AJOVY is contraindicated in patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients. Reactions have included anaphylaxis and angioedema [see Warnings and Precautions (5.1)].

Contraindications
AJOVY is contraindicated in patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients. (4)

Warnings and Precautions
Hypersensitivity Reactions: If hypersensitivity occurs, consider discontinuing AJOVY and institute appropriate therapy. (5.1)

Clinical Trials Experience
The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

Hypersensitivity Reactions [see Warnings and Precautions (5.1)]

Clinical Trials
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in clinical practice.

Patient Counseling Information
*Sections or subsections omitted from the full prescribing information are not listed.

DOSAGE FORMS AND STRENGTHS
Injection: 225 mg/1.5 mL solution in a single-dose prefilled autoinjector. (3)
Injection: 225 mg/1.5 mL solution in a single-dose prefilled syringe. (3)

ADVERSE REACTIONS
The most common adverse reactions (>5% and greater than placebo) were injection site reactions. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals at 1-888-483-8279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Remarks: AJOVY® (fremanezumab-vfrm) injection, for subcutaneous use

The 675 mg quarterly dosage is administered as three consecutive injections of 225 mg each. (2.1)

Dosing and Administration
Two subcutaneous dosing options of AJOVY are available to administer the recommended dosage:
- 225 mg monthly, or
- 675 mg every 3 months (quarterly). (2.1)

The 675 mg quarterly dosage is administered as three consecutive injections of 225 mg each. (2.1)

Pregnancy
Lactation
8.1 Pregnancy
8.2 Lactation

AJOVY® (fremanezumab-vfrm) injection, for subcutaneous use
Initial U.S. Approval: 2018

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AJOVY safely and effectively. See full prescribing information for AJOVY.

AJOVY® (fremanezumab-vfrm) injection, for subcutaneous use

DOSAGE AND ADMINISTRATION

Recommended Dosage
Two subcutaneous dosing options of AJOVY are available to administer the recommended dosage:
- 225 mg monthly, or
- 675 mg every 3 months (quarterly), which is administered as three consecutive subcutaneous injections of 225 mg each.

When switching dosage options, administer the first dose of the new regimen on the next scheduled date of administration. If a dose of AJOVY is missed, administer as soon as possible. Thereafter, AJOVY can be scheduled from the date of the last dose.

Administration Instructions
AJOVY may be administered by healthcare professionals, patients, and/or caregivers. Prior to use, provide proper training to patients and/or caregivers on the preparation and administration of AJOVY prefilled syringe, including aseptic technique [see Instructions for Use]:
- Remove AJOVY from the refrigerator. Prior to use, allow AJOVY to sit at room temperature for 30 minutes protected from direct sunlight. Do not warm by using a heat source such as hot water or a microwave. Do not use AJOVY if it has been at room temperature for 7 days or longer [see How Supplied/Storage and Handling (16.2)].
- Follow aseptic injection technique every time AJOVY is administered. (2.2)
- Follow aseptic injection technique every time AJOVY is administered [see Dosage Forms and Strengths (3)]. Do not use if the solution is cloudy, discolored, or contains particles.
- Administer AJOVY by subcutaneous injection into the abdomen, thigh, or upper arm that are not tender, bruised, red, or indurated. For multiple injections, you may use the same body site, but not the exact location of the previous injection. (2.2)
- Do not co-administer AJOVY with other injectable drugs at the same injection site.

Adverse Reactions Occurring with an Incidence of At Least 2% for Either Dosing Regimen of AJOVY at Least 2% Greater Than Placebo in Studies 1 and 2

Table 1:

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>AJOVY 225 mg Monthly</th>
<th>AJOVY 225 mg Monthly</th>
<th>Placebo Monthly</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=290)</td>
<td>(n=667)</td>
<td>(n=668)</td>
<td></td>
</tr>
<tr>
<td>Injection site reactionsb</td>
<td>43 %</td>
<td>45 %</td>
<td>38 %</td>
</tr>
</tbody>
</table>

b Injection site reactions include multiple related adverse event terms, such as injection site pain, induration, and erythema.
6.2 Immunogenicity
As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on 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 sample collection, concurrent medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to fremanezumab-vfrm in the studies described below with the incidence of antibodies in other studies to other products may be misleading. Clinical immunogenicity of AJOVY was monitored by analyzing anti-drug antibodies (ADA) and neutralizing antibodies in drug-treated patients. The data reflect the percentage of patients whose test results were positive for antibodies to AJOVY in specific assays.

In 3-month placebo-controlled studies, treatment-emergent ADA responses were observed in 6 out of 170 (0.4%) AJOVY-treated patients. One of the 6 patients developed anti-AJOVY neutralizing antibodies at Day 84. In the ongoing long-term open-label study, ADA were detected in 16% of patients (30 out of 1888). Out of 30 ADA-positive patients, 17 had a neutralizing activity in their post-dose samples. However, these data do not demonstrate an impact of anti-fremanezumab-vfrm antibody development on the efficacy or safety of AJOVY in these patients, the available data are too limited to make definitive conclusions.

6.3 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of AJOVY. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Immune System Disorders – Anaphylactic reactions and angioedema [see Containments (4) and Warnings and Precautions (5.3)].

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to AJOVY during pregnancy. Healthcare providers are encouraged to register pregnant patients, or pregnant women may enroll themselves in the registry by calling 1-833-927-2605 or visiting www.tevamigrainepregnancyregistry.com.

Risk Summary
There are no adequate data on the developmental risk associated with the use of AJOVY in pregnant women. AJOVY has a long half-life [see Clinical Pharmacology (12.3)]. This should be taken into consideration for women who are pregnant or plan to become pregnant while taking AJOVY. Administration of fremanezumab-vfrm to rats and rabbits during the period of organogenesis or to rats throughout pregnancy and lactation at doses resulting in plasma levels greater than those expected clinically did not result in adverse effects on development [see Animal Data]. In the U.S. general population, the estimated background risk of major birth defects and miscarriage 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 Embryo/Fetal Risk
Published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy. Data

Animal Data
When fremanezumab-v frm (0, 50, 100, or 200 mg/kg) was administered to male and female rats by weekly subcutaneous injection prior to and during mating and continuing in females throughout organogenesis, no adverse embryofetal effects were observed. The highest dose tested was associated with plasma exposures (AUC) approximately 2 times that in humans at a dose of 675 mg. Administration of fremanezumab-vfrm (0, 10, 50, or 100 mg/kg) weekly by subcutaneous injection to pregnant rabbits throughout the period of organogenesis produced no adverse effects on embryofetal development. The highest dose tested was associated with plasma AUC exposures (AUC) approximately 2 times that in humans at a dose of 675 mg.

Human Data
In Study 1 and Study 2, respectively.

Condition

Study 1 (NCT 02629861) included adults with a history of episodic migraine (patients with <15 headache days per month). All patients were randomized (1:1:1) to receive subcutaneous injections of either AJOVY 675 mg every three months (quarterly), AJOVY 225 mg monthly, or placebo monthly, over a 3-month treatment period. Patients were allowed to use acute headache treatments during the study. A subset of patients (21%) was allowed to use one additional concomitant preventive medication. The study excluded patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism.

The primary efficacy endpoint was the mean change from baseline in the monthly average number of migraine days during the 3-month treatment period. Secondary endpoints included the proportion of patients reaching at least a 50% reduction in monthly average number of migraine days during the 3-month treatment period, the mean change from baseline in the monthly average number of days of use of any acute headache medication during the 3-month treatment period, and the mean change from baseline in the number of migraine days during the first month of the treatment period. In Study 1, a total of 875 patients (742 females, 133 males), ranging in age from 18 to 70 years, were randomized. A total of 791 patients completed the 3-month double-blind phase. The mean migraine frequency at baseline was approximately 9 migraine days per month, and was similar across treatment groups.

11 DESCRIPTION
Fremanezumab-vfrm is a fully humanized IgG2A/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Fremanezumab-vfrm is produced by recombinant DNA technology in mammalian cell culture (CHO) cells. The antibody consists of 1224 amino acids and has a molecular weight of approximately 146 kDa. AJOVY (fremanezumab-vfrm) injection is a sterile, preservative-free, clear to opalescent, colorless to slightly yellow solution for subcutaneous injection, supplied in a single-dose 225 mg/1.5 mL prefilled autoinjector and a single-dose 225 mg/1.5 mL prefilled syringe.

AJOVY® (fremanezumab-vfrm) injection Each prefilled autoinjector or prefilled syringe delivers 15 mL of solution containing 225 mg fremanezumab-vfrm, disodium ethylenediaminetetraacetic acid dihydrate (EDTA) (0.04 mg), L-histidine (0.815 mg), L-histidine hydrochloride monohydrate (3.39 mg), polysorbate-80 (0.3 mg), sucrose (99 mg), and Water for Injection, and has a pH of 5.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Fremanezumab-vfrm is a humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor. The relationship between the pharmacodynamic activity and the mechanism(s) by which fremanezumab-vfrm exerts its clinical effects is unknown.

12.2 Pharmacodynamics
The relationship between the pharmacodynamic activity and the mechanism(s) by which fremanezumab-vfrm exerts its clinical effects is unknown.

12.3 Pharmacokinetics
Absorption
After single subcutaneous (SC) administrations of 225 mg, 675 mg, and 900 mg fremanezumab-vfrm, median time to maximum concentrations (tmax) was 5 to 7 days. Dose-proportionality, based on population PK, was observed between 225 mg to 900 mg. Steady state was achieved by approximately 168 days (about 6 months) following 225 mg SC monthly and 675 mg SC quarterly dosing regimens. Median accumulation ratio, based on once-monthly and once-quarterly dosing regimens, is approximately 2.3 and 1.2, respectively.

Distribution
Fremanezumab-vfrm has an apparent volume of distribution of approximately 6 liters, suggesting volume distribution to the extravascular tissues.

Metabolism
Similar to other monoclonal antibodies, fremanezumab-vfrm is degraded by enzymatic proteolysis into small peptides and amino acids.

Elimination
Fremanezumab-vfrm apparent clearance was approximately 0.41 L/day. Fremanezumab-vfrm was estimated to have a half-life of approximately 31 days.

Specific Populations
A population PK analysis assessing effects of age, race, sex, and weight was conducted on data from 2287 subjects. No dose adjustments are recommended for AJOVY.

Patients with Hepatic or Renal Impairment
Hepatic/renal impairment is not expected to affect the pharmaco kinetics of fremanezumab. A population PK analysis of integrated data from the AJOVY clinical studies did not reveal a difference in the pharmaco kinetics of fremanezumab in patients with mild hepatic impairment, relative to those with normal hepatic function. There were only 4 patients with moderate hepatic impairment, and no patient with severe hepatic impairment in fremanezumab clinical studies. No dedicated hepatic/renal impairment studies were conducted to assess the effect of hepatic or renal impairment on the pharmaco kinetics of fremanezumab.

Drug Interactions
Fremanezumab is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely. Additionally, the effects of medications for the acute treatment (specifically analgesics, ergots, and triptans) and preventive treatment of migraine were evaluated in a population PK model, and found not to influence fremanezumab exposure.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis
Carcinogenicity studies of fremanezumab-vfrm were not conducted.

Mutagenesis
Genetic toxicology studies of fremanezumab-vfrm were not conducted.

Impairment of Fertility
When fremanezumab-vfrm (0, 50, 100, or 200 mg/kg) was administered to male and female rats by weekly subcutaneous injection prior to and during mating and continuing in females throughout organogenesis, no adverse effects on male or female fertility were observed. The highest dose tested was associated with plasma exposures (AUC) approximately 2 times that in humans at a dose of 675 mg.

14 CLINICAL STUDIES
The efficacy of AJOVY was evaluated as a preventive treatment of episodic or chronic migraine in two multicenter, randomized, 3-month, double-blind, placebo-controlled studies (Study 1 and Study 2, respectively).

Episodic Migraine
Study 1 (NCT 02629861) included adults with a history of episodic migraine (patients with <15 headache days per month). All patients were randomized (1:1:1) to receive subcutaneous injections of either AJOVY 675 mg every three months (quarterly), AJOVY 225 mg monthly, or placebo monthly, over a 3-month treatment period. Patients were allowed to use acute headache treatments during the study. A subset of patients (21%) was allowed to use one additional concomitant preventive medication. The study excluded patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism.

The primary efficacy endpoint was the mean change from baseline in the monthly average number of migraine days during the 3-month treatment period. Secondary endpoints included the proportion of patients reaching at least a 50% reduction in monthly average number of migraine days during the 3-month treatment period, the mean change from baseline in the monthly average number of days of use of any acute headache medication during the 3-month treatment period, and the mean change from baseline in the number of migraine days during the first month of the treatment period. In Study 1, a total of 875 patients (742 females, 133 males), ranging in age from 18 to 70 years, were randomized. A total of 791 patients completed the 3-month double-blind phase. The mean migraine frequency at baseline was approximately 9 migraine days per month, and was similar across treatment groups.
AJOVY® (fremanezumab-vfrm) injection

Both monthly and quarterly dosing regimens of AJOVY demonstrated statistically significant improvements for efficacy endpoints compared to placebo over the 3-month period, as summarized in Table 2.

Table 2: Efficacy Endpoints in Study 1

<table>
<thead>
<tr>
<th>Study 1 Efficacy Endpoint</th>
<th>AJOVY 225 mg Monthly (N=287)</th>
<th>AJOVY 675 mg Quarterly (N=288)</th>
<th>Placebo (N=290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monthly migraine days (MMD)</td>
<td>8.9</td>
<td>9.2</td>
<td>9.1</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>-3.7</td>
<td>-3.4</td>
<td>-2.2</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥50% MDD responders</td>
<td>42.7%</td>
<td>44.4%</td>
<td>27.5%</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>19.8%</td>
<td>16.5%</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Monthly acute headache medication days</td>
<td>-3.0</td>
<td>-2.9</td>
<td>-1.6</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>-1.4</td>
<td>-1.3</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 1 displays the mean change from baseline in the average monthly number of migraine days in Study 1.

Figure 2 shows the distribution of change from baseline in mean monthly migraine days in bins of 2 days by treatment group in Study 1. A treatment benefit over placebo for both doses of AJOVY is seen across a range of changes from baseline in monthly migraine days.

Figure 2: Distribution of Change from Baseline in Mean Monthly Migraine Days by Treatment Group in Study 1

Chronic Migraine

Study 2 (NCT 02621931) included adults with a history of chronic migraine (patients with ≥15 headache days per month). All patients were randomized (1:1:1) to receive subcutaneous injections of either AJOVY 675 mg starting dose followed by 225 mg monthly, 675 mg every 3 months (quarterly), or placebo monthly, over a 3-month treatment period. Patients were allowed to use acute headache treatments during the study. A subset of patients (21%) was allowed to use one additional concomitant, preventive medication.

The study excluded patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism.

AJOVY® (fremanezumab-vfrm) injection

The primary efficacy endpoint was the mean change from baseline in the monthly average number of headache days of at least moderate severity during the 3-month treatment period. The secondary endpoints were the mean change from baseline in the monthly average number of migraine days during the 3-month treatment period, the proportion of patients reaching at least 50% reduction in the monthly average number of headache days of at least moderate severity during the 3-month treatment period, the mean change from baseline in the monthly average number of days of use of any acute headache medication during the 3-month treatment period, and the mean change from baseline in the number of headache days of at least moderate severity during the first month of treatment.

In Study 2, a total of 1130 patients (991 females, 139 males), ranging in age from 18 to 70 years, were randomized. A total of 1034 patients completed the 3-month double-blind phase.

Both monthly and quarterly dosing regimens of AJOVY treatment demonstrated statistically significant improvement for key efficacy outcomes compared to placebo, as summarized in Table 3.

Table 3: Efficacy Endpoints in Study 2

<table>
<thead>
<tr>
<th>Study 2 Efficacy Endpoint</th>
<th>AJOVY 225 mg Monthly (N=375)</th>
<th>AJOVY 675 mg Quarterly (N=375)</th>
<th>Placebo (N=371)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline headache days of any severity</td>
<td>20.3</td>
<td>20.4</td>
<td>20.3</td>
</tr>
<tr>
<td>Baseline headache days of at least moderate severity</td>
<td>12.8</td>
<td>13.2</td>
<td>13.3</td>
</tr>
<tr>
<td>Change from baseline in the monthly average number of headache days of at least moderate severity</td>
<td>-4.6</td>
<td>-4.3</td>
<td>-2.5</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>-2.1</td>
<td>-1.8</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change from baseline in monthly average number of migraine days in patients</td>
<td>-5.0</td>
<td>-4.9</td>
<td>-3.2</td>
</tr>
<tr>
<td>Change from baseline in monthly average number of headache days of at least moderate severity at 4 weeks after 1st dose</td>
<td>-4.6</td>
<td>-4.6</td>
<td>-2.3</td>
</tr>
<tr>
<td>Percentage of patients with ≥ 50% reduction in monthly average number of headache days of at least moderate severity</td>
<td>40.8%</td>
<td>37.6%</td>
<td>18.3%</td>
</tr>
<tr>
<td>Change from baseline in monthly average number of days of acute headache medication</td>
<td>-4.2</td>
<td>-3.7</td>
<td>-1.9</td>
</tr>
</tbody>
</table>

Figure 3 shows the distribution of change from baseline in monthly headache days of at least moderate severity in Study 2.

Figure 3: Change from Baseline in Monthly Headache Days of At Least Moderate Severity in Study 2

Figure 4 shows the distribution of change from baseline in monthly headache days of at least moderate severity at month 3 in bins of 3 days by treatment group. A treatment benefit over placebo for both dosing regimens of AJOVY is seen across a range of changes from baseline in headache days.

Figure 4: Change from Baseline in Monthly Headache Days of At Least Moderate Severity in Study 2

a LS (least-square) means and standard error of the mean are presented.
b Used for chronic migraine diagnosis.
c Used for primary endpoint analysis.
AJOVY® (fremanezumab-vfrm) injection

Figure 4: Distribution of Mean Change from Baseline in Monthly Headache Days of At Least Moderate Severity by Treatment Group in Study 2

*In Study 2, patients received a 675 mg starting dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

AJOVY (fremanezumab-vfrm) injection is a sterile, preservative-free, clear to opalescent, colorless to slightly yellow solution for subcutaneous administration.

AJOVY is not made with natural rubber latex.

AJOVY is supplied as follows:

• Prefilled Autoinjector
  - Pack of 1 autoinjector: 225 mg/1.5 mL single-dose prefilled autoinjector
  - Pack of 3 autoinjectors: 3 x 225 mg/1.5 mL single-dose prefilled autoinjectors

• Prefilled Syringe
  - Pack of 1 syringe: 225 mg/1.5 mL single-dose prefilled syringe

16.2 Storage and Handling

• Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original outer carton to protect from light.
• If necessary, AJOVY may be kept in the original carton at room temperature up to 30°C (86°F) for a maximum of 7 days. After removal from the refrigerator, AJOVY must be used within 7 days or discarded. Once stored at room temperature, do not place back in the refrigerator.
• Do not freeze.
• Do not expose to extreme heat or direct sunlight.
• Do not shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Information on Preparation and Administration

Provide guidance to patients and caregivers on proper subcutaneous administration technique, including aseptic technique, and how to use the single-dose prefilled syringe [(see Dosage and Administration (2.2)]. Instruct patients and/or caregivers to read and follow the Instructions for Use each time they use AJOVY.

Instruct patients prescribed the regimen of 225 mg every 3 months to administer the dosage as three consecutive subcutaneous injections of 225 mg each [(see Dosage and Administration (2.2)].

Hypersensitivity Reactions

Inform patients about the signs and symptoms of hypersensitivity reactions and that these reactions can occur up to 1 month after administration. Advise patients to contact their healthcare provider immediately if signs or symptoms of hypersensitivity reactions occur [(see Warnings and Precautions (5.4)].

Pregnancy

Advise women that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to AJOVY during pregnancy [(see Use in Specific Populations (8.1)].

Manufactured by:

Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454
US License No. 2016

AJOVY® (fremanezumab-vfrm), its use, or its process of manufacture, may be protected by one or more United States patents, including US 8,007,794, US 8,586,045 and US 9,896,502.

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AJO-008

continued
What are the possible side effects of AJOVY?

AJOVY may cause serious side effects, including:

- Allergic reactions. Allergic reactions, including itching, rash, and hives, can happen within hours and up to 1 month after receiving AJOVY. Call your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, mouth, tongue, or throat
  - trouble breathing

The most common side effects of AJOVY include:

- injection site reactions

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of AJOVY. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store AJOVY?

- Store AJOVY in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Keep AJOVY in the carton it comes in to protect from light.
- If needed, AJOVY may be stored at room temperature up to 86°F (30°C) in the carton it comes in for up to 7 days. Do not use AJOVY if it has been out of the refrigerator for 7 days or longer. Throw away (dispose of) AJOVY in a sharps disposal or puncture-resistant container if it has been out of the refrigerator for 7 days or longer. Once stored at room temperature, do not place back in the refrigerator.
- Do not freeze. If AJOVY freezes, throw it away in a sharps disposal container.
- Keep AJOVY out of extreme heat and direct sunlight.
- Do not shake AJOVY.

Keep AJOVY prefilled autoinjector and AJOVY prefilled syringe out of the reach of small children.

General information about the safe and effective use of AJOVY.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use AJOVY for a condition for which it was not prescribed. Do not give AJOVY to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about AJOVY that is written for health professionals.

What are the ingredients in AJOVY?

Active ingredient: fremanezumab-vfrm

Inactive ingredients: disodium ethylenediaminetetraacetic acid dihydrate (EDTA), L-histidine, L-histidine hydrochloride monohydrate, polysorbate-80, sucrose, and Water for Injection.

AJOVY prefilled syringe and prefilled autoinjector are not made with natural rubber latex.

Manufactured by: Teva Pharmaceuticals USA, Inc., North Wales, PA 19454
US License No. 2016
AJOPPL-005

For more information, go to www.AJOVY.com or call 1-888-483-8279.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 6/2021
Read this before you inject.

Step 1. Check the dose your healthcare provider has prescribed.
AJOVY comes as a single-dose (one time) prefilled autoinjector. Your healthcare provider will prescribe the dose that is best for you.
- If your healthcare provider has prescribed 225 mg of AJOVY each month for you, give 1 injection each month, using a 225 mg prefilled AJOVY autoinjector.
- If your healthcare provider has prescribed 675 mg of AJOVY every 3 months for you, give 3 separate injections, one after another, using a different 225 mg prefilled AJOVY autoinjector for each injection. Give these injections 1 time every 3 months.
Before you inject, always check the label of your single-dose prefilled autoinjector to make sure you have the correct medicine and the correct dose of AJOVY. If you are not sure of your dose, ask your healthcare provider.

How do I inject AJOVY?

Step 2. Remove the prefilled autoinjector from the carton.
- You may need to use more than 1 prefilled autoinjector depending on your prescribed dose.
- Remove the autoinjector from the carton (see Figure C).
- Do not shake the prefilled autoinjector at any time, as this could affect the way the medicine works.

Important: If there are any unused autoinjectors left in the carton, put the carton and unused autoinjectors back in the refrigerator.

Step 3. Gather the supplies you will need to inject AJOVY.
- Gather the following supplies (see Figure D) and the number of AJOVY 225 mg prefilled autoinjectors you will need to give your prescribed dose:
  - If your dose is 225 mg, you will need 1 AJOVY 225 mg prefilled autoinjector.
  - If your dose is 675 mg, you will need 3 AJOVY 225 mg prefilled autoinjectors.
  - Alcohol swabs (not supplied).
  - Gauze pads or cotton balls (not supplied).
  - Sharps disposal or puncture-resistant container (not supplied).

Step 4. Let AJOVY reach room temperature.
- Place the supplies you have gathered on a clean, flat surface.
- Wait for 30 minutes to allow the medicine to reach room temperature.
- Do not leave the prefilled autoinjector in direct sunlight.
- Do not warm up the AJOVY prefilled autoinjector using a heat source such as hot water or a microwave.

Step 5. Wash your hands.
- Wash your hands with soap and water and dry well with a clean towel.
  Be careful not to touch your face or hair after washing your hands.

Step 6. Look closely at your AJOVY prefilled autoinjector.
Note: You may see air bubbles in the prefilled autoinjector. This is normal. Do not remove the air bubbles from the prefilled autoinjector before giving your injection.

Injecting AJOVY with these air bubbles will not harm you.

- Check that the liquid medicine in the prefilled autoinjector viewing window is clear and colorless to slightly yellow before you give your injection. (See Figure E). If the liquid has any particles in it, or is discolored, cloudy, or frozen, do not use the prefilled autoinjector. Call your healthcare provider or pharmacist.

| Do not use the prefilled autoinjector if it has any visible damage, such as cracks or leaks. See disposal instructions in Step 12. |
| Check that AJOVY appears on the prefilled autoinjector. |
| Check the expiration date (EXP) printed on the prefilled autoinjector label. |

Step 7: Choose your injection area.

- Choose an injection area from the following areas (see Figure F):
  - your stomach area (abdomen), avoid about 2 inches around the belly button.
  - the front of your thighs, an area that is at least 2 inches above the knee and 2 inches below the groin.
  - the back of your upper arms, in the fleshy area of the upper back portion.

Note: There are some injection areas on your body that are hard to reach (like the back of your arm). You may need help from someone who has been instructed on how to give your injection if you cannot reach certain injection areas.

Step 8. Clean your injection area.
- Clean the chosen injection area using a new alcohol swab. Let your skin dry.
- Do not inject AJOVY into an area that is tender, red, bruised, callused, tattooed, hard, or that has scars or stretch marks.
- Do not inject AJOVY in the same injection site that you inject other medicine.
- If you want to use the same injection area for the 3 separate injections needed for the 675 mg dose, make sure the second and third injections are not at the same spot you used for the other injections.

Step 9. Remove protective cap and do not replace.
- Pick up the prefilled autoinjector in 1 hand.
- Hold the prefilled autoinjector as shown in Figure G and pull the protective cap straight off with your other hand. Do not twist.
- Throw away the protective cap right away.
Step 10. Give your injection.

10.1 Place the prefilled autoinjector at a 90 degree angle against your skin at the injection site you have cleaned (see Figure H).

10.2 Press down on the prefilled autoinjector and keep holding it down against the skin for about 30 seconds. Do not remove pressure until the 3 steps below are complete.

1. You hear the first “click” (this means the injection has started and the blue plunger starts to move).
2. You hear a second “click” (about 15 seconds after the first click. The plunger will be moving to the bottom of the viewing window as the medicine is being injected.)
3. You wait another 10 seconds. (to make sure all the medicine is injected).

10.3 Check that the blue plunger has filled the viewing window and remove the autoinjector from the skin by lifting the prefilled autoinjector straight up (see Figure I).

Note: When the blue plunger has filled the viewing window you will be able to see the gray stopper.

As the prefilled autoinjector is lifted from the skin, the needle shield returns to the original (before use) position and locks into place, covering the needle.

Do not try to put the protective cap back on the used prefilled autoinjector as it is no longer needed.

Do not try to re-use the prefilled autoinjector.

Step 11. Apply pressure to the injection site.

- Use a clean, dry cotton ball, or gauze pad to gently press on the injection site for a few seconds.
- Do not rub the injection site.
- Do not re-use the prefilled autoinjector.

Step 12. Dispose of your prefilled autoinjector right away.

- Put your used prefilled autoinjectors in a FDA-cleared sharps disposal container right away after use.
- Do not throw away (dispose of) prefilled autoinjectors in your household trash. Do not recycle your used sharps disposal container.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used autoinjectors. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Instructions for Use

AJOVY™ (a-JO-vee) (fremanezumab-vfrm) injection prefilled syringe, for subcutaneous use

For subcutaneous injection only.

Read and follow the Instructions for Use for your AJOVY prefilled syringe before you start using it and each time you get a refill.

Important:

- AJOVY prefilled syringe is for single-time (one-time) use only. Put AJOVY in a FDA-cleared sharps disposal or puncture-resistant container right away after use. Do not throw away (dispose of) your used sharps disposal container in your household trash.
- Before injecting, let AJOVY sit at room temperature for 30 minutes.
- Keep AJOVY prefilled syringe out of the reach of small children.
- After you remove the needle cap from AJOVY, to prevent infection, do not touch the needle.
- Do not pull back on the plunger at any time, as this can break the prefilled syringe.
- Do not inject AJOVY in your veins (intravenously).
How do I inject AJOVY?

Step 1. Check the dose your healthcare provider has prescribed. AJOVY comes as a single-dose (one time) prefilled syringe. Your healthcare provider will prescribe the dose that is best for you.

- If your healthcare provider has prescribed 225 mg of AJOVY each month for you, give 1 injection each month using a 225 mg prefilled AJOVY syringe.
- If your healthcare provider has prescribed 675 mg of AJOVY every 3 months for you, give 3 separate injections, one after another, using a different 225 mg prefilled AJOVY syringe for each injection. Give these injections 1 time every 3 months.

Before you inject, always check the label of your single-dose prefilled syringe to make sure you have the correct medicine and the correct dose of AJOVY. If you are not sure of your dose, ask your healthcare provider.

How do I inject AJOVY?

Step 2. Remove the prefilled syringe from the carton.

- You may need to use more than 1 prefilled syringe depending on your prescribed dose.
- Hold the prefilled syringe (as shown in Figure C).
- Remove the syringe from the carton.
- Do not shake the prefilled syringe at any time, as this could affect the way the medicine works.

Step 3. Gather the supplies you will need to inject AJOVY.

- Gather the following supplies (see Figure D) and the number of AJOVY 225 mg prefilled syringes you will need to give your prescribed dose:
  - If your dose is 225 mg, you will need 1 AJOVY 225 mg prefilled syringe.
  - If your dose is 675 mg, you will need 3 AJOVY 225 mg prefilled syringes.
  - alcohol swabs (not supplied).
  - gauze pads or cotton balls (not supplied).
  - sharps disposal or puncture-resistant container (not supplied).

Step 4. Let AJOVY reach room temperature.

- Place the supplies you have gathered on a clean, flat surface.
- Wait for 30 minutes to allow the medicine to reach room temperature.
- Do not leave the prefilled syringe in direct sunlight.
- Do not warm up the AJOVY prefilled syringe using a heat source such as hot water or a microwave.

Step 5. Wash your hands.

- Wash your hands with soap and water and dry well with a clean towel. Be careful not to touch your face or hair after washing your hands.

Step 6. Look closely at your AJOVY prefilled syringe.

Note: You may see air bubbles in the prefilled syringe. This is normal. Do not remove the air bubbles from the prefilled syringe before giving your injection. Injecting AJOVY with these air bubbles will not harm you.

- Check that the liquid medicine in the prefilled syringe is clear and colorless to slightly yellow before you give your injection (see Figure E). If the liquid has any particles in it, or is discolored, cloudy, or frozen, do not use the prefilled syringe. Call your healthcare provider or pharmacist.
- Do not use the prefilled syringe if it has any visible damage, such as cracks or leaks. See disposal instructions in Step 12.

- Check that AJOVY appears on the prefilled syringe.
- Do not use if you have been given the wrong medicine.

- Check the expiration date (EXP) printed on the prefilled syringe label.
- Do not use the prefilled syringe if the expiration date (EXP) has passed.
AJOVY® (fremanezumab-vfrm) injection

**Figure G**

Step 11. Remove the needle from your skin.
- After you have injected all of the medicine, **pull the needle straight out** (see Figure H).
- **Do not** recap the needle at any time to avoid injury and infection.

**Figure F**

**Note:** There are some injection areas on your body that are hard to reach (like the back of your arm). You may need help from someone who has been instructed on how to give your injection if you cannot reach certain injection areas.

Step 7. Choose your injection area.
- **Choose** an injection area from the following areas (see Figure F):
  - your **stomach area** (abdomen), avoid about 2 inches around the belly button.
  - the **front of your thighs**, an area that is at least 2 inches above the knee and 2 inches below the groin.
  - the **back of your upper arms**, in the fleshy area of the upper back portion.

Step 8. Clean your injection area.
- **Clean** the chosen injection area using a new alcohol swab. Let your skin dry.
- **Do not** inject AJOVY into an area that is tender, red, bruised, callused, tattooed, hard, or that has scars or stretch marks.
- **Do not** inject AJOVY in the same injection site that you inject other medicine.
- If you want to use the same injection area for the 3 separate injections needed for the 675 mg dose, make sure the second and third injections are not at the same spot you used for the other injections.

Step 9. Remove needle cap and do not replace.
- **Pick up** the body of the prefilled syringe with 1 hand.
- **Pull** the needle cap **straight off** with your other hand (see Figure G).
- **Do not** twist.
- **Throw away** the needle cap right away.
- **Do not** put the needle cap back on the prefilled syringe, to avoid injury and infection.

**Figure G**

Step 10. Give your injection following the 4 steps below.
1. **Use your free** hand to **gently pinch up** at least 1 inch of the skin that you have cleaned.
2. **Insert the** needle into the pinched skin at a 45 to 90 degree angle.
3. **When the** needle is all the way into your skin, **use your thumb to push the plunger.**
4. **Push the plunger slowly all the way down as far as it will go to inject all of the medicine.**

**Figure H**

Step 12. Apply pressure to the injection site.
- **Use a clean, dry cotton ball or gauze to gently press on the injection site** for a few seconds.
- **Do not** rub the injection site.
- **Do not** re-use the prefilled syringe.

Step 13. Dispose of your prefilled syringe right away.
- **Put your used prefilled syringes, needles, and sharps in a FDA-cleared sharps disposal container right away after use.**
- **Do not throw away** (dispose of) loose needles, syringes, or prefilled syringes in your household trash. Do not recycle your used sharps disposal container.
- **If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:**
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- **When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at:** http://www.fda.gov/safesharpsdisposal
- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. **Do not** recycle your used sharps disposal container.

Injection Complete

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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