

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrEMGALITY™

Galcanezumab Injection

120 mg/mL solution for subcutaneous injection

CGRP binding antibody

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Date of Initial Approval:
July 30, 2019

Submission Control No: 219521

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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.

EMGALITY should be initiated by physicians experienced in the diagnosis and treatment of migraine.

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 for subcutaneous use only.

3.2 Recommended Dose and Dosage Adjustment

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

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

3.3 Administration

A patient may self-inject EMGALITY by following the instructions for use.

Protect EMGALITY from direct sunlight. Do not warm EMGALITY by using a heat source such as hot water or a microwave.

Do not shake the product.

Inspect EMGALITY visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use EMGALITY if it is cloudy or there are visible

particles.

Administer EMGALITY in the abdomen, thigh, back of the upper arm, or buttocks subcutaneously.

Both prefilled syringe and prefilled pen are single-dose and deliver the entire contents.

3.4 Missed Dose

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

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 single-dose prefilled syringe or pen	L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride, and water for injection

EMGALITY is a sterile, preservative-free, clear and colorless to slightly yellow solution. Each single-dose prefilled syringe or pen contains 120 mg EMGALITY in 1 mL (120 mg/mL).

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. If a serious hypersensitivity reaction occurs, administration of EMGALITY should be discontinued immediately and appropriate therapy initiated. Serious hypersensitivity reactions could occur days after administration and may be prolonged.

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 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.

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 3156 patients and healthy volunteers were exposed to EMGALITY, representing more than 1258 patient years of exposure. Of these, 1647 patients were exposed to EMGALITY once monthly for at least 6 months and 279 patients were exposed for 12 months.

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.

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

Table 2: Adverse Reactions Reported with EMGALITY-treated Patients (and More Frequently than in Patients Receiving Placebo) By System Organ Class and Preferred Term

System Organ Class Preferred Term	EMGALITY 120 mg N = 705 (%)	EMGALITY 240 mg N = 730 (%)	Placebo N = 1451 (%)
General disorders and administration site conditions			
Injection site reactions ^a	128 (18.2)	166 (22.7)	183 (12.6)
Gastrointestinal disorders			
Constipation	7 (1.0)	11 (1.5)	8 (0.6)
Neurologic disorders			
Vertigo	5 (0.7)	9 (1.2)	3 (0.2)
Skin and subcutaneous tissue disorders			
Pruritus	5 (0.7)	9 (1.2)	4 (0.3)
Urticaria	2 (0.3)	1 (0.1)	5 (0.3)

^a Injection site reactions include multiple preferred terms, such as injection site pain, injection site erythema, injection site pruritus, injection site bruising and injection site swelling.

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 3 and 4 were observed to occur at or above 1% during the double-blind treatment phase.

Table 3: 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 4: Incidence of Treatment-emergent Adverse Events in ≥ 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.

8.3 Less Common Clinical Trial Adverse Reactions

None.

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).

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.

Table 5: Steady-State Pharmacokinetic Parameters of EMGALITY^{a, b}

C_{max} mean (%CV)	28 mcg/mL (35)
AUC_{tau} mean (%CV)	15,900 mcg x hour/mL (42)
C_{min} mean (% CV)	15 mcg/mL (53)

^a Based on population PK analysis.

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

Absorption: Following a 120 mg dose of galcanezumab at steady-state, the median time to maximum concentration was 5 days (range: 3 to 14 days).

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 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-dose 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 colorless 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 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 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.

Table7: 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				
≥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		
$\geq 50\%$ 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.

14 NON-CLINICAL TOXICOLOGY

General Toxicology

Galcanzumab was well tolerated in cynomolgus monkeys and Sprague Dawley rats at weekly subcutaneous doses of up to 100 mg/kg and 20 mg/kg (156 and 8 times greater than the human exposure at the 120 mg once monthly dose based on AUC), respectively, for up to 6 months. There was no evidence of galcanzumab-related systemic toxicity in cynomolgus monkeys; however, in rats, two male deaths were observed at a dose of 250 mg/kg (19 times greater than the human exposure at 120 mg once monthly dose based on AUC) for which a drug-related effect could not be ruled out. In both rats and monkeys, galcanzumab-related non-adverse macroscopic and microscopic changes were limited to the injection sites and were consistent with inflammation. There were no galcanzumab-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 galcanzumab.

Genotoxicity

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

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 galcanzumab-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 (7.9 and 38 times greater than the human exposure at the 120 mg once monthly dose based on AUC in males and females, respectively).

No galcanzumab-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 38 and 64 times higher than the human exposure at the 120 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 (34 times greater than the human exposure at the 120 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 to prevent migraine in adults who have at least 4 migraine days per month.

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.

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
- 120 mg solution for injection in a 1 mL prefilled pen

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.

- 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-dose (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:

The recommended dose of EMGALITY is a first dose of 240 mg (2 injections) followed by 120 mg (1 injection) every month thereafter.

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

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:

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

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

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 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., Toronto, Ontario, M1N 2E8

Last Revised July 30, 2019

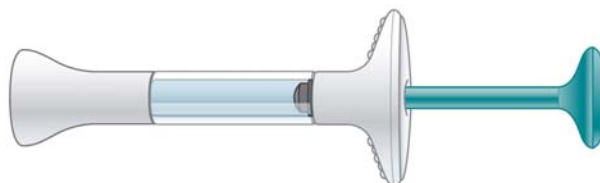
EMG-0001-CA-PM-201900730

INSTRUCTIONS FOR USE

PrEMGALITY™ (em-GAL-it-ē)

galcanezumab injection

120 mg/mL solution for subcutaneous use
prefilled syringe



www.lilly.ca

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

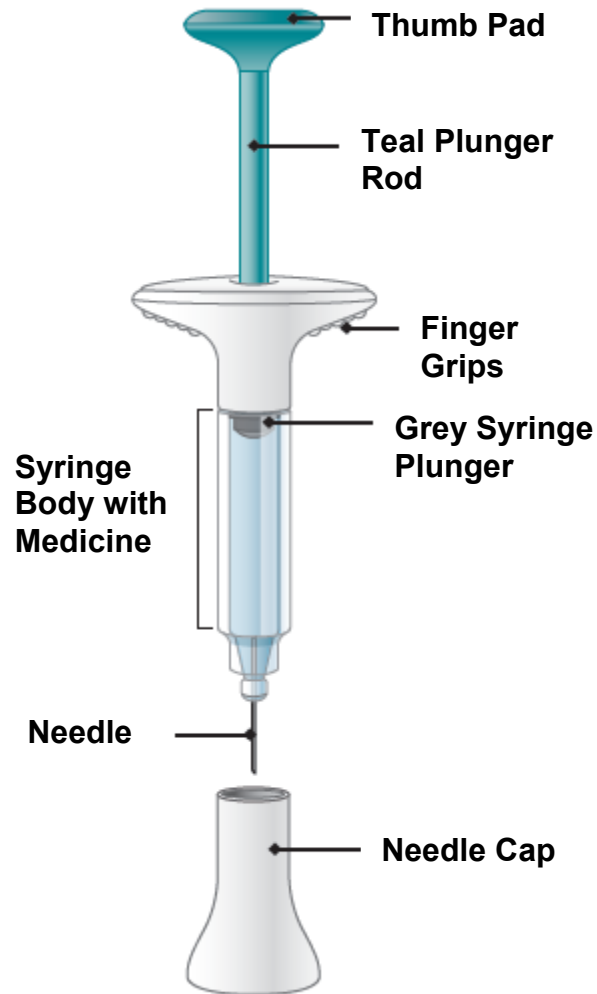
Important Information

- 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 these Instructions for Use and refer to them 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.

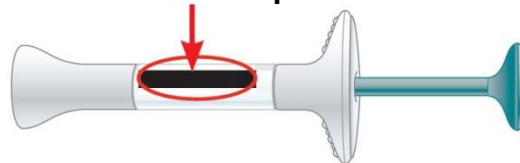
Inspect the Prefilled Syringe and the medicine

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



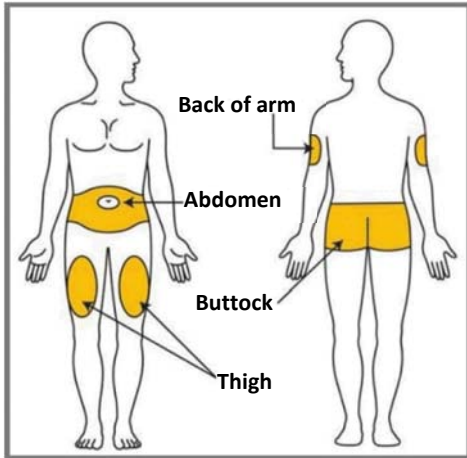
Prepare for injection

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.

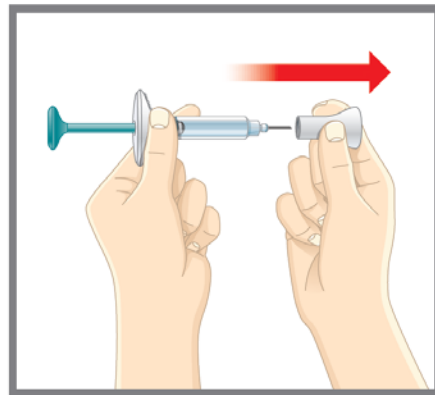
- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 2 inches of the belly button (navel).



- **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 and dry the injection site before you inject.**

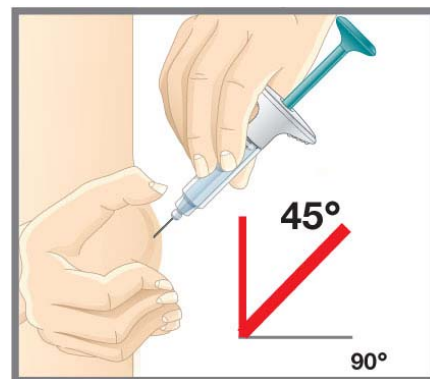
1 Uncap

- **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

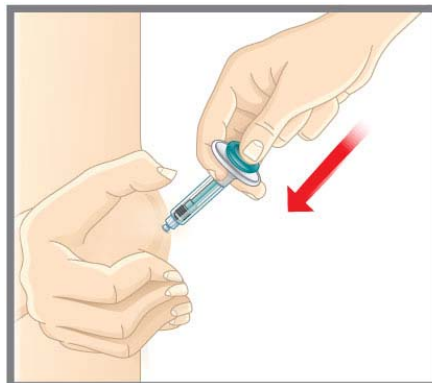
- Gently pinch and hold a fold of skin where you will inject.
- Insert the needle at a 45-degree angle.



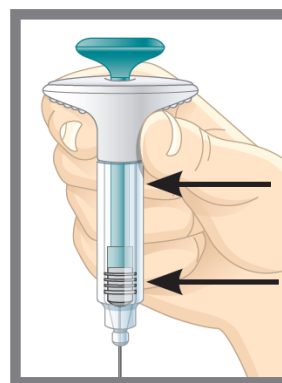
3 Inject

- 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.



Teal plunger rod

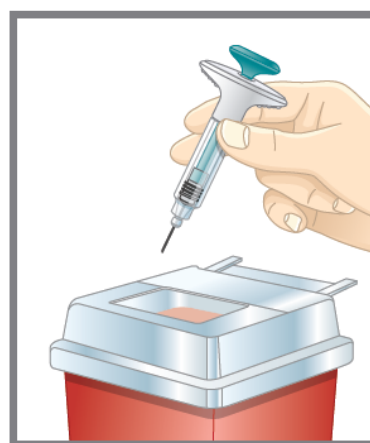
Grey syringe plunger

- Remove the needle from your skin and gently let go of your skin.
- **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. What if there is a drop of liquid or blood on my skin after my injection?

A. This is normal. Press a cotton ball or gauze over the injection site. Do not rub the injection site.

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-LillyRx (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., Toronto, Ontario, M1N 2E8

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Document Revision Date: July 30, 2019

EMG-120MG-PFS-0001-CA-IFU-20190730

INSTRUCTIONS FOR USE

Pr**EMGALITY**[™] (em-GAL-it-ē)

galcanezumab injection

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



www.lilly.ca

Lilly

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

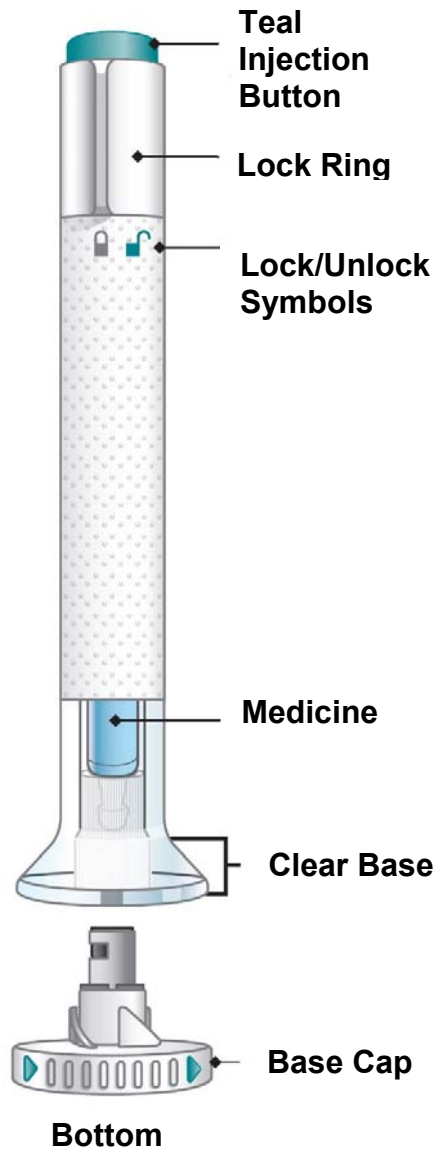
Important Information

- 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 these Instructions for Use and refer to them 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.

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 discolored, or has small particles
- the Expiration Date printed on the label has passed
- the medicine is frozen

Expiration Date



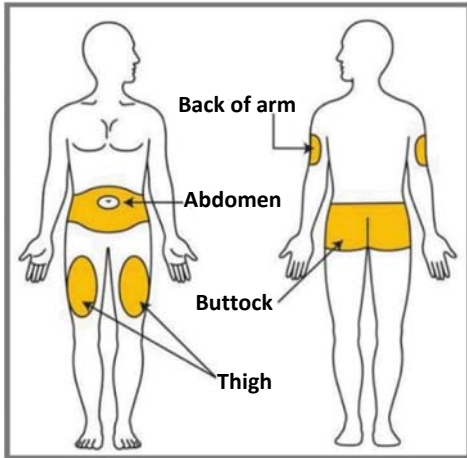
Prepare for injection

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.

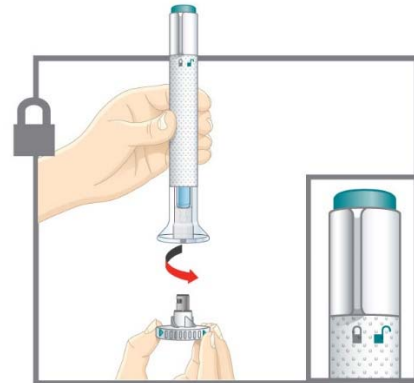
- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 2 inches of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttocks.




- **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 and dry the injection site before you inject.**

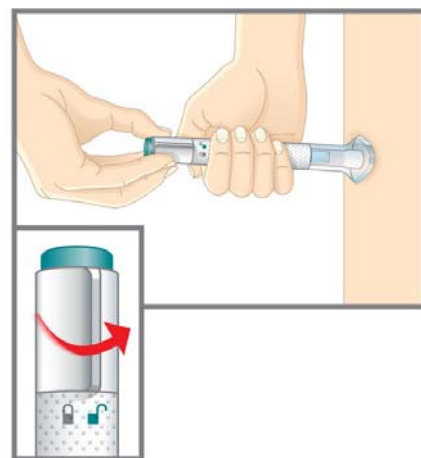
1 Uncap the Pen

-  **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.



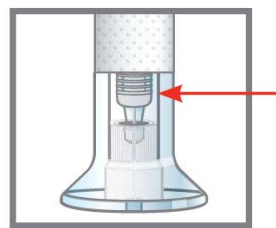
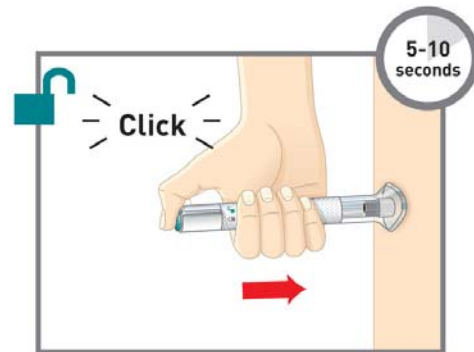
2 Place and Unlock

- 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.



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 there is a drop of liquid or blood on my skin after my injection?

A. This is normal. Press a cotton ball or gauze over the injection site. Do not rub the injection site.

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-LillyRx (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.

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Document revision date: July 30, 2019

EMG-120MG-PEN-0001-CA-IFU-201900730