALITY 300 mg should not be administered more than once every month during a cluster period.

EMGALITY is not intended for the acute treatment of individual cluster headache attacks; patients should not exceed the monthly dose prescribed by the healthcare professional.

EMGALITY **should not** be used after the end of a cluster period and during the remission time.

Overdose:

If you think you have taken too much EMGALITY, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

For migraine: If you miss a dose take your dose as soon as you can. Thereafter resume monthly dosing.

For episodic cluster headache: If you take a partial dose (only 1 or 2 of the three prefilled syringes), take the missed injection(s) as soon as you can. If your healthcare provider determines that you should continue treatment, take the next complete dose one month from the date you took the missed injection(s).

What are possible side effects from using EMGALITY?

These are not all the possible side effects you may feel when taking EMGALITY. If you experience any side effects not listed here, contact your healthcare professional.

Very Common (≥ 1 in 10):

- injection site itching, redness, or swelling
- injection site pain
- injection site bruising
- injection site hardness

Common (≥ 1 in 100 and < 1 in 10)

- constipation
- dizziness
- itching
- rash

Uncommon (≥ 1 in 1000 and < 1 in 100):

- hives

Rare (≥ 1 in 10,000 and < 1 in 1000)

- serious allergic reaction

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store EMGALITY in a refrigerator at 2°C to 8°C until time of use. Keep the syringe or pen in the carton in order to protect from light.

If needed, EMGALITY may be left out of the refrigerator at a temperature up to 30°C for up to 7 days. EMGALITY should be discarded if not used within this 7-day period.

Do not freeze or shake the syringe or pen.

Keep out of reach and sight of children.

If you want more information about EMGALITY:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website www.lilly.ca, or by calling 1-888-545-5972.
- Instructions for Use can be found on www.lilly.ca

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

EMGALITY is a registered trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

You may need to read this package insert again.
Please do not throw it away until you have finished your medicine.

This leaflet was prepared by Eli Lilly Canada, Inc.

Last Revised September 11, 2020

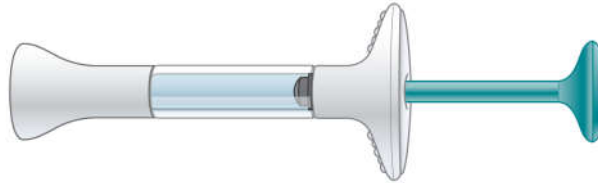
A3.0-EMG-NL0002-CA-PM-YYYYMMDD

INSTRUCTIONS FOR USE

Pr**EMGALITY**[®] (em-GAL-it-ē)

galcanezumab injection

**120 mg/mL solution for subcutaneous use
prefilled syringe**



www.lilly.ca

The Lilly logo, which consists of the word "Lilly" in a red, cursive script font.

This Instructions for Use is for patients with migraine.

- **If you are using EMGALITY for episodic cluster headache, there is a different Instructions for Use because the dose and number of syringes needed is different.**

For subcutaneous injection only.

Before you use the EMGALITY prefilled syringe, read and carefully follow all the step-by-step instructions.

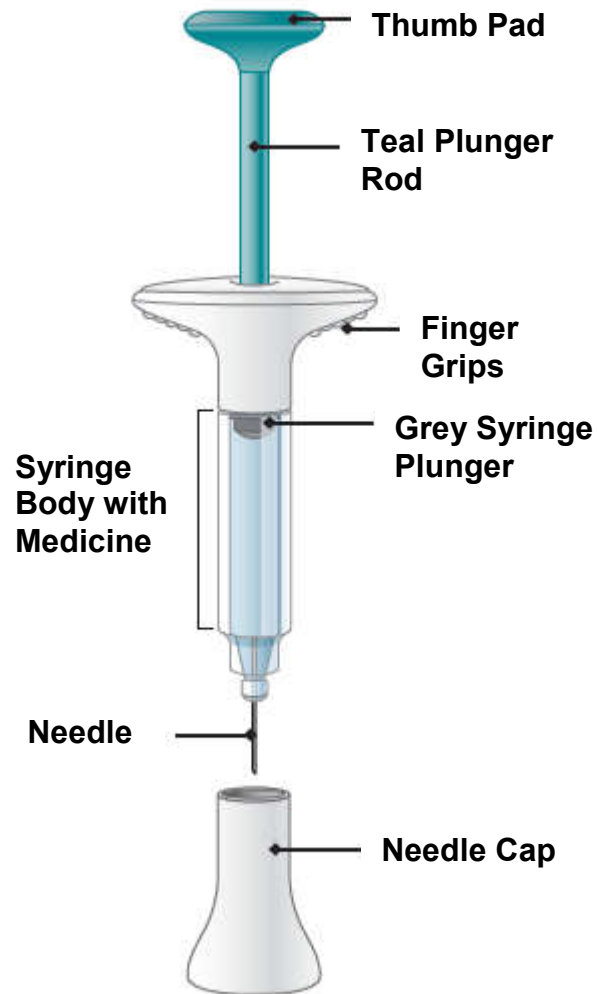
Important Information

- Your healthcare professional should show you how to prepare and inject EMGALITY using the prefilled syringe. Do not inject yourself or someone else until you have been shown how to inject EMGALITY.
- Keep this Instructions for Use and refer to it as needed.
- Each EMGALITY prefilled syringe is for **one-time use only**. Do not share or reuse your EMGALITY prefilled syringe. You may give or get an infection.
- Your healthcare professional may help you decide where on your body to inject your dose. You can also read the “**Choose your injection site**” section of these instructions to help you choose which area can work best for you.
- If you have vision problems, **do not** use EMGALITY prefilled syringe without help from a caregiver.

INSTRUCTIONS FOR USE

Before you use the EMGALITY prefilled syringe, read and carefully follow all the step-by-step instructions.

Parts of the EMGALITY Prefilled Syringe



Before You Get Started

Take the Prefilled Syringe from the refrigerator

Put the original package with any unused syringes back in the refrigerator.

Leave the needle cap on until you are ready to inject.

For a more comfortable injection, leave the prefilled syringe at room temperature for 30 minutes before injecting.

Do not microwave the prefilled syringe, run hot water over it, or leave it in direct sunlight.

Do not shake.

Gather Supplies

For each injection you will need:

- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See “**After You Inject Your Medicine.**”

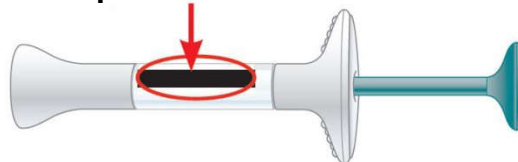
Inspect the Prefilled Syringe and the medicine

Make sure you have the right medicine. The medicine inside should be clear. Its colour may be colourless to slightly yellow.

Do not use the prefilled syringe, and dispose of as directed by your healthcare professional or pharmacist if:

- it looks damaged
- the medicine is cloudy, is discoloured, or has small particles
- the Expiration Date printed on the label has passed
- the medicine is frozen

Expiration Date

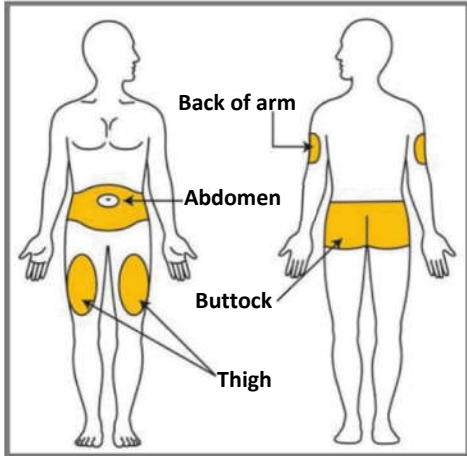


Prepare for injection

Wash your hands with soap and water before you inject your EMGALITY. Make sure a sharps disposal container is close by.

Choose your injection site

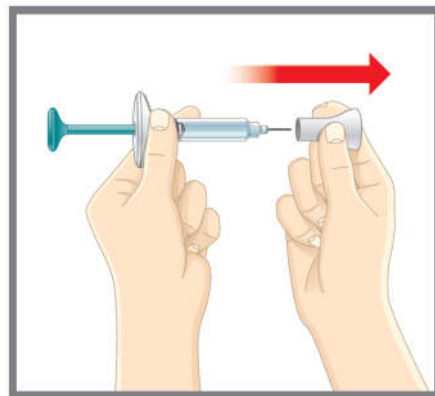
Your healthcare professional can help you choose the injection site that is best for you.



- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 2 inches of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttocks.
- **Do not** inject in the exact same spot. For example, if your first injection was in your abdomen, your next injection could be in another area of your abdomen.
- **Clean the injection site with an alcohol wipe. Let the injection site dry before you inject.**

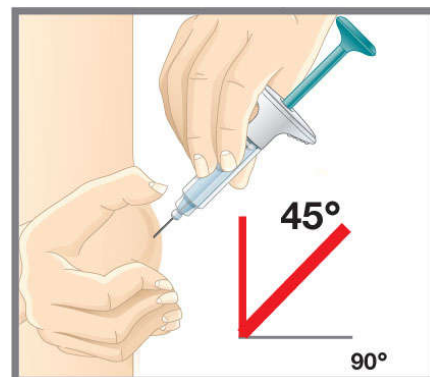
1 Uncap

- **Leave the needle cap on until you are ready to inject.**
- Pull the needle cap off and throw it away in your household trash.
- **Do not** put the needle cap back on – you could damage the needle or stick yourself by accident.
- **Do not** touch the needle.



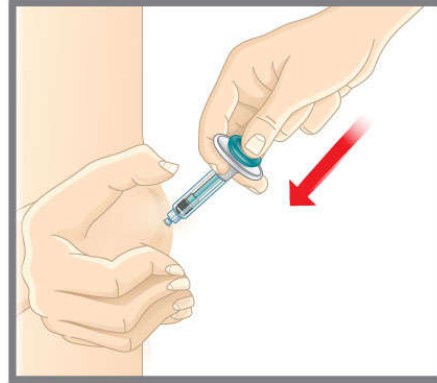
2 Insert

- Gently pinch and hold a fold of skin where you will inject.
- Insert the needle at a 45-degree angle.

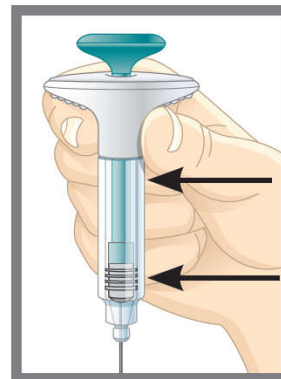


3 Inject

- Slowly push on the thumb pad to push the plunger all the way in until all the medicine is injected.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.



- You should see the teal plunger rod show through the syringe body when the injection is complete as shown.
- Remove the needle from your skin and gently let go of your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site. Do not rub the injection site.



Teal plunger rod

Grey syringe plunger

- **Do not** put the needle cap back on the prefilled syringe.

After You Inject Your Medicine

Throw away the used prefilled syringe

- Put the used EMGALITY prefilled syringe in a sharps disposal container right away after use. **Do not** throw away (dispose of) the EMGALITY prefilled syringe in your household trash.



- If you do not have a sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
 - upright and stable during use,
 - leak-resistant, and
 - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be provincial or local laws about how you should throw away needles and syringes. For more information about the proper way to dispose of the container contact your healthcare professional.
- **Do not** recycle your used sharps disposal container.

Commonly Asked Questions

Q. What if I see air bubbles in my EMGALITY prefilled syringe?

A. It is normal to have air bubbles in the prefilled syringe. EMGALITY is injected under your skin (subcutaneous injection).

Q. What if there is a drop of liquid on the tip of the needle when I remove the needle cap?

A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I cannot push in the plunger?

A. If the plunger is stuck or damaged:

- **Do not** continue to use the syringe
- Remove the needle from your skin
- Dispose of the syringe and get a new one

Q. How can I tell if my injection is complete?

A. When your injection is complete:

- The teal plunger rod should show through the body of the syringe.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.

If you have more questions about how to use the EMGALITY prefilled syringe:

- Call your healthcare professional
- Call 1-888-545-5972
- Visit www.lilly.ca

Storage and Handling

- Store your prefilled syringe in the refrigerator between 2°C to 8°C.
- Your prefilled syringe may be stored unrefrigerated for up to 7 days. Do not store above 30°C.
- Do not freeze your prefilled syringe.
- Protect your prefilled syringe from light until use.
- Do not shake your prefilled syringe.
- Discard your prefilled syringe if any of the above conditions are not followed.
- **Keep your prefilled syringe and all medicines out of the reach of children.**

Read the Patient Medication Information for EMGALITY inside this box to learn more about your medicine.

Eli Lilly Canada Inc., P.O. Box 73, Toronto, Ontario, M5X 1B1

EMGALITY is a trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

Copyright © 2019, YYYY, Eli Lilly and Company. All rights reserved.

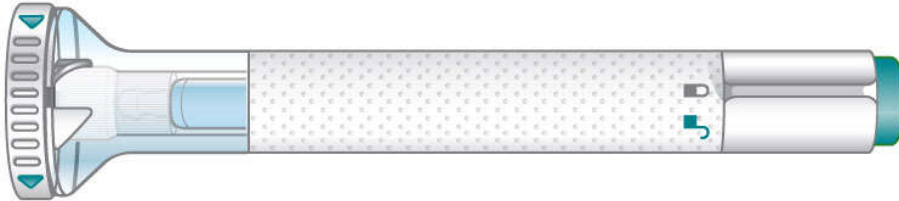
Document Revision Date: September 11, 2020

A 3.0-EMG-120MG-PFS-NL0002-CA-IFU-YYYYMMDD

INSTRUCTIONS FOR USE

PrEMGALITY® (em-GAL-it-ē) galcanezumab injection

120 mg/mL solution for subcutaneous use
prefilled pen



www.lilly.ca

Lilly

This Instructions for Use is for patients with migraine.

For subcutaneous injection only.

Before you use the EMGALITY prefilled pen (Pen), read and carefully follow all the step-by-step instructions.

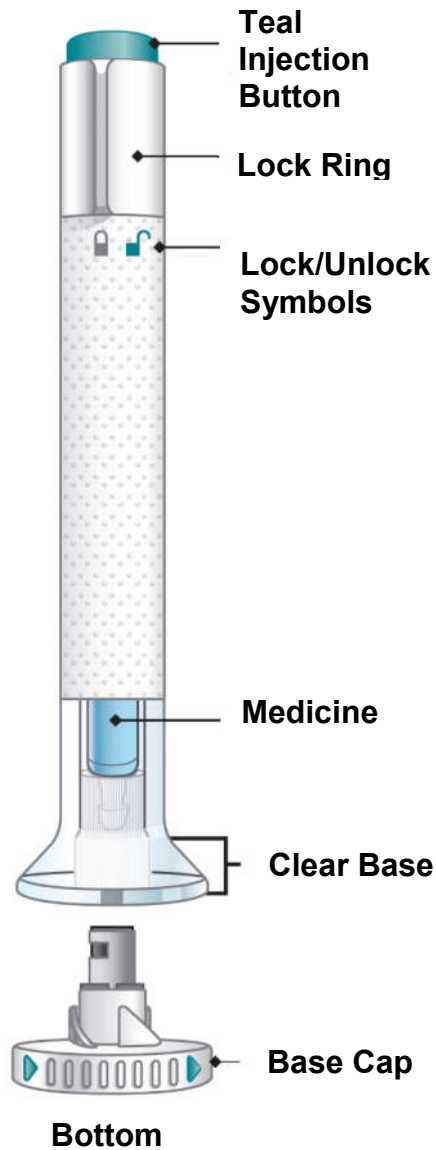
Important Information

- Your healthcare professional should show you how to prepare and inject EMGALITY using the Pen. Do not inject yourself or someone else until you have been shown how to inject EMGALITY.
- Keep this Instructions for Use and refer to it as needed.
- Each EMGALITY Pen is for **one-time use only**. Do not share or reuse your EMGALITY Pen. You may give or get an infection.
- The Pen contains glass parts. Handle it carefully. If you drop it on a hard surface, do not use it. Use a new Pen for your injection.
- Your healthcare professional may help you decide where on your body to inject your dose. You can also read the “**Choose your injection site**” section of these instructions to help you choose which area can work best for you.
- If you have vision or hearing problems, **do not** use EMGALITY Pen without help from a caregiver.

INSTRUCTIONS FOR USE

Before you use the EMGALITY Pen, read and carefully follow all the step-by-step instructions.

Parts of the EMGALITY Pen



Before You Get Started

Take the Pen from the refrigerator

Put the original package with any unused Pens back in the refrigerator.

Leave the base cap on until you are ready to inject.

For a more comfortable injection, leave the Pen at room temperature for 30 minutes before injecting.

Do not microwave the Pen, run hot water over it, or leave it in direct sunlight.

Do not shake.

Gather Supplies

For each injection you will need:

- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See “**After You Inject Your Medicine.**”

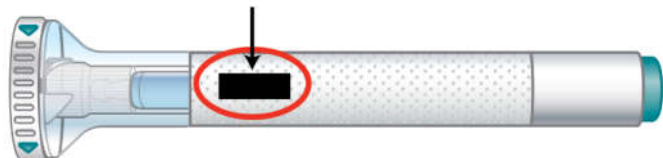
Inspect the Pen and the medicine

Make sure you have the right medicine. The medicine inside should be clear. Its colour may be colourless to slightly yellow.

Do not use the Pen, and dispose of as directed by your healthcare professional or pharmacist if:

- it looks damaged
- the medicine is cloudy, is discoloured, or has small particles
- the Expiration Date printed on the label has passed
- the medicine is frozen

Expiration Date

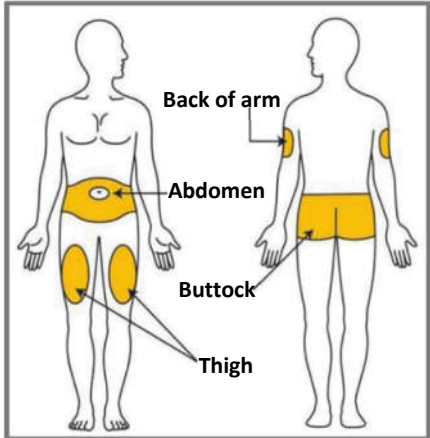


Prepare for injection

Wash your hands with soap and water before you inject your EMGALITY. Make sure a sharps disposal container is close by.


Choose your injection site

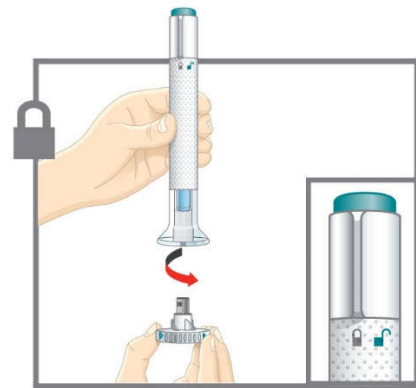
Your healthcare professional can help you choose the injection site that is best for you.




- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 2 inches of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttocks.
- **Do not** inject in the exact same spot. For example, if your first injection was in your abdomen, your next injection could be in another area of your abdomen.
- **Clean the injection site with an alcohol wipe. Let the injection site dry before you inject.**

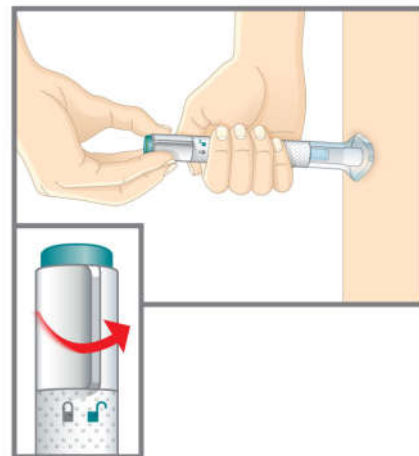
1 Uncap the Pen

-  **Make sure the Pen is locked. Leave the base cap on until you are ready to inject.**
- Twist off the base cap and throw it away in your household trash.
- **Do not** put the base cap back on – this could damage the needle.
- **Do not** touch the needle.



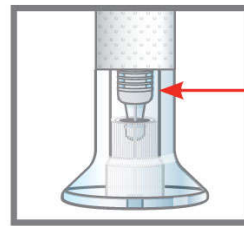
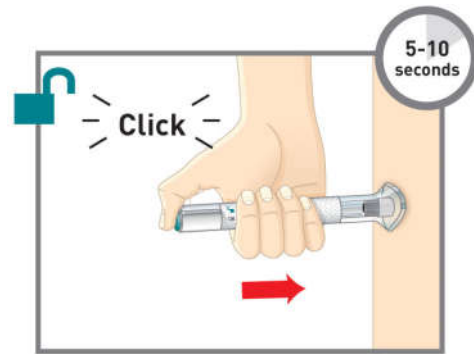
2 Place and Unlock

- Place and hold the clear base flat and firmly against your skin.
-  Turn the lock ring to the **unlock** position.



3 Press and Hold for 10 Seconds

- Press and hold the teal injection button; you will hear a loud click.
- **Keep holding the clear base firmly against your skin.** You will hear a second click in about 10 seconds after the first one. This second click tells you that your injection is complete.
- Remove the Pen from your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site. Do not rub the injection site.

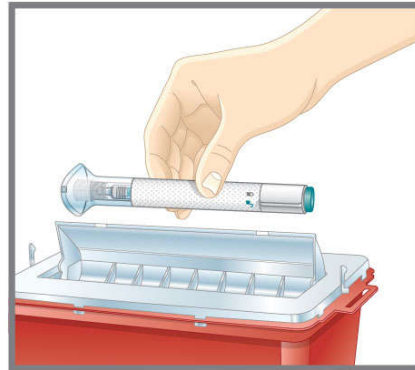


You will know your injection is complete when the grey plunger is visible.

After You Inject Your Medicine

Throw away the used Pen

- Put the used EMGALITY Pen in a sharps disposal container right away after use. **Do not** throw away (dispose of) the EMGALITY Pen in your household trash.
- If you do not have a sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
 - upright and stable during use,
 - leak-resistant, and
 - properly labeled to warn of hazardous waste inside the container.



- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be provincial or local laws about how you should throw away needles and pens. For more information about the proper way to dispose of the container contact your healthcare professional.
- **Do not** recycle your used sharps disposal container.

Commonly Asked Questions

Q. What if I see bubbles in the Pen?

A. It is normal to have air bubbles in the Pen. EMGALITY is injected under your skin (subcutaneous injection).

Q. What if there is a drop of liquid on the tip of the needle when I remove the base cap?

A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I unlocked the Pen and pressed the teal injection button before I twisted off the base cap?

A. Do not remove the base cap. Dispose of the Pen and get a new one.

Q. Do I need to hold the injection button down until the injection is complete?

A. This is not necessary, but it may help you keep the Pen steady and firm against your skin.

Q. What if the needle did not retract after my injection?

A. Do not touch the needle or replace the base cap. Store in a safe place to avoid an accidental needlestick and contact 1-888-545-5972 for instructions on how to return the Pen.

Q. What if I heard more than 2 clicks during my injection – 2 loud clicks and a soft one? Did I get my complete injection?

A. Some patients may hear a soft click right before the second loud click. That is the normal operation of the Pen. Do not remove the Pen from your skin until you hear the second loud click.

Q. How can I tell if my injection is complete?

A. After you press the teal injection button, you will hear 2 loud clicks. The second click tells you that your injection is complete. You will also see the grey plunger at the top of the clear base.

If you have more questions about how to use the EMGALITY prefilled pen:

- Call your healthcare professional

- Call 1-888-545-5972
- Visit www.lilly.ca

Storage and Handling

- Store your prefilled pen in the refrigerator between 2°C to 8°C.
- Your prefilled pen may be stored unrefrigerated for up to 7 days. Do not store above 30°C.
- Do not freeze your prefilled pen.
- Protect your prefilled pen from light until use.
- Do not shake your prefilled pen.
- Discard your prefilled pen if any of the above conditions are not followed.
- **Keep your prefilled pen and all medicines out of the reach of children.**

The Pen meets the current dose accuracy and functional requirements of ISO 11608-1 and 11608-5.

Read the Patient Medication Information for EMGALITY inside this box to learn more about your medicine.

Eli Lilly Canada Inc., P.O. Box 73, Toronto, Ontario, M5X 1B1

EMGALITY is a registered trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

Copyright © 2019, YYYY, Eli Lilly and Company. All rights reserved.

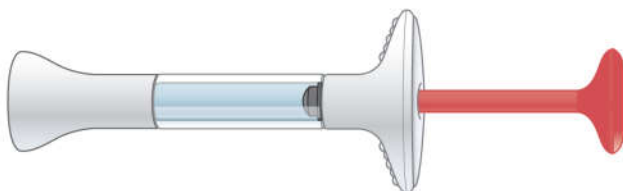
Document revision date: September 08, 2020

A2.0-EMG-120MG-PEN-NL0002-CA-IFU-YYYYMMDD

INSTRUCTIONS FOR USE

PrEMGALITY® (em-GAL-it-ē) galcanezumab injection

100 mg/mL solution for subcutaneous use
prefilled syringe



www.lilly.ca

Lilly

This Instructions for Use is for patients with episodic cluster headache.

- If you are using EMGALITY for preventive treatment of migraine, there is a different Instructions for Use because the dose and number of syringes needed is different.

For subcutaneous injection only.

Before you use the EMGALITY prefilled syringe, read and carefully follow all the step-by-step instructions.

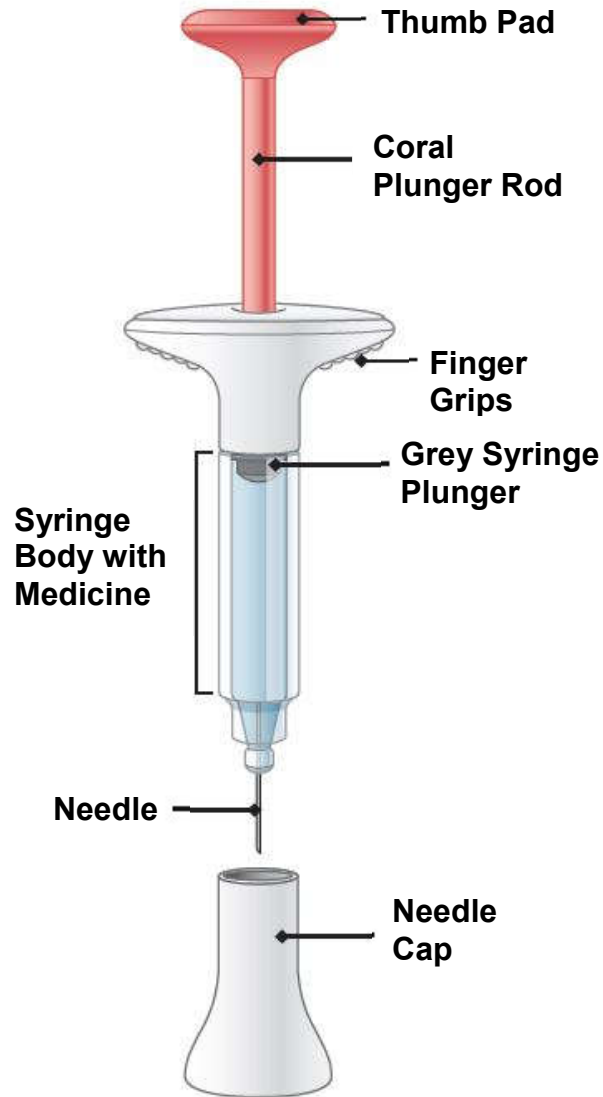
Important Information

- Your healthcare professional should show you how to prepare and inject EMGALITY using the prefilled syringe. Do not inject yourself or someone else until you have been shown how to inject EMGALITY.
- Keep this Instructions for Use and refer to it as needed.
- Each EMGALITY prefilled syringe is for **one-time use only**. Do not share or reuse your EMGALITY prefilled syringe. You may give or get an infection.
- Your healthcare professional may help you decide where on your body to inject your dose. You can also read the “**Choose your injection site**” section of these instructions to help you choose which area can work best for you.
- If you have vision problems, **do not** use EMGALITY prefilled syringe without help from a caregiver.

INSTRUCTIONS FOR USE

Before you use the EMGALITY prefilled syringe, read and carefully follow all the step-by-step instructions.

Parts of the EMGALITY Prefilled Syringe



Before You Get Started

Take the Prefilled Syringes from the refrigerator

Take 3 EMGALITY prefilled syringes from the refrigerator.

Leave the needle cap on until you are ready to inject.

For a more comfortable injection, leave the prefilled syringes at room temperature for 30 minutes before injecting.

Do not microwave the prefilled syringe, run hot water over it, or leave it in direct sunlight.

Do not shake.

Gather Supplies

For each injection you will need:

- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See “**After You Inject Your Medicine.**”

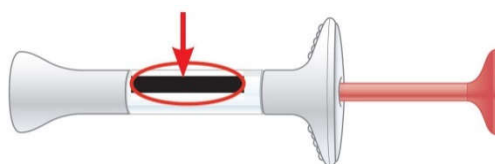
Inspect the Prefilled Syringe and the medicine

Make sure you have the right medicine. The medicine inside should be clear. Its colour may be colourless to slightly yellow.

Do not use the prefilled syringe, and dispose of as directed by your healthcare professional or pharmacist if:

- it looks damaged
- the medicine is cloudy, is discoloured, or has small particles
- the Expiration Date printed on the label has passed
- the medicine is frozen

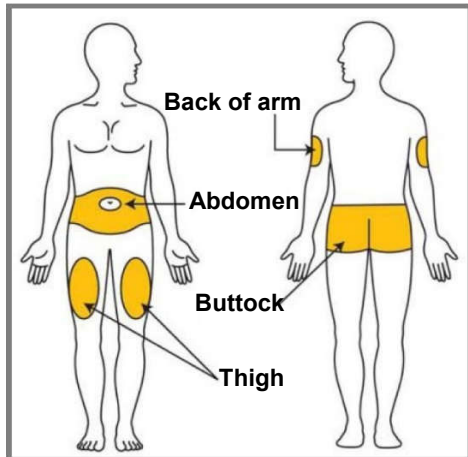
Expiration Date



Prepare for injection

Wash your hands with soap and water before you inject your EMGALITY. Make sure a sharps disposal container is close by.

Choose your injection site

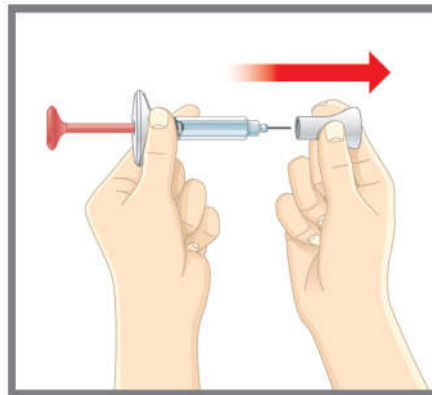


Your healthcare professional can help you choose the injection site that is best for you.

- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 2 inches of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttocks.
- **Do not** inject in the exact same spot. For example, if your first injection was in your abdomen, your next injection could be in another area of your abdomen.
- **Clean the injection site with an alcohol wipe. Let the injection site dry before you inject.**

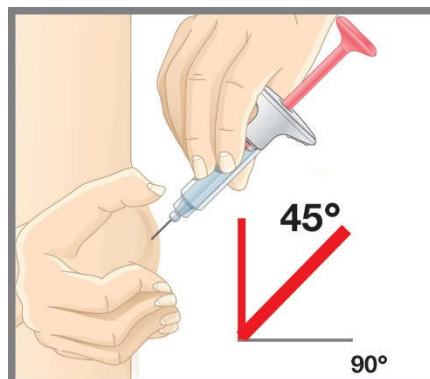
1 Uncap

- **Leave the needle cap on until you are ready to inject.**
- Pull the needle cap off and throw it away in your household trash.
- **Do not** put the needle cap back on - you could damage the needle or stick yourself by accident.
- **Do not** touch the needle.



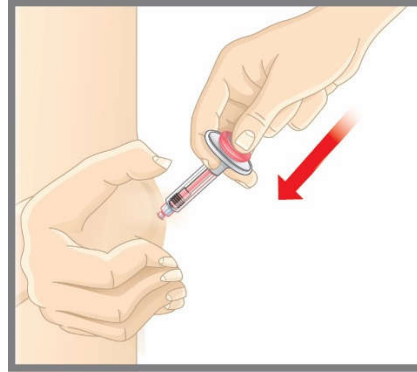
2 Insert

- Gently pinch and hold a fold of skin where you will inject.
- Insert the needle at a 45-degree angle.

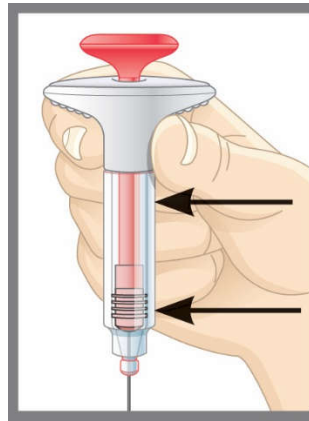


3 Inject

- Slowly push on the thumb pad to push the plunger all the way in until all the medicine is injected.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.



- You should see the coral plunger rod show through the syringe body when the injection is complete as shown.
- Remove the needle from your skin and gently let go of your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site. Do not rub the injection site.
- **Do not** put the needle cap back on the prefilled syringe.



Coral plunger rod

Grey syringe plunger

After You Inject Your Medicine

Throw away the used prefilled syringe

- Put the used EMGALITY prefilled syringe in a sharps disposal container right away after use. **Do not** throw away (dispose of) the EMGALITY prefilled syringe in your household trash.



- If you do not have a sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,

- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be provincial or local laws about how you should throw away needles and syringes. For more information about the proper way to dispose of the container contact your healthcare professional.
- **Do not** recycle your used sharps disposal container.

For each of the 3 injections, repeat all instructions with a new prefilled syringe.

Commonly Asked Questions

Q. What if I see air bubbles in my EMGALITY prefilled syringe?

A. It is normal to have air bubbles in the prefilled syringe. EMGALITY is injected under your skin (subcutaneous injection).

Q. What if there is a drop of liquid on the tip of the needle when I remove the needle cap?

A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I cannot push in the plunger?

A. If the plunger is stuck or damaged:

- **Do not** continue to use the syringe
- Remove the needle from your skin
- Dispose of the syringe and get a new one

Q. How can I tell if my injection is complete?

A. When your injection is complete:

- The coral plunger rod should show through the body of the syringe.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.

If you have more questions about how to use the EMGALITY prefilled syringe:

- Call your healthcare professional
- Call 1-888-545-5972
- Visit www.lilly.ca

Storage and Handling

- Store your prefilled syringe in the refrigerator between 2°C to 8°C.

- Your prefilled syringe may be stored unrefrigerated for up to 7 days. Do not store above 30°C.
- Do not freeze your prefilled syringe.
- Protect your prefilled syringe from light until use.
- Do not shake your prefilled syringe.
- Discard your prefilled syringe if any of the above conditions are not followed.
- **Keep your prefilled syringe and all medicines out of the reach of children.**

Read the Patient Medication Information for EMGALITY inside this box to learn more about your medicine.

Eli Lilly Canada Inc., P.O. Box 73, Toronto, Ontario, M5X 1B1
EMGALITY is a registered trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.
Copyright © YYYY, Eli Lilly and Company. All rights reserved.
Document Revision Date: September 11, 2020

A3.0-EMG-100MG-PFS-NL0000-CA-IFU-YYYYMMDD