ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Emgality 120 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled pen contains 120 mg of galcanezumab in 1 mL.

Galcanezumab is a recombinant humanised monoclonal antibody produced in Chinese Hamster Ovary cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emgality is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month.

4.2 Posology and method of administration

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

Posology

The recommended dose is 120 mg galcanezumab injected subcutaneously once monthly, with a 240 mg loading dose as the initial dose.

Patients should be instructed to inject a missed dose as soon as possible and then resume monthly dosing.

The treatment benefit should be assessed within 3 months after initiation of treatment. Any further decision to continue treatment should be taken on an individual patient basis. Evaluation of the need to continue treatment is recommended regularly thereafter.

Elderly (≥ 65 years)
There is limited information in subjects aged ≥ 65 years. No dose adjustment is required as the pharmacokinetics of galcanezumab are not affected by age.

Renal impairment/hepatic impairment
No dose adjustment is required in patients with mild to moderate renal impairment or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of galcanezumab in children aged 6 to 18 years have not yet been established. No data are available.

There is no relevant use of galcanezumab in children below the age of 6 years for the prevention of migraine.

Method of administration

Subcutaneous use.

A patient may self-inject galcanezumab by following the Instructions for Use. Galcanezumab is to be injected subcutaneously in the abdomen, thigh, back of the upper arm, or in the gluteal region. After training, patients may self-inject galcanezumab if a healthcare professional determines that it is appropriate. Comprehensive instructions for administration are given in the Package Leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

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

Cardiovascular risk

Patients with certain major cardiovascular diseases were excluded from clinical studies (see section 5.1). No safety data are available in these patients.

Serious hypersensitivity

Serious hypersensitivity reactions including cases of anaphylaxis, angioedema and urticaria have been reported (see section 4.8). Serious hypersensitivity reactions may occur within 1 day after galcanezumab administration, however cases with a delayed onset (ranging from more than 1 day to 4 weeks after administration) have been reported. In some cases, hypersensitivity reactions had a prolonged duration. If a serious hypersensitivity reaction occurs, administration of galcanezumab should be discontinued immediately and appropriate therapy initiated (see section 4.3). Patients should be informed on the possibility of a delayed onset hypersensitivity reaction and instructed to contact their physician.

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per 120 mg dose, that is to say essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies were conducted. No pharmacokinetic drug interactions are expected based on the characteristics of galcanezumab.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of galcanezumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Human immunoglobulin (IgG) is known to cross the placental barrier. As a precautionary measure, it is preferable to avoid the use of galcanezumab during pregnancy.

Breast-feeding

It is unknown whether galcanezumab is excreted in human milk. Human IgG is known to be excreted in breast milk during the first days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to breast-fed infants cannot be excluded during this short period. Afterwards, use of galcanezumab could be considered during breast-feeding only if clinically needed.

Fertility

The effect of galcanezumab on human fertility has not been evaluated. Fertility studies in animals do not indicate harmful effects with respect to male and female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Galcanezumab may have a minor influence on the ability to drive and use machines. Vertigo may occur following the administration of galcanezumab (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

Over 2 500 patients were exposed to galcanezumab in migraine prophylaxis studies supporting the initial registration of galcanezumab. Over 1 400 patients were exposed to galcanezumab during the double-blind treatment phase of the placebo-controlled phase 3 studies. 279 patients were exposed for 12 months.

The reported adverse drug reactions for 120 mg and 240 mg in the migraine clinical trials were injection site pain (10.1 %/11.6 %), injection site reactions (9.9 %/14.5 %), vertigo (0.7 %/1.2 %), constipation (1.0 %/1.5 %), pruritus (0.7 %/1.2 %) and urticaria (0.3 %/0.1 %). Most of the reactions were mild or moderate in severity. Less than 2.5 % of patients in these studies discontinued due to adverse reactions.

Tabulated list of adverse reactions

Table 1. List of adverse reactions in clinical studies and post-marketing reports
Frequency estimate: Very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000).

System organ class	Very common	Common	Uncommon	Rare
Immune system disorders				Anaphylaxis Angioedema
Ear and labyrinth disorders		Vertigo		
Gastrointestinal disorders		Constipation		
Skin and subcutaneous tissue disorders		Pruritus Rash	Urticaria	
General disorders and administration site conditions	Injection site pain Injection site reactions[a]			

[a] Most frequently reported terms (≥ 1 %) were: Injection site reaction, Injection site erythema, Injection site pruritus, Injection site bruising, Injection site swelling.

Description of selected adverse reactions

Injection site pain or reactions
The majority of reactions related to the injection site were mild to moderate and less than 0.5 % of patients exposed to galcanezumab during the phase 3 studies discontinued the treatment due to an injection site reaction. The majority of injection site reactions were reported within 1 day and on average resolved within 5 days. In 86 % of the patients reporting injection site pain, the reaction occurred within 1 hour of injection and resolved on average in 1 day. One percent of the patients exposed to galcanezumab during the phase 3 studies experienced severe pain at the injection site.

Urticaria
While urticaria is uncommon, serious cases of urticaria have been reported in galcanezumab clinical studies.

Immunogenicity
In the clinical studies, the incidence of anti-drug antibody development during the double-blind treatment phase was 4.8 % in patients receiving galcanezumab once monthly (all but one of whom had *in vitro* neutralizing activity). With 12 months of treatment, up to 12.5 % of galcanezumab-treated patients developed anti-drug antibodies, most of which were of low titre and tested positive for neutralising activity *in vitro*. However, the presence of anti-drug antibodies did not affect the pharmacokinetics, efficacy, or safety of galcanezumab.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 600 mg have been administered subcutaneously to humans without 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: analgesics, calcitonin gene-related peptide (CGRP) antagonists, ATC code: N02CD02

Mechanism of action

Galcanezumab is a humanised IgG4 monoclonal antibody that binds calcitonin gene-related peptide (CGRP) thus preventing its biological activity. Elevated blood concentrations of CGRP have been associated with migraine attacks. Galcanezumab binds to CGRP with high affinity (K_D = 31 pM) and high specificity (> 10 000-fold vs related peptides adrenomedullin, amylin, calcitonin and intermedin).

Clinical efficacy and safety

The efficacy and safety of galcanezumab has been studied in 3 phase 3, randomized, placebo-controlled, double-blind studies in adult patients (N = 2 886). The 2 episodic migraine studies (EVOLVE-1 and EVOLVE-2) enrolled patients who met International Classification of Headache Disorders (ICHD) criteria for a diagnosis of migraine with or without aura with 4-14 migraine headache days per month. The chronic migraine study (REGAIN) enrolled patients who met ICHD criteria for chronic migraine with ≥ 15 headache days per month, of which at least 8 had the features of migraine. Patients with recent acute cardiovascular events (including MI, unstable angina, CABG, stroke, DVT) and/or those deemed to be at serious cardiovascular risk were excluded from the galcanezumab clinical trials. Patients > 65 years of age were also excluded.

Patients received placebo, galcanezumab 120 mg/month (with an initial loading dose of 240 mg for the first month) or galcanezumab 240 mg/month and were allowed to use medication for the acute treatment of migraine. Across the 3 studies, patients were predominantly female (> 83 %) with a mean age of 41 years, and an average migraine history of 20 to 21 years. Approximately one-third of patients across the studies had at least 1 prior failure on a migraine prophylactic treatment for efficacy reasons and approximately 16 % of patients across the studies had at least 2 prior failure on a prophylactic treatment for efficacy reasons.

In all 3 studies, the overall mean change from baseline in number of monthly Migraine Headache Days (MHDs) was the primary efficacy measure. Response rate is the mean percentage of patients meeting a defined threshold in the reduction of the number of monthly MHDs (≥ 50 %, ≥ 75 % and 100 %) across the double-blind treatment period. The impact of migraine on functioning was assessed by the Role Function-Restrictive domain of the Migraine-Specific Quality of Life Questionnaire (MSQ) version 2.1, and by the Migraine Disability Assessment (MIDAS) Questionnaire. The MSQ measures impact of migraine on work or daily activities, relationships with family and friends, leisure time, productivity, concentration, energy, and tiredness. Scoring ranges from 0 to 100, with higher scores indicating less impairment , that is, patients experience fewer restrictions on the performance of day-to-day activities. For the MIDAS, higher scores indicate more disability. The baseline scores of the MIDAS reflected severe migraine related disability of patients in EVOLVE-1 and EVOLVE-2 (mean of 33.1) and a very severely disabled population (mean of 67.2) in REGAIN.

Episodic migraine
Studies EVOLVE-1 and EVOLVE-2 had a 6 month, double-blind, placebo-controlled treatment period. Completion rate of the double-blind treatment phase for patients who received galcanezumab ranged from 82.8 % to 87.7 %.

Both galcanezumab 120 mg and 240 mg treatment groups demonstrated statistically significant and clinically meaningful improvements from baseline compared to placebo on mean change in MHD (see Table 2). Patients treated with galcanezumab had greater response rates and greater reductions in the number of monthly MHDs that acute medication was taken compared with placebo-treated patients. Galcanezumab-treated patients had a greater improvement in functioning (as measured by the MSQ Role Function-Restrictive domain score) compared with placebo-treated patients, beginning at month 1. More patients treated with galcanezumab achieved clinically significant levels of improvement in functioning (responder rate based on MSQ Role Function Restrictive domain) compared with those treated with placebo. Galcanezumab was associated with a statistically significant reduction in disability over placebo.

Compared with placebo-treated patients, patients treated with galcanezumab 120 mg or 240 mg had significantly greater mean decreases from baseline in the number of monthly MHDs at month 1 and at all subsequent months up to month 6 (see Figure 1). Additionally, in month 1, patients treated with galcanezumab (loading dose of 240 mg) demonstrated significantly fewer weekly MHDs compared with placebo-treated patients, at week 1 and each subsequent week.

Figure 1 Reduction in monthly migraine headache days over time in studies EVOLVE-1 and EVOLVE-2

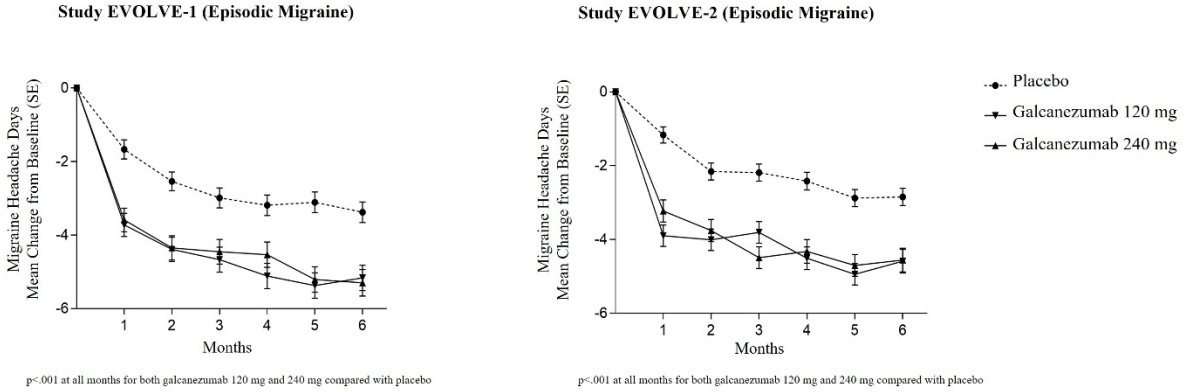


Table 2. Efficacy and patient reported outcome measures

	EVOLVE-1 – Episodic Migraine			EVOLVE-2 - Episodic Migraine		
	Emgality		Placebo	Emgality		Placebo
	120 mg	240 mg		120 mg	240 mg	
	N = 210	N = 208	N = 425	N = 226	N = 220	N = 450
Efficacy Outcomes[a]						
MHD						
Baseline	9.21	9.14	9.08	9.07	9.06	9.19
Mean Change	-4.73	-4.57	-2.81	-4.29	-4.18	-2.28
Treatment Difference	-1.92	-1.76		-2.02	-1.90	
$CI_{95\,\%}$	(-2.48, -1.37)	(-2.31, -1.20)		(-2.55, -1.48)	(-2.44, -1.36)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
≥ 50 % MHD Responders						
Percentage, %	62.3	60.9	38.6	59.3	56.5	36.0
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
≥ 75 % MHD Responders						
Percentage, %	38.8	38.5	19.3	33.5	34.3	17.8
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
100 % MHD Responders						
Percentage, %	15.6	14.6	6.2	11.5	13.8	5.7
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
MHD with Acute Medication Use						
Baseline	7.42	7.34	7.38	7.47	7.47	7.62
Mean Change	-3.96	-3.76	-2.15	-3.67	-3.63	-1.85
Treatment Difference	-1.81	-1.61		-1.82	-1.78	
$CI_{95\,\%}$	(-2.28, -1.33)	(-2.09, -1.14)		(-2.29, -1.36)	(-2.25, -1.31)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
Patient-reported Outcome Measures						
MSQ Role Function-Restrictive Domain[b]						
N	189	184	377	213	210	396
Baseline	51.39	48.76	52.92	52.47	51.71	51.35
Mean Change	32.43	32.09	24.69	28.47	27.04	19.65
Treatment Difference	7.74	7.40		8.82	7.39	
$CI_{95\,\%}$	(5.20, 10.28)	(4.83, 9.97)		(6.33, 11.31)	(4.88, 9.90)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
MSQ Role Function Restrictive Domain Responders[c]						
N	189	184	377	213	210	396
Percentage, %	63.5	69.6	47.2	58.2	60.0	43.4
P-value	< .001[f]	< .001[f]		< .001[f]	< .001[f]	
MIDAS Total Score[e]						
N	177	170	345	202	194	374
Baseline	32.93	36.09	31.84	30.87	32.75	34.25
Mean Change	-21.16	-20.06	-14.87	-21.17	-20.24	-12.02
Treatment Difference	-6.29	-5.19		-9.15	-8.22	
$CI_{95\%}$	(-9.45, -3.13)	(-8.39, -1.98)		(-12.61, -5.69)	(-11.71, -4.72)	
P-value	< .001[f]	.002[f]		< .001[f]	< .001[f]	

N = number of patients; $CI_{95\,\%}$ = 95 % confidence interval.

[a]Efficacy outcomes were evaluated across Months 1-6.

[b]Evaluated across Months 4-6.

[c]Defined as those with an improvement of ≥ 25 points for Episodic Migraine at Months 4-6 average.

[d]Statistically significant after adjustment for multiple comparisons.
[e]Evaluated at Month 6.
[f]Not adjusted for multiple comparisons.

In pooled data from studies EVOLVE-1 and EVOLVE-2, in patients who failed one or more prophylactic treatments for efficacy reasons, the treatment difference for the reduction of mean monthly MHDs observed between galcanezumab 120 mg and placebo was -2.69 days ($p < 0.001$) and between galcanezumab 240 mg and placebo -2.78 days ($p < 0.001$). In patients failing two or more prophylactic treatments, the treatment difference was -2.64 days ($p < 0.001$) between 120 mg and placebo and -3.04 days ($p < 0.001$) between 240 mg and placebo.

Chronic migraine
Study REGAIN had a 3 month, double-blind, placebo-controlled treatment period followed by a 9 month open-label extension. Approximately 15 % of the patients continued concurrent treatment with topiramate or propranolol as allowed by the protocol for prophylaxis of migraine. Completion rate of the double-blind treatment phase for patients who received galcanezumab was 95.3 %.

Both galcanezumab 120 mg and 240 mg treatment groups demonstrated statistically significant and clinically meaningful improvements from baseline compared to placebo on mean change in MHD (see Table 3). Patients treated with galcanezumab had greater response rates and greater reductions in the number of monthly MHDs that acute medication was taken compared with placebo-treated patients. Galcanezumab-treated patients had a greater improvement in functioning (as measured by the MSQ Role Function-Restrictive domain score) compared with placebo-treated patients, beginning at month 1. More patients treated with galcanezumab achieved clinically significant levels of improvement in functioning (responder rate based on MSQ Role Function Restrictive domain) compared with those treated with placebo. The 120 mg dose was associated with a statistically significant reduction in disability over placebo.

Compared with placebo-treated patients, patients treated with galcanezumab 120 mg or 240 mg had significantly greater mean decreases from baseline in the number of monthly MHDs at the first month and at all subsequent months up to month 3 (see Figure 2). Additionally, in month 1, patients treated with galcanezumab (loading dose of 240 mg) demonstrated significantly fewer weekly MHDs compared with placebo-treated patients, at week 1 and each subsequent week.

Figure 2 Reduction in monthly migraine headache days over time in study REGAIN

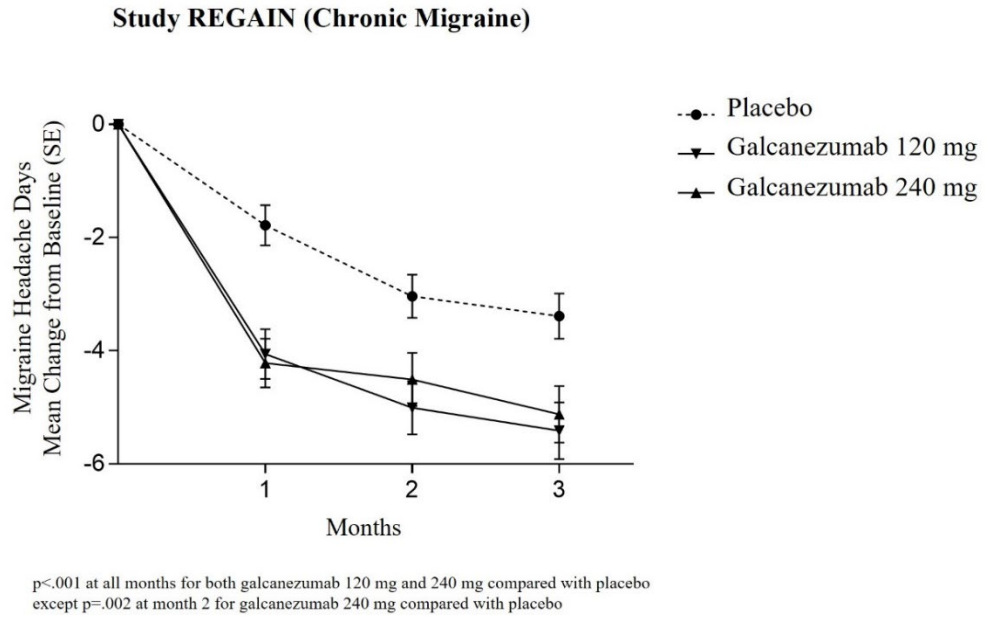


Table 3. Efficacy and patient reported outcome measures

	REGAIN – Chronic Migraine		
	Emgality		Placebo
	120 mg N = 273	240 mg N = 274	N = 538
Efficacy Outcomes[a]			
MHD			
Baseline	19.36	19.17	19.55
Mean Change	-4.83	-4.62	-2.74
Treatment Difference	-2.09	-1.88	
$CI_{95\ \%}$	(-2.92, -1.26)	(-2.71, -1.05)	
P-value	< .001[c]	< .001[c]	
≥ 50 % MHD Responders			
Percentage, %	27.6	27.5	15.4
P-value	< .001[c]	< .001[c]	
≥ 75 % MHD Responders			
Percentage, %	7.0	8.8	4.5
P-value	.031[d]	< .001[c]	
100 % MHD Responders			
Percentage, %	0.7	1.3	0.5
P-value	> .05[d]	> .05[d]	
MHD with Acute Medication Use			
Baseline	15.12	14.49	15.51
Mean Change	-4.74	-4.25	-2.23
Treatment Difference	-2.51	-2.01	
$CI_{95\ \%}$	(-3.27, -1.76)	(-2.77, -1.26)	
P-value	< .001[d]	< .001[c]	
Patient-reported Outcome Measures[b]	-	-	-
MSQ Role Function-Restrictive Domain			
N	252	253	494
Baseline	39.29	38.93	38.37
Mean Change	21.81	23.05	16.76
Treatment Difference	5.06	6.29	
$CI_{95\ \%}$	(2.12, 7.99)	(3.03, 9.55)	
P-value	< .001[d]	< .001[c]	
MSQ Role Function Restrictive Domain Responders			
N	252	253	494
Percentage, %	64.3	64.8	54.1
P-value	.003[e]	.002[e]	
MIDAS Total Score			
N	254	258	504
Baseline	62.46	69.17	68.66
Mean Change	-20.27	-17.02	-11.53
Treatment Difference	-8.74	-5.49	
$CI_{95\ \%}$	(-16.39, -1.08)	(-13.10, 2.12)	
P-value	.025[e]	> .05[e]	

N = number of patients; $CI_{95\ \%}$ = 95 % confidence interval.

[a]Efficacy outcomes were evaluated across Months 1-3.

[b]Patient-reported outcomes were evaluated at Month 3. MSQ role function restrictive domain responders were defined as those with an improvement of ≥ 17.14 points for Chronic Migraine at Month 3.

[c]Statistically significant after adjustment for multiple comparisons.

[d]Not statistically significant after adjustment for multiple comparisons.

[e]Not adjusted for multiple comparisons.

In patients who failed one or more prophylactic treatments for efficacy reasons, the treatment difference for the reduction of mean monthly MHDs observed between galcanezumab 120 mg and placebo was -3.54 days ($p < 0.001$) and between galcanezumab 240 mg and placebo -1.37 days ($p < 0.05$). In patients failing two or more prophylactic treatments, the treatment difference was -4.48 days ($p < 0.001$) between 120 mg and placebo and -1.86 days ($p < 0.01$) between 240 mg and placebo.

Sixty-four percent of the patients had acute headache medication overuse at baseline. In these patients, the treatment difference observed between galcanezumab 120 mg and placebo and between galcanezumab 240 mg and placebo for the reduction of MHDs in these patients was respectively -2.53 days ($p < 0.001$) and -2.26 days ($p < 0.001$).

Long term efficacy
Efficacy was sustained for up to 1 year in an open-label study in which patients with either episodic or chronic migraine (with an average baseline of 10.6 monthly MHDs) received galcanezumab 120 mg/month (with an initial loading dose of 240 mg for the first month) or galcanezumab 240 mg/month. 77.8 % of patients completed the treatment period. The overall mean reduction from baseline in the number of monthly MHDs averaged over the treatment phase was 5.6 days for the 120 mg dose group and 6.5 days for the 240 mg dose group. Over 72 % of patients completing the study reported a 50 % reduction in MHDs at month 12. In pooled data from studies EVOLVE-1 and EVOLVE-2, more than 19 % of the patients treated with galcanezumab maintained a ≥ 50 % response from Month 1 to Month 6 versus 8 % of the patients on placebo ($p < 0.001$).

Phase 3 study in a population with previous failure to 2 to 4 migraine preventive medication categories
Study CONQUER, in episodic and chronic migraine patients that experienced previous failures to 2 to 4 prophylactic medication categories in the past 10 years, supports the main findings of the previous migraine efficacy studies, i.e. galcanezumab treatment led to a mean reduction in monthly migraine headache days (4.1 days compared to 1.0 days in the placebo group; $p<.0001$). Mean reduction in monthly migraine headache days was also observed within the subpopulations of episodic migraine (2.9 days for galcanezumab compared with 0.3 days for placebo; $p<.0001$) and chronic migraine (5.9 days for galcanezumab compared with 2.2 days for placebo; $p<.0001$).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with galcanezumab in one or more subsets of the paediatric population in the prophylaxis of migraine headaches (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Based on a population pharmacokinetic (PK) analysis, following a loading dose of 240 mg the maximum serum concentration (C_{max}) of galcanezumab was approximately 30 µg/mL (27 % coefficient of variation, (CV)) and the time to C_{max} was 5 days postdose.

Monthly doses of 120 mg or 240 mg achieved a steady-state C_{max} ($C_{max, ss}$) of approximately 28 µg/mL (35 % CV) or 54 µg/mL (31 % CV), respectively. The galcanezumab $C_{max, ss}$ at monthly doses of 120 mg is achieved after the 240 mg loading dose.

Injection site location (abdomen, thigh, buttocks and arm) did not significantly influence the absorption of galcanezumab.

Distribution

Based on a population PK analysis, the apparent volume of distribution of galcanezumab was 7.3 L.

Biotransformation

As a humanised 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 of galcanezumab was approximately 0.008 L/hour and the half life of galcanezumab was 27 days.

Linearity/non-linearity

Galcanezumab exposure increases proportionally with dose.

Based on a population PK analysis that included doses ranging from 5 – 300 mg, the rate of absorption, apparent clearance and apparent volume of distribution was independent of dose.

Age, sex, weight, race, ethnicity

No dose adjustment is needed on the basis of age (18 to 65 years), sex, weight, race or ethnicity as there was no clinically meaningful effect of these factors on the apparent clearance or apparent volume of distribution of galcanezumab.

Renal or hepatic impairment

Specific clinical pharmacology studies to evaluate the effects of renal impairment and hepatic impairment on the PK of galcanezumab have not been conducted. Renal elimination of IgG monoclonal antibody is low. Similarly, IgG monoclonal antibodies are mainly eliminated via intracellular catabolism and hepatic impairment is not expected to influence the clearance of galcanezumab. Based on a population PK analysis, bilirubin concentration or Cockcroft-Gault creatinine clearance (range: 24 to 308 mL/min) did not significantly influence the apparent clearance of galcanezumab.

5.3 Preclinical safety data

Non-clinical data revealed no special hazards for humans based on repeat-dose toxicity studies conducted in rats and cynomolgus monkeys and safety pharmacology evaluations conducted in cynomolgus monkeys at exposures approximately 10 to 80 times higher than clinical exposures in patients receiving 240 mg.

Nonclinical studies have not been conducted to evaluate the carcinogenic or mutagenic potential of galcanezumab. There is no evidence to suggest that chronic treatment with galcanezumab would increase the risk of carcinogenesis based on data from pharmacology and chronic toxicology studies with galcanezumab, as well as an assessment of the literature regarding CGRP.

No effects on fertility parameters such as oestrous cycle, sperm analysis, or mating and reproductive performance were observed in rats that were administered galcanezumab (exposures approximately 4 to 20 times the human exposure at 240 mg). In male fertility study, right testis weight was significantly reduced at exposures to 4 times the human exposure at 240 mg.

At Gestational Day 20, an increase in the number of foetuses and litters with short ribs and a decrease in the mean number of ossified caudal vertebrae occurred in the rat embryo-foetal toxicity development study at an exposure approximately 20 times the human exposure at 240 mg. These

findings were noted at no maternal toxicity and were considered to be related to galcanezumab but non-adverse.

At Gestational Day 29, in rabbit embryo-foetal development toxicity study skull anomaly was found in one male foetus from mother treated with galcanezumab at an exposure approximately 33 times the human exposure at 240 mg.

In a juvenile toxicology study in which rats were administered galcanezumab twice weekly from Postnatal Day 21 through 90, systemic effects were limited to reversible, minimal, nonadverse decreases in total bone mineral content and bone mineral density at exposures approximately 50 times the human exposure at 240 mg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-histidine
L-histidine hydrochloride monohydrate
Polysorbate 80
Sodium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.
Store in the original package in order to protect from light.

Emgality may be stored unrefrigerated for up to 7 days when stored at temperatures up to 30 °C. If these conditions are exceeded, the pre-filled pen must be discarded.

6.5 Nature and contents of container

Type I clear glass syringe. The syringe is encased in a disposable, single-dose pen. Packs of 1, 2 or 3 pre-filled pens. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use

The instructions for using the pen included with the Package Leaflet, must be followed carefully. The pre-filled pen is for total use only.

The pre-filled pen should be inspected visually prior to administration. Emgality should not be used if the solution is cloudy, discoloured or contains particles, or if any part of the device appears to be damaged.

Do not shake.

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

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1330/001
EU/1/18/1330/002
EU/1/18/1330/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 November 2018
Date of latest renewal: 01 September 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Emgality 120 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 120 mg of galcanezumab in 1 mL.

Galcanezumab is a recombinant humanised monoclonal antibody produced in Chinese Hamster Ovary cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emgality is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month.

4.2 Posology and method of administration

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

Posology

The recommended dose is 120 mg galcanezumab injected subcutaneously once monthly, with a 240 mg loading dose as the initial dose.

Patients should be instructed to inject a missed dose as soon as possible and then resume monthly dosing.

The treatment benefit should be assessed within 3 months after initiation of treatment. Any further decision to continue treatment should be taken on an individual patient basis. Evaluation of the need to continue treatment is recommended regularly thereafter.

Elderly (≥ 65 years)
There is limited information in subjects aged ≥ 65 years. No dose adjustment is required as the pharmacokinetics of galcanezumab are not affected by age.

Renal impairment/hepatic impairment
No dose adjustment is required in patients with mild to moderate renal impairment or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of galcanezumab in children aged 6 to 18 years have not yet been established. No data are available.

There is no relevant use of galcanezumab in children below the age of 6 years for the prevention of migraine.

Method of administration

Subcutaneous use.

A patient may self-inject galcanezumab by following the Instructions for Use. Galcanezumab is to be injected subcutaneously in the abdomen, thigh, back of the upper arm, or in the gluteal region. After training, patients may self-inject galcanezumab if a healthcare professional determines that it is appropriate. Comprehensive instructions for administration are given in the Package Leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

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

Cardiovascular risk

Patients with certain major cardiovascular diseases were excluded from clinical studies (see section 5.1). No safety data are available in these patients.

Serious hypersensitivity

Serious hypersensitivity reactions including cases of anaphylaxis, angioedema and urticaria have been reported (see section 4.8). Serious hypersensitivity reactions may occur within 1 day after galcanezumab administration, however cases with a delayed onset (ranging from more than 1 day to 4 weeks after administration) have been reported. In some cases, hypersensitivity reactions had a prolonged duration. If a serious hypersensitivity reaction occurs, administration of galcanezumab should be discontinued immediately and appropriate therapy initiated (see section 4.3). Patients should be informed on the possibility of a delayed onset hypersensitivity reaction and instructed to contact their physician.

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per 120 mg dose, that is to say essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies were conducted. No pharmacokinetic drug interactions are expected based on the characteristics of galcanezumab.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of galcanezumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Human immunoglobulin (IgG) is known to cross the placental barrier. As a precautionary measure, it is preferable to avoid the use of galcanezumab during pregnancy.

Breast-feeding

It is unknown whether galcanezumab is excreted in human milk. Human IgG is known to be excreted in breast milk during the first days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to breast-fed infants cannot be excluded during this short period. Afterwards, use of galcanezumab could be considered during breast-feeding only if clinically needed.

Fertility

The effect of galcanezumab on human fertility has not been evaluated. Fertility studies in animals do not indicate harmful effects with respect to male and female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Galcanezumab may have a minor influence on the ability to drive and use machines. Vertigo may occur following the administration of galcanezumab (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

Over 2 500 patients were exposed to galcanezumab in migraine prophylaxis studies supporting the initial registration of galcanezumab. Over 1 400 patients were exposed to galcanezumab during the double-blind treatment phase of the placebo-controlled phase 3 studies. 279 patients were exposed for 12 months.

The reported adverse drug reactions for 120 mg and 240 mg in the migraine clinical trials were injection site pain (10.1 %/11.6 %), injection site reactions (9.9 %/14.5 %), vertigo (0.7 %/1.2 %), constipation (1.0 %/1.5 %), pruritus (0.7 %/1.2 %) and urticaria (0.3 %/0.1 %). Most of the reactions were mild or moderate in severity. Less than 2.5 % of patients in these studies discontinued due to adverse reactions.

Tabulated list of adverse reactions

Table 1. List of adverse reactions in clinical studies and post-marketing reports
Frequency estimate: Very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000).

System organ class	Very common	Common	Uncommon	Rare
Immune system disorders				Anaphylaxis Angioedema
Ear and labyrinth disorders		Vertigo		
Gastrointestinal disorders		Constipation		
Skin and subcutaneous tissue disorders		Pruritus Rash	Urticaria	
General disorders and administration site conditions	Injection site pain Injection site reactions[a]			

[a] Most frequently reported terms (≥ 1 %) were: Injection site reaction, Injection site erythema, Injection site pruritus, Injection site bruising, Injection site swelling.

Description of selected adverse reactions

Injection site pain or reactions
The majority of reactions related to the injection site were mild to moderate and less than 0.5 % of patients exposed to galcanezumab during the phase 3 studies discontinued the treatment due to an injection site reaction. The majority of injection site reactions were reported within 1 day and on average resolved within 5 days. In 86 % of the patients reporting injection site pain, the reaction occurred within 1 hour of injection and resolved on average in 1 day. One percent of the patients exposed to galcanezumab during the phase 3 studies experienced severe pain at the injection site.

Urticaria
While urticaria is uncommon, serious cases of urticaria have been reported in galcanezumab clinical studies.

Immunogenicity
In the clinical studies, the incidence of anti-drug antibody development during the double-blind treatment phase was 4.8 % in patients receiving galcanezumab once monthly (all but one of whom had *in vitro* neutralizing activity). With 12 months of treatment, up to 12.5 % of galcanezumab-treated patients developed anti-drug antibodies, most of which were of low titre and tested positive for neutralising activity *in vitro*. However, the presence of anti-drug antibodies did not affect the pharmacokinetics, efficacy, or safety of galcanezumab.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 600 mg have been administered subcutaneously to humans without 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: analgesics, calcitonin gene-related peptide (CGRP) antagonists, ATC code: N02CD02

Mechanism of action

Galcanezumab is a humanised IgG4 monoclonal antibody that binds calcitonin gene-related peptide (CGRP) thus preventing its biological activity. Elevated blood concentrations of CGRP have been associated with migraine attacks. Galcanezumab binds to CGRP with high affinity (K_D = 31 pM) and high specificity (> 10 000-fold vs related peptides adrenomedullin, amylin, calcitonin and intermedin).

Clinical efficacy and safety

The efficacy and safety of galcanezumab has been studied in 3 phase 3, randomized, placebo-controlled, double-blind studies in adult patients (N = 2 886). The 2 episodic migraine studies (EVOLVE-1 and EVOLVE-2) enrolled patients who met International Classification of Headache Disorders (ICHD) criteria for a diagnosis of migraine with or without aura with 4-14 migraine headache days per month. The chronic migraine study (REGAIN) enrolled patients who met ICHD criteria for chronic migraine with ≥ 15 headache days per month, of which at least 8 had the features of migraine. Patients with recent acute cardiovascular events (including MI, unstable angina, CABG, stroke, DVT) and/or those deemed to be at serious cardiovascular risk were excluded from the galcanezumab clinical trials. Patients > 65 years of age were also excluded.

Patients received placebo, galcanezumab 120 mg/month (with an initial loading dose of 240 mg for the first month) or galcanezumab 240 mg/month and were allowed to use medication for the acute treatment of migraine. Across the 3 studies, patients were predominantly female (> 83 %) with a mean age of 41 years, and an average migraine history of 20 to 21 years. Approximately one-third of patients across the studies had at least 1 prior failure on a migraine prophylactic treatment for efficacy reasons and approximately 16 % of patients across the studies had at least 2 prior failure on a prophylactic treatment for efficacy reasons.

In all 3 studies, the overall mean change from baseline in number of monthly Migraine Headache Days (MHDs) was the primary efficacy measure. Response rate is the mean percentage of patients meeting a defined threshold in the reduction of the number of monthly MHDs (≥ 50 %, ≥ 75 % and 100 %) across the double-blind treatment period. The impact of migraine on functioning was assessed by the Role Function-Restrictive domain of the Migraine-Specific Quality of Life Questionnaire (MSQ) version 2.1, and by the Migraine Disability Assessment (MIDAS) Questionnaire. The MSQ measures impact of migraine on work or daily activities, relationships with family and friends, leisure time, productivity, concentration, energy, and tiredness. Scoring ranges from 0 to 100, with higher scores indicating less impairment , that is, patients experience fewer restrictions on the performance of day-to-day activities. For the MIDAS, higher scores indicate more disability. The baseline scores of the MIDAS reflected severe migraine related disability of patients in EVOLVE-1 and EVOLVE-2 (mean of 33.1) and a very severely disabled population (mean of 67.2) in REGAIN.

Episodic migraine
Studies EVOLVE-1 and EVOLVE-2 had a 6 month, double-blind, placebo-controlled treatment period. Completion rate of the double-blind treatment phase for patients who received galcanezumab ranged from 82.8 % to 87.7 %.

Both galcanezumab 120 mg and 240 mg treatment groups demonstrated statistically significant and clinically meaningful improvements from baseline compared to placebo on mean change in MHD (see Table 2). Patients treated with galcanezumab had greater response rates and greater reductions in the number of monthly MHDs that acute medication was taken compared with placebo-treated patients. Galcanezumab-treated patients had a greater improvement in functioning (as measured by the MSQ Role Function-Restrictive domain score) compared with placebo-treated patients, beginning at month 1. More patients treated with galcanezumab achieved clinically significant levels of improvement in functioning (responder rate based on MSQ Role Function Restrictive domain) compared with those treated with placebo. Galcanezumab was associated with a statistically significant reduction in disability over placebo.

Compared with placebo-treated patients, patients treated with galcanezumab 120 mg or 240 mg had significantly greater mean decreases from baseline in the number of monthly MHDs at month 1 and at all subsequent months up to month 6 (see Figure 1). Additionally, in month 1, patients treated with galcanezumab (loading dose of 240 mg) demonstrated significantly fewer weekly MHDs compared with placebo-treated patients, at week 1 and each subsequent week.

Figure 1 Reduction in monthly migraine headache days over time in studies EVOLVE-1 and EVOLVE-2

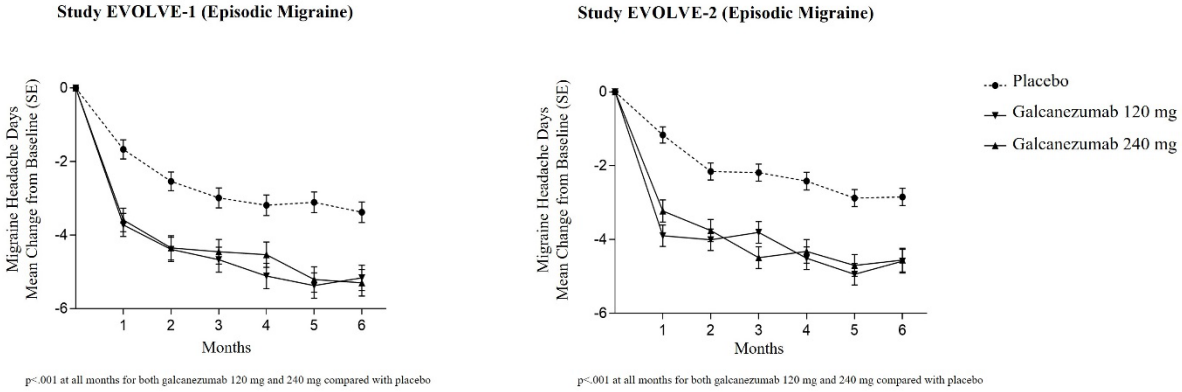


Table 2. Efficacy and patient reported outcome measures

	EVOLVE-1 – Episodic Migraine			EVOLVE-2 - Episodic Migraine		
	Emgality		Placebo	Emgality		Placebo
	120 mg	240 mg		120 mg	240 mg	
	N = 210	N = 208	N = 425	N = 226	N = 220	N = 450
Efficacy Outcomes[a]						
MHD						
Baseline	9.21	9.14	9.08	9.07	9.06	9.19
Mean Change	-4.73	-4.57	-2.81	-4.29	-4.18	-2.28
Treatment Difference	-1.92	-1.76		-2.02	-1.90	
$CI_{95\,\%}$	(-2.48, -1.37)	(-2.31, -1.20)		(-2.55, -1.48)	(-2.44, -1.36)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
≥ 50 % MHD Responders						
Percentage, %	62.3	60.9	38.6	59.3	56.5	36.0
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
≥ 75 % MHD Responders						
Percentage, %	38.8	38.5	19.3	33.5	34.3	17.8
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
100 % MHD Responders						
Percentage, %	15.6	14.6	6.2	11.5	13.8	5.7
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
MHD with Acute Medication Use						
Baseline	7.42	7.34	7.38	7.47	7.47	7.62
Mean Change	-3.96	-3.76	-2.15	-3.67	-3.63	-1.85
Treatment Difference	-1.81	-1.61		-1.82	-1.78	
$CI_{95\,\%}$	(-2.28, -1.33)	(-2.09, -1.14)		(-2.29, -1.36)	(-2.25, -1.31)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
Patient-reported Outcome Measures						
MSQ Role Function-Restrictive Domain[b]						
N	189	184	377	213	210	396
Baseline	51.39	48.76	52.92	52.47	51.71	51.35
Mean Change	32.43	32.09	24.69	28.47	27.04	19.65
Treatment Difference	7.74	7.40		8.82	7.39	
$CI_{95\,\%}$	(5.20, 10.28)	(4.83, 9.97)		(6.33, 11.31)	(4.88, 9.90)	
P-value	< .001[d]	< .001[d]		< .001[d]	< .001[d]	
MSQ Role Function Restrictive Domain Responders[c]						
N	189	184	377	213	210	396
Percentage, %	63.5	69.6	47.2	58.2	60.0	43.4
P-value	< .001[f]	< .001[f]		< .001[f]	< .001[f]	
MIDAS Total Score[e]						
N	177	170	345	202	194	374
Baseline	32.93	36.09	31.84	30.87	32.75	34.25
Mean Change	-21.16	-20.06	-14.87	-21.17	-20.24	-12.02
Treatment Difference	-6.29	-5.19		-9.15	-8.22	
$CI_{95\%}$	(-9.45, -3.13)	(-8.39, -1.98)		(-12.61, -5.69)	(-11.71, -4.72)	
P-value	< .001[f]	.002[f]		< .001[f]	< .001[f]	

N = number of patients; $CI_{95\,\%}$ = 95 % confidence interval.

[a]Efficacy outcomes were evaluated across Months 1-6.

[b]Evaluated across Months 4-6.

[c]Defined as those with an improvement of ≥ 25 points for Episodic Migraine at Months 4-6 average.

[d]Statistically significant after adjustment for multiple comparisons.
[e]Evaluated at Month 6.
[f]Not adjusted for multiple comparisons.

In pooled data from studies EVOLVE-1 and EVOLVE-2, in patients who failed one or more prophylactic treatments for efficacy reasons, the treatment difference for the reduction of mean monthly MHDs observed between galcanezumab 120 mg and placebo was -2.69 days ($p < 0.001$) and between galcanezumab 240 mg and placebo -2.78 days ($p < 0.001$). In patients failing two or more prophylactic treatments, the treatment difference was -2.64 days ($p < 0.001$) between 120 mg and placebo and -3.04 days ($p < 0.001$) between 240 mg and placebo.

Chronic migraine
Study REGAIN had a 3 month, double-blind, placebo-controlled treatment period followed by a 9 month open-label extension. Approximately 15 % of the patients continued concurrent treatment with topiramate or propranolol as allowed by the protocol for prophylaxis of migraine. Completion rate of the double-blind treatment phase for patients who received galcanezumab was 95.3 %.

Both galcanezumab 120 mg and 240 mg treatment groups demonstrated statistically significant and clinically meaningful improvements from baseline compared to placebo on mean change in MHD (see Table 3). Patients treated with galcanezumab had greater response rates and greater reductions in the number of monthly MHDs that acute medication was taken compared with placebo-treated patients. Galcanezumab-treated patients had a greater improvement in functioning (as measured by the MSQ Role Function-Restrictive domain score) compared with placebo-treated patients, beginning at month 1. More patients treated with galcanezumab achieved clinically significant levels of improvement in functioning (responder rate based on MSQ Role Function Restrictive domain) compared with those treated with placebo. The 120 mg dose was associated with a statistically significant reduction in disability over placebo.

Compared with placebo-treated patients, patients treated with galcanezumab 120 mg or 240 mg had significantly greater mean decreases from baseline in the number of monthly MHDs at the first month and at all subsequent months up to month 3 (see Figure 2). Additionally, in month 1, patients treated with galcanezumab (loading dose of 240 mg) demonstrated significantly fewer weekly MHDs compared with placebo-treated patients, at week 1 and each subsequent week.

Figure 2 Reduction in monthly migraine headache days over time in study REGAIN

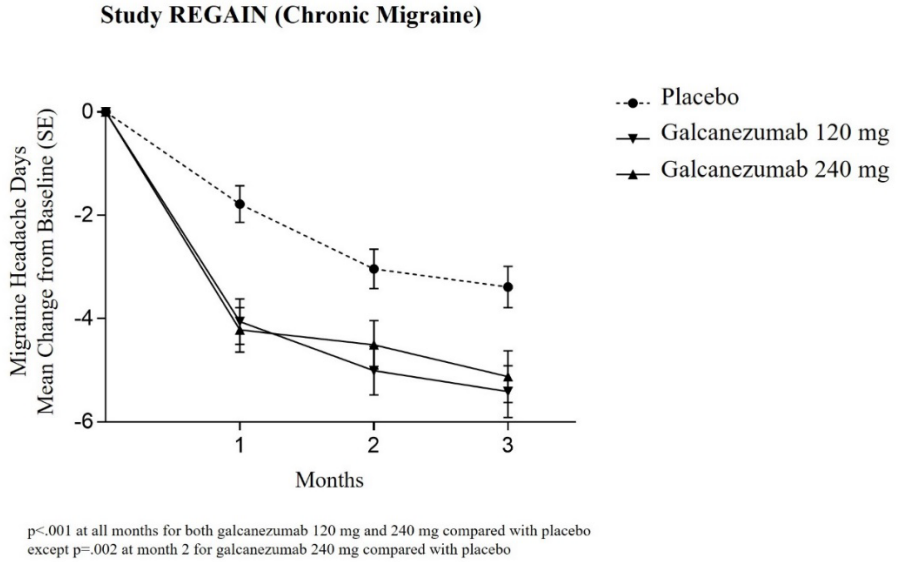


Table 3. Efficacy and patient reported outcome measures

	REGAIN – Chronic Migraine		
	Emgality		Placebo
	120 mg N = 273	240 mg N = 274	N = 538
Efficacy Outcomes[a]			
MHD			
Baseline	19.36	19.17	19.55
Mean Change	-4.83	-4.62	-2.74
Treatment Difference	-2.09	-1.88	
$CI_{95\ \%}$	(-2.92, -1.26)	(-2.71, -1.05)	
P-value	< .001[c]	< .001[c]	
≥ 50 % MHD Responders			
Percentage, %	27.6	27.5	15.4
P-value	< .001[c]	< .001[c]	
≥ 75 % MHD Responders			
Percentage, %	7.0	8.8	4.5
P-value	.031[d]	< .001[c]	
100 % MHD Responders			
Percentage, %	0.7	1.3	0.5
P-value	> .05[d]	> .05[d]	
MHD with Acute Medication Use			
Baseline	15.12	14.49	15.51
Mean Change	-4.74	-4.25	-2.23
Treatment Difference	-2.51	-2.01	
$CI_{95\ \%}$	(-3.27, -1.76)	(-2.77, -1.26)	
P-value	< .001[d]	< .001[c]	
Patient-reported Outcome Measures[b]	-	-	-
MSQ Role Function-Restrictive Domain			
N	252	253	494
Baseline	39.29	38.93	38.37
Mean Change	21.81	23.05	16.76
Treatment Difference	5.06	6.29	
$CI_{95\ \%}$	(2.12, 7.99)	(3.03, 9.55)	
P-value	< .001[d]	< .001[c]	
MSQ Role Function Restrictive Domain Responders			
N	252	253	494
Percentage, %	64.3	64.8	54.1
P-value	.003[e]	.002[e]	
MIDAS Total Score			
N	254	258	504
Baseline	62.46	69.17	68.66
Mean Change	-20.27	-17.02	-11.53
Treatment Difference	-8.74	-5.49	
$CI_{95\ \%}$	(-16.39, -1.08)	(-13.10, 2.12)	
P-value	.025[e]	> .05[e]	

N = number of patients; $CI_{95\ \%}$ = 95 % confidence interval.

[a]Efficacy outcomes were evaluated across Months 1-3.

[b]Patient-reported outcomes were evaluated at Month 3. MSQ role function restrictive domain responders were defined as those with an improvement of ≥ 17.14 points for Chronic Migraine at Month 3.

[c]Statistically significant after adjustment for multiple comparisons.

[d]Not statistically significant after adjustment for multiple comparisons.

[e]Not adjusted for multiple comparisons.

In patients who failed one or more prophylactic treatments for efficacy reasons, the treatment difference for the reduction of mean monthly MHDs observed between galcanezumab 120 mg and placebo was -3.54 days ($p < 0.001$) and between galcanezumab 240 mg and placebo -1.37 days ($p < 0.05$). In patients failing two or more prophylactic treatments, the treatment difference was -4.48 days ($p < 0.001$) between 120 mg and placebo and -1.86 days ($p < 0.01$) between 240 mg and placebo.

Sixty-four percent of the patients had acute headache medication overuse at baseline. In these patients, the treatment difference observed between galcanezumab 120 mg and placebo and between galcanezumab 240 mg and placebo for the reduction of MHDs in these patients was respectively -2.53 days ($p < 0.001$) and -2.26 days ($p < 0.001$).

Long term efficacy
Efficacy was sustained for up to 1 year in an open-label study in which patients with either episodic or chronic migraine (with an average baseline of 10.6 monthly MHDs) received galcanezumab 120 mg/month (with an initial loading dose of 240 mg for the first month) or galcanezumab 240 mg/month. 77.8 % of patients completed the treatment period. The overall mean reduction from baseline in the number of monthly MHDs averaged over the treatment phase was 5.6 days for the 120 mg dose group and 6.5 days for the 240 mg dose group. Over 72 % of patients completing the study reported a 50 % reduction in MHDs at month 12. In pooled data from studies EVOLVE-1 and EVOLVE-2, more than 19 % of the patients treated with galcanezumab maintained a ≥ 50 % response from Month 1 to Month 6 versus 8 % of the patients on placebo ($p < 0.001$).

Phase 3 study in a population with previous failure to 2 to 4 migraine preventive medication categories
Study CONQUER, in episodic and chronic migraine patients that experienced previous failures to 2 to 4 prophylactic medication categories in the past 10 years, supports the main findings of the previous migraine efficacy studies, i.e. galcanezumab treatment led to a mean reduction in monthly migraine headache days (4.1 days compared to 1.0 days in the placebo group; $p<.0001$). Mean reduction in monthly migraine headache days was also observed within the subpopulations of episodic migraine (2.9 days for galcanezumab compared with 0.3 days for placebo; $p<.0001$) and chronic migraine (5.9 days for galcanezumab compared with 2.2 days for placebo; $p<.0001$).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with galcanezumab in one or more subsets of the paediatric population in the prophylaxis of migraine headaches (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Based on a population pharmacokinetic (PK) analysis, following a loading dose of 240 mg the maximum serum concentration (C_{max}) of galcanezumab was approximately 30 µg/mL (27 % coefficient of variation, (CV)) and the time to C_{max} was 5 days postdose.

Monthly doses of 120 mg or 240 mg achieved a steady-state C_{max} ($C_{max, ss}$) of approximately 28 µg/mL (35 % CV) or 54 µg/mL (31 % CV), respectively. The galcanezumab $C_{max, ss}$ at monthly doses of 120 mg is achieved after the 240 mg loading dose.

Injection site location (abdomen, thigh, buttocks and arm) did not significantly influence the absorption of galcanezumab.

Distribution

Based on a population PK analysis, the apparent volume of distribution of galcanezumab was 7.3 L.

Biotransformation

As a humanised 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 of galcanezumab was approximately 0.008 L/hour and the half life of galcanezumab was 27 days.

Linearity/non-linearity

Galcanezumab exposure increases proportionally with dose.

Based on a population PK analysis that included doses ranging from 5 – 300 mg, the rate of absorption, apparent clearance and apparent volume of distribution was independent of dose.

Age, sex, weight, race, ethnicity

No dose adjustment is needed on the basis of age (18 to 65 years), sex, weight, race or ethnicity as there was no clinically meaningful effect of these factors on the apparent clearance or apparent volume of distribution of galcanezumab.

Renal or hepatic impairment

Specific clinical pharmacology studies to evaluate the effects of renal impairment and hepatic impairment on the PK of galcanezumab have not been conducted. Renal elimination of IgG monoclonal antibody is low. Similarly, IgG monoclonal antibodies are mainly eliminated via intracellular catabolism and hepatic impairment is not expected to influence the clearance of galcanezumab. Based on a population PK analysis, bilirubin concentration or Cockcroft-Gault creatinine clearance (range: 24 to 308 mL/min) did not significantly influence the apparent clearance of galcanezumab.

5.3 Preclinical safety data

Non-clinical data revealed no special hazards for humans based on repeat-dose toxicity studies conducted in rats and cynomolgus monkeys and safety pharmacology evaluations conducted in cynomolgus monkeys at exposures approximately 10 to 80 times higher than clinical exposures in patients receiving 240 mg.

Nonclinical studies have not been conducted to evaluate the carcinogenic or mutagenic potential of galcanezumab. There is no evidence to suggest that chronic treatment with galcanezumab would increase the risk of carcinogenesis based on data from pharmacology and chronic toxicology studies with galcanezumab, as well as an assessment of the literature regarding CGRP.

No effects on fertility parameters such as oestrous cycle, sperm analysis, or mating and reproductive performance were observed in rats that were administered galcanezumab (exposures approximately 4 to 20 times the human exposure at 240 mg). In male fertility study, right testis weight was significantly reduced at exposures to 4 times the human exposure at 240 mg.

At Gestational Day 20, an increase in the number of foetuses and litters with short ribs and a decrease in the mean number of ossified caudal vertebrae occurred in the rat embryo-foetal toxicity development study at an exposure approximately 20 times the human exposure at 240 mg. These

findings were noted at no maternal toxicity and were considered to be related to galcanezumab but non-adverse.

At Gestational Day 29, in rabbit embryo-foetal development toxicity study skull anomaly was found in one male foetus from mother treated with galcanezumab at an exposure approximately 33 times the human exposure at 240 mg.

In a juvenile toxicology study in which rats were administered galcanezumab twice weekly from Postnatal Day 21 through 90, systemic effects were limited to reversible, minimal, nonadverse decreases in total bone mineral content and bone mineral density at exposures approximately 50 times the human exposure at 240 mg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-histidine
L-histidine hydrochloride monohydrate
Polysorbate 80
Sodium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.
Store in the original package in order to protect from light.

Emgality may be stored unrefrigerated for up to 7 days when stored at temperatures up to 30 °C. If these conditions are exceeded, the pre-filled syringe must be discarded.

6.5 Nature and contents of container

Type I clear glass single-dose syringe. Pack sizes of 1, 2 or 3 pre-filled syringes. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use

The instructions for using the syringe included with the Package Leaflet, must be followed carefully. The pre-filled syringe is for total use only.

The pre-filled syringe should be inspected visually prior to administration. Emgality should not be used if the solution is cloudy, discoloured or contains particles, or if any part of the device appears to be damaged.

Do not shake.

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

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1330/003
EU/1/18/1330/004
EU/1/18/1330/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 November 2018
Date of latest renewal: 01 September 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

ImClone Systems LLC
33 ImClone Drive
Branchburg
New Jersey
NJ 08876
United States

Names and addresses of the manufacturer(s) responsible for batch release

Pre-filled pen

Eli Lilly Italia S.p.A.
Via Gramsci, 731-733
50019
Sesto Fiorentino (FI)
Italy

Lilly, S.A.
Avda. de la Industria, 30
28108 Alcobendas, Madrid
Spain.

Pre-filled syringe

Eli Lilly Italia S.p.A.
Via Gramsci, 731-733
50019
Sesto Fiorentino (FI)
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON - PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT

Emgality 120 mg solution for injection in pre-filled pen
galcanezumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 120 mg of galcanezumab

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride monohydrate, sodium chloride, polysorbate 80, water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
1 pre-filled pen
3 pre-filled pens
2 pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
For single use only.
Do not shake.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.
Store in the original package in order to protect from light.
Emgality may be stored unrefrigerated for a single period up to 7 days when stored at temperatures up to 30 °C

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1330/001 (1 pre-filled pen)
EU/1/18/1330/002 (3 pre-filled pens)
EU/1/18/1330/005 (2 pre-filled pens)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emgality

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

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

Emgality 120 mg injection
galcanezumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Emgality 120 mg solution for injection in pre-filled syringe
galcanezumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 120 mg of galcanezumab

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride monohydrate, sodium chloride, polysorbate 80, water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
1 pre-filled syringe
3 pre-filled syringes
2 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
For single use only.
Do not shake.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.
Emgality may be stored unrefrigerated for a single period up to 7 days when stored at temperatures up to 30 °C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1330/003 (1 pre-filled syringe)
EU/1/18/1330/004 (3 pre-filled syringes)
EU/1/18/1330/006 (2 pre-filled syringes)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emgality

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

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

Emgality 120 mg injection
galcanezumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Emgality 120 mg solution for injection in pre-filled pen

galcanezumab

.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Emgality is and what it is used for
2. What you need to know before you use Emgality
3. How to use Emgality
4. Possible side effects
5. How to store Emgality
6. Contents of the pack and other information

1. What Emgality is and what it is used for

Emgality contains galcanezumab, a medicine that stops the activity of a naturally occurring substance in the body called calcitonin gene-related peptide (CGRP). People with migraine may have increased levels of CGRP.

Emgality is used to prevent migraine in adult patients who have at least 4 migraines days per month.

Emgality can reduce the frequency of migraine headache and improve your quality of life. It starts working in about a week.

2. What you need to know before you use Emgality

Do not use Emgality:

- if you are allergic to galcanezumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before or during treatment with Emgality if:

- you have a serious cardiovascular disease. Emgality has not been studied in patients with serious cardiovascular diseases.

Look out for allergic reactions

Emgality can potentially cause serious allergic reactions. Serious allergic reactions happen mainly within 1 day after having taken Emgality, but some reactions can be delayed (happen more than 1 day to 4 weeks after having taken Emgality). Some allergic reactions can be prolonged in duration. You must look out for signs of these reactions while you are using Emgality. Stop using Emgality and tell

your doctor or seek medical help immediately if you notice any signs of a serious allergic reaction. Such signs are listed under “Serious side effects” in section 4.

Children and adolescents
This medicine should not be given to children and adolescents under 18 years of age because it has not been studied in this age group.

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

Pregnancy and breast-feeding
If you are a woman able to have children, you are advised to avoid becoming pregnant while using Emgality.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. It is preferable to avoid the use of Emgality in pregnancy as the effects of this medicine in pregnant women are not known.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine. You and your doctor should decide if you should breast feed and use Emgality .

Driving and using machines
Galcanezumab could have a minor effect on your ability to drive and use machines. Some patients have had vertigo whilst using Emgality.

Emgality contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 120 mg dose, that is to say essentially “sodium-free”.

3. How to use Emgality

Always use this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Emgality pre-filled pen is for single use only and contains one dose of Emgality (120 mg).
- The first time you receive Emgality your doctor or nurse will inject two pens (total 240 mg).
- After the first dose, you will use one pen (120 mg) every month.

Your doctor will decide for how long you should use Emgality.

Emgality is given by injection under your skin (subcutaneous injection). You and your doctor or nurse should decide if you can inject Emgality yourself.

It is important not to try to inject yourself until you have been trained by your doctor or nurse. A caregiver may also give you your Emgality injection after proper training.

The pen must not be shaken.

Read the “Instructions for Use” for the pen carefully before using Emgality.

If you use more Emgality than you should
If you have injected more Emgality than you should, e.g. if after the first dose of 240 mg, you have injected it twice in a single month, or if anyone else has accidentally used Emgality, contact your doctor immediately.

If you forget to use Emgality
Do not take a double dose to make up for forgotten injection

If you have forgotten to inject a dose of Emgality, inject the missed dose as soon as possible and then inject the next dose after a month from that date.

If you stop using Emgality
You should not stop using Emgality without speaking to your doctor first.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Allergic reactions with Emgality are usually mild to moderate (such as rash or itching). Serious allergic reactions may occur rarely (may affect up to 1 in 1 000 people) 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.

Tell your doctor or get emergency medical help straight away if you notice any of those signs.

Other side effects that have been reported.

Very common side effects (may affect more than 1 in 10 people):
- Injection site pain
- Injection site reactions (e.g. red skin, itching, bruising, swelling)

Common side effects (may affect up to 1 in 10 people):
- Vertigo (a feeling of dizziness or “spinning”)
- Constipation
- Itching
- Rash

Uncommon side effects (may affect up to 1 in 100 people):
- Hives (raised itchy areas of skin)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Emgality

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and on the carton after “EXP.” The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C). Do not freeze.

Store in the original package in order to protect from light.

Emgality may be stored unrefrigerated for a single period up to 7 days when stored at temperatures up to 30 °C. If the pen is stored at a higher temperature or for a longer period it must be discarded.

Do not use this medicine if you notice that the pen is damaged, or the medicine is cloudy or has particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your doctor, nurse or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Emgality contains
The active substance is galcanezumab. Each pre-filled pen contains 120 mg of galcanezumab in 1 mL solution.

The other ingredients are: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride and water for injections.

What Emgality looks like and contents of the pack
Emgality is a solution for injection in a clear glass syringe. Its colour may vary from colourless to slightly yellow.

The syringe is encased in a disposable, single-dose pen. Pack sizes of 1, 2 or 3 pre-filled pens.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Eli Lilly Nederland B. V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

Manufacturer:
Eli Lilly Italia S.p.A., Via Gramsci 731/733, 50019, Sesto Fiorentino (FI), Italy.
Lilly, S.A., Avda. de la Industria, 30, 28108 Alcobendas, Madrid Spain.

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

Belgique/België/Belgien
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

България
ТП "Ели Лили Недерланд" Б.В. - България
тел. + 359 2 491 41 40

Česká republika
ELI LILLY ČR, s.r.o.
Tel: + 420 234 664 111

Danmark
Eli Lilly Danmark A/S
Tlf.: +45 45 26 60 00

Lietuva
Eli Lilly Lietuva
Tel. +370 (5) 2649600

Luxembourg/Luxemburg
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

Magyarország
Lilly Hungária Kft.
Tel: + 36 1 328 5100

Malta
Charles de Giorgio Ltd.
Tel: + 356 25600 500

Deutschland
Organon Healthcare GmbH
Tel. + 0800 3384 726 (+49 (0) 8920 400 2210)
dpoc.germany@organon.com

Eesti
Eli Lilly Nederland B. V.
Tel: +372 6 817 280

Ελλάδα
ΦΑΡΜΑΣΕΡΒ-ΛΙΛΛΥ Α.Ε.Β.Ε.
Τηλ: +30 210 629 4600

España
Organon Salud, S.L.
Tel: +34 91 591 12 79

France
Organon France
Tél: +33-(0) 1 57 77 32 00

Hrvatska
Eli Lilly Hrvatska d.o.o.
Tel: +385 1 2350 999

Ireland
Eli Lilly and Company (Ireland) Limited
Tel: + 353-(0) 1 661 4377

Ísland
Icepharma hf.
Sími + 354 540 8000

Italia
Eli Lilly Italia S.p.A.
Tel: + 39- 055 42571

Κύπρος
Phadisco Ltd
Τηλ: +357 22 715000

Latvija
Eli Lilly (Suisse) S.A Pārstāvniecība Latvijā
Tel: +371 67364000

Nederland
Eli Lilly Nederland B.V.
Tel: + 31-(0) 30 60 25 800

Norge
Eli Lilly Norge A.S.
Tlf: + 47 22 88 18 00

Österreich
Eli Lilly Ges.m.b.H.
Tel: + 43-(0) 1 711 780

Polska
Eli Lilly Polska Sp. z o.o.
Tel: +48 22 440 33 00

Portugal
Lilly Portugal Produtos Farmacêuticos, Lda
Tel: + 351-21-4126600

România
Eli Lilly România S.R.L.
Tel: + 40 21 4023000

Slovenija
Eli Lilly farmacevtska družba, d.o.o.
Tel: +386 (0)1 580 00 10

Slovenská republika
Eli Lilly Slovakia s.r.o.
Tel: + 421 220 663 111

Suomi/Finland
Oy Eli Lilly Finland Ab
Puh/Tel: + 358-(0) 9 85 45 250

Sverige
Eli Lilly Sweden AB
Tel: + 46-(0) 8 7378800

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site:
https://www.ema.europa.eu

Instructions for use

Emgality 120 mg solution for injection in pre-filled pen

Galcanezumab

For subcutaneous use

Before using your pre-filled pen (pen):

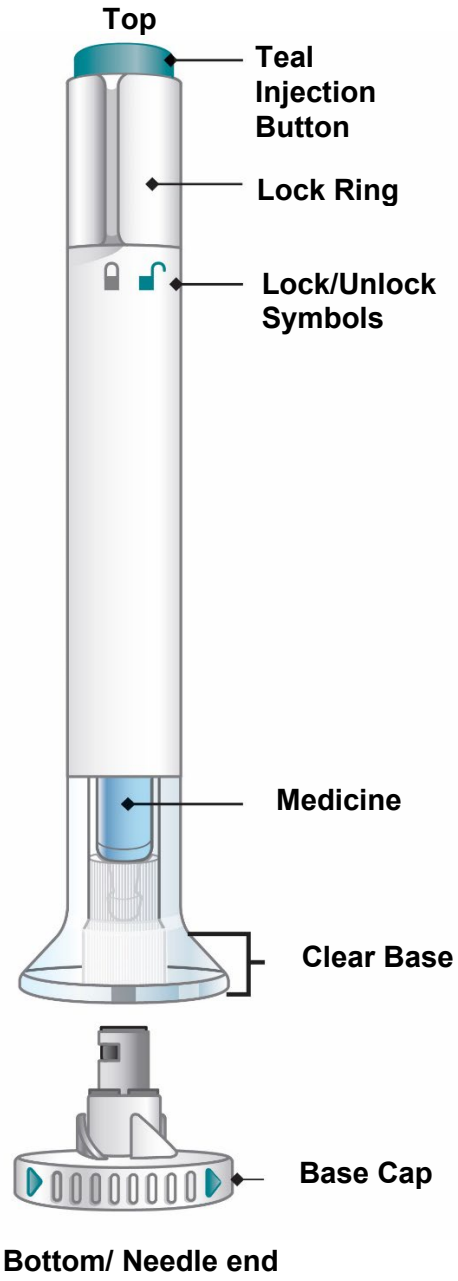
Important Information

- Your doctor or nurse 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 and refer to them as needed.
- Each pen is for **ONE-TIME USE ONLY.** Do not share or reuse your pen. Otherwise, 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 doctor, pharmacist or nurse can 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 the 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.

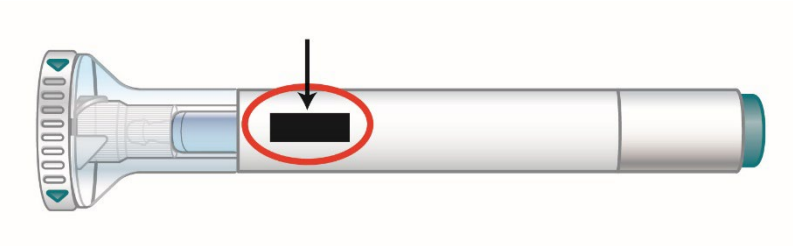
Do not shake**.**
For a more comfortable injection, leave the pen at room temperature for 30 minutes before injecting.
Do not microwave the pen, run hot water over it, or leave it in direct sunlight.

Inspect the pen and the medicine

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

Do not use the pen, and dispose of as directed by your doctor, pharmacist or nurse 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

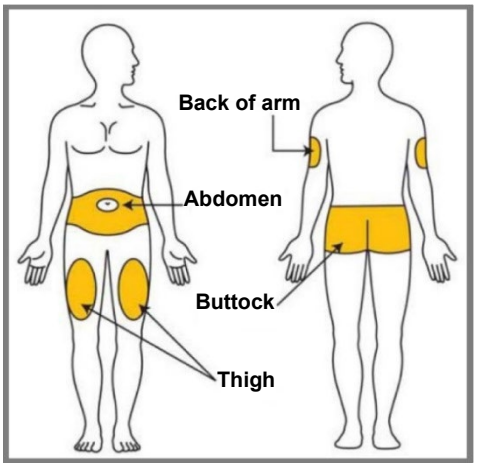


Prepare for injection

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

Choose your injection site

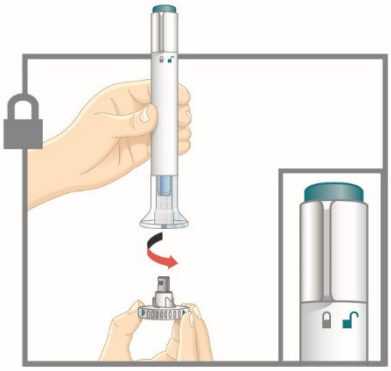
Your doctor, pharmacist or nurse can help you choose the injection site that is best for you.



- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 5 centimeters of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttock.
- **Do not** inject in the same spot as before. 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.**

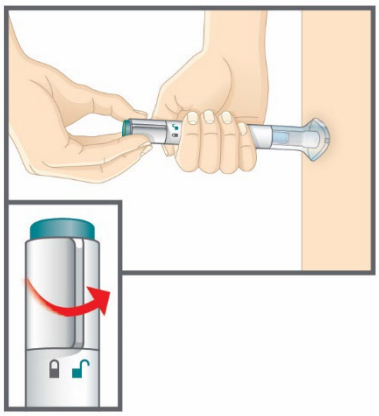
1 Uncap the Pen

Make sure the pen is locked. Leave the base cap on until you are ready to inject.



- When you are ready to inject, twist off the base cap and throw it away in the bin.
- **Do not** put the base cap back on – this could damage the needle.
- **Do not** touch the needle.

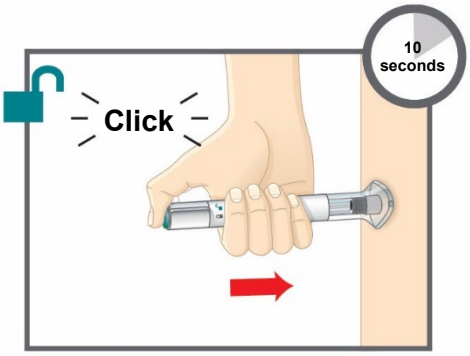
2 Place and Unlock



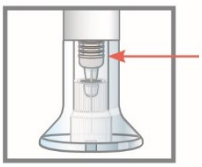
- Place and hold the clear base flat and firmly against your skin.

Turn the lock ring to the **unlock** position.

3 Press and Hold



- 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 5 to 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 you can see the grey plunger.

After You Injection Your Medicine

Dispose of the pen

DO NOT put the base cap back on. Dispose of the pen in a sharps disposal container or as directed by your doctor, pharmacist or nurse.

When you dispose of the pen and the sharps disposal container:

- Do not recycle the filled sharps container.
- Ask your doctor, pharmacist or nurse about how to dispose of medicines you no longer use.

Commonly Asked Questions

Q. What if I see air bubbles in my 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. Contact your doctor, pharmacist or nurse 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 hear 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.

Read the full Package Leaflet for Emgality inside this box to learn more about your medicine.

Revision date:

Package leaflet: Information for the patient

Emgality 120 mg solution for injection in pre-filled syringe

galcanezumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Emgality is and what it is used for
2. What you need to know before you use Emgality
3. How to use Emgality
4. Possible side effects
5. How to store Emgality
6. Contents of the pack and other information

1. What Emgality is and what it is used for

Emgality contains galcanezumab, a medicine that stops the activity of a naturally occurring substance in the body called calcitonin gene-related peptide (CGRP). People with migraine may have increased levels of CGRP.

Emgality is used to prevent migraine in adult patients who have at least 4 migraines days per month.

Emgality can reduce the frequency of migraine headache and improve your quality of life. It starts working in about a week.

2. What you need to know before you use Emgality

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

Warnings and precautions
Talk to your doctor, pharmacist or nurse before or during treatment with Emgality if:
- you have a serious cardiovascular disease. Emgality has not been studied in patients with serious cardiovascular diseases.

Look out for allergic reactions
Emgality can potentially cause serious allergic reactions. Serious allergic reactions happen mainly within 1 day after having taken Emgality, but some reactions can be delayed (happen more than 1 day to 4 weeks after having taken Emgality). Some allergic reactions can be prolonged in duration. You must look out for signs of these reactions while you are using Emgality. Stop using Emgality and tell

your doctor or seek medical help immediately if you notice any signs of a serious allergic reaction. Such signs are listed under “Serious side effects” in section 4.

Children and adolescents
This medicine should not be given to children and adolescents under 18 years of age because it has not been studied in this age group.

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

Pregnancy and breast-feeding
If you are a woman able to have children, you are advised to avoid becoming pregnant while using Emgality.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. It is preferable to avoid the use of Emgality in pregnancy as the effects of this medicine in pregnant women are not known.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine. You and your doctor should decide if you should breast feed and use Emgality .

Driving and using machines
Galcanezumab could have a minor effect on your ability to drive and use machines. Some patients have had vertigo whilst using Emgality.

Emgality contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 120 mg dose, that is to say essentially “sodium-free”.

3. How to use Emgality

Always use this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Emgality pre-filled syringe is for single use only and contains one dose of Emgality (120 mg).
- The first time you receive Emgality your doctor or nurse will inject two syringes (total 240 mg).
- After the first dose, you will use one syringe (120 mg) every month.

Your doctor will decide for how long you should use Emgality.

Emgality is given by injection under your skin (subcutaneous injection). You and your doctor or nurse should decide if you can inject Emgality yourself.

It is important not to try to inject yourself until you have been trained by your doctor or nurse. A caregiver may also give you your Emgality injection after proper training.

The syringe must not be shaken.

Read the “Instructions for Use” for the syringe carefully before using Emgality.

If you use more Emgality than you should
If you have injected more Emgality than you should, e.g. if after the first dose of 240 mg, you have injected it twice in a single month, or if anyone else has accidentally used Emgality, contact your doctor immediately.

If you forget to use Emgality
Do not take a double dose to make up for forgotten injection

If you have forgotten to inject a dose of Emgality, inject the missed dose as soon as possible and then inject the next dose after a month from that date.

If you stop using Emgality
You should not stop using Emgality without speaking to your doctor first.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Allergic reactions with Emgality are usually mild to moderate (such as rash or itching). Serious allergic reaction may occur rarely (may affect up to 1 in 1 000 people) 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.

Tell your doctor or get emergency medical help straight away if you notice any of those signs.

Other side effects that have been reported.

Very common side effects (may affect more than 1 in 10 people):
- Injection site pain
- Injection site reactions (e.g. red skin, itching, bruising, swelling)

Common side effects (may affect up to 1 in 10 people):
- Vertigo (a feeling of dizziness or “spinning”)
- Constipation
- Itching
- Rash

Uncommon side effects (may affect up to 1 in 100 people):
- Hives (raised itchy areas of skin)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Emgality

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and on the carton after “EXP.” The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C). Do not freeze.

Store in the original package in order to protect from light.

Emgality may be stored unrefrigerated for a single period up to 7 days when stored at temperatures up to 30 °C. If the syringe is stored at a higher temperature or for a longer period it must be discarded.

Do not use this medicine if you notice that the syringe is damaged, or the medicine is cloudy or has particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your doctor, nurse or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Emgality contains
The active substance is galcanezumab. . Each pre-filled syringe contains 120 mg of galcanezumab in 1 mL solution.

The other ingredients are: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride and water for injections.

What Emgality looks like and contents of the pack
Emgality is a solution for injection in a clear glass single-dose syringe. Its colour may vary from colourless to slightly yellow. Pack sizes of 1, 2 or 3 pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Eli Lilly Nederland B. V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

Manufacturer:
Eli Lilly Italia S.p.A., Via Gramsci 731/733, 50019, Sesto Fiorentino (FI), Italy.

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

Belgique/België/Belgien
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

България
ТП "Ели Лили Недерланд" Б.В. - България
тел. + 359 2 491 41 40

Česká republika
ELI LILLY ČR, s.r.o.
Tel: + 420 234 664 111

Danmark
Eli Lilly Danmark A/S
Tlf.: +45 45 26 60 00

Lietuva
Eli Lilly Lietuva
Tel. +370 (5) 2649600

Luxembourg/Luxemburg
Eli Lilly Benelux S.A./N.V.
Tél/Tel: + 32-(0)2 548 84 84

Magyarország
Lilly Hungária Kft.
Tel: + 36 1 328 5100

Malta
Charles de Giorgio Ltd.
Tel: + 356 25600 500

Deutschland
Organon Healthcare GmbH
Tel. + 0800 3384 726 (+49 (0) 8920 400 2210)
dpoc.germany@organon.com

Eesti
Eli Lilly Nederland B. V.
Tel: +372 6 817 280

Ελλάδα
ΦΑΡΜΑΣΕΡΒ-ΛΙΛΛΥ Α.Ε.Β.Ε.
Τηλ: +30 210 629 4600

España
Organon Salud, S.L.
Tel: +34 91 591 12 79

France
Organon France
Tél: +33-(0) 1 57 77 32 00

Hrvatska
Eli Lilly Hrvatska d.o.o.
Tel: +385 1 2350 999

Ireland
Eli Lilly and Company (Ireland) Limited
Tel: + 353-(0) 1 661 4377

Ísland
Icepharma hf.
Sími + 354 540 8000

Italia
Eli Lilly Italia S.p.A.
Tel: + 39- 055 42571

Κύπρος
Phadisco Ltd
Τηλ: +357 22 715000

Latvija
Eli Lilly (Suisse) S.A Pārstāvniecība Latvijā
Tel: +371 67364000

Nederland
Eli Lilly Nederland B.V.
Tel: + 31-(0) 30 60 25 800

Norge
Eli Lilly Norge A.S.
Tlf: + 47 22 88 18 00

Österreich
Eli Lilly Ges.m.b.H.
Tel: + 43-(0) 1 711 780

Polska
Eli Lilly Polska Sp. z o.o.
Tel: +48 22 440 33 00

Portugal
Lilly Portugal Produtos Farmacêuticos, Lda
Tel: + 351-21-4126600

România
Eli Lilly România S.R.L.
Tel: + 40 21 4023000

Slovenija
Eli Lilly farmacevtska družba, d.o.o.
Tel: +386 (0)1 580 00 10

Slovenská republika
Eli Lilly Slovakia s.r.o.
Tel: + 421 220 663 111

Suomi/Finland
Oy Eli Lilly Finland Ab
Puh/Tel: + 358-(0) 9 85 45 250

Sverige
Eli Lilly Sweden AB
Tel: + 46-(0) 8 7378800

This leaflet was last revised in

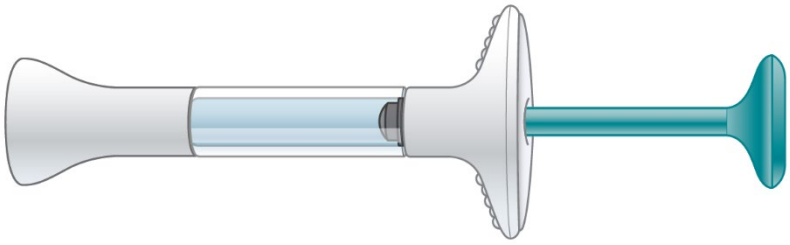
Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu

Instructions for use

Emgality 120 mg solution for injection in pre-filled syringe

Galcanezumab

For subcutaneous use



Before using your pre-filled syringe:

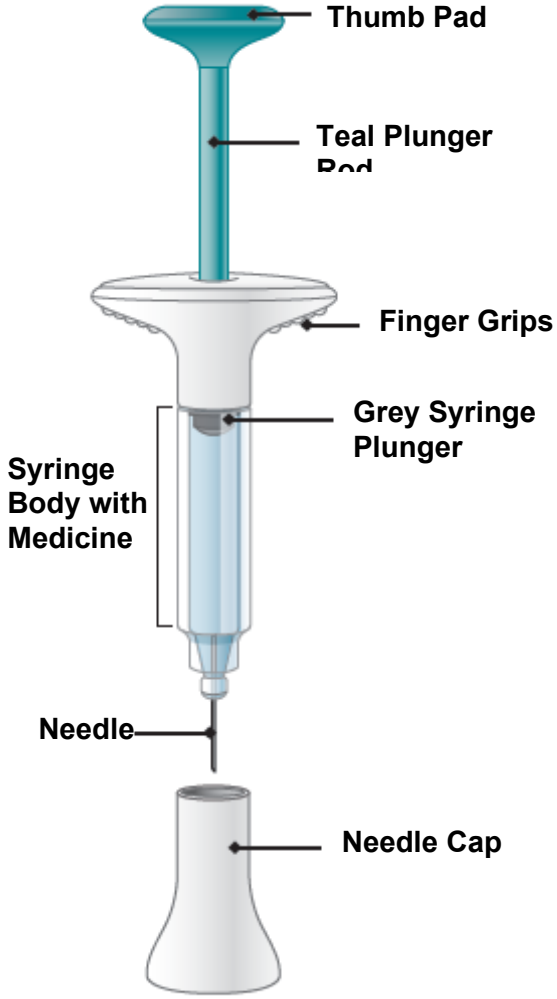
Important Information

- Your doctor or nurse should show you how to prepare and inject Emgality using the syringe. Do not inject yourself or someone else until you have been shown how to inject Emgality.
- Keep these instructions and refer to them as needed.
- Each syringe is for **ONE-TIME USE ONLY.** Do not share or reuse your syringe. Otherwise, you may give or get an infection.
- Your doctor, pharmacist or nurse can 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 syringe without help from a caregiver.

INSTRUCTIONS FOR USE

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

Parts of the Emgality Syringe



Before You Get Started

Take the 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.

Do not shake.

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

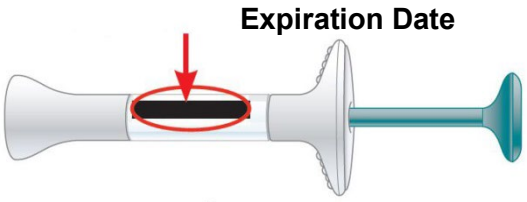
Do not microwave the syringe, run hot water over it, or leave it in direct sunlight.

Inspect the syringe and the medicine

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

Do not use the syringe, and dispose of as directed by your doctor, pharmacist or nurse 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

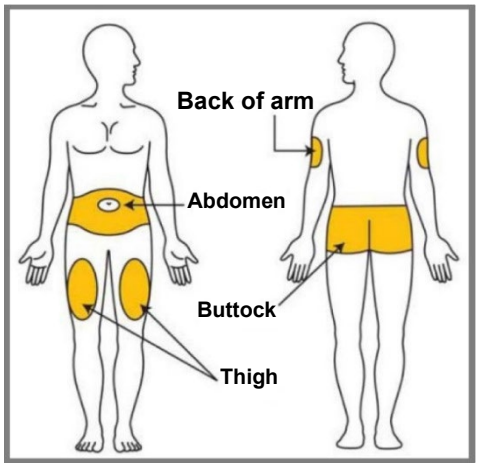


Prepare for injection

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 doctor, pharmacist or nurse can help you choose the injection site that is best for you.

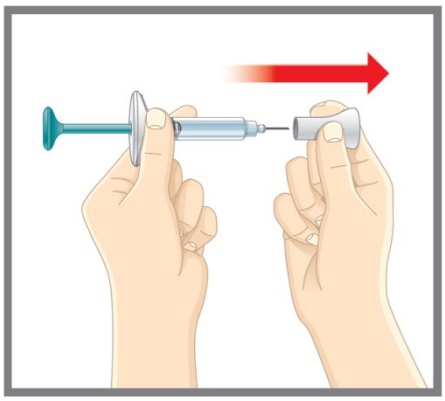


- **You** may inject the medicine into your stomach area (abdomen) or thigh. Do not inject within 5 centimeters of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm or buttock.

- **Do not** inject in the same spot as before. 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.**

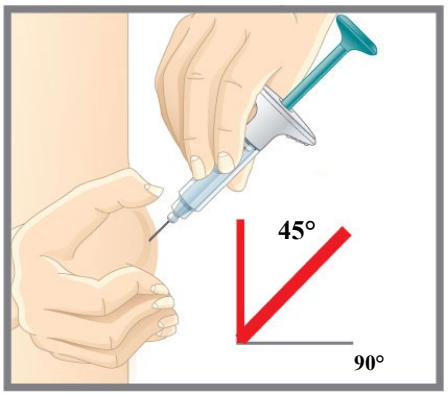
1 Uncap

- **Leave the needle cap on until you are ready to inject.**
- When you are ready to inject, pull the needle cap off and throw it away in the bin.
- **Do not** put the needle cap back on – you could damage the needle or injure yourself by accident.
- **Do not** touch the needle.



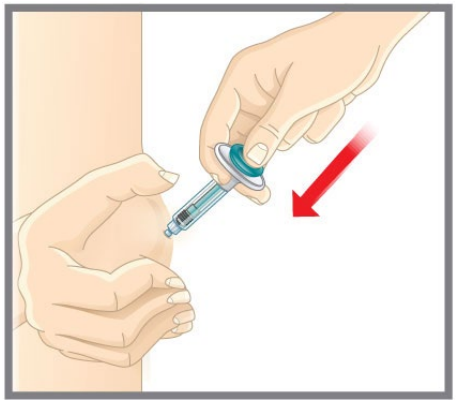
2 Insert

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

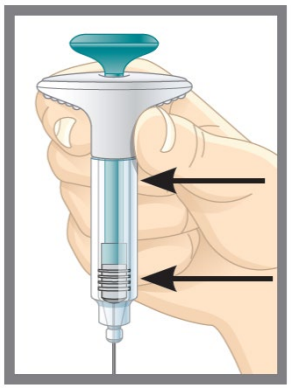


3 Inject

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



Teal plunger rod

Grey syringe plunger

After You Inject Your Medicine

Dispose of the syringe

DO NOT put the needle cap back on. Dispose of the syringe in a sharps disposal container or as directed by your doctor, pharmacist or nurse.

When you dispose of the syringe and the sharps disposal container:

- Do not recycle the filled sharps container.
- Ask your doctor, pharmacist or nurse abou how to dispose of medicines you no longer use.

Commonly Asked Questions

Q. **What if I see air bubbles in my Emgality syringe?**

A. It is normal to have air bubbles in the 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 end of the syringe.

Read the full Package Leaflet for Emgality inside this box to learn more about your medicine.

Revision date: