AJOVY® (FREMANEZUMAB)

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

AJOVY solution for injection in pre-filled syringe 225 mg/1.5ml
AJOVY solution for injection in pre-filled pen 225 mg/1.5ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One pre-filled syringe contains 225 mg fremanezumab.
One pre-filled pen contains 225 mg fremanezumab.

Fremanezumab is a humanised monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Clear to opalescent, colourless to slightly yellow solution with a pH of 5.5 and an osmolality of 300-450 mOsm/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AJOVY is indicated for the preventive treatment of migraine in adults.

4.2 Posology and method of administration

The treatment should be initiated by a physician experienced in the diagnosis and treatment of migraine.

Posology

Two dosing options are available:
- 225 mg once monthly (monthly dosing) or
- 675 mg every three months (quarterly dosing)

When switching dosing regimens, the first dose of the new regimen should be administered on the next scheduled dosing date of the prior regimen.

When initiating treatment with fremanezumab, concomitant migraine preventive treatment may be continued if considered necessary by the prescriber (see section 5.1).

The treatment benefit should be assessed within 3 months after initiation of 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.

Missed dose
If a fremanezumab injection is missed on the planned date, dosing should resume as soon as possible on the indicated dose and regimen. A double dose must not be administered to make up for a missed dose.

Special Populations

Elderly
There is limited data available on the use of fremanezumab in patients ≥65 years of age. Based on the results of population pharmacokinetic analysis, no dose adjustment is required (see section 5.2).

Renal or hepatic impairment
No dose adjustment is necessary in patients with mild to moderate renal impairment or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of AJOVY in children and adolescents below the age of 18 years have not yet been established. No data are available.

Method of administration

Subcutaneous use.

AJOVY is for subcutaneous injection only. It should not be administered by the intravenous or intramuscular route. AJOVY can be injected into areas of the abdomen, thigh, or upper arm that are not tender, bruised, red, or indurated. For multiple injections, injection sites should be alternated.

Patients may self-inject if instructed in subcutaneous self-injection technique by a healthcare professional. For further instructions on administration, please refer to the patient information leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Serious hypersensitivity reactions

Anaphylactic reactions have been reported rarely with fremanezumab (see section 4.8). Most reactions have occurred within 24 hours of administration although some reactions have been delayed. Patients should be warned about the symptoms associated with hypersensitivity reactions. If a serious hypersensitivity reaction occurs, initiate appropriate therapy and do not continue treatment with fremanezumab (see section 4.3).

Major cardiovascular diseases

Patients with certain major cardiovascular diseases were excluded from clinical studies (see section 5.1). No safety data are available in these patients.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., is essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

No formal clinical drug interaction studies have been performed with AJOVY. No pharmacokinetic drug interactions are expected based on the characteristics of fremanezumab. Furthermore, concomitant use of acute migraine treatments (specifically analgesics, ergots, and triptans) and migraine preventive medicinal products during the clinical studies did not affect the pharmacokinetics of fremanezumab.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is a limited amount of data from the use of AJOVY in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of AJOVY during pregnancy.

Breast-feeding

It is unknown whether fremanezumab is excreted in human milk. Human IgG is known to be excreted in breast milk during the first days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to breast-fed infants cannot be excluded during this short period. Afterwards, use of fremanezumab could be considered during breast-feeding only if clinically needed.

Fertility

There are no fertility data in humans. Available non-clinical data do not suggest an effect on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

AJOVY has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

A total of over 2,500 patients (more than 1,900 patient years) have been treated with AJOVY in registration studies. More than 1,400 patients were treated for at least 12 months.

Commonly reported adverse drug reactions (ADRs) were local reactions at the injection site (pain [24%], induration [17%], erythema [16%] and pruritus [2%]).

Tabulated list of adverse reactions

ADRs from clinical studies and post-marketing reports are presented according to MedDRA system organ classification. Within each frequency grouping, ADRs are presented in the order of decreasing seriousness. Frequency categories are based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each system organ class, ADRs are ranked by frequency, most frequent reactions first.

The following ADRs have been identified for AJOVY (Table 1).

Table 1: Adverse reactions

MedDRA System Organ Class	Frequency	Adverse Reaction
Immune system disorders	Uncommon	Hypersensitivity reactions such as rash, pruritus, urticaria and swelling
	Rare	Anaphylactic reaction
General disorders and administration site conditions	Very common	Injection site pain
		Injection site induration
		Injection site erythema
	Common	Injection site pruritus
	Uncommon	Injection site rash

Description of selected adverse reactions

Injection site reactions
The most frequently observed local reactions at the injection site were pain, induration and erythema. All 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. All injection site reactions resolved, mostly within a few hours or days. Injection site reactions generally did not necessitate discontinuation of the medicinal product.

Serious hypersensitivity reactions
Anaphylactic reactions have been reported rarely. These reactions mostly occurred within 24 hours of administration although some reactions have been delayed.

Immunogenicity
In 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 neutralising antibodies. With 12 months of treatment, ADA were detected in 2.3% of the patients (43 out of 1,888). The safety and efficacy of fremanezumab were not affected by ADA development.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

Doses up to 2,000 mg have been administered intravenously in clinical trials without dose-limiting toxicity. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcitonin gene-related peptide (CGRP) antagonists.
ATC code: N02CD03

Mechanism of action

Fremanezumab is a humanised IgG2Δa/kappa monoclonal antibody derived from a murine precursor. Fremanezumab selectively binds the calcitonin gene-related peptide (CGRP) ligand and blocks both CGRP isoforms (α-and β-CGRP) from binding to the CGRP receptor. While the precise mechanism of action by which fremanezumab prevents migraine attacks is unknown, it is believed that prevention of migraine is obtained by its effect modulating the trigeminal system. CGRP levels have been shown to increase significantly during migraine and return to normal with headache relief.

Fremanezumab is highly specific for CGRP and does not bind to closely related family members (e.g., amylin, calcitonin, intermedin and adrenomedullin).

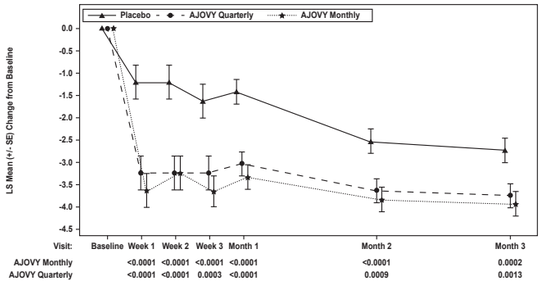
Clinical efficacy and safety

The efficacy of fremanezumab was assessed in two randomised, 12-week, double-blind, placebo-controlled phase III studies in adult patients with episodic (Study 1) and chronic migraine (Study 2). The patients enrolled had at least a 12-month history of migraine (with and without aura) according to the International Classification of Headache Disorders (ICHD-III) diagnostic criteria. Elderly patients (>70 years), patients using opioids or barbiturates on more than 4 days per month, and patients with pre-existing myocardial infarction, cerebrovascular accident, and thromboembolic events were excluded.

Episodic migraine study (Study 1)
The efficacy of fremanezumab was evaluated in episodic migraine in a randomised, multicentre, 12-week, placebo-controlled, double-blind study (Study 1). Adults with a history of episodic migraine (less than 15 headache days per month) were included in the study. A total of 875 patients (742 females, 133 males) were randomised into one of three arms: 675 mg fremanezumab every three months (quarterly, n=291), 225 mg fremanezumab once a month (monthly, n=290), or monthly administration of placebo (n=294) administered via subcutaneous injection. Demographics and baseline disease characteristics were balanced and comparable between the study arms. Patients had a median age of 42 years (range: 18 to 70 years), 85% were female, and 80% were white. The mean migraine frequency at baseline was approximately 9 migraine days per month. Patients were allowed to use acute headache treatments during the study. A sub-set of patients (21%) was also allowed to use one commonly used concomitant, preventive medicinal product (beta-blockers, calcium channel blocker/benzocycloheptene, antidepressants, anticonvulsants). Overall, 19% of the patients had previously used topiramate. A total of 791 patients completed the 12-week double-blind treatment period.

The primary efficacy endpoint was the mean change from baseline in the monthly average number of migraine days during the 12-week treatment period. Key secondary endpoints were the achievement of at least 50% reduction from baseline in monthly migraine days (50% responder rate), mean change from baseline in the patient reported MIDAS score, 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 (see Table 2). The effect also occurred from as early as the first month and sustained over the treatment period (see Figure 1).

Figure 1: Mean Change from Baseline in the Monthly Average Number of Migraine Days for Study 1



Mean at baseline (monthly average number of migraine days): Placebo: 9.1, AJOVY Quarterly: 9.2, AJOVY Monthly: 8.9.

Table 2: Key Efficacy Outcomes in Study 1 in Episodic Migraine

Efficacy Endpoint	Placebo (n=290)	Fremanezumab 675 mg quarterly (n=288)	Fremanezumab 225 mg monthly (n=287)
MMD			
Mean change[a] (95% CI)	-2.2 (-2.68, -1.71)	-3.4 (-3.94, -2.96)	-3.7 (-4.15, -3.18)
TD (95% CI)[b]	-	-1.2 (-1.74, -0.69)	-1.4 (-1.96, -0.90)
Baseline (SD)	9.1 (2.65)	9.2 (2.62)	8.9 (2.63)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*
MHD			
Mean change[a] (95% CI)	-1.5 (-1.88, -1.06)	-3.0 (-3.39, -2.55)	-2.9 (-3.34, -2.51)
TD (95% CI)[b]	-	-1.5 (-1.95, -1.02)	-1.5 (-1.92, -0.99)
Baseline (SD)	6.9 (3.13)	7.2 (3.14)	6.8 (2.90)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*
50% Responder Rate MMD			
Percentage [%]	27.9%	44.4%	47.7%
P-value (vs. placebo)	-	*p<0.0001*	*p<0.0001*
75% Responder Rate MMD			
Percentage [%]	9.7%	18.4%	18.5%
P-value (vs. placebo)	-	*p=0.0025*	*p=0.0023*
MIDAS total			
Mean change[a] (95% CI)	-17.5 (-20.62, -14.47)	-23.0 (-26.10, -19.82)	-24.6 (-27.68, -21.45)
Baseline (SD)	37.3 (27.75)	41.7 (33.09)	38 (33.30)
P-value (vs. placebo)[a]	-	*p=0.0023*	*p<0.0001*
MAHMD			
Mean change[a] (95% CI)	-1.6 (-2.04, -1.20)	-2.9 (-3.34, -2.48)	-3.0 (-3.41, -2.56)
TD (95% CI)[b]	-	-1.3 (-1.73, -0.78)	-1.3 (-1.81, -0.86)
Baseline (SD)	7.7 (3.60)	7.7 (3.70)	7.7 (3.37)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*

CI = confidence interval; MAHMD = monthly acute headache medication days; MHD = monthly headache days of at least moderate severity; MIDAS = Migraine Disability Assessment; MMD = monthly migraine days; SD = standard deviation; TD = treatment difference

[a] For all endpoints mean change and CIs are 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] Treatment difference is based on the MMRM analysis with treatment, gender, region, and baseline preventive medication use (yes/no), month, and treatment month as fixed effects and corresponding baseline value and years since onset of migraine as covariates.

In patients on one other concomitant, migraine preventive medicinal product, the treatment difference for the reduction of monthly migraine days (MMD) observed between fremanezumab 675 mg quarterly and placebo was -1.8 days (95% CI: -2.95, -0.55) and between fremanezumab 225 mg monthly and placebo -2.0 days (95% CI: -3.21, -0.86).

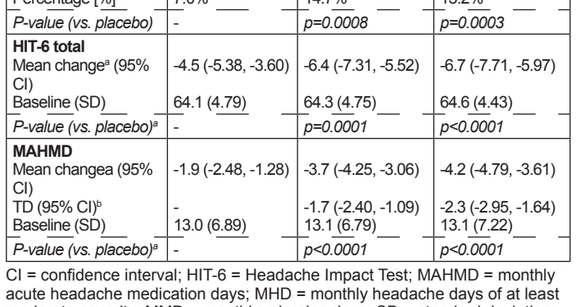
In patients who had previously used topiramate the treatment difference for the reduction of monthly migraine days (MMD) observed between fremanezumab 675 mg quarterly and placebo was -2.3 days (95% CI: -3.64, -1.00) and between fremanezumab 225 mg monthly and placebo -2.4 days (95% CI: -3.61, -1.13).

Chronic migraine study (Study 2)

Fremanezumab was evaluated in chronic migraine in a randomised, multicentre, 12-week, placebo-controlled, double-blind study (Study 2). The study population included adults with a history of chronic migraine (15 headache days or higher per month). A total of 1,130 patients (991 females, 139 males) were randomised into one of three arms: 675 mg fremanezumab starting dose followed by 225 mg fremanezumab once a month (monthly, n=379), 675 mg fremanezumab every three months (quarterly, n=376), or monthly administration of placebo (n=375) administered via subcutaneous injection. Demographics and baseline disease characteristics were balanced and comparable between the study arms. Patients had a median age of 41 years (range: 18 to 70 years), 88% were female, and 79% were white. The mean headache frequency at baseline was approximately 21 headache days per month (of which 13 headache days were of at least moderate severity). Patients were allowed to use acute headache treatments during the study. A sub-set of patients (21%) was also allowed to use one commonly used concomitant, preventive medicinal product (beta-blockers, calcium channel blocker/benzocycloheptene, antidepressants, anticonvulsants). Overall, 30% of the patients had previously used topiramate and 15% onabotulinumtoxin A. A total of 1,034 patients completed the 12-week double-blind treatment period.

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 12-week treatment period. Key secondary endpoints were the achievement of at least 50% reduction from baseline in monthly headache days of at least moderate severity (50% responder rate), mean change from baseline in the patient reported HIT-6 score, 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 (see Table 3). The effect also occurred from as early as the first month and sustained over the treatment period (see Figure 2).

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



Mean at baseline (monthly average number of headache days of at least moderate severity): Placebo: 13.3, AJOVY Quarterly: 13.2, AJOVY Monthly: 12.8.

Table 3: Key Efficacy Outcomes in Study 2 in Chronic Migraine

Efficacy Endpoint	Placebo (n=371)	Fremanezumab 675 mg quarterly (n=375)	Fremanezumab 225 mg monthly with 675 mg starting dose (n=375)
MHD			
Mean change[a] (95% CI)	-2.5 (-3.06, -1.85)	-4.3 (-4.87, -3.66)	-4.6 (-5.16, -3.97)
TD (95% CI)[b]	-	-1.8 (-2.45, -1.13)	-2.1 (-2.77, -1.46)
Baseline (SD)	13.3 (5.80)	13.2 (5.45)	12.8 (5.79)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*
MMD			
Mean change[a] (95% CI)	-3.2 (-3.86, -2.47)	-4.9 (-5.59, -4.20)	-5.0 (-5.70, -4.33)
TD (95% CI)[b]	-	-1.7 (-2.44, -0.92)	-1.9 (-2.61, -1.09)
Baseline (SD)	16.3 (5.13)	16.2 (4.87)	16.0 (5.20)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*
50% Responder Rate MHD			
Percentage [%]	18.1%	37.6%	40.8%
P-value (vs. placebo)	-	*p<0.0001*	*p<0.0001*
75% Responder Rate MHD			
Percentage [%]	7.0%	14.7%	15.2%
P-value (vs. placebo)	-	*p=0.0008*	*p=0.0003*
HIT-6 total			
Mean change[a] (95% CI)	-4.5 (-5.38, -3.60)	-6.4 (-7.31, -5.52)	-6.7 (-7.71, -5.97)
Baseline (SD)	64.1 (4.79)	64.3 (4.75)	64.6 (4.43)
P-value (vs. placebo)[a]	-	*p=0.0001*	*p<0.0001*
MAHMD			
Mean changea (95% CI)	-1.9 (-2.48, -1.28)	-3.7 (-4.25, -3.06)	-4.2 (-4.79, -3.61)
TD (95% CI)[b]	-	-1.7 (-2.40, -1.09)	-2.3 (-2.95, -1.64)
Baseline (SD)	13.0 (6.89)	13.1 (6.79)	13.1 (7.22)
P-value (vs. placebo)[a]	-	*p<0.0001*	*p<0.0001*

CI = confidence interval; HIT-6 = Headache Impact Test; MAHMD = monthly acute headache medication days; MHD = monthly headache days of at least moderate severity; MMD = monthly migraine days; SD = standard deviation; TD = treatment difference

[a] For all endpoints mean change and CIs are 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] Treatment difference is based on the MMRM analysis with treatment, gender, region, and baseline preventive medication use (yes/no), month, and treatment month as fixed effects and corresponding baseline value and years since onset of migraine as covariates.

In patients on one other concomitant, migraine preventive medicinal product, the treatment difference for the reduction of monthly headache days (MHD) of at least moderate severity observed between fremanezumab 675 mg quarterly and placebo was -1.3 days (95% CI: -2.66, 0.03) and between fremanezumab 225 mg monthly with 675 mg starting dose and placebo -2.0 days (95% CI: -3.27, -0.67).

In patients who had previously used topiramate the treatment difference for the reduction of monthly headache days (MHD) of at least moderate severity observed between fremanezumab 675 mg quarterly and placebo was -2.7 days (95% CI: -3.88, -1.51) and between fremanezumab 225 mg monthly with 675 mg starting dose and placebo -2.9 days (95% CI: -4.10, -1.78). In patients who had previously used onabotulinumtoxin A the treatment difference for the reduction of monthly headache days (MHD) of at least moderate severity observed between fremanezumab 675 mg quarterly and placebo was -1.3 days (95% CI: -3.01, -0.37) and between fremanezumab 225 mg monthly with 675 mg starting dose and placebo -2.0 days (95% CI: -3.84, -0.22).

Approximately 52% of the patients in the study had acute headache medication overuse. The observed treatment difference for the reduction of monthly headache days (MHD) of at least moderate severity between fremanezumab 675 mg quarterly and placebo in these patients was -2.2 days (95% CI: -3.14, -1.22) and between fremanezumab 225 mg monthly with 675 mg starting dose and placebo -2.7 days (95% CI: -3.71, -1.78).

Long-term study (Study 3)

For all episodic and chronic migraine patients, efficacy was sustained for up to 12 additional months in the long-term study (Study 3), in which patients received 225 mg fremanezumab monthly or 675 mg quarterly. 79% of patients completed the 12-month treatment period of Study 3. Pooled across the two dosing regimens, a reduction of 6.6 monthly migraine days was observed after 15 months relative to Study 1 and Study 2 baseline. 61% of patients completing Study 3 achieved a 50% response in the last month of the study. No safety signal was observed during the 15-month combined treatment period.

Intrinsic and extrinsic factors

The efficacy and safety of fremanezumab was demonstrated regardless of age, gender, race, use of concomitant preventive medicinal products (beta-blockers, calcium channel blocker/benzocycloheptene, antidepressants, anticonvulsants), use of topiramate or onabotulinumtoxin A for migraine in the past, and acute headache medication overuse.
There is limited data available on the use of fremanezumab in patients ≥65 years of age (2% of the patients).

Paediatric population

See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Absorption

After single subcutaneous administrations of 225 mg and 675 mg fremanezumab, median time to maximum concentrations (t_{max}) in healthy subjects was 5 to 7 days. The absolute bioavailability of fremanezumab after subcutaneous administration of 225 mg and 900 mg in healthy subjects was 55% (±SD of 23%) to 66% (±SD of 26%). Dose proportionality, based on population pharmacokinetics, was observed between 225 mg to 675 mg. 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

Assuming the model-derived estimated bioavailability of 66% (±SD of 26%) holds for the patient population, the volume of distribution for a typical patient was 3.6 L (35.1% CV) following subcutaneous administration of 225 mg, 675 mg and 900 mg of fremanezumab.

Biotransformation

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

Elimination

Assuming the model-derived estimated bioavailability of 66% (±SD of 26%) holds for the patient population, central clearance for a typical patient was 0.09 L/day (23.4% CV) following subcutaneous administration of 225 mg, 675 mg and 900 mg of fremanezumab. The formed small peptides and amino acids may be re-used in the body for de novo synthesis of proteins or are excreted by the kidney. Fremanezumab has an estimated half-life of 30 days.

Special populations

A population pharmacokinetic analysis looking at age, race, gender, and weight was conducted on data from 2,546 subjects. Approximately twice as much exposure is expected in the lowest body weight quartile (43.5 to 60.5 kg) compared to the highest body weight quartile (84.4 to131.8 kg). However, body weight did not have an observed effect on the clinical efficacy based on the exposure-response analyses in episodic and chronic migraine patients. No dose adjustments are required for fremanezumab. No data on exposure-efficacy relationship in subjects with body weight >132 kg is available.

Renal or hepatic impairment

Since monoclonal antibodies are not known to be eliminated via renal pathways or metabolised in the liver, renal and hepatic impairment are not expected to impact the pharmacokinetics of fremanezumab. Patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2) have not been studied. Population pharmacokinetic analysis of integrated data from the AJOVY clinical studies did not reveal a difference in the pharmacokinetics of fremanezumab in patients with mild to moderate renal impairment or hepatic impairment relative to those with normal renal or hepatic function (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction and development.

As fremanezumab is a monoclonal antibody, no genotoxicity or carcinogenicity studies have been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-histidine
L-histidine hydrochloride monohydrate
Sucrose
Disodium ethylenediaminetetraacetic acid (EDTA) dihydrate
Polysorbate 80 (E 433)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Please refer to carton.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Keep the pre-filled syringe(s) or pre-filled pen(s) in the outer carton in order to protect from light.
AJOVY may be stored unrefrigerated for up to 7 days at a temperature up to 30°C. AJOVY must be discarded if it has been out of the refrigerator for longer than 7 days.

6.5 Nature and contents of container

Pre-filled syringe

1.5 mL solution in a 2.25 mL Type I glass syringe with plunger stopper (bromobutyl rubber) and needle.

Pack sizes of 1 or 3 pre-filled syringes. Not all pack sizes may be marketed.

Pre-filled pen

Pre-filled pen containing 1.5 mL solution in a 2.25 mL Type I glass syringe with plunger stopper (bromobutyl rubber) and needle.

Pack sizes of 1 or 3 pre-filled pens. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use

The detailed instructions for use provided in patient information leaflet must be followed step-by-step carefully.
The pre-filled syringe and the pre-filled pen are 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 pre-filled syringe and the pre-filled pen should not be shaken.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

Vetter Pharma-Fertigung GmbH & Co. KG
Mooswiesen 2
88214 Ravensburg
Germany

8. DATE OF REVISION OF THE TEXT

07-2022.