

Product Monograph
Including Patient Medication Information

PrAJOVY®

Fremanezumab injection

CHO (Chinese Hamster Ovary) cells

solution for subcutaneous injection

225 mg in 1.5 mL (150 mg/mL) pre-filled syringe

225 mg in 1.5 mL (150 mg/mL) autoinjector

Professed Standard

Calcitonin Gene-related Peptide (CGRP) antagonist

Distributed by:

Teva Canada Limited

Toronto, Ontario M1B 2K9

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Teva Canada Innovation

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RECENT MAJOR LABEL CHANGES

1. Indications, 1.1 Pediatrics	2026/01
4. Dosage and Administration, 4.2 Recommended Dose and Dose Adjustment	2026/01
7.1 Special Populations 7.1.3 Pediatrics	2026/01

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Part 1: Healthcare Professional Information

1 INDICATIONS

PrAJOVY® (fremanezumab solution for subcutaneous injection) is indicated for:

- the prevention of migraine in adults who have at least 4 migraine days per month.
- the prevention of episodic migraine (fewer than 15 migraine days per month) in pediatric patients aged 6 to 17 years and weighing at least 45 kg.

AJOVY should be initiated by healthcare professionals experienced in the diagnosis and treatment of migraine.

1.1 Pediatrics

Pediatrics (6 to 17 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of AJOVY in pediatric patients 6-17 years, weighing at least 45 kg and with a clinical diagnosis of episodic migraine (fewer than 15 migraine days per month) have been established (see [Recommended Dose and Dosage Adjustment](#)). Therefore, Health Canada has authorized an indication for pediatric use in these patients.

The safety and efficacy of AJOVY in children below 6 years of age have not been established.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Clinical studies of AJOVY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. (See [WARNINGS AND PRECAUTIONS, Geriatrics](#))

2 CONTRAINDICATIONS

AJOVY (fremanezumab) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, (see [DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING](#)).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

AJOVY is administered subcutaneously through single dose prefilled syringes or single dose prefilled autoinjectors. AJOVY may be self-administered by patients 13 years of age and older, or administered by healthcare professionals and/or adult caregivers. In pediatric patients 6 to 12 years of age, AJOVY must be administered by a healthcare professional or adult caregiver. Administration should be performed by an individual who has been trained to administer the product. ([See Administration and Instructions for Use leaflets](#))

4.2 Recommended Dose and Dosage Adjustment

- Adults

Two subcutaneous dosing options of AJOVY are available to administer the recommended dosage ([See Clinical Trials](#)):

- 225 mg (1 subcutaneous injection) once a month (monthly dosing), or
- 675 mg (3 separate subcutaneous injections of 225 mg one after another) every 3 months (quarterly dosing).

The dose regimen must be followed as prescribed. Patients should be advised that monthly dosing consists of a single subcutaneous injection.

When switching dosage options, the first dose of the new regimen should be given on the next scheduled dosing date of the prior regimen.

- Pediatrics (6 to 17 years of age) and weighing at least 45 kg

The recommended dosage in pediatric patients aged 6 to 17 years, weighing at least 45 kg is:

- 225 mg (1 subcutaneous injection) once a month (monthly dosing)

Do not administer AJOVY to pediatric patients weighing less than 45 kg as an appropriate strength presentation is not available. ([see CLINICAL TRIALS](#)).

For both adult and pediatric patients, the treatment benefit should be assessed within 3 months after initiation of the treatment. Any further decision to continue treatment should be taken on an individual patient basis. Evaluation of the need to continue treatment is recommended regularly thereafter. ([See CLINICAL TRIALS](#)).

4.4 Administration

AJOVY is for subcutaneous use only.

AJOVY may be administered by healthcare professionals, patients and/or caregivers. Only healthcare professionals and/or caregivers may administer AJOVY to pediatric patients aged 12 years and younger.

Prior to use, provide proper training to patients and/or caregivers on the preparation and administration of AJOVY prefilled syringe or prefilled autoinjector, including aseptic technique [\[see respective Instructions for Use\]](#).

- 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. [\(See STORAGE, STABILITY AND DISPOSAL\)](#).
- Follow aseptic injection technique every time AJOVY is administered. Inspect AJOVY for particles or discoloration prior to administration. Do not use if the solution is cloudy, discoloured, or contains particles. [\(See DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING\)](#).
- Administer AJOVY by subcutaneous injection into areas of 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.
- Do not co-administer AJOVY with other injectable drugs at the same injection site

4.5 Missed Dose

If an AJOVY injection is missed on the planned date, the missed dose should be administered as soon as possible. The regular dosing regimen should resume from the new dosing day.

A double dose must not be administered to make up for a missed dose.

5 OVERDOSE

In case of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse effects and given appropriate symptomatic treatment if necessary.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous injection	Injection: 225 mg/1.5 mL solution in a single- dose prefilled syringe Injection: 225 mg/1.5 mL solution in a single-dose prefilled autoinjector	Disodium ethylenediaminetetraacetic acid dihydrate (EDTA), L-histidine, polysorbate 80, sucrose, and Water for Injection.

AJOVY is a sterile, preservative-free, clear to opalescent, colourless to slightly yellow solution practically free from particles.

AJOVY prefilled syringe cap is not made with natural rubber latex. AJOVY prefilled syringe cap is made from natural latex-free material.

Prefilled Syringe

AJOVY is supplied as a carton of one 225 mg/1.5 mL (150 mg/mL) single-dose pre-filled syringe.

Prefilled Autoinjector

AJOVY is supplied as a carton of one 225 mg/1.5 mL (150 mg/mL) single-dose prefilled autoinjector

Description

AJOVY contains fremanezumab, a fully humanized IgG2Δa/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Fremanezumab is produced by recombinant DNA technology in Chinese hamster ovary (CHO) cells. The antibody consists of 1324 amino acids and has a molecular weight of approximately 148 kDa.

7 WARNINGS AND PRECAUTIONS

Cardiovascular

No safety data are available in these populations. Patients with significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism were excluded from the clinical trials. (See [CLINICAL TRIALS](#)).

Hepatic/Biliary/Pancreatic/Renal

No safety data are available in these populations. Fremanezumab as a monoclonal antibody is not expected to undergo hepatic metabolism or renal clearance. Patients with severe hepatic impairment and severe renal impairment (eGFR <30 mL/min/1.73 m²) have not been studied in AJOVY clinical trials. (See [CLINICAL TRIALS](#)).

Sensitivity/Resistance

Serious hypersensitivity reactions, including rash, angioedema, and anaphylactic reactions, were reported with the CGRP- class products including AJOVY in clinical trials and in post-market experience.

These reactions may occur within minutes, although some may occur up to one month after administration.

If a hypersensitivity reaction occurs, consider discontinuing AJOVY, and institute appropriate therapy.

7.1 Special Populations

7.1.1 Pregnancy

There are no adequate data on the developmental risk associated with the use of AJOVY in pregnant individuals. AJOVY has a long half-life (see [CLINICAL PHARMACOLOGY](#)). This should be taken into consideration for individuals who are pregnant or plan to become pregnant while using AJOVY. (See [Non-Clinical Toxicology](#)).

7.1.2 Breast-feeding

It is unknown if the drug is excreted in human milk. Because many drugs are excreted in human milk, precaution should be exercised.

There are no data on the presence of fremanezumab 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.

7.1.3 Pediatrics

Episodic migraine

Safety and efficacy of AJOVY in patients aged 6-17 years and older, suffering from episodic migraine and weighing at least 45 kg have been established, and are similar to the safety and efficacy profile seen in clinical trials in adults with migraine.

The safety and efficacy of AJOVY in children below 6 years of age have not been established.

Chronic migraine

The safety and efficacy of AJOVY in pediatric patients (<18 years of age) with chronic migraine have not been established.

Bone growth and development (pediatrics): Longterm effects of CGRP pathway inhibition on skeletal growth and maturation in children are unknown. In the pediatric program, growth and puberty were monitored (e.g., height/weight; Tanner staging); however, clinical exposure is limited in duration, which may be insufficient to detect delayed changes. Health care

professionals should periodically monitor growth velocity and pubertal development during treatment (e.g., height z-scores and Tanner staging), and reassess therapy if concerns arise.

7.1.4 Geriatrics

Geriatrics (≥ 65 years of age): Clinical studies of AJOVY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Adults

Hypersensitivity reactions, including rash, pruritus and urticaria were reported with fremanezumab in less than 1% of patients in clinical trials. Most reactions were mild to moderate, but some led to discontinuation or required corticosteroid treatment. Most reactions were reported from within hours to one month after administration.

Hypersensitivity reactions, including urticaria, pruritus, rash and swelling/edema have also been reported with fremanezumab in post-marketing experience.

Very common reported adverse drug reactions (ADRs) from the clinical trials were local reactions at the injection site pain, induration, erythema and pruritus.

The adverse reactions that most commonly led to discontinuations were injection site reactions.

Pediatrics

No new clinical trial safety findings were noted for AJOVY use in the pediatric population compared to the known safety profile from the adult clinical trials.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

The safety of AJOVY was evaluated in 2512 adult patients with migraine who received at least one dose of AJOVY 225 mg monthly or AJOVY 675 mg quarterly for at least six months; 775 patients for at least 12 months; and 138 patients for at least 15 months. In placebo-controlled clinical trials (Studies 1 and 2), 662 patients received AJOVY 225 mg monthly for 12 weeks (with or without a loading dose of 675 mg), and 663 patients received AJOVY 675 mg quarterly for 12 weeks (See CLINICAL TRIALS) . In the controlled trials, 87% of patients were female, 80% were White, and the mean age was 41 years.

The most common adverse reactions in the clinical trials for the preventive treatment of migraine were injection site reactions. The adverse reactions that most commonly led to discontinuations were injection site reactions.

Patients with significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism were excluded from the clinical trials. (See CLINICAL TRIALS)

Table 2: Adverse Reactions Occurring with an Incidence of $\geq 1\%$ and Greater Than Placebo in Episodic and Chronic Migraine Studies

System Organ Class Preferred Term	AJOVY 225 mg monthly N=290	AJOVY 675 mg quarterly N=667	Placebo N=668
Injection site reactions*	43 %	45 %	38 %

*Injection site reactions include multiple related adverse event terms, such as injection site pain, induration, and erythema

Table 3: Treatment Emergent adverse events occurring with an incidence of $\geq 1\%$ in the Placebo Controlled Studies

System Organ Class Preferred Term	AJOVY 225 mg monthly N=290 n= (%)	AJOVY 675 mg quarterly N=667 n= (%)	Placebo N=668 n= (%)
Patients with at least 1 AE	192 (66)	458 (69)	411 (62)

System Organ Class Preferred Term	AJOVY 225 mg monthly N=290 n= (%)	AJOVY 675 mg quarterly N=667 n= (%)	Placebo N=668 n= (%)
Gastrointestinal Disorders			
Nausea	4 (1)	11 (2)	16 (2)
Diarrhoea	2 (<1)	5 (<1)	8 (1)
General disorders and administration site conditions			
Injection site pain	87 (30)	200 (30)	180 (27)
Injection site induration	71 (24)	131 (20)	113 (17)
Injection site erythema	52 (18)	135 (20)	101 (15)
Injection site haemorrhage	3 (1)	16 (2)	16 (2)
Injection site pruritus	4 (1)	10 (1)	2 (<1)
Fatigue	2 (<1)	9 (1)	9 (1)
Injection site rash	3 (1)	5 (<1)	0
Injection site swelling	3 (1)	4 (<1)	0
Infections and infestations			
Upper respiratory tract infection	16 (6)	29 (4)	30 (4)
Nasopharyngitis	11 (4)	30 (4)	29 (4)
Urinary tract infection	7 (2)	14 (2)	11 (2)
Bronchitis	6 (2)	9 (1)	6 (<1)
Sinusitis	4 (1)	12 (2)	18 (3)
Influenza	2 (<1)	8 (1)	(1)
Gastroenteritis	4 (1)	4 (<1)	5 (<1)
Cystitis	3 (1)	1 (<1)	1 (<1)

System Organ Class Preferred Term	AJOVY 225 mg monthly N=290 n= (%)	AJOVY 675 mg quarterly N=667 n= (%)	Placebo N=668 n= (%)
Herpes zoster	3 (1)	0	1 (<1)
Injury, poisoning and procedural complications			
Ligament sprain	1 (<1)	3 (<1)	2 (<1)
Investigations			
Blood creatine phosphokinase increased	1 (<1)	3 (<1)	7 (1)
Alanine aminotransferase increased	1 (<1)	3 (<1)	1 (<1)
Aspartate aminotransferase increased	1 (<1)	3 (<1)	1 (<1)
Musculoskeletal and connective tissue disorders			
Back pain	3 (1)	11 (2)	9 (1)
Musculoskeletal pain	3 (1)	4 (<1)	0
Arthralgia	3 (1)	2 (<1)	1 (<1)
Nervous system disorders			
Dizziness	3 (1)	9 (1)	9 (1)
Paraesthesia	2 (<1)	9 (1)	4 (<1)
Migraine	1 (<1)	6 (<1)	11 (2)
Respiratory, thoracic and mediastinal disorders			
Cough	1 (<1)	8 (1)	6 (<1)
Skin and subcutaneous tissue disorders			
Pruritus	0	8 (1)	1 (<1)

Injection site reactions

The most frequently observed local reactions at the injection site were pain, induration and erythema. Most local injection site reactions were transient and predominantly mild to moderate in severity. Pain, induration and erythema were typically observed immediately after injection while pruritus and rash appeared within a median of 24 and 48 hours, respectively. Most injection site reactions resolved, generally within a few hours or days. If the intensity of Injection site reactions is severe, discontinuation of fremanezumab should be considered.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Over 400 pediatric patients with migraine, 6 to 17 years of age, have been treated with AJOVY in registration studies. This included 123 pediatric patients in the placebo-controlled trial with episodic migraine (EM). The only adverse reactions of AJOVY observed in this study were injection site reactions, which is similar to the overall safety profile observed in adult clinical studies. The injection site reactions reported were injection site erythema, injection site pain, and injection site swelling. Table 4 summarizes adverse reactions reported in the 3-month placebo-controlled study.

Table 4: Adverse Reactions Occurring with an Incidence of \geq 1% in Pediatric Patients with Episodic Migraine

Adverse Reaction	AJOVY N=123 n= (%)	Placebo N=112 n= (%)
Injection site reactions ^a	20 (%)	12 (%)

^aInjection site reactions include multiple related adverse event terms, such as injection site erythema, swelling, and pain.

8.3 Less Common Clinical Trial Adverse Reactions

From all clinical trials with AJOVY in adult patients with chronic and episodic migraine, the following less common adverse events of <1% have been observed. Causality to AJOVY has not been established.

Cardiac disorders (palpitations, angina pectoris).

Eyes disorders (vision blurred, diplopia, eye irritations).

Gastrointestinal disorders (nausea, diarrhea, constipation, vomiting, abdominal distension).

General disorders (chest pain, malaise).

Hepatobiliary disorders (weight increased, Gamma-glutamyltransferase increased).

Musculoskeletal and connective tissue disorders (pain, myalgia).

Nervous system disorders (migraine, headache, somnolence).

Psychiatric disorders (insomnia, anxiety, depression, suicidal ideation).

Skin disorders (rash, urticaria)

Vascular disorder (hypertension)

8.5 Post-Market Adverse Reactions

The following adverse reactions are based on post-marketing spontaneous reports. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate the frequency.

Isolated cases of serious hypersensitivity reactions including angioedema and anaphylaxis have been reported in the post-marketing experience.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No formal clinical drug interaction studies have been performed with AJOVY. 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. Furthermore, concomitant use of acute migraine treatments (specifically analgesics, ergots and triptans) and preventive treatment of migraine were found not to influence fremanezumab exposure.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

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

10.2 Pharmacodynamics

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

10.3 Pharmacokinetics

Table 5 provides a summary of the pharmacokinetic parameters of fremanezumab following subcutaneous administration in adult healthy participants and adult and pediatric migraine patients.

Table 5: Summary of mean (%CV) pharmacokinetic parameters of fremanezumab in healthy participants and migraine patients after subcutaneous doses

Dose regimen	Age group	Population	C _{max} ^a (µg/mL)	AUC ^b (µg×day/mL)	Clearance ^c (L/day)	Volume of distribution ^d (L)	t _{1/2} (day)
225 mg single dose	Adults	Healthy participants	29.7 (13.7)	1771 (17.5)	0.129 (17.8)	6.43 (14.0)	35.0 (11.5)
675 mg single dose			104.8 (28.8)	5534 (31.7)	0.127 (30.1)	5.71 (27.5)	32.2 (21.5)
225 mg monthly ^e		Migraine patients	71.2 (29.2)	1670 (31.2)	0.098 (33.0)	2.02 (34.4)	30.4 (21.3)
675 mg quarterly ^e			116 (24.3)	5050 (31.0)			
225 mg monthly ^e	Pediatrics 6 to 17 years weighing at least 45 kg	Migraine patients	93.5 (12.9)	1744 (13.4)	0.110 (28.5)	1.55 (467.9)	-

^aC_{max} for single dose and C_{max,ss} for multiple doses; ^bAUC_{0-∞} for single dose and AUC_{τ,ss} for multiple doses; ^cCL/F from NCA for single dose and CL from population PK for multiple doses; ^dV_z/F from NCA for single dose and V_c from population PK for multiple doses; ^eestimated by population PK analysis.

AUC_{0-∞}: area under the concentration-time curve from time of dosing to infinity; AUC_{τ,ss}: area under the concentration-time curve for a dosing interval at steady state; C_{max}: maximum concentration; C_{max,ss}: maximum concentration during a dosing interval at steady state; CL: clearance; CL/F: apparent clearance; V_c= central volume of distribution; V_z/F=apparent volume of distribution during the terminal phase.

Absorption

After single subcutaneous administrations of 225 mg, 675 mg and 900mg fremanezumab, median time to maximum concentrations (t_{max}) in healthy subjects was 5 to 7 days. Dose proportionality, based on population pharmacokinetics, was observed from 225 mg to 900

mg. The absolute bioavailability was 54% and 57% for doses at 225 mg and 900 mg, respectively. Steady state was achieved by approximately 168 days (about 6 months) following 225 mg monthly and 675 mg quarterly dosing regimens. Median accumulation ratio, based on once monthly and once quarterly dosing regimens, is approximately 2.4 and 1.2, respectively.

Distribution

The apparent volume of distribution was approximately 6 L following subcutaneous administration of fremanezumab.

Metabolism

Similar to other monoclonal antibodies, fremanezumab is expected to be degraded by enzymatic proteolysis into small peptides and amino acids.

Elimination

Based on a population pharmacokinetic analysis, the estimated apparent clearance was 0.14 L/day (23% CV) and the estimated half-life was 30 days (21% CV) following subcutaneous administration of fremanezumab.

Special Populations and Conditions

Pediatrics

Based on population pharmacokinetic analysis of pediatric patients with migraine, fremanezumab has an apparent volume of distribution of approximately 3.19 L and an apparent clearance of 0.0974 L/day. Following subcutaneous administration of 225 mg fremanezumab monthly in the pediatric population weighing at least 45 kg, the predicted steady-state exposures (maximum plasma concentration [C_{max}], area under the plasma concentration-time curve [AUC], average plasma concentration [C_{av}]) to fremanezumab generally overlapped with those of adults, with 31% higher mean C_{max} and approximately 4% higher mean AUC and C_{av} in the pediatric population.

Hepatic Insufficiency

No dedicated hepatic/renal impairment studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of fremanezumab. Population pharmacokinetic analysis did not reveal a difference in the pharmacokinetics of fremanezumab in patients with hepatic or renal impairment relative to those with normal hepatic or renal function. Patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) have not been studied in AJOVY clinical trials.

10.4 Immunogenicity

All therapeutic proteins have the 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 sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

In 3-month placebo-controlled studies, 0.4 % of patients (6 out of 1,701) treated with fremanezumab developed anti-drug antibodies (ADA). The antibody responses were of low titer. One of these 6 patients developed neutralizing antibodies. With 12 months of treatment, ADA were detected in 2.3% of the patients (38 out of 1,888) with 0.95% of the patients developing neutralizing antibodies.

In a 3-month placebo-controlled study in pediatric patients 6 to 17 years of age with episodic migraine (TV48125-CNS-30083), 1.6% (2 of 123) of participants treated with fremanezumab tested positive for treatment-emergent ADA. Neutralizing antibodies were observed in one of the two participants who developed treatment-emergent ADA (overall 1 of 123, 0.8%).

11 STORAGE, STABILITY AND DISPOSAL

- Store refrigerated at 2°C to 8°C in the original outer carton to protect from light until time of use.
- If necessary, AJOVY may be kept in the original carton at room temperature up to 25°C for a maximum of 7 days. After removal from the refrigerator, AJOVY must be used within 7 days or discarded.
- Do not freeze. Do not expose to extreme heat or direct sunlight. Do not shake.
- Disposal: Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

12 SPECIAL HANDLING INSTRUCTIONS

- Detailed instructions for use are provided respectively for the prefilled syringe, and the prefilled autoinjector at the end of the package leaflet and must be followed step-by-step carefully.

- The prefilled syringe and the prefilled autoinjector are each for single use only.
- AJOVY should not be used if the solution is cloudy or discoloured or contains particles.
 - AJOVY should not be used if the solution has been frozen.
- The prefilled syringe and the prefilled autoinjector should not be shaken.

Part 2: Scientific Information

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: fremanezumab

Chemical name: Immunoglobulin G2, anti-(human alpha-calcitonin gene-related peptide/beta-calcitonin gene-related peptide)

Molecular formula and molecular mass: $C_{6470}H_{9952}N_{1716}O_{2016}S_{46}$ - Approximately 148 kDa

Structural formula: fremanezumab is composed of 2 heavy chains, each predicted to contain 448 amino acids residues and 2 light chains containing 214 amino acid residues.

Physicochemical properties: AJOVY (fremanezumab) injection is a sterile, preservative-free, clear to opalescent, colorless to slightly yellow solution for subcutaneous administration with a pH of 5.5.

Pharmaceutical standard: Professed

Product Characteristics:

Fremanezumab is a fully humanized IgG2Δa/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Fremanezumab is produced by recombinant DNA technology in Chinese hamster ovary (CHO) cells. The antibody consists of 1324 amino acids and has a molecular weight of approximately 148 kDa.

Each prefilled syringe and prefilled autoinjector delivers 1.5 mL of solution containing 225 mg fremanezumab, disodium ethylenediaminetetraacetic acid dihydrate (EDTA) (0.204 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.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Adults – Episodic Migraine

The efficacy of AJOVY was evaluated as a preventive treatment of episodic migraine in adult patients in a multicenter, randomized, 3-month, double-blind, placebo-controlled study TV48125-CNS-30050.

Table 6: Summary of Patient Demographics in Episodic Migraine Study TV48125-CNS-30050

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
TV48125-CNS-30050 (Efficacy and safety) Episodic migraine	Randomized, double-blind, placebo-controlled, parallel-group study	3-month treatment period ^a : sc PBO monthly (PBO/PBO/PBO) sc fremanezumab at 675 mg followed by monthly doses of PBO (675 mg/PBO/PBO) sc fremanezumab 225 mg monthly (225/225/225 mg)	Enrolled: 875 Treated: 874 Completed: 791	41.8 (18-70)	M: 133(15%) F: 742 (85%)

^aIn order to maintain blinding throughout the study, the number of injections at each visit was the same for all patients regardless of the treatment group to which they were randomized.

AJOVY was evaluated for the preventive treatment of episodic migraine in study TV48125-CNS-30050 which 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. Randomization was stratified based on sex, country, and baseline preventive migraine medication use (yes, no). The total number of patients who received concomitant migraine preventive medication during the study was pre-specified not to exceed 30% of the total sample size of the study. Overall, 21% of randomized patients received concomitant migraine preventive medication during the study.

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.

Headache information was captured daily throughout study participation using the electronic headache diary device. 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 TV48125-CNS-30050, a total of 875 patients (742 females, 133 males), ranging in age from 18 to 70 years, were randomized. A total of 791 (90.4%) patients completed the 3-month double-blind phase.

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 7.

Table 7: Results of study TV48125-CNS-30050 in Episodic Migraine- Adults

Efficacy Endpoint	Placebo (n=290)	Fremanezumab 675 mg quarterly (n=288)	Fremanezumab 225 mg monthly (n=287)
Monthly Migraine Days (MMD)			
Baseline MMD	9.1	9.2	8.9
LS mean change from baseline ^a	-2.2	-3.4	-3.7
LS mean difference from placebo (95% CI) ^a	-	-1.2 (-1.74, -0.69)	-1.4 (-1.96, 0.90)
<i>P-value (vs. placebo)^a</i>	-	<i>p</i> <0.0001	<i>p</i> <0.0001
50% Responder Rate MMD			

Efficacy Endpoint	Placebo (n=290)	Fremanezumab 675 mg quarterly (n=288)	Fremanezumab 225 mg monthly (n=287)
Percentage [%]	27.9%	44.4%	47.7%
Estimated difference from placebo (95% CI)	-	16.5 (8.8, 24.2)	19.8 (12.1, 27.6)
<i>P-value (vs. placebo)^b</i>	-	<i>p<0.0001</i>	<i>p<0.0001</i>
Monthly Acute Headache Medication Days (MAHMD)			
Baseline MAHMD	7.7	7.7	7.7
LS mean change from baseline ^a	-1.6	-2.9	-3.0
LS mean difference from placebo (95% CI) ^a	-	-1.3 (-1.73, -0.78)	-1.3 (-1.81, -0.86)
<i>P-value (vs. placebo)^a</i>	-	<i>p<0.0001</i>	<i>p<0.0001</i>

FAS (Full Analysis Set): Includes all randomized patients who received at least 1 dose of study drug and had at least 10 days of post-baseline efficacy assessments on the primary endpoint.

CI = confidence interval

LS = least squares

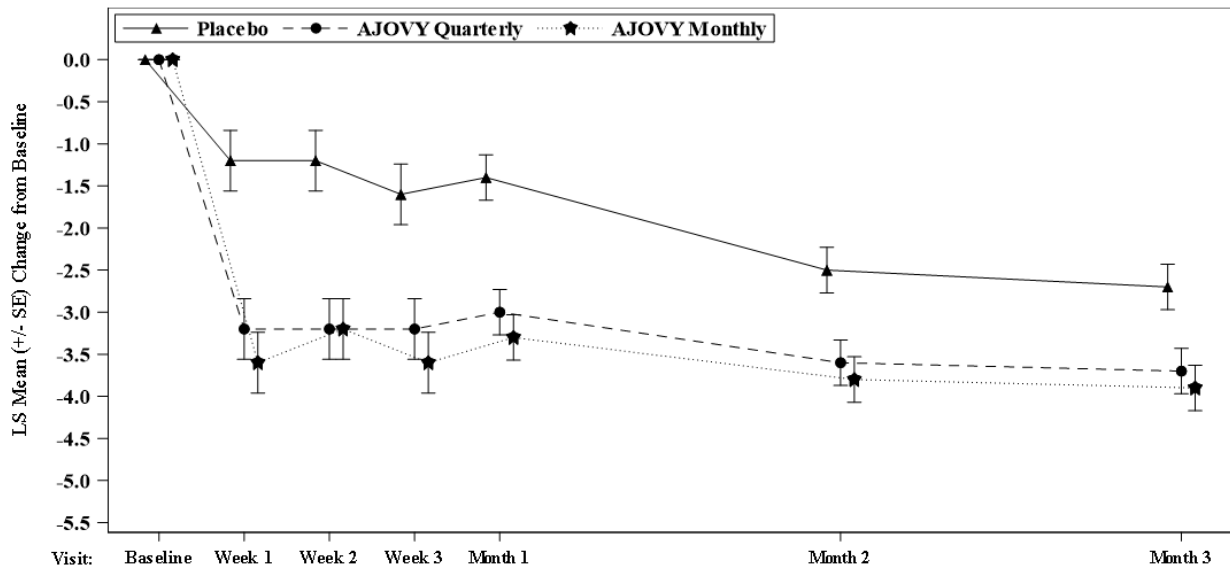
A fixed-sequence (hierarchical) testing procedure was implemented to control the type 1 error rate at 0.05.

^a Based on the ANCOVA model that included treatment, gender, region, and baseline preventive medication use (yes/no) as fixed effects and corresponding baseline value and years since onset of migraine as covariates.

^b P-value was based on the Cochran-Mantel-Haenszel test stratified by baseline preventive medication use (yes/no). The early discontinued patients were considered as non-responders for overall analysis.

Figure 1 displays the mean change from baseline in the average of monthly number of migraine days in Study TV45128-CNS-30050.

Figure 1: Mean Change from Baseline in the Monthly Average Number of Migraine Days for TV45128-CNS-30050



Note: Least squares (LS) mean and standard error (SE) of the mean are presumed in the figure.

Adults – Chronic Migraine

Table 4: Summary of patient demographics for clinical trials in Adult Patients with Chronic Migraine

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
TV48125-CNS-30049 (Efficacy and safety) Chronic migraine	Randomized, double-blind, placebo-controlled, parallel-group study	3-month treatment period ^a : sc PBO monthly (PBO/PBO/PBO) sc fremanezumab at 675 mg followed by monthly doses of PBO (675 mg/PBO/PBO) sc fremanezumab 225 mg monthly with a starting dose of 675 mg (675/225/225 mg)	Enrolled:1130 Treated: 1130 Completed: 1034	41.3 (18-71)	M: 139 (12%) F: 991 (88%)

^aIn order to maintain blinding throughout the study, the number of injections at each visit was the same for all patients regardless of the treatment group to which they were randomized.

The study 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. Randomization was stratified based on sex, country, and baseline preventive migraine medication use (yes, no). The total number of patients who received concomitant migraine preventive medication during the study was pre-specified not to exceed 30% of the total sample size of the study. Overall, 21% of randomized patients received concomitant migraine preventive medication during the study.

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.

Headache information was captured daily throughout study participation using the electronic headache diary device. 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 TV48125-CNS-30049, a total of 1130 patients (991 females, 139 males), ranging in age from 18 to 70 years, were randomized. A total of 1034 (91.5%) patients completed the 3-month double-blind phase.

Table 5: Key Efficacy outcomes in Chronic Migraine – Study TV48125-CNS-30049 Based on FAS

Efficacy Endpoint	Placebo (n=371)	Fremanezumab 675 mg quarterly (n=375)	Fremanezumab 225 mg monthly with 675 mg starting dose (n=375)
Monthly Headache Days of At Least Moderate Severity (MHD)			
Baseline MHD	13.3	13.2	12.8
LS mean change from baseline ^a	-2.5	-4.3	-4.6
LS mean difference from placebo (95% CI) ^a	-	-1.8 (-2.45, -1.13)	-2.1 (-2.77, -1.46)
<i>P-value (vs. placebo)^a</i>	-	<i>p<0.0001</i>	<i>p<0.0001</i>

Efficacy Endpoint	Placebo (n=371)	Fremanezumab 675 mg quarterly (n=375)	Fremanezumab 225 mg monthly with 675 mg starting dose (n=375)
Monthly Migraine Days (MMD)			
Baseline MMD	16.3	16.2	16.0
LS mean change from baseline ^a	-3.2	-4.9	-5.0
LS mean difference from placebo (95% CI) ^a	-	-1.7 (-2.44, -0.92)	-1.9 (-2.61, -1.09)
<i>P-value (vs. placebo)^a</i>	-	<i>p<0.0001</i>	<i>p<0.0001</i>
50% Responder Rate MHD			
Percentage [%]	18.1%	37.6%	40.8%
Estimated difference from placebo (95% CI)	-	19.5 (13.2, 25.7)	22.9 (16.5, 29.2)
<i>P-value (vs. placebo)^b</i>	-	<i>p<0.0001</i>	<i>p<0.0001</i>
Monthly Acute Headache Medication Days (MAHMD)			
Baseline MAHMD	13.0	13.1	13.1
LS mean change from baseline ^a	-1.9	-3.7	-4.2

FAS (Full Analysis Set): Includes all randomized patients who received at least 1 dose of study drug and had at least 10 days of post-baseline efficacy assessments on the primary endpoint.

CI = confidence interval

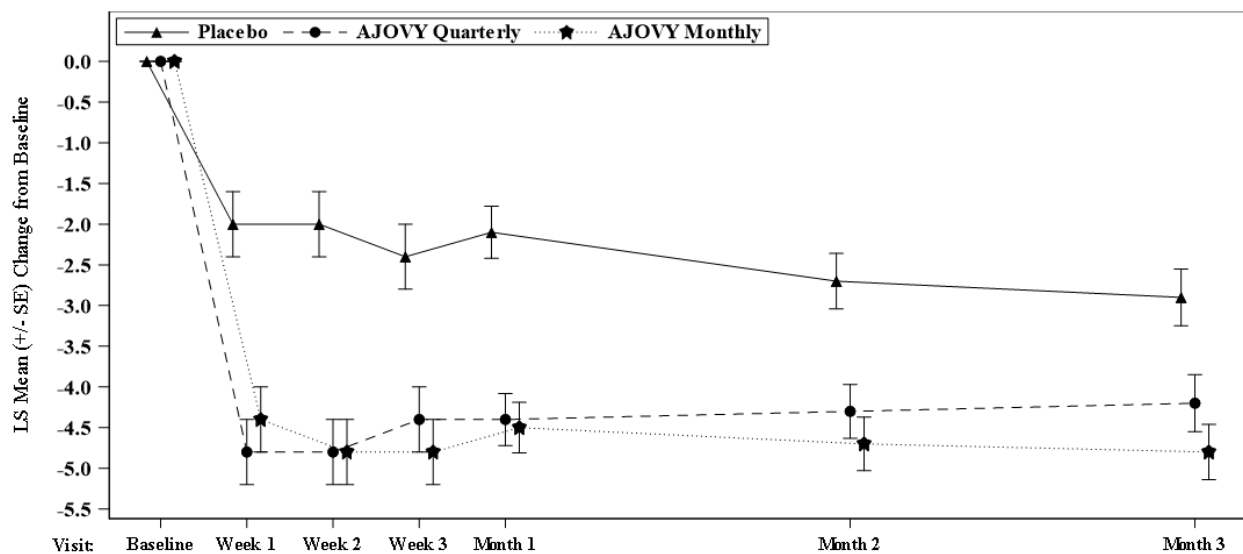
LS = least squares

A fixed-sequence (hierarchical) testing procedure was implemented to control the type 1 error rate at 0.05.

^a Based on the ANCOVA model that included treatment, gender, region, and baseline preventive medication use (yes/no) as fixed effects and corresponding baseline value and years since onset of migraine as covariates.

^b P-value was based on the Cochran-Mantel-Haenszel test stratified by baseline preventive medication use (yes/no). The early discontinued patients were considered as non-responders for overall analysis.

Figure 2: Mean Change from Baseline in the Monthly Average Number of Headache Days of At Least Moderate Severity for Study TV48125-CNS-30049



Note: Least squares (LS) mean and standard error (SE) of the mean are presumed in the figure.

Difficult to treat migraine

The efficacy and safety of fremanezumab in a total of 838 episodic and chronic migraine patients with documented inadequate response to two to four classes of prior migraine preventive medicinal products was assessed in a randomised study (FOCUS), which was composed of a 12-week double-blind, placebo-controlled treatment period.

All patients were randomized (1:1:1) to receive subcutaneous injections of either AJOVY 675 mg every three months (quarterly), AJOVY 225 mg monthly (with the starting dose 675 mg for chronic migraine only), or placebo monthly. Randomization was stratified based on sex,

country, and a special treatment failure group defined as having documented inadequate response to valproic acid and 2 to 4 classes of prior preventive migraine medications. Patients were allowed to use acute headache treatments during the study.

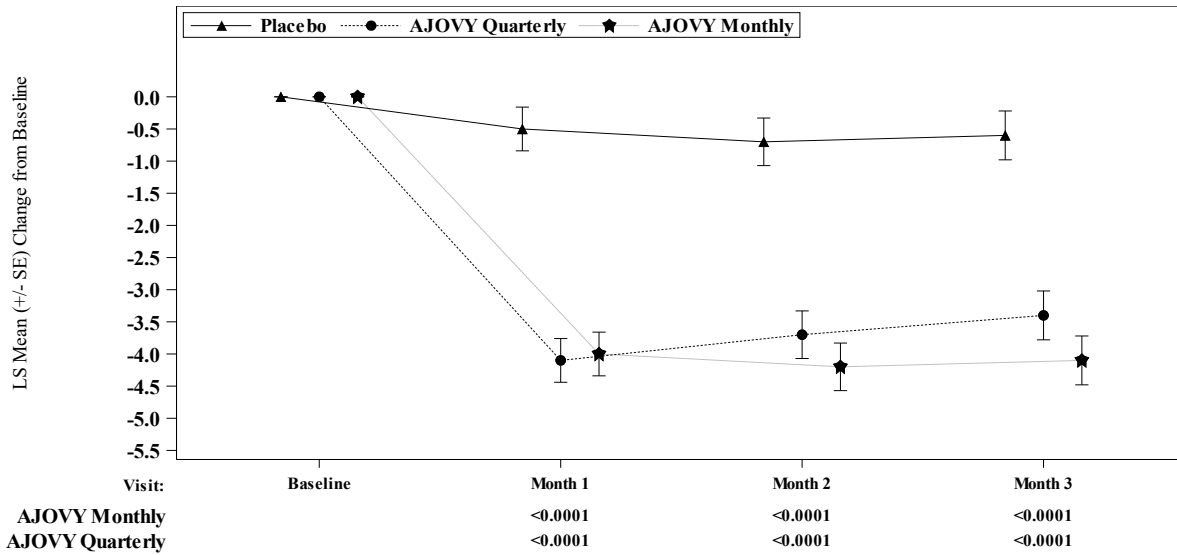
The study excluded patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism. A total of 838 patients (700 females, 138 males), ranging in age from 18 to 70 years, were randomized. A total of 807 (96.3%) patients completed the 3-month double-blind phase.

Headache information was captured daily throughout study participation using the electronic headache diary device. The primary efficacy endpoint was the mean change from baseline in the monthly average number of migraine days during the 12-week double-blind treatment period. Key secondary endpoints were the achievement of at least 50% reduction from baseline in monthly migraine days, the mean change from baseline in the monthly average number of headache days of at least moderate severity and change from baseline in monthly average number of days of acute headache medicinal product use.

Both monthly and quarterly dosing regimens of fremanezumab demonstrated statistically significant and clinically meaningful improvement from baseline compared to placebo for key endpoints.

For the primary endpoint, the mean reduction in monthly migraine days (MMD) were -3.7 (95% CI: -4.38, -3.05) in fremanezumab quarterly group and -4.1 (95% CI: -4.73, -3.41) in fremanezumab monthly group compared to -0.6 (95% CI: -1.25, 0.07) in placebo group. 34% of patients in fremanezumab quarterly group and 34% of patients in fremanezumab monthly group achieved at least 50% reduction in MMD, during the 12-week treatment period, compared to 9% of patients in placebo group ($p < 0.0001$). The effect also occurred from as early as the first month and was sustained over the 12-week double-blind treatment period.

Figure 3: Mean Change from Baseline in Monthly Average Number of Migraine Days for Difficult to Treat Migraine - FOCUS Study



Mean at baseline (monthly average number of migraine days): Placebo: 14.4, AJOVY Quarterly: 14.1, AJOVY Monthly: 14.1.

Note: Least squares (LS) mean and standard error (SE) of the mean are presumed in the figure.

Pediatrics (6 to 17 years of age) EPISODIC MIGRAINE

The efficacy of AJOVY was evaluated as a preventive treatment of episodic migraine in pediatric patients 6 to 17 years of age in one multicenter, randomized, 3-month, double-blind, placebo-controlled study (TV48125-CNS-30083).

Table 10: Summary of patient demographics for clinical trials in Pediatric Patients with Episodic Migraine

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
TV48125-CNS-30083 (Efficacy and safety) Episodic migraine	Randomized, double-blind, placebo-controlled, group study	3-month treatment period sc fremanezumab 225 mg or 120 mg, or placebo monthly	Enrolled: 235 Treated: 235 Completed: 225	13.3 (6 – 17)	M: 105 (45%) F: 130 (55%)

The study included pediatric patients 6 to 17 years of age with a history of episodic migraine (patients with <15 headache days per month). All participants were randomized (1:1) to receive subcutaneous injections of either AJOVY or placebo monthly, over a 3-month period. Patients who weighed 45 kg or more received 225 mg fremanezumab and patients who weighed under 45 kg received 120 mg fremanezumab. Patients were allowed to use acute headache treatments during the study. A subset of patients (21%) was allowed to use one or two additional concomitant preventive medication(s). The study excluded patients with clinically significant cardiovascular disease. Efficacy measures were derived from headache variables collected daily using an electronic diary device.

The primary endpoint was the mean change from baseline (28-day baseline period) in the monthly average number of migraine days during the 12-week period after the first dose of trial drug.

Secondary endpoints included:

- Mean change from baseline (28-day baseline period) in monthly average number of headache days of at least moderate severity during the 12-week period after the first dose of trial drug.
- Proportion of patients reaching at least 50% reduction in the monthly average number of migraine days during the 12-week period after the first dose of trial drug.
- Mean change from baseline (28-day baseline period) in the monthly average number of days of use of any acute headache medications during the 12-week period after the first dose of trial drug.

In study 30083, a total of 235 patients were randomized. A total of 225 patients completed the 3-month, double-blind treatment period.

Table 11: Efficacy Endpoints in Study TV48125-CNS-30083 Based on Full Analysis Set (FAS)

Efficacy Endpoint	Placebo (N=111) *	Fremanezumab combined (N=123)**
Monthly migraine days (MMD) #		
Baseline	7.5	7.8

Efficacy Endpoint	Placebo (N=111) *	Fremanezumab combined (N=123)**
LS mean change from baseline ^a	-1.4	-2.5
LS mean difference from placebo (95% CI) ^a		-1.0 (-1.90, -0.16)
<i>P-value (vs. placebo)^a</i>		0.0210
Monthly headache days of at least moderate severity[#]		
Baseline	7.9	8.2
LS mean change from baseline ^a	-1.5	-2.6
LS mean difference from placebo (95% CI) ^a		-1.1 (-2.06, -0.20)
<i>P-value (vs. placebo)^a</i>		0.0172
≥ 50% MMD responders		
Percentage [%]	27.0%	47.2%
Estimated difference from placebo		20.1%
<i>P-value (vs. placebo)^b</i>		0.0016
Monthly acute headache medication days[#]		
Baseline	5.6	5.8
LS mean change from baseline ^a	-1.0	-2.1
LS mean difference from placebo (95% CI) ^a		-1.1 (-1.77, -0.42)

Efficacy Endpoint	Placebo (N=111) *	Fremanezumab combined (N=123)**
<i>P-value (vs. placebo)^a</i>		0.0016

FAS (Full Analysis Set): Includes all randomized patients who received at least 1 dose of study drug and had at least 10 days of post-baseline efficacy assessments on the primary endpoint.

CI = confidence interval.

LS= least squares

A fixed-sequence (hierarchical) testing procedure was implemented to control the type I error rate at 0.05.

* One patient in the placebo group was excluded from the analysis due to not having at least 10 days of post-baseline efficacy data.

**Fremanezumab combined group (N = 123) includes 36 patients treated with 120 mg and 87 patients treated with 225 mg.

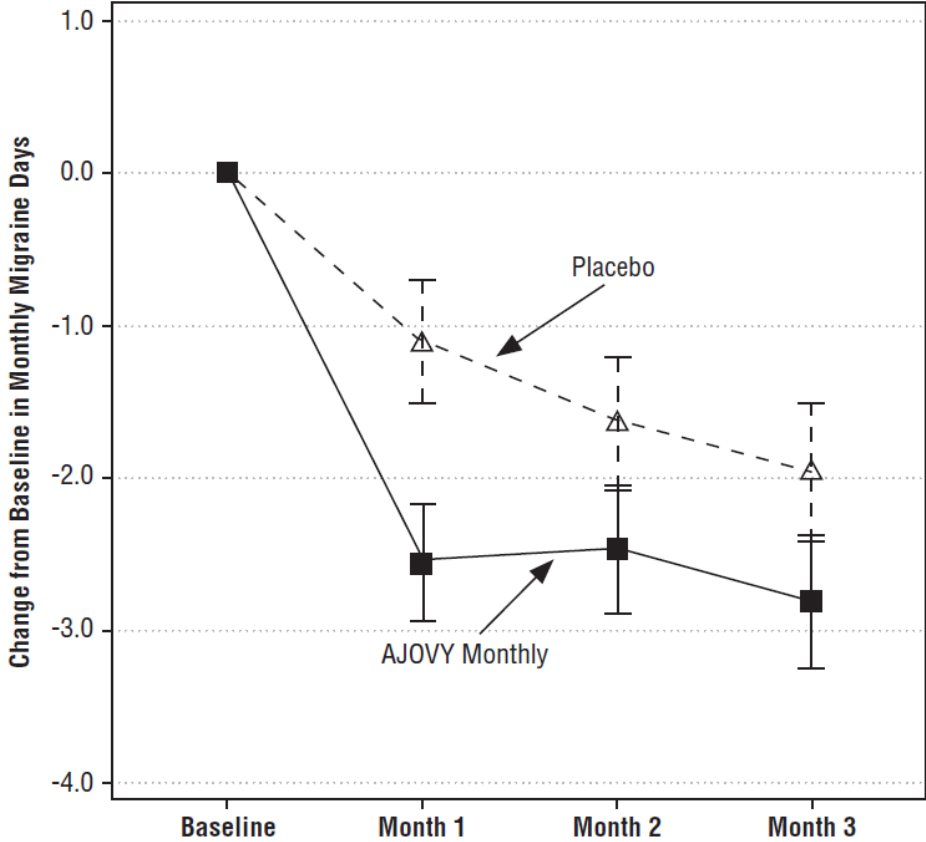
Those efficacy endpoints are continuous. No missing data imputation is done for those endpoints as all patients in FAS have their monthly average number of days of efficacy variables during the 12-week period.

^a Based on the ANCOVA model that included treatment, gender, region, and baseline preventive medication use (yes/no) as fixed effects and corresponding baseline value and years since onset of migraine as covariates.

^b p-value is from a logistic regression model with the following factors: treatment, sex, region, puberty status, weight category, and preventive migraine medication use at baseline (Yes/No).

Figure 2 displays the mean change from baseline in the average monthly number of migraine days in Study TV48125-CNS-30083.

Figure 4: Change from Baseline in Monthly Migraine Days (Fremanezumab 120 mg and 225 mg combined versus placebo) in Study TV48125-CNS-30083^a



^a LS (least-square) means and standard error of the mean are presented.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: The safety of fremanezumab was evaluated in repeat-dose toxicity studies in rats and monkeys for the duration of 3 months, and in chronic toxicity studies in cynomolgus monkeys for the duration of 6 months. Both the iv and sc routes were tested following once weekly dosing.

In rats, the no-observed-adverse-effect-level (NOAEL) was the highest dose tested in the 3month repeat dose study (300 mg/kg sc) and safety margins (based on AUC) were 21 times higher than the exposure in humans at the recommended clinical sc dose regimen of 225 mg once monthly.

In monkeys, in the 6-month chronic toxicity study, at the NOAEL dose of 300 mg/kg/weekly, safety margins (based on AUC) were at least 158 times higher than the human exposure at the 225 mg once monthly sc dose.

Other studies in rats and monkeys via sc dosing were of shorter duration and therefore, safety margins were slightly lower than the values mentioned above, ranging from 18 to 48 times higher than the clinical exposure at the 225 mg once monthly sc dose. In one study in monkeys via iv dosing, the NOAEL (10 mg/kg) and corresponding safety margin (approximately 4-fold higher) were lower due to incidental findings which were not reproducible in the chronic toxicity study

Other studies in rats and monkeys via sc dosing were of shorter duration and therefore, safety margins were slightly lower than the values mentioned above, ranging from 18 to 48 times higher than the clinical exposure at the 225 mg once monthly sc dose. In one study in monkeys via iv dosing, the NOAEL (10 mg/kg) and corresponding safety margin (approximately 4-fold higher) were lower due to incidental findings (perivasculitis of the ciliary vessel of the eye) which were not reproducible in the chronic toxicity study.

Carcinogenicity: Animal studies have not been performed to evaluate the carcinogenic potential of fremanezumab.

Genotoxicity: No studies have been performed to evaluate the genotoxic potential of fremanezumab.

Reproductive and Developmental Toxicology: When fremanezumab (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 calculated safety margins of approximately 43-fold and 9-fold in male and female rats, respectively, based on AUC over the human exposure following 225 mg once monthly sc dosing.

Administration of fremanezumab (0, 10, 50, or 100 mg/kg) weekly by subcutaneous injection to pregnant rabbits throughout the period of organogenesis produced no adverse effects on embryo-fetal development. The highest dose tested was associated with a calculated safety margin (based on AUC) of 20-fold relative to the human exposure administered a monthly sc dose of 225 mg.

Administration of fremanezumab (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. Exposure at the NOAEL (based on AUC) was 14 times higher than the human exposure at 225 mg monthly sc dose.

Special Toxicology: Safety pharmacology endpoints were evaluated in the general toxicology studies (up to 300 mg/kg/week) and in an additional stand-alone single dose study (100 mg/kg) in conscious telemetered cynomolgus monkeys, as well as single dose respiratory and CNS studies in rats (up to 300 mg/kg). No treatment-related effects were identified after single or repeated administrations up to 6 months via once weekly administration at doses of up to 300 mg/kg.

Juvenile Toxicity: A GLP study in 4-week old juvenile rats evaluated the potential effects of fremanezumab following 6 weekly sc injections at dose levels of 0 (vehicle control), 50, 150, and 450 mg/kg/week, up to 9 weeks of age, followed by a 6-week treatment-free period.

No toxicological effects were observed on incidence of clinical signs or food consumption. No effects on growth and development parameters, including body weight, tibia length measurement, and bone densitometry, neuro-behavioral development, and sexual maturation, were observed up to 9 weeks of age. A statistically significant reduction of total white blood cell count characterized by reduced absolute lymphocyte count in males and females across all dose groups relative to the control group was observed following the dosing phase, and in high-dose females at the end of the 6-week treatment-free period. However, all values were within historical control ranges and were not associated with any clinical signs or adverse effects. Fertility in dosed males and females and fetal development up to gestational day 13 in dosed females were not adversely affected following mating at 13 weeks of age. The NOAEL was the highest dose tested (450 mg/kg bw/week), equivalent to 58-fold the maximum recommended human dose in pediatric patients (225 mg dose/month), based on AUC in male and female animals.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrAJOVY®

fremanezumab

This patient medication information is written for the person who will be taking AJOVY.

This maybe you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This patient medication information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about AJOVY, talk to a healthcare professional.

What AJOVY is used for:

- AJOVY is a prescription medicine used for the prevention of migraine in adults who have at least 4 migraine days per month.
- AJOVY is also used for the preventive treatment of episodic migraine (fewer than 15 migraine days per month) in children aged 6 – 17 years and weighing at least 45 kg (99 pounds).

AJOVY has not been studied in children younger than 6 years of age.

AJOVY has not been studied in children with chronic migraine.

How AJOVY works:

AJOVY works by blocking the activity of a molecule called calcitonin gene-related peptide (CGRP). Increased CGRP levels in the blood may cause migraine attacks.

The ingredients in AJOVY are:

Medicinal ingredients: fremanezumab

Non-medicinal ingredients: Disodium ethylenediaminetetraacetic acid dihydrate (EDTA), L-histidine, polysorbate80, sucrose, and water for Injection

AJOVY comes in the following dosage forms:

Subcutaneous injection in a prefilled syringe or a prefilled autoinjector, each containing

225mg/1.5mL(150mg/mL) and each for a single use.

Do not use AJOVY if:

Do not use AJOVY if you are allergic to fremanezumab or any of the ingredients in AJOVY. See the “What are the ingredients of AJOVY” above for a complete list of the ingredients in AJOVY.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take AJOVY. Talk about any health conditions or problems you may have, including if you:

- If you have severe kidney disease
- If you have severe liver disease
- are pregnant or plan to become pregnant. It is not known if AJOVY will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if AJOVY passes into your breast milk. Talk to your healthcare professional about the best way to feed your baby while using AJOVY

Talk to your doctor, pharmacist or nurse right away if you get:

- Severe injection site reactions such as area of swelling, bleeding
- Severe allergic reactions such as trouble breathing, swelling of the lips and tongue, itching or severe rash after injecting AJOVY.

These reactions may occur within minutes, although some may occur up to one month after administration.

Tell your doctor if you have or have had cardiovascular disease (problems with the heart and blood vessels) before using this medication, because AJOVY has not been studied in patients with certain cardiovascular diseases.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take AJOVY:

- See the detailed “Instructions for Use” for information on how to prepare and inject a dose of AJOVY.
- Use AJOVY exactly as your healthcare professional tells you to use it.
- AJOVY is injected under your skin (subcutaneously).
- Your healthcare professional should show you or your caregiver how to prepare and inject your first dose of AJOVY. A child 13 years of age and older may give AJOVY themselves under the supervision of an adult or may receive AJOVY by a caregiver. A child younger than 13 years of age will receive AJOVY by a caregiver.
- Your healthcare professional will tell you how much AJOVY to use and when to use it. See Usual Dose section for more information.

Adults

- Your healthcare professional will tell you if you should use AJOVY 225 mg one time every month or AJOVY 675 mg one time every 3 months.
- If your prescribed dose is AJOVY 675 mg every 3 months, you must use 3 separate syringes or 3 separate autoinjectors. You will give 3 separate injections, one after another, one time every 3 months.
- If you are giving 3 injections of AJOVY for your prescribed dose, you may use the same body site for all 3 injections. Do NOT use the same spot for all 3 injections
- **Do not** inject AJOVY in the same injection site that you inject other medicine.
- If your doctor changes the frequency of injections, the new dose regimen should be given on the next scheduled dosing date of the old dose regimen.

If you have questions about your schedule, ask your healthcare professional.

Children 6 to 17 years of age and weighing and least 45 kg (99 pounds)

- Use AJOVY 225 mg one time every month
- **Do not** inject AJOVY in the same injection site that you inject other medicine.

If you have questions about your schedule, ask your healthcare professional.

Usual dose:

AJOVY comes as single-use (1 time) pre-filled syringe or a prefilled autoinjector, each containing a single-dose. Your healthcare professional will prescribe the dose that is best for you.

Adult

- If your healthcare professional prescribes the 225 mg monthly dose for you, take 1 injection every month, using a prefilled syringe or a prefilled autoinjector.
- Be aware that the monthly dose consists of a single subcutaneous injection.

- If your healthcare professional prescribes the 675 mg every 3 months dose for you, take 3 separate injections one after another. Use a different prefilled syringe or a different prefilled autoinjector for each injection. You will take these injections once every 3 months.

It is important to follow the dose regimen as prescribed by your doctor.

Children 6 to 17 years of age and weighing at least 45 kg (99 pounds):

Use AJOVY 225 mg one time every month, using a prefilled syringe or a prefilled autoinjector.

It is important to follow the dose regimen as prescribed by your doctor.

Be aware that the monthly dose consists of a single subcutaneous injection.

Overdose:

If you think you, or a person you are caring for, have taken too much AJOVY, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed Dose:

If you miss a dose of AJOVY, take it as soon as possible. If you need to take the dose late, you will need to adjust your schedule:

- If you take 225 mg of AJOVY, inject your next dose 1 month after the late dose.
- If you take 675 mg of AJOVY, inject your next dose 3 months after the late dose.

If you have questions about your schedule, ask your healthcare professional.

Possible side effects from using AJOVY:

These are not all the possible side effects you may feel when taking AJOVY. If you experience any side effects not listed here, contact your healthcare professional.

Very common (may affect more than 1 in 10 people)

The following mild to moderate, short-lasting skin reactions around the injection area can occur:

Pain, localized hardening in the skin-raised red or purple skin patches, redness of the skin, severe itching at the injection site

Common (may affect up to 1 in 10 people)

Itching at the injection site

Uncommon (may affect up to 1 in 100 people)

Rash at injection site. Hives, rash, dizziness, fatigue, gastrointestinal discomfort, joint pain, back pain.

If you have a troublesome symptom or side effect that is not listed above or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store refrigerated at 2°C to 8°C in the original outer carton to protect from light until time of use.
- If necessary, AJOVY may be kept in the original carton at room temperature up to 25°C for a maximum of 7 days. After removal from the refrigerator, AJOVY must be used within 7 days or discarded.
- Do not freeze. Do not expose to extreme heat or direct sunlight. Do not shake.

Keep out of reach and sight of children.

If you want more information about AJOVY:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada Drug Product Database website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website at <http://www.tevacanadainnovation.ca> or by calling Toll free number 1-833-302-0121.

This leaflet was prepared by Teva Canada Innovation

Last Revised 2026-01-30

INSTRUCTIONS FOR USE – PREFILLED SYRINGE

AJOVY® (FREMANEZUMAB) INJECTION FOR SUBCUTANEOUS USE

Prefilled syringe 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 one-time use only. Put AJOVY in sharps disposal 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.

AJOVY may be self-administered by patients 13 years of age and older or administered by healthcare professionals and/or adult caregivers. In pediatric patients 6 to 12 years of age, AJOVY must be administered by a healthcare professional or adult caregiver. Administration should be performed by an individual who has been trained to administer the product.

Storage Conditions:

- Store AJOVY in the refrigerator between 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 25 °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 AJOVY in a sharps disposal container if it has been out of the refrigerator for 7 days or longer.
- **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 the syringe out of the reach of children.

AJOVY prefilled syringe (Before use). See Figure A. Appearance of the syringe before use

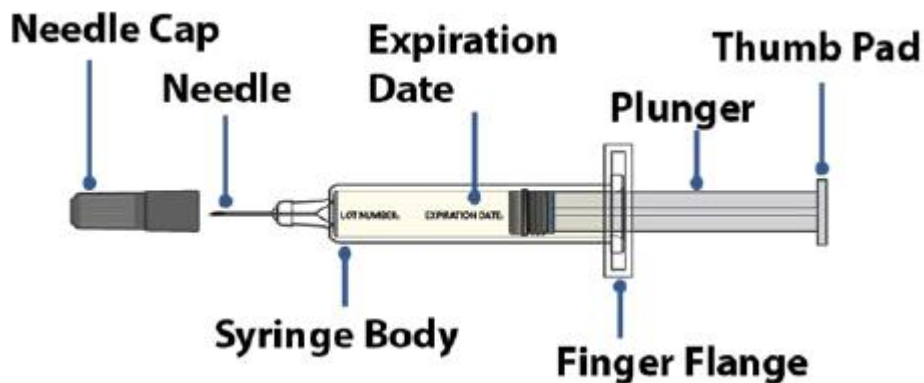


Figure A - AJOVY prefilled syringe

After use: See Figure B.



Figure B - Appearance of the syringe after use

How do I inject AJOVY?



Read this before you inject.

Step 1. Check your prescription.

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

- If your healthcare professional prescribes the 225 mg monthly dose for you, take 1 injection monthly, using a prefilled syringe.
- If your healthcare professional prescribes the 675 mg every 3 months dose for you, take 3 separate injections one after another, using a different prefilled syringe for each injection. You will take these injections once 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 professional.

Step 2. Remove the prefilled syringe from the carton.

- You may need to use more than 1 prefilled syringe based 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.

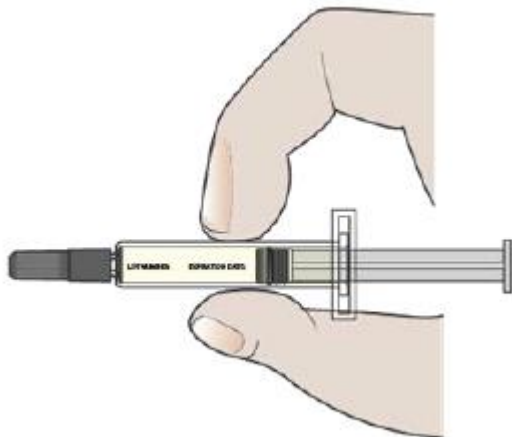


Figure C - How to manipulate the syringe

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.
 - alcohol swabs (not supplied)
 - gauze pads or cotton balls (not supplied)
 - sharps disposal or puncture-resistant container (not supplied).
 - 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).



Figure D - Supplies needed for the injection of AJOVY

Tell your pharmacist or healthcare provider if you do not already have a sharps or puncture-resistant container.

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, as this could damage the liquid medicine.
- **Do NOT** warm up the AJOVY prefilled syringe using hot water, a microwave, or any other way than instructed, as this could damage the liquid medicine.



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.

<ul style="list-style-type: none">• Check that the liquid medicine in the prefilled syringe is clear and colourless to slightly yellow before you give your injection. (See Figure E). If the liquid has any particles in it, or is discoloured, cloudy, or frozen,	<ul style="list-style-type: none">• Do not use the prefilled syringe if it has any visible damage, such as cracks or leaks. See disposal instructions in Step 12.
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do not use the prefilled autoinjector. Call your healthcare provider or pharmacist.	
<ul style="list-style-type: none">• Check that AJOVY appears on the prefilled syringe.	<ul style="list-style-type: none">• Do not use if you have been given the wrong medicine.
<ul style="list-style-type: none">• Check the expiration date printed on the prefilled syringe label.	<ul style="list-style-type: none">• Do not use the prefilled syringe if the expiration date has passed.

The above checks are all important to make sure the medicine is safe to use.

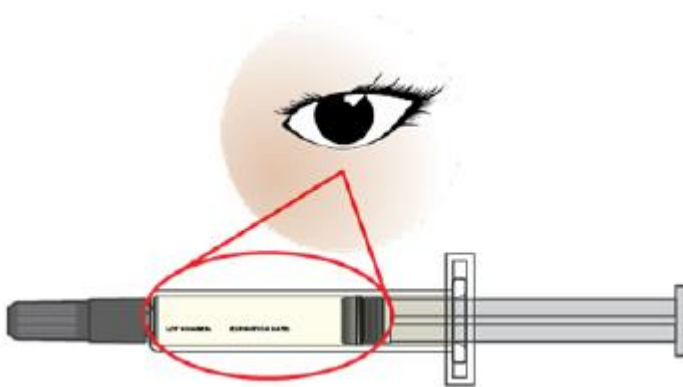


Figure E - Checking the content of the prefilled syringe

Step 7. Choose your injection area.

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



Figure F - Injection areas

Note: There are some injection areas on your body that are hard to reach (like the back of your arm). You will 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
- **Wait** 10 seconds to allow the skin to dry before injecting.
- **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 body site for the three 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.

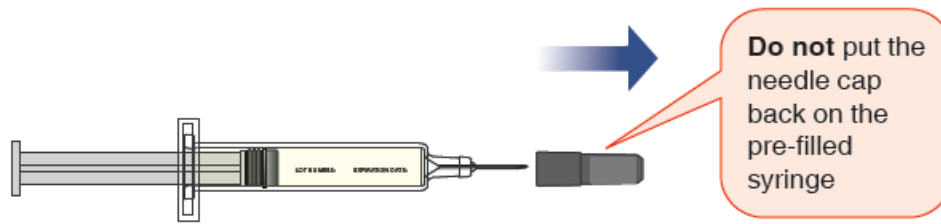
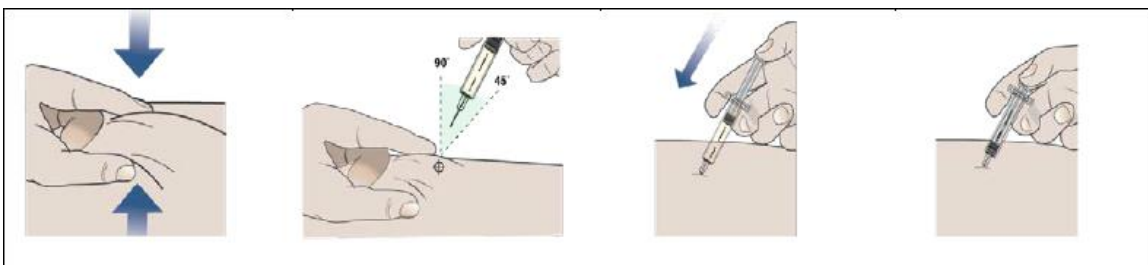


Figure G - Removing the needle cap

Step 10. Give your injection following the 4 steps below.

<p>1. Use your free hand to gently pinch up at least 1 inch of the skin that you have cleaned.</p>	<p>2. Insert the needle into the pinched skin at 45 to 90 degree angle</p>	<p>3. When the needle is all the way into your skin, use your thumb to push the plunger.</p>	<p>4. Push the plunger slowly all the way down as far as it will go to inject all of the medicine.</p>
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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.

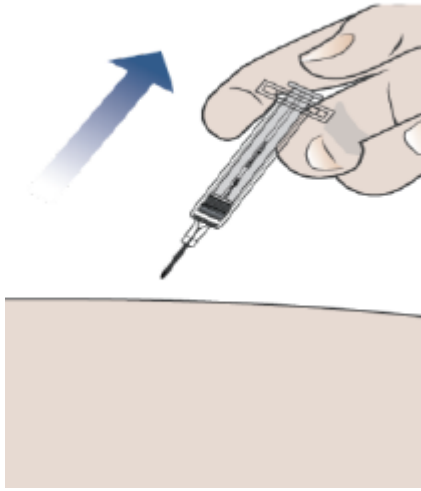


Figure H - Removing the needle

Step 12. Apply pressure at 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 Health Canada -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 Health Canada -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 labelled 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 provincial or local laws about how you should throw away used syringes.

- **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

INSTRUCTIONS FOR USE – PREFILLED AUTOINJECTOR

AJOVY® (fremanezumab) injection for subcutaneous use

Prefilled autoinjector 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 sharps disposal 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.

AJOVY may be self-administered by patients 13 years of age and older or administered by healthcare professionals and/or adult caregivers. In pediatric patients 6 to 12 years of age, AJOVY must be administered by a healthcare professional or adult caregiver. Administration should be performed by an individual who has been trained to administer the product.

Storage Conditions:

- Store AJOVY in the refrigerator between 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 20°C to 25°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 AJOVY in a sharps disposal container if it has been out of the refrigerator for 7 days or longer.

- **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.

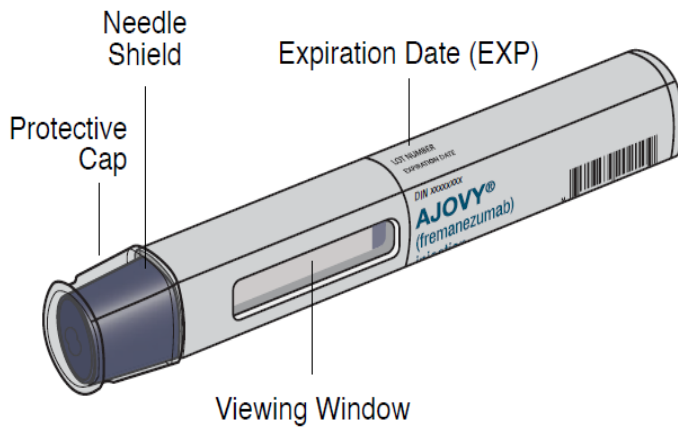


Figure A AJOVY prefilled autoinjector

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

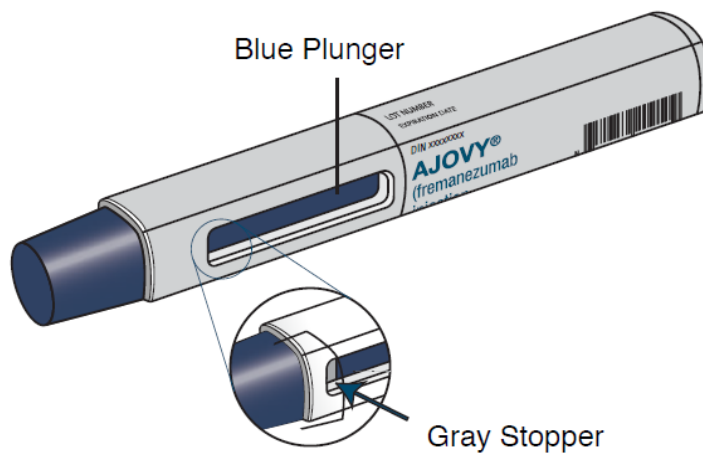


Figure B Appearance of the autoinjector after use

- 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 your prescription.

AJOVY comes as a single-dose (1 time) prefilled autoinjector. Your healthcare provider will prescribe the dose that is best for you.

- If your healthcare professional prescribes the 225 mg of AJOVY monthly dose for you, take 1 injection monthly, using a 225 mg prefilled AJOVY autoinjector.
- If your healthcare professional prescribes the 675 mg of AJOVY every 3 months dose for you, take 3 separate injections, one after another, using a different 225 mg prefilled AJOVY autoinjector for each injection. You will take these injections once 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 professional.

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.

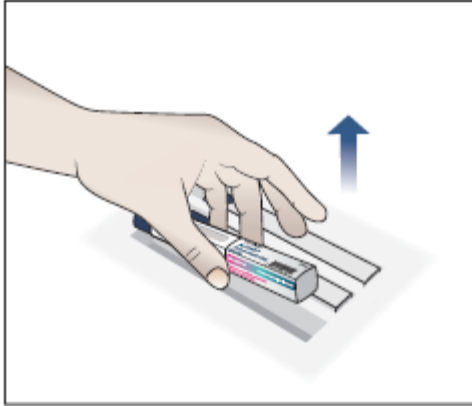


Figure C How to remove the prefilled autoinjector from the carton

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:
 - Alcohol swabs (not supplied).
 - Gauze pads or cotton balls (not supplied).
 - Sharps disposal or puncture-resistant container (not supplied).
 - If your dose is 225 mg, you will need 1 AJOVY 225 mg prefilled autoinjector.
 - Alcohol swabs (not supplied).
 - Gauze pads or cotton balls (not supplied).
 - Sharps disposal or puncture-resistant container (not supplied).

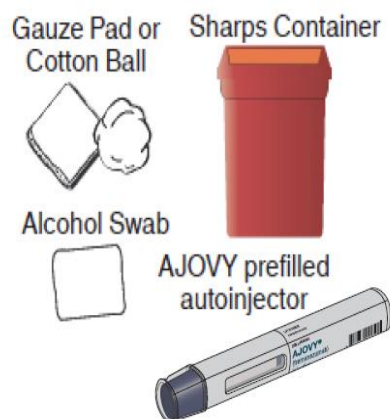


Figure D Supplies needed for the injection of AJOVY

Tell your pharmacist or healthcare provider if you do not already have a sharps or puncture-resistant container.

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 as this could damage the liquid medicine.
- **Do NOT** warm up the AJOVY prefilled autoinjector using hot water, a microwave, or any other way than instructed, as this could damage the liquid medicine.



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.

- | | |
|---|---|
| <ul style="list-style-type: none">• Check that the liquid medicine in the prefilled autoinjector viewing window is clear and colourless to slightly yellow before you give your injection. (See Figure E). If the liquid has any particles in it, or is discoloured, cloudy, or frozen, do not use the prefilled autoinjector. | <ul style="list-style-type: none">• Do not use the prefilled autoinjector if it has any visible damage, such as cracks or leaks. See disposal instructions in Step 12. |
|---|---|

Call your healthcare provider or pharmacist.	
<ul style="list-style-type: none"> • Check that AJOVY appears on the prefilled autoinjector. 	<ul style="list-style-type: none"> • Do not use if you have been given the wrong medicine.
<ul style="list-style-type: none"> • Check the expiration date (EXP) printed on the prefilled autoinjector label. 	<ul style="list-style-type: none"> • Do not use the prefilled autoinjector if the expiration date (EXP) has passed.

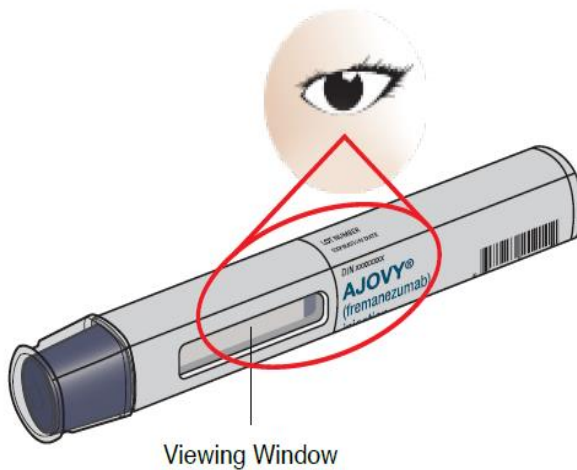


Figure E Checking the content of the prefilled autoinjector

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.



Figure F Injection areas

Note: There are some injection areas on your body that are hard to reach (like the back of your arm). You will 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.
- **Wait** 10 seconds to allow your skin to dry before injecting.
- **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.
- **Do NOT** put the protective cap back on the prefilled autoinjector, to avoid injury and infection.

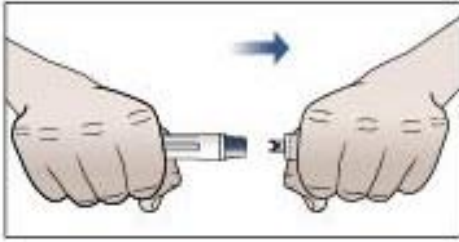


Figure G Removing the protective cap

Step 10. Give your injection following the 3 steps below.

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

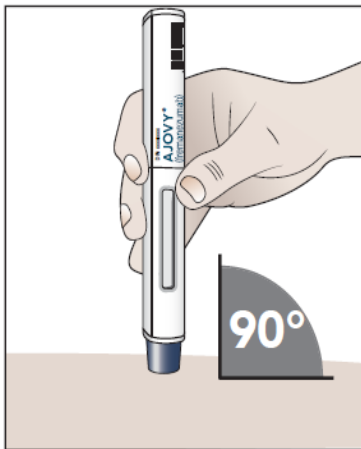
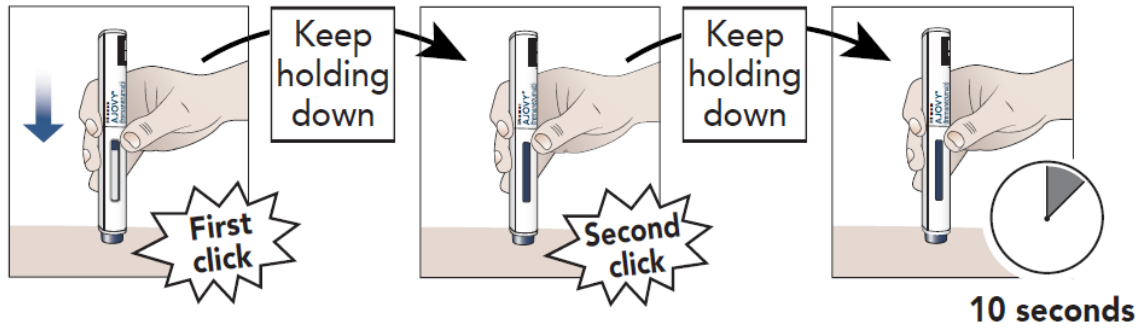


Figure H Give your injection

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.

<p>1. You hear the first “click” (this means the injection has started and the blue plunger starts to move).</p>	<p>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.)</p>	<p>3. You wait another 10 seconds. (to make sure all the medicine is injected).</p>
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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.

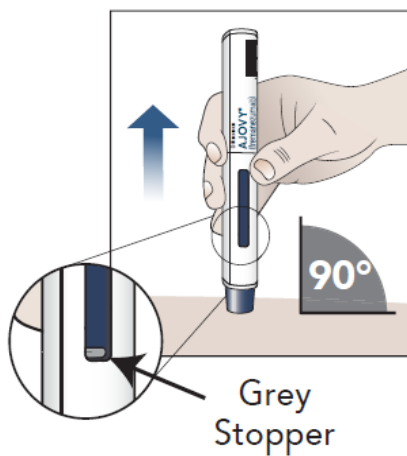


Figure I Blue plunger filled the viewing window, you can see the gray stopper.

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 Health Canada – 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 Health Canada -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 labelled 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 provincial or local laws about how you should throw away used autoinjectors.

- **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