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 to slightly brown.

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

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. If a serious hypersensitivity reaction occurs, administration of galcanezumab should be discontinued immediately and appropriate therapy initiated. Serious hypersensitivity reactions may occur within 1 day after galcanezumab administration, however cases with a delayed onset have also been reported.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 120 mg dose, i.e., is 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 clinical studies in migraine prophylaxis. 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 events.

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 System		Vertigo		
Gastrointestinal System		Constipation		
Skin and Subcutaneous Tissue		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 events 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 event 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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form *https://sideeffects.health.gov.il*

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

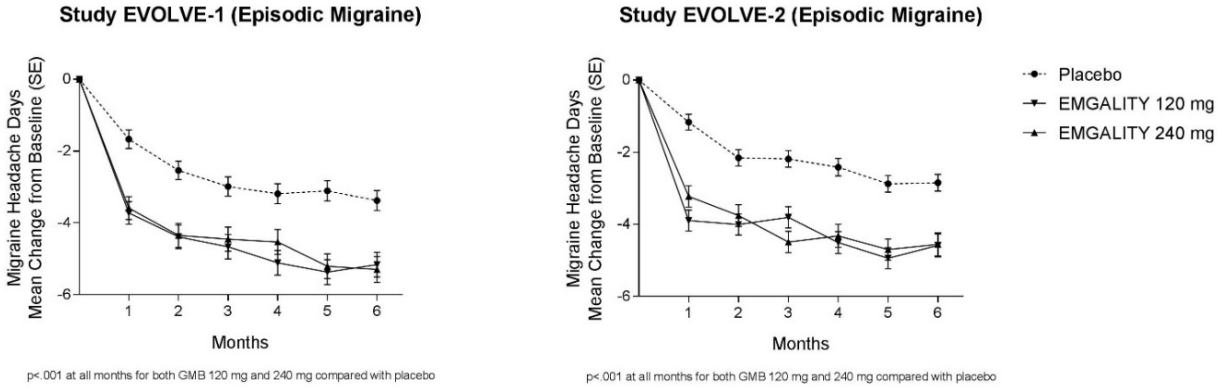

Table 2. Efficacy and patient reported outcome measures

	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

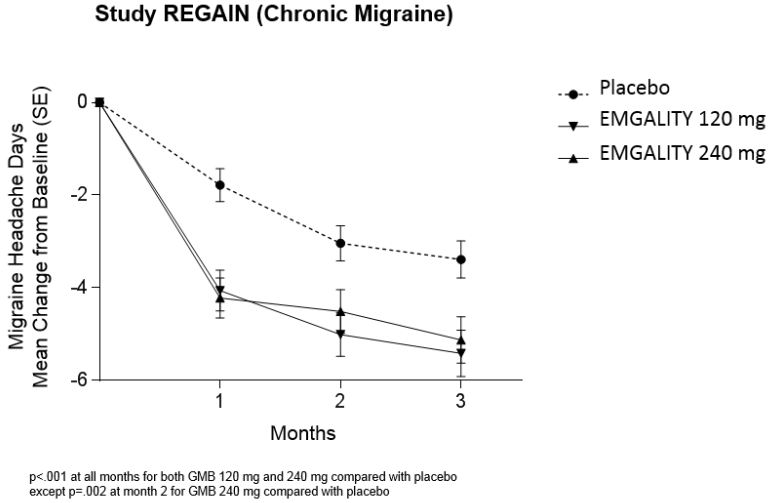

Table 3. Efficacy and patient reported outcome measures

	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).

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

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

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

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

6.4 Special precautions for storage

Store in a refrigerator (2ºC – 8ºC).
Do not freeze or shake.
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. Once the device has been stored at room temperature, do not return to the refrigerator and discard if unused within this 7-day period.

6.5 Nature and contents of container

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

The needle included in the pack is only suitable for sub-cutaneous injection.

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. License Holder

Eli Lilly Israel Limited
4 HaSheizaf Street, POB 4246 Ra'anana 4366411, Israel

8. Manufacturer

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana (IN) 46285
United States (USA)

9. License Number

Emgality 120 mg: 162-90-35852-00

Revised in August 2021 according to MOHs guidelines.

X EMGAPN S 05