Approved Use

VYEPTI is a prescription medicine used for the preventive treatment of migraine in adults.

Important Safety Information

Do not receive VYEPTI if you have a known allergy to eptinezumab-jjmr or its ingredients.

VYEPTI may cause allergic reactions. Call your healthcare provider or get emergency medical help right away if you have any symptoms of an allergic reaction: rash; swelling of your face, lips, tongue, or throat; if you have trouble breathing; hives; or redness in your face.

Before starting VYEPTI, tell your healthcare provider about all your medical conditions, including if you are pregnant or plan to become pregnant, or you are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including any prescription and over-the-counter medicines, vitamins, or herbal supplements.

The most common side effects of VYEPTI include stuffy nose and scratchy throat, and allergic reactions. These are not all the possible side effects of VYEPTI. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more information, see the full Prescribing Information and Patient Information.

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INDICATIONS AND USAGE

VYEPTI is a calcitonin gene-related peptide antagonist indicated for the preventive treatment of migraine in adults.

DOSE AND ADMINISTRATION

- **Recommended Dosing**
  - The recommended dosage is 100 mg administered by intravenous infusion every 3 months. Some patients may benefit from a dosage of 300 mg (2.1, 2.2)
  - Dilute only in 100 mL of 0.9% Sodium Chloride Injection, USP (2.2)

DOSAGE FORMS AND STRENGTHS

- Placebo

ADVERSE REACTIONS

- Hypersensitivity reactions* (1)
- Nasopharyngitis (6.1)
- Rash (6.1)
- Pruritus (6.1)
- flushing/hot flush (6.1)

CONTRAINDICATIONS

- VYEPTI is contraindicated in patients with serious hypersensitivity to eptinezumab-jjmr or to any of the excipients (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions: Reactions have included angioedema, urticaria, facial flushing, and rash. If a hypersensitivity reaction occurs, consider discontinuing VYEPTI and initiate appropriate therapy (5.1)
- The most common adverse reactions (2% and 2% or greater than placebo) were nasopharyngitis and hypersensitivity (6.1)

PREGNANCY

- Teratogenic effects: Animal reproduction studies have not been conducted with VYEPTI. It is also not known whether VYEPTI can cause fetal harm when administered to a pregnant woman. Use VYEPTI during pregnancy only if the potential benefit justifies the potential risk to the fetus (8.1)

NURSING MOTHERS

- There is no information on the excretion of VYEPTI in human milk. Because many drugs are excreted in human milk, consider the potential clinical significance of this exposure and the importance of the nursing relationship (8.3)

Pediatric Use

- VYEPTI is not indicated for use in children under 18 years of age (8.4)

Geriatric Use

- Experience in geriatric patients: The safety and effectiveness of VYEPTI in geriatric patients have not been established (8.5)

ADVERSE REACTIONS

- The most common adverse reactions (≥2% and 2% or greater than placebo) were nasopharyngitis, rhinitis, conjunctivitis, headache, and diarrhea (6.1)

Table 1. Adverse Reactions Occurring with an Incidence of at Least 2% for VYEPTI

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>VYEPTI 100 mg N=579</th>
<th>VYEPTI 300 mg N=574</th>
<th>Placebo N=588</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Hypersensitivity reactions*</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Adverse Reactions Occurring with an Incidence of at Least 2% for VYEPTI and at Least 2% Greater than Placebo in Studies 1 and 2

Table 1. Adverse Reactions Occurring with an Incidence of at Least 2% for VYEPTI and at Least 2% Greater than Placebo in Studies 1 and 2

- Hypersensitivity reactions includes multiple related adverse event terms, such as hypersensitivity, pruritus, and flushing/hot flush that occurred on the day of dosing.

*Hypersensitivity reactions includes multiple related adverse event terms, such as hypersensitivity, pruritus, and flushing/hot flush that occurred on the day of dosing.

contraindications

VYEPTI is contraindicated in patients with serious hypersensitivity to eptinezumab-jjmr or to any of the excipients.

Warnings and Precautions

Hypersensitivity reactions: Reactions have included angioedema, urticaria, facial flushing, and rash. If a hypersensitivity reaction occurs, consider discontinuing VYEPTI and institute appropriate therapy.

Adverse Reactions

The most common adverse reactions were nasopharyngitis and hypersensitivity.

Pregnancy

Teratogenic effects: Animal reproduction studies have not been conducted with VYEPTI. It is also not known whether VYEPTI can cause fetal harm when administered to a pregnant woman. Use VYEPTI during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Experience in geriatric patients: The safety and effectiveness of VYEPTI in geriatric patients have not been established.

Pediatric Use

VYEPTI is not indicated for use in children under 18 years of age.

Geriatric Use

Experience in geriatric patients: The safety and effectiveness of VYEPTI in geriatric patients have not been established.

Adverse Reactions

The most common adverse reactions were nasopharyngitis and hypersensitivity.

Table 1. Adverse Reactions Occurring with an Incidence of at Least 2% for VYEPTI and at Least 2% Greater than Placebo in Studies 1 and 2

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<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*Hypersensitivity reactions includes multiple related adverse event terms, such as hypersensitivity, pruritus, and flushing/hot flush that occurred on the day of dosing.
12.2 Pharmacodynamics
The relationship between the pharmacodynamic activity and the mechanism(s) by which eptinezumab-jjmr exerts its clinical effects is unknown.

12.3 Pharmacokinetics
Eptinezumab-jjmr exhibits linear pharmacokinetics and exposure increases proportionally with doses from 100 mg to 300 mg after intravenous administration. Steady-state plasma concentration is attained after the first dose with a once every 3-month dosing schedule.

Distribution
The central volume of distribution (Vc) for eptinezumab-jjmr is approximately 3.7 liters.

Metabolism & Elimination
Eptinezumab-jjmr is expected to be degraded by proteolytic enzymes into small peptides and amino acids.

The apparent clearance of eptinezumab-jjmr was 0.006 L/h, and the terminal elimination half-life was approximately 27 days.

Specific Populations
A population pharmacokinetic analysis assessing the effects of age, race, sex, and body weight did not suggest any clinically significant impact of these covariates on eptinezumab exposures.

Patients with Renal or Hepatic Impairment
No dedicated studies were conducted to assess the effects of renal or hepatic impairment on the pharmacokinetics of eptinezumab-jjmr. However, hepatic or renal impairment is not expected to affect the pharmacokinetics of eptinezumab-jjmr. A population pharmacokinetic analysis of integrated data from eptinezumab-jjmr clinical studies did not reveal clinically significant impact on pharmacokinetics of patients with hepatic or renal impairment.

Drug Interaction Studies
P450 Enzymes
Eptinezumab-jjmr is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

Sumatriptan
The co-administration of a single dose of 300 mg eptinezumab-jjmr administered as an intravenous infusion (over a period of 1 hour ± 15 min) with a single dose of 6 mg sumatriptan administered subcutaneously did not significantly influence the pharmacokinetics of eptinezumab-jjmr or sumatriptan.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
The carcinogenic potential of eptinezumab-jjmr has not been assessed.

Mutagenesis
Genetic toxicity studies of eptinezumab-jjmr have not been conducted.

Impairment of Fertility
When eptinezumab-jjmr (0, 75, or 150 mg/kg) was administered weekly by intravenous injection to male and female rats prior to and during mating and continuing in females to gestation day 3-4, no adverse effects on fertility were observed. The higher dose tested (150 mg/kg) is 30 times the maximum recommended human dose (MRHD) of 300 mg, on a body weight basis (mg/kg).

14 CLINICAL STUDIES
The efficacy of VYEPTI was evaluated as a preventive treatment of episodic and chronic migraine in two randomized, multicenter, placebo-controlled studies, both with 6-month double-blind periods: one study in patients with episodic migraine (Study 1) and one study in patients with chronic migraine (Study 2). VYEPTI was administered by intravenous infusion every 3 months in both studies; however, the primary endpoint was measured at 12 weeks.

Study 1: Episodic Migraine
Study 1 (NCT02559895) included adults with a history of episodic migraine (4 to 14 headache days per month, of which at least 4 were migraine days). A total of 665 patients were randomized to receive placebo (N=222), 100 mg VYEPTI (N=221), or 300 mg VYEPTI (N=222) every 3 months for 12 months. Patients were allowed to use concurrent acute migraine or headache medications, including migraine-specific medications (e.g., triptans, ergotamine derivatives), during the trial.

The study excluded patients with a history of cardiovascular disease (hypertension, ischemic heart disease), neurological disease, or cerebrovascular disease.

The primary efficacy endpoint was the change from baseline in mean monthly migraine days over Months 1-3. Secondary endpoints included the percentages of patients with 50% or greater, and 75% or greater reductions from baseline in monthly migraine days over Months 1-3.

Patients had a median age of 39 years (range: 18 to 71 years), 84% were female, and 84% were white. The mean migraine frequency at baseline was approximately 8.6 migraine days per month and was similar across treatment groups.

VYEPTI treatment demonstrated statistically significant improvements compared to placebo for the primary efficacy endpoint, as shown in Table 2; secondary endpoints are also summarized in Table 2.

Table 2. Efficacy Endpoint Results in Study 1

<table>
<thead>
<tr>
<th></th>
<th>VYEPTI 100 mg</th>
<th>VYEPTI 300 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly Migraine Days (MMD)</td>
<td>N=221</td>
<td>N=222</td>
<td>N=222</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>-3.9</td>
<td>-4.3</td>
<td>-3.2</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>-0.7</td>
<td>-1.1</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.018</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

In Study 1 and Study 2, 1.9% of patients treated with VYEPTI discontinued treatment because of adverse reactions (see Warnings and Precautions (5.1)).

6.2 Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of samples, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to eptinezumab-jjmr in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In patients receiving VYEPTI 100 mg or 300 mg every 3 months, the incidence of anti-eptinezumab-jjmr antibody development in Study 1 (up to 56 weeks) was 20.6% (82/447), and 41.3% (39/92) of those patients developed anti-eptinezumab-jjmr neutralizing antibodies. In Study 2 (up to 32 weeks), the incidence of anti-eptinezumab-jjmr antibody development was 18.3% (129/706), and 34.9% (45/129) of those patients developed anti-eptinezumab-jjmr neutralizing antibodies. In an open-label study with 84 weeks of treatment, 18% (23/128) of patients developed anti-eptinezumab-jjmr neutralizing antibodies.

Although the results from both studies showed no clear evidence of an impact from development of anti-eptinezumab-jjmr antibodies, including neutralizing antibodies, on the safety and efficacy profiles of VYEPTI, the available data are too limited to make definitive conclusions.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
There are no adequate data on developmental risks associated with the use of VYEPTI in pregnant women.

No adverse developmental effects were observed following administration of eptinezumab-jjmr to pregnant animals at doses greater than those used clinically [see Data].

In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively. The estimated rate of major birth defects (2.2%-2.9%) and miscarriage (17%) among deliveries to women with migraine are similar to rates reported in women without migraine.

Clinical Considerations
Disease-Associated Maternal and/or Fetal Risk
Published data have suggested that women with migraine may be at increased risk of preclampsia and gestational hypertension during pregnancy.

Data
Animal Data
When eptinezumab-jjmr (0, 75, or 150 mg/kg) was administered weekly to female rats and rabbits by intravenous injection throughout organogenesis, no adverse effects on embryofetal development were observed. The higher dose tested (150 mg/kg) is 30 times the maximum recommended human dose (MRHD) of 300 mg, on a body weight basis (mg/kg).

When eptinezumab-jjmr (0, 75, or 150 mg/kg) was administered weekly to female rats throughout pregnancy and lactation, no adverse effects on pre- and postnatal development were observed. The higher dose tested (150 mg/kg) is 30 times the MRHD, on a mg/kg basis.

8.2 Lactation
Risk Summary
There are no data on the presence of eptinezumab-jjmr in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for VYEPTI and any potential adverse effects on the breastfed infant from VYEPTI or from the underlying maternal condition.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Clinical studies of VYEPTI did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

11 DESCRIPTION
Eptinezumab-jjmr is a humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Eptinezumab-jjmr has an approximate molecular weight of 143 kD. Eptinezumab-jjmr is produced in Pichia pastoris yeast cells by recombinant DNA technology.

VEPTEI (eptinezumab-jjmr) injection is sterile, preservative-free, clear to slightly opalescent, colorless to brownish-yellow solution, for intravenous infusion. VYEPTI is supplied as a 100 mg/mL single-dose vial. Each mL contains 100 mg eptinezumab-jjmr formulated in L-histidine (1 mg), L-histidine hydrochloride monohydrate (2.8 mg), polysorbate 80 (100 mg/mL), sorbitol (40.5 mg), and Water for Injection, USP, at a pH of 5.8.
Study 1: Acute Migraine

Table 2. Efficacy Endpoint Results in Study 1 (continued)

<table>
<thead>
<tr>
<th></th>
<th>VYEPTI 100 mg N=221</th>
<th>VYEPTI 300 mg N=222</th>
<th>Placebo N=222</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50% MMD responders – Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Responders</td>
<td>49.8%</td>
<td>56.3%</td>
<td>37.4%</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>12.4%</td>
<td>18.9%</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.009*</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>≥75% MMD responders – Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Responders</td>
<td>22.2%</td>
<td>29.7%</td>
<td>16.2%</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>6.0%</td>
<td>13.5%</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>NS**</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

*Nominal statistical significance
**NS = Not statistically significant

Figure 1 shows the mean change from baseline in average monthly migraine days in Study 1. Patients treated with VYEPTI at both doses had greater mean decreases from baseline in average monthly migraine days compared to placebo-treated patients.

Study 2: Chronic Migraine

Table 2. Efficacy Endpoint Results in Study 2

<table>
<thead>
<tr>
<th></th>
<th>VYEPTI 100 mg N=356</th>
<th>VYEPTI 300 mg N=350</th>
<th>Placebo N=366</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monthly Migraine Days (MMD) – Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from baseline</td>
<td>-7.7</td>
<td>-8.2</td>
<td>-5.6</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>-2.0</td>
<td>-2.6</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>≥50% MMD responders – Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Responders</td>
<td>57.6%</td>
<td>61.4%</td>
<td>39.3%</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>18.2%</td>
<td>22.1%</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>≥75% MMD responders – Months 1-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Responders</td>
<td>26.7%</td>
<td>33.1%</td>
<td>15.0%</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>11.7%</td>
<td>18.1%</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2 shows the distribution of change from baseline in mean monthly migraine days through Month 3 by treatment group in 2-day increments.

Figure 3 demonstrates that greater percentages of placebo-treated patients had migraines on most days during the first 7 days of treatment compared to VYEPTI-treated patients in Study 1.

Figure 4 shows the mean change from baseline in average monthly migraine days for Study 2. Patients treated with VYEPTI at both doses had greater mean decreases from baseline in mean monthly migraine days compared to placebo-treated patients.
Figure 5 shows the distribution of change from baseline in mean monthly migraine days through Month 3 by treatment group in 3-day increments.

Figure 5. Distribution of Change from Baseline in Mean Monthly Migraine Days over Months 1-3 by Treatment Group in Study 2

Figure 6 demonstrates that greater percentages of placebo-treated patients had migraines on individual days during the first 7 days of treatment compared to VYEPTI-treated patients in Study 2.

Figure 6. Percentage of Patients with a Migraine from Day -1 (Day Prior to Infusion) to Day 7 in Study 2

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied
VYEPTI (eptinezumab-jjmr) injection is a clear to slightly opalescent, colorless to brownish-yellow solution supplied as:
Carton containing one 100 mg/mL single-dose vial - NDC 67386-130-51.

16.2 Storage and Handling
Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light until time of use. Do not freeze or shake.
The vial stopper is not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION
Advertise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity Reactions
Inform patients that hypersensitivity reactions, including angioedema, urticaria, facial flushing, and rash, can occur. Advise patients to contact their healthcare provider immediately if signs or symptoms of hypersensitivity reactions occur [see Warnings and Precautions (5.1)].

Pregnancy
Advise patients to notify their healthcare provider if they become pregnant during treatment or plan to become pregnant [see Use in Specific Populations (8.1)].

Lactation
Inform patients to notify their healthcare provider if they are breastfeeding or plan to breastfeed [see Use in Specific Populations (8.2)].

Manufactured by: Lundbeck Seattle BioPharmaceuticals, Inc.
11804 North Creek Parkway South
Bothell, WA 98011 USA
U.S. License No. 2097

Vyepti is a trademark of Lundbeck Seattle BioPharmaceuticals, Inc. EPT-L-100005

PATIENT INFORMATION
VYEPTI™ (vye ep’ tee)
eptinezumab-jjmr
injection, for intravenous use

What is VYEPTI?
VYEPTI is a prescription medicine used for the preventive treatment of migraine in adults.

It is not known if VYEPTI is safe and effective in children.

Do not receive VYEPTI if you are allergic to eptinezumab-jjmr or any of the ingredients in VYEPTI. See the end of this Patient Information leaflet for a complete list of ingredients in VYEPTI.

Before you receive VYEPTI, tell your healthcare provider about all of your medical conditions, including if you:
- are pregnant or plan to become pregnant. It is not known if VYEPTI will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if VYEPTI passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while using VYEPTI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive VYEPTI?
- VYEPTI will be given by a healthcare provider in a healthcare setting.
- VYEPTI is given by intravenous (IV) infusion in your vein.
- VYEPTI will be given over 30 minutes every 3 months.

If you have questions about your infusion schedule, ask your healthcare provider.

What are the possible side effects of VYEPTI?
VYEPTI may cause serious side effects, including:
- Allergic reactions. Allergic reactions can happen after receiving VYEPTI. Call your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - rash
  - swelling of your face, lips, tongue or throat
  - trouble breathing
  - hives
  - redness in your face

The most common side effects of VYEPTI include:
- stuffy nose and scratchy throat
- allergic reactions

These are not all of the possible side effects of VYEPTI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of VYEPTI.
Medicines are sometimes prescribed for purposes other than those listed in the Patient Information leaflet.

You can ask your pharmacist or healthcare provider for information about VYEPTI that is written for health professionals.

What are the ingredients in VYEPTI?
Active ingredient: eptinezumab-jjmr

Inactive ingredients: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sorbitol, and Water for Injection.

The vial stopper is not made with natural rubber latex.

Manufactured by: Lundbeck Seattle BioPharmaceuticals, Inc., 11804 North Creek Parkway South, Bothell, WA 98011

US License Number: 2097

Vyepti is a trademark of Lundbeck Seattle BioPharmaceuticals, Inc.

For more information, call 1-833-4-VYEPTI (833-489-3784) or go to www.Vyepti.com.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: 2/2020