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

**INDICATIONS AND USAGE**

AJOVY is a calcitonin gene-related peptide antagonist indicated for the preventive treatment of migraine in adults. (1)

**DOSE 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). (2,2)

- The 675 mg quarterly dosage is administered as three consecutive injections of 225 mg each. (2,2)

- For subcutaneous use only. (2,2)

**CONTRAINDICATIONS**

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).)

**PRECAUTIONS (5.1)**

**WARNINGS AND PRECAUTIONS**

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

**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.

Revised: 9/2021
AJOVY® (fremanezumab-vfrm) injection

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, and 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 1701 (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. Although 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 uncertain 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 Contraindications (4) and Warnings and Precautions (5.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure 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 using 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 Embryofetal 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-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 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 fetal development. The highest dose tested was associated with plasma AUC approximately 3 times that in humans (675 mg). Administration of fremanezumab-vfrm (0, 50, 100, or 200 mg/kg) weekly by subcutaneous injection to female rats throughout pregnancy and lactation resulted in no adverse effects on pre- and postnatal development. The highest dose tested was associated with plasma AUC approximately 2 times that in humans (675 mg).

8.2 Lactation

Risk Summary

There are no data on the presence of fremanezumab-vfrm 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 AJOVY and any potential adverse effects on the breastfed infant from AJOVY 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 AJOVY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

Fremanezumab-vfrm is a fully humanized lgG2a/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Fremanezumab-vfrm is produced by recombinant DNA technology in Chinese hamster ovary (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 1.5 mL of solution containing 225 mg fremanezumab-vfrm, disodium ethylendiaminetetraacetic acid dihydrate (EDTA) (0.04 mg), L-histidine (0.815 mg), L-histidine hydrochloride monohydrate (3.93 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.

12.2 Pharmacodynamics

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

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Fremanezumab-vfrm 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 02629661) 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.
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>Baseline migraine days</td>
<td>8.9</td>
<td>9.2</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>-1.5</td>
<td>-1.2</td>
<td>p-value &lt;0.001</td>
</tr>
<tr>
<td>&gt;50% MDD responders</td>
<td>47.7%</td>
<td>44.4%</td>
<td>27.5%</td>
</tr>
<tr>
<td>% responders</td>
<td>19.8%</td>
<td>16.5%</td>
<td>p-value &lt;0.001</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Monthly acute headache medication days</td>
<td>Change from baseline</td>
<td>-3.0</td>
<td>-2.9</td>
</tr>
<tr>
<td>Difference from placebo</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

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>p-value &lt;0.001</td>
</tr>
<tr>
<td>Change from baseline in the 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 &gt;50% reduction in monthly average number of headache days of at least moderate severity</td>
<td>40.8%</td>
<td>37.6%</td>
<td>18.1%</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>

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.
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No change or decrease in monthly average moderate-severity headache days per month

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=371)</td>
<td>0%</td>
</tr>
<tr>
<td>AJOVY 675 mg Quarterly (N=375)</td>
<td>10%</td>
</tr>
<tr>
<td>AJOVY 225 mg Monthly* (N=375)</td>
<td>15%</td>
</tr>
</tbody>
</table>

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

**HOW SUPPLIED/STORAGE AND HANDLING**

**16.1 How Supplied**

AJOVY (fremanezumab-vfrm) injection is a sterile, preservative-free, 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
  - Pack of 3 syringes: 3 x 225 mg/1.5 mL single-dose prefilled syringes

**16.2 Storage and Handling**

- Do not freeze.
- If necessary, AJOVY may be kept in the original carton at room temperature up to 30°C (86°F) for 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 shake.
- Do not expose to extreme heat or direct sunlight.
- Do not shake.

**17 PATIENT COUNSELING INFORMATION**

Advisors the patient and/or caregivers 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.
- Instruct patients and/or caregivers to read and follow the Instructions for Use each time they use AJOVY.

**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.

**Pregnancy**

- Advise women that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to AJOVY during pregnancy.

Manufactured by: Teva Pharmaceuticals USA, Inc. North Wales, PA 19454

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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-009

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
AJOPL-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: 9/2021

Instructions for Use

AJOVY® (a-JO-vee) (fremanezumab-vfrm) injection prefilled autoinjector, for subcutaneous use

For subcutaneous injection only.

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

Important:

• AJOVY prefilled autoinjector 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 autoinjector out of the reach of small children.
• After you remove the protective cap from AJOVY, to prevent infection, do not touch the needle.
• Do not inject AJOVY in your veins (intravenously).
• Do not re-use your AJOVY prefilled autoinjector as this could cause injury or infection.
• Do not share your AJOVY prefilled autoinjector with another person. You may give another person an infection or get an infection from them.

You may give AJOVY yourself. If you feel uncomfortable, you should not get your first dose of AJOVY until you or your caregiver receive training from a healthcare provider on the right way to use AJOVY.

Storage Conditions:

• 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.

AJOVY prefilled autoinjector (Before use). See Figure A.

AJOVY prefilled autoinjector (After use). See Figure B.

• The blue plunger moves down the viewing window during the injection. The blue plunger fills the window when the injection is complete. Note: When the blue plunger has filled the viewing window you will still be able to see the gray stopper, as shown in Figure B.
• When injecting AJOVY, hold the prefilled autoinjector so that your hand does not cover the viewing window.
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 AJOVY appears on the prefilled autoinjector.
- Check the expiration date (EXP) printed on the prefilled autoinjector label.
- Do not use the prefilled autoinjector if it has any visible damage, such as cracks or leaks. See disposal instructions in Step 12.

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.
AJOVY® (fremanezumab-vfrm) injection

- Throw away the protective cap right away.
- Do not put the protective cap back on the prefilled autoinjector, to avoid injury and infection.

**Figure G**

**Step 10. Give your injection.**

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

**Figure H**

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.**

   - 10.2 Press down on the prefilled autoinjector and keep holding it down against the skin for about 30 seconds.
   - 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 right away after use.

3. **You wait another 10 seconds. (to make sure all the medicine is injected).**

   **10 Seconds**

**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.

**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.
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 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.

**Injection Complete**

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

Manufactured by:
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North Wales, PA 19454
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AJOIFU-AI-004
Approved: 10/2020

**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).
- Do not re-use your AJOVY prefilled syringe, as this could cause injury or infection.
- Do not share your AJOVY prefilled syringe with another person. You may give another person an infection or get an infection from them.
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.

STOP
Read this before you inject.
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 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.

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.

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.

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:
    o made of a heavy-duty plastic,
    o can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    o upright and stable during use,
    o leak-resistant, and
    o 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.

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