RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	Vyepti™
Generic Name	eptinezumab-jjmr
Drug Manufacturer	Lundbeck seattle, BioPharmaceuticals, Inc.

New Drug Approval

FDA Approval Date: February 21, 2020
Review Designation: None
Review Type: Biologics license application 761119

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Migraine is an episodic disorder, the centerpiece of which is a severe headache generally associated with nausea and/or light and sound sensitivity. It is one of the most common complaints encountered by neurologists in day-to-day practice. The pathophysiology, clinical manifestations, diagnosis, and complications of migraine will be reviewed here. Other aspects of migraine are discussed separately. (See "Acute treatment of migraine in adults" and "Preventive treatment of migraine in adults" and "Chronic migraine" and "Migraine with brainstem aura (basilar-type migraine)" and "Hemiplegic migraine" and "Vestibular migraine" and "Headache, migraine, and stroke".)

Migraine is a common disorder that affects up to 12 percent of the general population. It is more frequent in women than in men, with attacks occurring in up to 17 percent of women and 6 percent of men each year. Migraine without aura is the most common type, accounting for approximately 75 percent of cases. Migraine is most common in those aged 30 to 39, an age span in which prevalence in men and women reaches 7 and 24 percent, respectively. Migraine also tends to run in families. Migraine, although not fatal, is a major cause of disability, and ranked second worldwide in 2016 among all diseases with respect to years of life lived with disability. Data from several retrospective nationwide cohort studies in Taiwan, all from the same group of investigators, suggest that migraine is a potential risk factor for Bell's palsy, sensorineural hearing loss, and oculomotor cranial nerve palsies; independent reports are needed to confirm these associations.

Efficacy

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 (i.e., 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.

Study 2: Chronic Migraine

Study 2 (NCT02974153) included adults with a history of chronic migraine (15 to 26 headache days per month, of which at least 8 were migraine days). A total of 1072 patients were randomized and received placebo (N=366), 100 mg VYEPTI (N=356), or 300 mg VYEPTI (N=350) every 3 months for 6 months. Patients were allowed to use and to continue an established stable regimen of acute migraine or headache preventive medication (except onabotulinumtoxinA). Patients with a dual diagnosis of chronic migraine and medication overuse headache attributable to acute medication overuse (triptans, ergotamine, or combination analgesics greater than 10 days per month) were included in the study population. Patients using opioids or butalbital-containing products greater than 4 days per month were not allowed. 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

Safety

ADVERSE EVENTS

- >10%:
- Immunologic: Antibody development (18% to 21%; neutralizing: 35% to 41%)
- 1% to 10%:
- Gastrointestinal: Nausea (2% [Lipton 2020])
- Hypersensitivity: Hypersensitivity reaction (1% to 2% [placebo: 0%])
- Nervous system: Fatigue (2% [Lipton 2020])
- Respiratory: Nasopharyngitis (8%)
- Frequency not defined: Hypersensitivity: Angioedema

WARNINGS & PRECAUTIONS

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

CONTRAINDICATIONS

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

Clinical Pharmacology

MECHANISMS OF ACTION

Eptinezumab-jjmr is a humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor.

Dose & Administration

ADULTS

Migraine prophylaxis: IV: Initial: 100 mg every 3 months; some patients may benefit from 300 mg every 3 months.

PEDIATRICS

None

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GERIATRICS

Refer to adult dosing

RENAL IMPAIRMENT

None

HEPATIC IMPAIRMENT

None

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: 100 mg/mL solution in a single-dose vial