EMGALITY® (GALCANEZUMAB-GNLM) – MEDICAL VALUE SUMMARY

I. VALUE SUMMARY

Prevention of Migraine

- In a 2018 large prospective, web-based patient survey of 21,143 people with migraine (OVERCOME):
  - Only 15.4% of individuals with ≥4 monthly headache days (MHD) and moderate or severe headache-related disability consulted a healthcare professional, received an accurate diagnosis and took a recommended preventive medication[1].
  - Patients with ≥4MHDs sought care for their migraine in primary care (45%), neurology (20%), the emergency department (19%), pain specialists (13%) or headache specialists (12%), and amongst other sites, and could select more than one site of care[2].
  - Higher ratios of opioids to triptans was seen in patients who sought care at pain specialists (2.7) and in emergency departments (2.4), compared to those who sought care at neurology (0.4) and headache specialists (0.5) [2].
- There are opportunities to improve the diagnosis and management of disabling migraine given the availability of preventive therapies.

EMGALITY for the preventive treatment of Migraine:

- Emgality® significantly reduced the average number of monthly migraine headache days in adults with episodic migraine over 6 months of treatment, and in adults with chronic migraine over 3 months of treatment, compared with placebo.
- Significantly more patients on Emgality had a ≥50%; ≥75%; and 100% mean reduction in MHDs in any given month in adults with episodic migraine, and ≥50% mean reduction in MHDs in adults with chronic migraine, compared with placebo.
- With Emgality®, <2% of patients across clinical trials discontinued due to treatment-related adverse events during double-blind treatment, which was approximately the same for patients on placebo.

EMGALITY for the treatment of Episodic Cluster Headache

- Emgality® significantly reduced overall mean change from baseline in weekly cluster headache attack frequency across weeks 1 to 3, compared with placebo.
- Significantly more patients on Emgality® had a ≥50% reduction in weekly cluster headache attack frequency at week 3.
- There were no substantial between-group differences in the incidence of adverse events, except that 8% of the patients in the galcanezumab group had injection-site pain[3]

II. INDICATIONS[4]

- Emgality® is a calcitonin-gene related peptide antagonist indicated in adults for the:
  - preventive treatment of migraine
  - treatment of episodic cluster headache.

III. CONTRAINDICATIONS[4]

- Emgality® is contraindicated in patients with serious hypersensitivity to galcanezumab-gnlm or any of the excipients.

IV. DOSAGE AND ADMINISTRATION[4]

- Migraine: 240 mg (two consecutive subcutaneous injections of 120 mg) once, thereafter monthly subcutaneously doses of 120 mg
- Episodic cluster headache: 300 mg (administered as three consecutive subcutaneous injections of 100 mg each) at the onset of the cluster period, and then monthly until the end of the cluster period

V. DOSAGE FORMS AND STRENGTHS[4]

- Emgality® is available in a 120 mg/mL in a single-dose prefilled pen or 120 mg/mL in a single-dose prefilled syringe for the preventive treatment of migraine, and 100 mg/mL in a single-dose prefilled syringe (three syringes per package/dose) for the treatment of episodic cluster headache.

VI. EFFICACY SUMMARY[4]

Migraine – preventive treatment:

- Efficacy of EMGALITY was evaluated in three multicenter, randomized, double-blind, placebo-controlled studies: two 6-month studies in patients with episodic migraine (EM) and one 3-month study in patients with chronic migraine (CM). Patients over 18 years of age were eligible if they had a history of migraine: episodic with 4-14 migraine days per month; chronic with ≥15 headache days per month of which ≥8 were migraine headache.
- The efficacy endpoints for studies 1-3 are shown in Table.1

	Study 1 (Episodic Migraine)		**Study 2 (Episodic Migraine)**		**Study 3 (Chronic Migraine)**	
	Emgality® 120mg N = 210	**Placebo N = 425**	**Emgality®120 mg N = 226**	**Placebo N = 450**	**Emgality®120 mg N = 273**	**Placebo N = 538**
Monthly Migraine Headache Days (over Months 1 to 6)						
Baseline migraine headache	9.2	9.1	9.1	9.2	19.4	19.6
Mean change from baseline	-4.7	-2.8	-4.3	-2.3	-4.8	-2.7
Difference from placebo	-1.9*		-2.0*		-2.1*	
≥50% Migraine Headache Days Responders (over Months 1 to 6)						
% Responders	62%*	39%	59%*		28%*	15%
100% Migraine Headache Days Responders (over Months 1 to 6)						
% Responders	16%*	6%	12%*		NS	NS
Monthly Migraine Headache Days (MHD) that Acute Medication was Taken (over Months 1						
Mean change from baseline	-4.0*	-	-3.7*		a	a

^N= 189 for Emgality® 120 mg and N = 377 for placebo in Study 1; N = 213 for Emgality® 120 mg and N = 396 for placebo in Study 2.

* p<0.001; NS= Not significant; MSQ - Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1)
[a]In Study 3, patients treated with Emgality® 120 mg showed a nominally greater reduction in the number of monthly migraine headache days that acute medication was taken (-4.7 for Emgality® 120 mg vs. -2.2 for placebo; nominal p-value <0.001).
See prescribing information for additional efficacy information on reduction in ≥75% MHD, and improvement in the MSQ Role Function-Restrictive Domain.

In 2020, the CONQUER study- a study of the efficacy and safety of EMGALITY in patients with 2-4 documented failures of prior preventives- demonstrated that Emgality® significantly reduced MHDs (- 4.1 days vs. placebo -1.0, p<0.0001)[5]. In an analysis of the 3-month double-blind period of the study, Emgality® significantly improved work productivity(WPAI, -14.3% vs placebo -3.5%; p<0.01) and reduced interictal burden (MIBS, -1.8 vs placebo -0.8; p<0.0001), defined as health and well-being between migraine attacks. Gains in productivity appeared to be driven by statistically significant improvements in presenteeism and work and non-work-related activity in the Emgality group compared to placebo[6].

WPAI= Work Productivity and Activity Impairment Questionnaire, MIBS= Migraine Interictal Burden Scale

Episodic Cluster Headache

- Efficacy of EMGALITY for the treatment of episodic cluster headache was evaluated in a randomized, 8-week, double-blind, placebo-controlled study. Patients were over 18 years of age, met the International Classification of Headache Disorders 3rd edition (beta version) diagnostic criteria for episodic cluster headache, had a maximum of 8 attacks per day, a minimum of one attack every other day, and at least 4 attacks during the prospective 7-day baseline period[4]. The study evaluated efficacy of 300mg dose administered every 30 days during the study.
- The efficacy endpoints are shown in Table.2

	Study 4 (Episodic Cluster Headache)	
	Emgality® 300 mg, N = 49	**Placebo, N = 57**
Mean Reduction in Weekly Cluster Headache Attack Frequency (over Weeks 1 to 3)		
Prospective Baseline Cluster Headache Attack Frequency	17.8	17.3
Mean change from baseline	-8.7	-5.2
Difference from placebo (p-value)	-3.5 (0.036)	
≥50% Weekly Cluster Headache Attack Frequency Responders (at Week 3)		
% responders	71.4%	52.6%
Difference from placebo (p-value)	18.8% (0.046)	

VII. SAFETY SUMMARY[4]

- Please see the full prescribing information at http://pi.lilly.com/us/emgality-uspi.pdf for complete safety information
- Hypersensitivity reactions, including anaphylaxis, angioedema, dyspnea, urticaria, and rash, have been reported with Emgality®. If a serious or severe hypersensitivity reaction occurs, discontinue administration of EMGALITY and initiate appropriate therapy. Hypersensitivity reactions can occur days after administration and may be prolonged.
- The most common adverse reaction was injection site reactions. In Studies 1, 2, and 3, 18% of patients on Emgality® 120 mg and 13% of patients on placebo reported injection site reactions. In these studies, 1.8% of patients discontinued double-blind treatment because of adverse events. In study 4 (episodic cluster headache), 2 Emgality®-treated patients discontinued double-blind treatment because of adverse events.
- Overall, the safety profile observed in patients with episodic cluster headache treated with Emgality® 300 mg monthly is consistent with the safety profile in migraine patients.

VIII. USE IN SPECIFIC POPULATIONS[4]

PREGNANCY AND LACTATION: No adequate data is available on the use of Emgality® in pregnancy or lactation.
PEDIATRIC or GERIATRIC USE: No information

References:

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2. Buse DC, Nicholson RA, Araujo AB, et al. Migraine care across the healthcare landscape in the United States among those with ≥4 migraine headache days per month: results of the OVERCOME study. 61st Annual Scientific Meeting American Headache Society July 11 -14 2019 Pennsylvania Convention Center Philadelphia, PA. Headache: The Journal of Head and Face Pain 2019; 59 S1:16-7. doi.org/10.1111/head.13549.
3. Goadsby PJ, Dodick DW, Leone M, Bardos JN, Oakes TM, Millen BA, Zhou C, Dowsett SA, Aurora SK, Ahn AH, Yang JY, Conley RR, Martinez JM. Trial of Galcanezumab in Prevention of Episodic Cluster Headache. N Engl J Med. 2019;381(2):132-141.
4. Emgality® [package insert]. Indianapolis, IN: Eli Lilly and Company, 2019. Available at http://pi.lilly.com/us/emgality-uspi.pdf
5. Mulleners WM, Kim B, Lainez MJA, Lanteri-Minet M, Aurora SK, Nichols RM, Wang S, Tockhorn-Heidenreich A, Detke HC. A Randomized, Placebo-Controlled Study of Galcanezumab in Patients with Treatment-Resistant Migraine: Double-Blind Results from the CONQUER Study. Neurology. 2020;94(15 Suppl):162.
6. García-Azorín D. et.al. Changes in Work Productivity and Interictal Burden: Results from a Randomized, Double-Blind, Placebo-Controlled Clinical Trial Evaluating Galcanezumab in Adults with Treatment- Resistant Migraine (CONQUER). 6th European Academy of Neurology (EAN) Congress; Virtual 2020, May 2020.