vyepti® (eptinezumab)

Vyepti® (eptinezumab) KEY CLINICAL EVIDENCE

Eptinezumab in episodic migraine: A randomized, double-blind, placebo-controlled study (PROMISE-1)[1]
Ashina M, Saper J, Cady R *et al. Cephalalgia* 2020; 40:241–54.

Efficacy and safety of eptinezumab in patients with chronic migraine: PROMISE-2[2]
Lipton RB, Goadsby PJ, Smith J *et al Neurology* 2020; 94:e136–e1377.

Efficacy, tolerability, and safety of eptinezumab in patients with a dual diagnosis of chronic migraine and medication overuse headache: Subgroup analysis of PROMISE-2[3]
Diener HC, Marmura MJ, Tepper SJ *et al. Headache*. 2020; 00:1–12.

Long-term safety and tolerability of eptinezumab in patients with chronic migraine: a 2-year, open-label, phase 3 trial[4]
Kudrow D, Cady RK, Allan B *et al. BMC Neurology*. 2021; 21:126.

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KEY FINDINGS

- In adults with episodic migraine (PROMISE-1) and adults with chronic migraine (PROMISE-2), monthly migraine days (MMDs) were significantly reduced across weeks 1–12 with Vyepti compared with placebo (PROMISE-1: –3.2 with placebo,–3.9 with 100 mg, –4.3 with 300 mg; p=0.0182 and p=0.0001 vs placebo, respectively; PROMISE-2: –5.6 with placebo, –7.7 with 100 mg, –8.2 with 300 mg; p<0.0001 vs placebo for both comparisons)[1,2]

- In a post-hoc analysis of adults with chronic migraine and MOH, MMDs were significantly reduced across weeks 1–12 with Vyepti compared with placebo (–8.4 with 100 mg, –8.6 with 300 mg, -5.4 with placebo; p<0.0001 vs placebo for both comparisons)[3]

- Vyepti 100 mg and 300 mg were well tolerated across all studies and populations studied.[1–5]
  Please see Approved Australian Product Information for full safety and tolerability information.

- In adults with chronic migraine (PREVAIL), Vyepti 300 mg demonstrated a favourable tolerability profile, limited long-term immunogenicity, early (week 4) and sustained (week 48) reductions in migraine-related burden, and improvements in health-related quality of life over 2 years[4]*

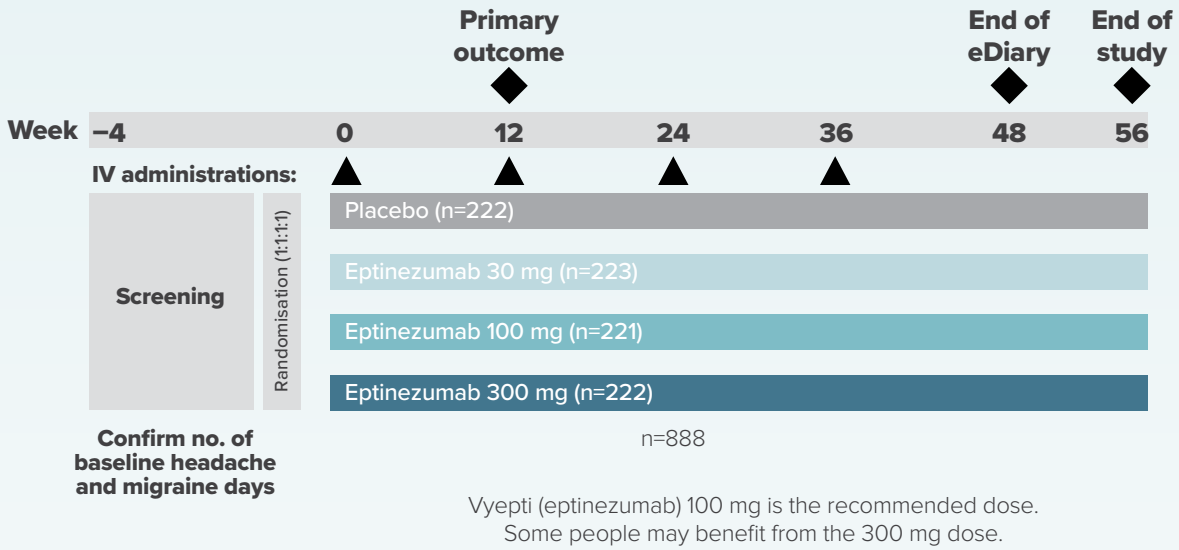
* Migraine-related burden was assessed by most bothersome symptoms (MBS). At week 4, 58.7% of individuals indicated that their MBS was “much improved” or “very much improved”, and this increased to 75.0% at week 48 (statistical comparisons not reported).[4] Patient-identified MBS was not collected beyond week 48. Health-related quality of life was assessed by Migraine Disability Assessment (MIDAS), Patient Global Impression of Change (PGIC) and 6-item Headache Impact Test (HIT-6). The proportion of individuals reporting severe disability (MIDAS grade IV) reduced from 84.4% at baseline to 26.8% (week 12) and to 20.8% (week 104, statistical outcomes not reported). The proportion of individuals reporting PGIC as “much improved” or “very much improved” was 61.1% (week 4) and 81.0% (week 48 to study end, statistical outcomes not reported). The proportion of individuals reporting HIT-6 as “severe life impact” decreased from 92.2% at baseline to 39.7% (week 4) and 38.5% (week 104, statistical outcomes not reported).

PROMISE-1[1]

Ashina M *et al. Cephalalgia* 2020; 40:241–54.

Study design[1]

PROMISE-1 was a parallel-group, double-blind, placebo-controlled trial to evaluate the safety and efficacy of Vyepti for the preventative treatment of episodic migraine in adults[1]



Vyepti (eptinezumab) 100 mg is the recommended dose.
Some people may benefit from the 300 mg dose.

Endpoints[1]

Primary

- Change from baseline in monthly migraine days (MMDs) over weeks 1–12, assessed using eDiary data

Key secondary

- ≥75% migraine responder rate over weeks 1–4
- ≥75% migraine responder rate over weeks 1–12
- ≥50% migraine responder rate over weeks 1–12
- Percentage of patients with a migraine on the day after dosing

Headache information was captured daily throughout study participation using an electronic headache diary device (eDiary).

Results[1]

Baseline characteristics and demographics were similar across treatment groups[1]

	Age	Weight	Females	Duration diagnosis	Migraines per month*	Headaches per month*	Medication use per month†
Vyepti 100 mg (n=223)	40.0 (10.7) years	82.4 (23.4) kg	80%	17.4 (11.2) years	8.7 (2.9) days	10.0 (3.0) days	24.7 (17.4) days
Vyepti 300 mg (n=224)	40.2 (11.7) years	80.2 (20.9) kg	89%	18.2 (11.8) years	8.6 (2.9) days	10.1 (3.1) days	26.1 (19.4) days
Placebo (n=222)	39.9 (11.7) years	82.4 (21.7) kg	84%	16.9 (11.2) years	8.4 (2.7) days	9.9 (2.8) days	24.7 (19.1) days

All values are mean (SD) unless otherwise indicated. 30 mg data not presented.

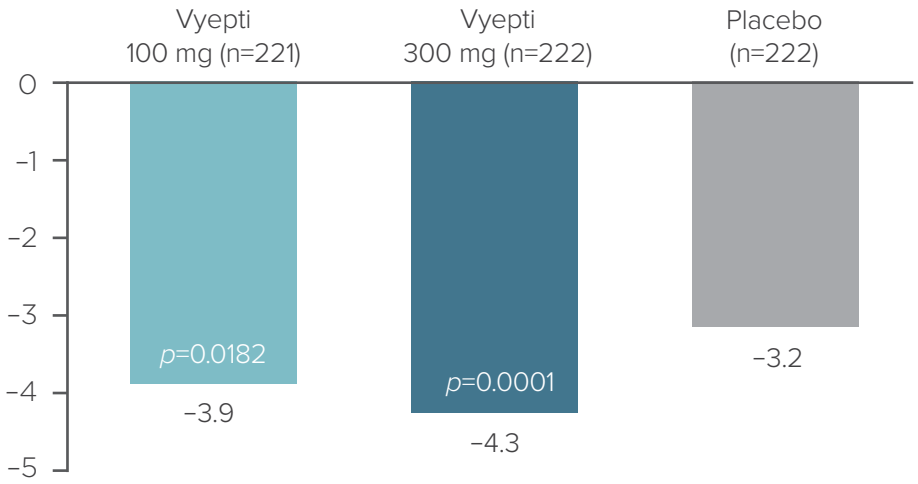
* Full analysis population; mean eDiary-reported migraine and headache characteristics during the 28-day screening period.

† eDiary-reported medications (for each patient, the denominator for the percentage was the number of days with a non-missing evening report for the selected interval; only patients who completed the evening report at least half the time for the selected interval were included).

Efficacy[1]

- Number of migraine days was statistically significantly reduced from baseline in the Vyepti 100 mg (–0.69 [95% confidence interval –1.25, –0.12], *p*=0.0182 vs placebo) and Vyepti 300 mg groups (–1.1 [–1.68, –0.54], *p*=0.0001 vs placebo)
- ≥75% migraine responder rates were statistically significantly higher for Vyepti 100 mg and 300 mg at weeks 1–4 (*p*=0.0112 and *p*=0.0066 vs placebo, respectively) and for Vyepti 300 mg at weeks 1–12 (*p*=0.0007 vs placebo)

Reduction in MMDs in weeks 1–12

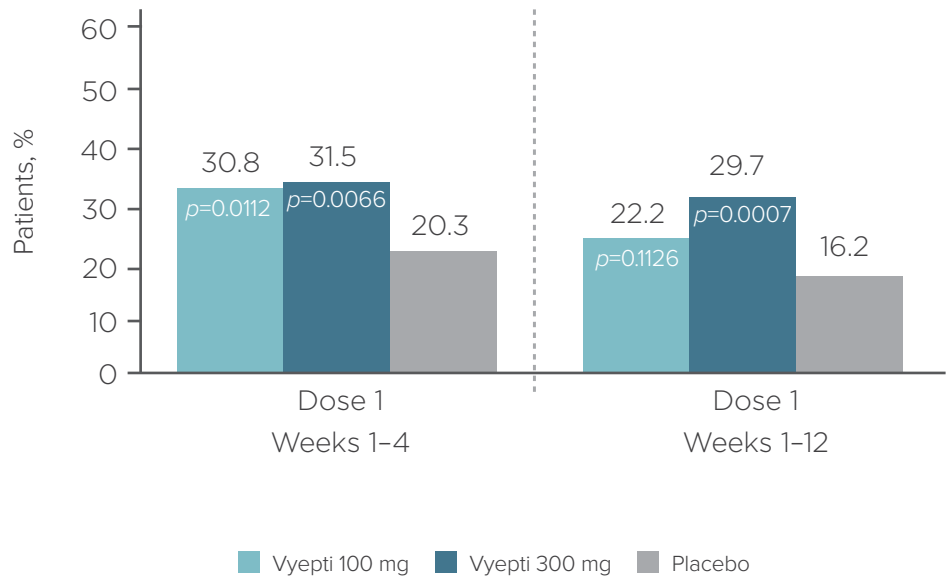


p values are versus placebo.
MMD: monthly migraine day

Baseline: 8.6 migraine days per month.

Migraine incidence on day 1 was reduced by 51.8% in the Vyepti 100 mg group (p=0.0312 vs placebo [not significant per the testing hierarchy]) and 54.7% in the Vyepti 300 mg (p=0.0159 vs placebo [not significant per the testing hierarchy])[1]

≥75% Migraine responder rates



Tolerability[1]

- Most common treatment-emergent adverse events were nasopharyngitis and upper respiratory tract infection in PROMISE-1[1]
- Nasopharyngitis and hypersensitivity reactions were a common adverse event across clinical trials[5]
- Please review the Vyepti® Product Information for full tolerability information

Treatment emergent adverse events reported in ≥2% of patients (safety population)[1]

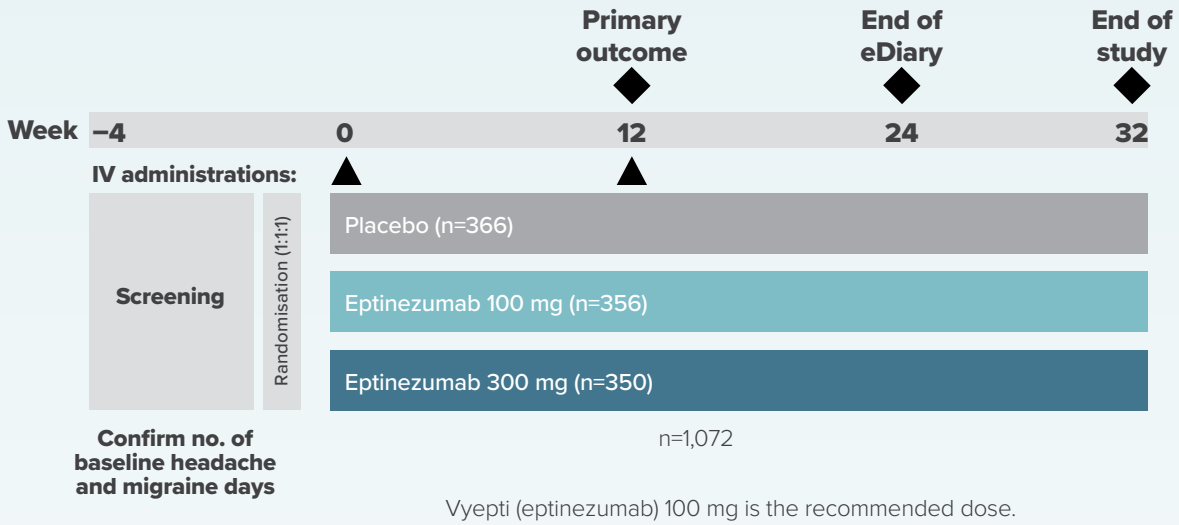
Adverse event	Vyepti 100 mg (n=221)	Vyepti 300 mg (n=222)	Placebo (n=222)
Any AE, n (%)	141 (63.2)	129 (57.6)	132 (59.5)
Respiratory tract disorders			
Upper respiratory tract infection	22 (9.9)	23 (10.3)	16 (7.2)
Nasopharyngitis	17 (7.6)	14 (6.3)	12 (5.4)
Sinusitis	6 (2.7)	11 (4.9)	14 (6.3)
Bronchitis	6 (2.7)	7 (3.1)	8 (3.6)
Cough	8 (3.6)	6 (2.7)	7 (3.2)
Influenza	4 (1.8)	8 (3.6)	5 (2.3)
Neurological system disorders			
Dizziness	10 (4.5)	4 (1.8)	8 (3.6)
Gastrointestinal disorders			
Nausea	5 (2.2)	5 (2.2)	8 (3.6)
Diarrhoea	3 (1.3)	8 (3.6)	3 (1.4)
Asthenic disorders			
Fatigue	8 (3.6)	8 (3.6)	1 (<1)
Musculoskeletal disorders			
Back pain	7 (3.1)	3 (1.3)	7 (3.2)

PROMISE-2[2]

Lipton RB *et al. Neurology* 2020; 94:e1365-e1377.

Study design[2]

PROMISE-2 was a parallel-group, double-blind, placebo-controlled trial to evaluate the safety and efficacy of Vyepti for the preventative treatment of chronic migraine in adults[2]



Vyepti (eptinezumab) 100 mg is the recommended dose.
Some people may benefit from the 300 mg dose.

Endpoints[2]

Primary

- Change from baseline in monthly migraine days (MMDs) over weeks 1–12, assessed using eDiary data

Key secondary

- ≥75% migraine responder rate over weeks 1–4
- ≥75% migraine responder rate over weeks 1–12
- ≥50% migraine responder rate over weeks 1–12
- Percentage of patients with a migraine on the day after dosing

Headache information was captured daily throughout study participation using an electronic headache diary device (eDiary).

Results[2]

Baseline characteristics and demographics were similar across treatment groups[2]

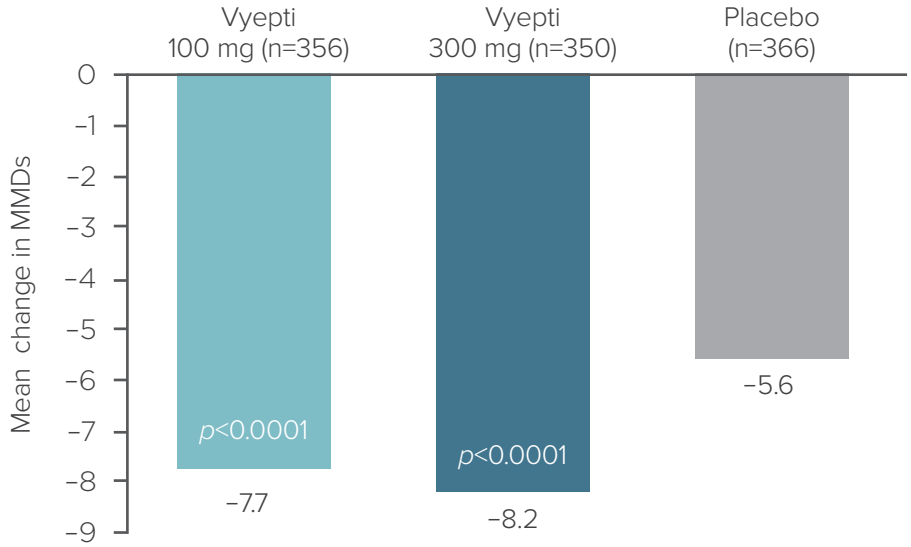
	Age	MOH + CM	BMI	Females	Age at diagnosis	Duration of diagnosis	Migraines per month*	Headaches per month*
Vyepti 100 mg (n=356)	41.0 (11.7) years	39%	26.4 (5.0)	86%	18.3 (12.2) years	11.6 (11.7) years	16.1 (4.6) days	20.4 (3.1) days
Vyepti 300 mg (n=350)	41.0 (10.4) years	42%	26.2 (5.0)	90%	19.0 (11.5) years	12.4 (11.2) years	16.1 (4.8) days	20.4 (3.2) days
Placebo (n=366)	39.6 (11.3) years	40%	27.0 (5.6)	89%	17.0 (11.6) years	11.6 (10.9) years	16.2 (4.6) days	20.6 (2.99) days

All values are mean (SD) unless otherwise indicated.

Efficacy[2]

- Number of migraine days was significantly reduced from baseline in the Vyepti 100 mg (–2.0 [95% CI –2.9, –1.2], $p<0.0001$ vs placebo) and Vyepti 300 mg groups (–2.6 [–3.4, –1.7], $p<0.0001$ vs placebo)[2]
- ≥75% migraine responder rates during weeks 1–4 and 1–12 were significantly higher in the Vyepti groups than the placebo group (all comparisons $p\leq0.0001$ vs placebo)[2]

Chronic migraine reduction in MMDs Weeks 1–12

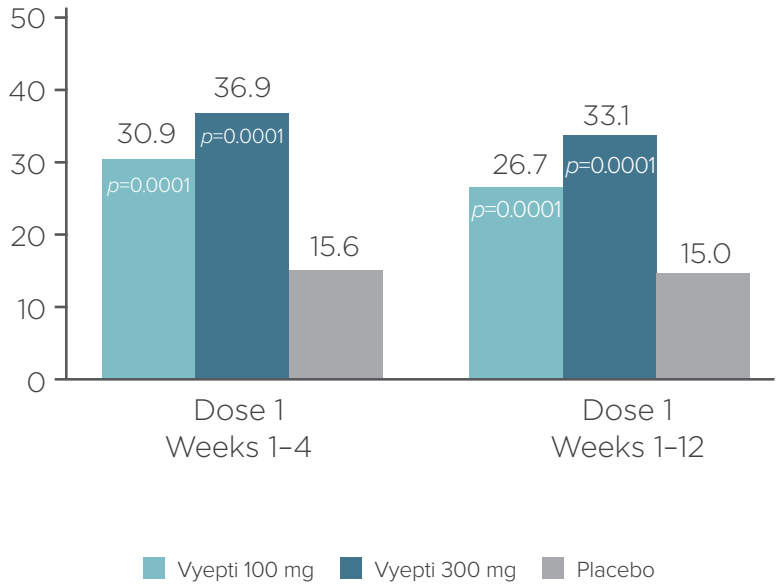


p values are versus placebo.
MMD: monthly migraine day

Baseline: 16 migraine days per month.

Migraine incidence on day 1 was reduced by 50.3% in the Vyepti 100 mg group (p<0.0001 vs placebo) and 51.6% in the Vyepti 300 mg (p<0.0001 vs placebo)[2]

≥75% chronic migraine responder rates



Tolerability[2]

- Most common treatment emergent adverse events were nasopharyngitis and upper respiratory tract infection in PROMISE-2[2]
- Nasopharyngitis and hypersensitivity reactions were a common adverse event across clinical trials[5]
- Please review the Vyepti® Product Information for full tolerability information

Treatment emergent adverse events reported in ≥2% of patients (safety population)[2]

Adverse event	Vyepti 100 mg (n=356)	Vyepti 300 mg (n=350)	Placebo (n=366)
Any AE, n (%)	155 (43.5)	182 (52.0)	171 (46.7)
Respiratory tract disorders			
Nasopharyngitis	19 (5.3)	33 (9.4)	22 (6.0)
Upper respiratory tract infection	15 (4.2)	19 (5.4)	20 (5.5)
Sinusitis	7 (2.0)	9 (2.6)	15 (4.1)
Neurological system disorders			
Migraine	6 (1.7)	8 (2.3)	16 (4.4)
Gastrointestinal disorders			
Nausea	6 (1.7)	12 (3.4)	7 (1.9)
Asthenic disorders			
Fatigue	8 (2.2)	6 (1.7)	7 (1.9)
Genitourinary disorders			
Urinary tract infection	8 (2.2)	12 (3.4)	6 (1.6)

PROMISE-2: MOH POST-HOC ANALYSIS[3]

Diener HC *et al. Headache.* 2021: 61:125–136.

MOH diagnostic criteria[3,6]

Trained investigators diagnosed MOH at screening based on 3 months of medication history using ICHD-3 beta criteria[3,6]

Headache occurring on ≥15 days/ month in a patient with a pre-existing headache disorder

Regular overuse for >3 months of ≥1 drugs that can be taken for acute and / or symptomatic treatment of headache

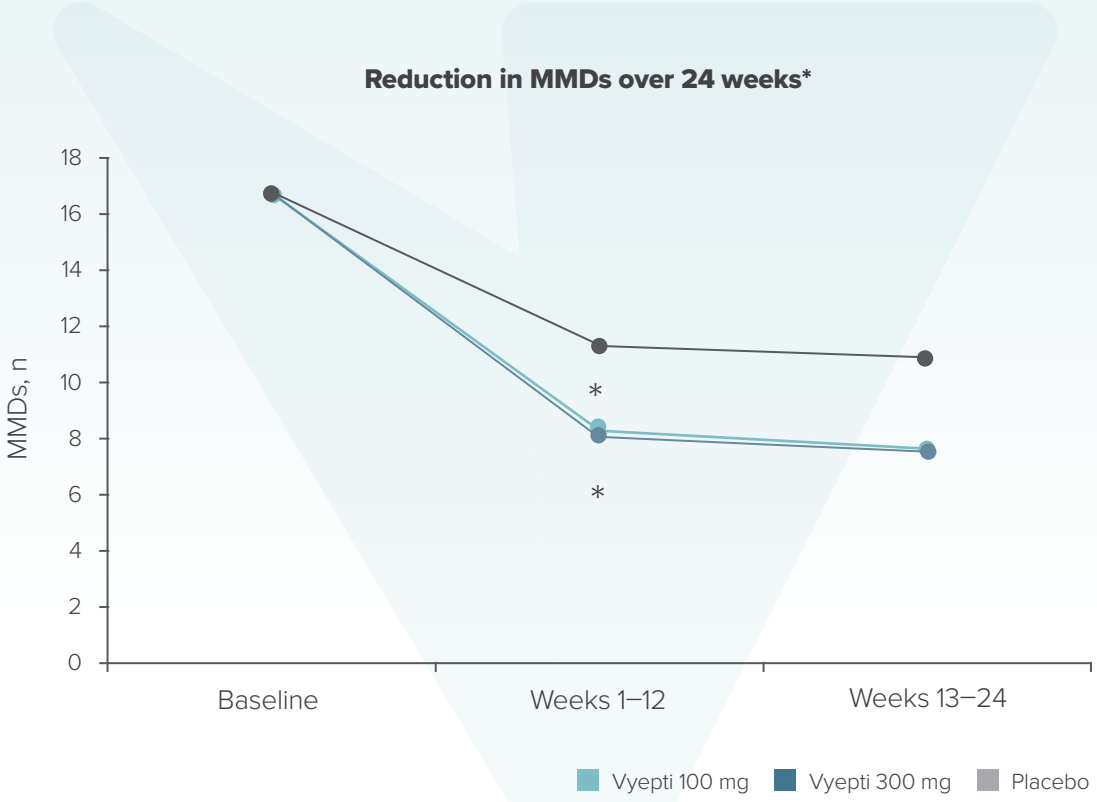
ICHD-3

Not better accounted for by another ICHD-3 diagnosis

- Patients in the PROMISE-2 study were prospectively screened for and diagnosed with medication overuse headache (MOH) as per the ICHD-3 beta criteria as a pre-specified subpopulation of the study[3]
- Although MOH was diagnosed at screening, investigators were not actively treating MOH during the PROMISE-2 study[3]

Efficacy and safety in MOH[3]

- Vyepti 100 and 300 mg resulted in a statistically significant (weeks 1–12, all comparisons $p<0.0001$ vs placebo) greater reduction in the number of MMDs compared to placebo[3]
- Vyepti was well tolerated by patients with MOH. Tolerability in the MOH subgroup and the overall study population was similar[3]



* Weeks 1–12, all comparisons $p<0.0001$ vs placebo
Weeks 13–24 statistical comparisons not reported.
MMD: monthly migraine days

PREVAIL[4]

Kudrow D *et al. BMC Neurology.* 2021; 21:126

Study design[4]

PREVAIL was an open-label, phase 3 trial comprising a 48-week treatment phase followed by a second 48-week treatment phase of Vyepti 300 mg in patients with chronic migraine (n=128)[4]

Key endpoints[4]

- Long-term safety
- Change from baseline in Migraine Disability Assessment Score (MIDAS)
- 6-Item Headache Impact Test (HIT-6)

Safety[4]

- ≥1 TEAEs considered related to study drug occurred in 18 patients (14.1%), the most common of which were hypersensitivity (5 events, 3.9%) and fatigue (4 events, 3.1%)[4]
- 8 TEAEs (6.3%) led to study drug withdrawal and 10 TEAEs (7.8%) led to study drug interruption[4]
- Hypersensitivity reactions were a common adverse event across clinical trials[5] and resulted in study drug withdrawal in 3 patients (2.3%) in PREVAIL[4]
- One patient experienced an anaphylactic reaction following the fifth infusion, which manifested as hives on legs, itchy scalp, and lower lip swelling*
- Please review the Vyepti® Product Information for full tolerability information
  - If a serious hypersensitivity reaction occurs with the infusion of Vyepti, further treatment with VYEPTI® should be discontinued.[1] If the hypersensitivity reaction is less severe, continuation of further treatment with Vyepti is up to the discretion of the treating physician.[1]

Treatment emergent adverse events reported in ≥2% of patients (safety population)[4]

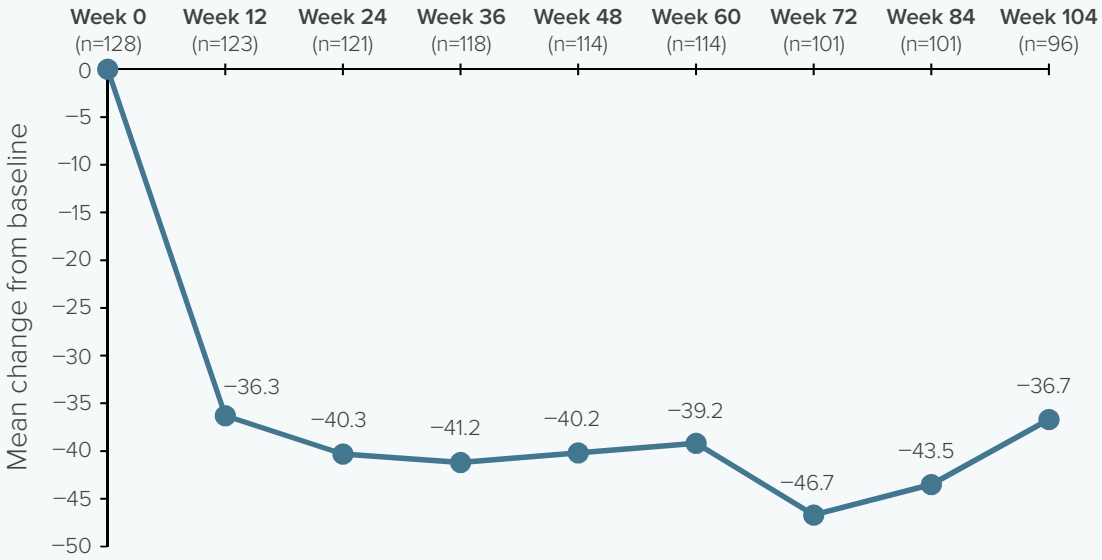
Adverse event, n (%)	Vyepti 300 mg (n=128)
Any AE, n (%)	91 (71.1)
Respiratory tract disorders	
Nasopharyngitis	27 (21.1)
Upper respiratory tract infection	18 (14.1)
Sinusitis	13 (10.2)
Influenza	11 (8.6)
Bronchitis	8 (6.3)
Neurological system disorders	
Migraine	10 (7.8)

Patient-reported outcomes[4]

- Clinically meaningful improvements in patient-reported measures were observed after the initial Vyepti dose and were maintained or improved after each subsequent dose (statistical comparisons not reported)[4]
- At week 4, 58.7% of individuals indicated that their most bothersome symptom (MBS) was “much improved” or “very much improved”, and this increased to 75.0% at week 48 (statistical comparisons not reported)[4]
  - The proportion of individuals reporting severe disability (MIDAS grade IV) reduced from 84.4% at baseline to 26.8% (week 12) and to 20.8% (week 104, statistical outcomes not reported)[4]
  - The proportion of individuals reporting PGIC as “much improved” or “very much improved” was 61.1% (week 4) and 81.0% (week 48 to study end, statistical outcomes not reported)[4]
  - The proportion of individuals reporting HIT-6 as “severe life impact” decreased from 92.2% at baseline to 39.7% (week 4) and 38.5% (week 104, statistical outcomes not reported)[4]

Patient reported outcomes[4]

Mean change from baseline in MIDAS



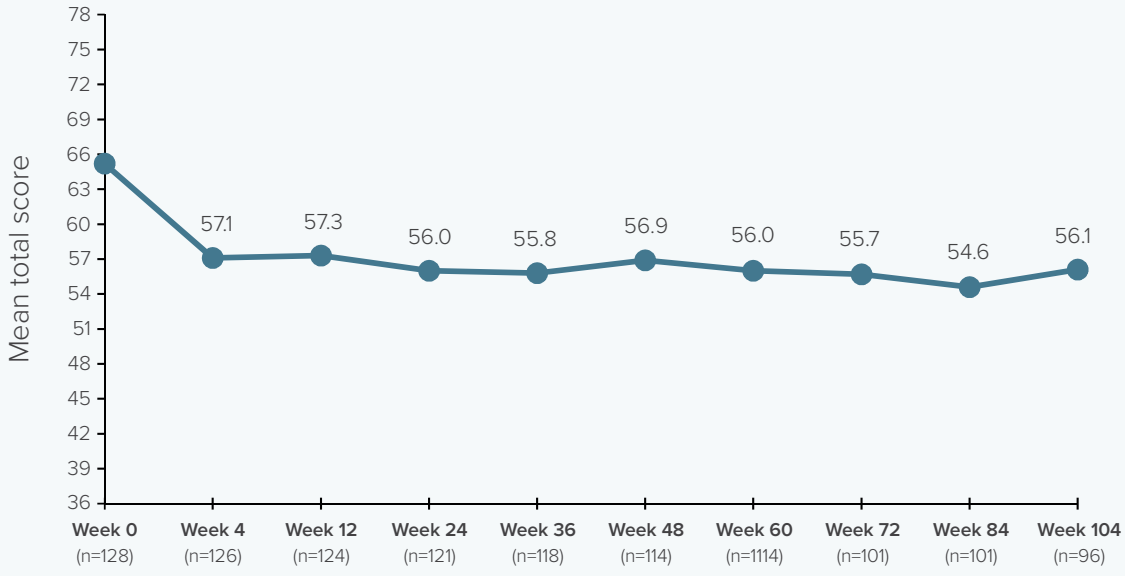
Statistical comparisons not reported.

MIDAS: Migraine Disability Assessment Score.

MIDAS total score at baseline: 56.8.

Patient reported outcomes[4]

Mean change in HIT-6



Statistical comparisons not reported.

HIT-6: 6-iten Headache Impact Test

HIT-6 score at baseline: 65.2.

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at **https://australia.progress.im/en** to access the latest news, resources and insights within your field

Vyepti® PBS Information: This product is not listed on the PBS.

Vyepti® is indicated for the preventive treatment of migraine in adults.[5]

Please review the full Approved Product Information for Vyepti before prescribing, available by calling Lundbeck on 1300 721 277.

Minimum Product Information: Vyepti® (eptinezumab). **Indications:** Vyepti is indicated for the preventive treatment of migraine in adults. **Contraindications:** Hypersensitivity to eptinezumab or any of the excipients. **Precautions:** Serious hypersensitivity reactions, including anaphylactic reactions may occur within minutes of the infusion. **Adverse Effects:** The common adverse events are nasopharyngitis and hypersensitivity. Most hypersensitivity reactions occurred during the infusion and were not serious; angioedema, urticaria, facial flushing and rash have been reported. Infusion-site related reactions occurred infrequently. **Dosage & Administration:** The recommended dose is 100 mg administered by intravenous infusion every 12 weeks and initiated and supervised by a healthcare professional. Vyepti 100 mg/mL is available as a single-dose vial. Treatment benefit should be assessed 3–6 months after initiation of treatment. Administration: Vyepti is for intravenous infusion only after dilution. Infusion takes place over approximately 30 minutes. For preparation and infusion instructions consult Approved PI. No dosage adjustments are recommended for age, gender or race. No dedicated hepatic and renal impairment studies were conducted; however, population pharmacokinetic analysis revealed no differences that would require dose adjustments. Insufficient data are available for use in elderly, children or adolescents. **Black triangle scheme:** This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at https://www.tga.gov.au/reporting-problems. **Date of Minimum PI:** 17 June 2021

References: 1. Ashina M *et al. Cephalalgia* 2020; 40:241–54 2. Lipton RB *et al. Neurology* 2020; 94:e1365–e1377. 3. Diener HC *et al. Headache.* 2020; 00:1–12. 4. Kudrow D *et al. BMC Neurology*. 2021; 21:126. 5. Vyepti® Approved Australian Prescribing Information. 6. Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia* 2018; 38:1–211.

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