ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼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

Aimovig 70 mg solution for injection in pre-filled syringe
Aimovig 70 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aimovig 70 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 70 mg erenumab.

Aimovig 70 mg solution for injection in pre-filled pen

Each pre-filled pen contains 70 mg erenumab.

Erenumab is a fully human IgG2 monoclonal antibody produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear to opalescent, colourless to light yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Aimovig is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month.

4.2 Posology and method of administration

Treatment should be initiated by physicians experienced in the diagnosis and treatment of migraine.

Posology

Treatment is intended for patients with at least 4 migraine days per month when initiating treatment with erenumab.

The recommended dose is 70 mg erenumab every 4 weeks. Some patients may benefit from a dose of 140 mg every 4 weeks (see section 5.1).

Each 140 mg dose is given as two subcutaneous injections of 70 mg.

Clinical studies have demonstrated that the majority of patients responding to therapy showed clinical benefit within 3 months. Consideration should be given to discontinuing treatment in patients who have shown no response after 3 months of treatment. Evaluation of the need to continue treatment is recommended regularly thereafter.

Special populations
Elderly (aged 65 years and over)
Aimovig has not been studied in elderly patients. No dose adjustment is required as the pharmacokinetics of erenumab are not affected by age.

Renal impairment / 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 Aimovig in children below the age of 18 years have not yet been established. No data are available.

Method of administration

Aimovig is for subcutaneous use.

Aimovig is intended for patient self-administration after proper training. The injections can also be given by another individual who has been appropriately instructed. The injection can be administered into the abdomen, thigh or into the outer area of the upper arm (the arm should be used only if the injection is being given by a person other than the patient; see section 5.2). Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard.

Pre-filled syringe
The entire contents of the Aimovig pre-filled syringe should be injected. Each pre-filled syringe is for single use only and designed to deliver the entire contents with no residual content remaining.

Comprehensive instructions for administration are given in the instructions for use in the package leaflet.

Pre-filled pen
The entire contents of the Aimovig pre-filled pen should be injected. Each pre-filled pen is for single use only and designed to deliver the entire contents with no residual content remaining.

Comprehensive instructions for administration are given in the instructions for use in the package 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

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

Latex-sensitive individuals

The removable cap of the Aimovig pre-filled syringe/pen contains dry natural rubber latex, which may cause allergic reactions in individuals sensitive to latex.

4.5 Interaction with other medicinal products and other forms of interaction

No effect on exposure of co-administered medicinal products is expected based on the metabolic pathways of monoclonal antibodies. No interaction with oral contraceptives (ethinyl estradiol/norgestimate) or sumatriptan was observed in studies with healthy volunteers.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are a limited amount of data from the use of erenumab 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 Aimovig during pregnancy.

Breast-feeding

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

Fertility

Animal studies showed no impact on female and male fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Aimovig is expected to have 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 2,600 patient years) have been treated with Aimovig in registration studies. Of these, more than 1,300 patients were exposed for at least 12 months.

The reported adverse drug reactions for 70 mg and 140 mg were injection site reactions (5.6%/4.5%), constipation (1.3%/3.2%), muscle spasms (0.7%/2.0%) and pruritus (1.0%/1.8%). Most of the reactions were mild or moderate in severity. Less than 2% of patients in these studies discontinued due to adverse events.

Tabulated list of adverse reactions

Table 1 lists all adverse drug reactions that occurred in Aimovig-treated patients during the 12-week placebo-controlled periods of the studies. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is 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).

Table 1 List of adverse reactions in clinical studies

System Organ Class	**Adverse reaction preferred term**	**Frequency category**
Gastrointestinal disorders	Constipation	Common
Skin and subcutaneous tissue disorders	Pruritus[a]	Common
Musculoskeletal and connective tissue disorders	Muscle spasms	Common
General disorders and administration site conditions	Injection site reactions[b]	Common
[a] Pruritus includes preferred terms of generalised pruritus, pruritus and pruritic rash. [b] See section "Injection site reactions" below.		

Description of selected adverse reactions

Injection site reactions
In the integrated 12-week placebo-controlled phase of the studies, injection site reactions were mild and mostly transient. There were no cases of discontinuation due to injection site reactions. The most frequent injection site reactions were localised pain, erythema and pruritus. Injection site pain typically subsided within 1 hour after administration.

Cutaneous reactions
Non-serious cases of rash, pruritus and swelling/oedema were observed, which in the majority of cases were mild and did not lead to treatment discontinuation.

Immunogenicity
In the clinical studies, the incidence of anti-erenumab antibody development during the double-blind treatment phase was 6.3% (56/884) among subjects receiving a 70 mg dose of erenumab (3 of whom had *in vitro* neutralising activity) and 2.6% (13/504) among subjects receiving a 140 mg dose of erenumab (none of whom had *in vitro* neutralising activity). There was no impact of anti-erenumab antibody development on efficacy or safety.

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 listed in Appendix V.

4.9 Overdose

No cases of overdose have been reported in clinical studies.

Doses up to 280 mg have been administered subcutaneously in clinical studies with no evidence of dose-limiting toxicity.

In the event of an overdose, the patient should be treated symptomatically and supportive measures instituted as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgetics, antimigraine preparations, ATC code: N02CX07

Mechanism of action

Erenumab is a human monoclonal antibody that binds to the calcitonin gene-related peptide (CGRP) receptor. The CGRP receptor is located at sites that are relevant to migraine pathophysiology, such as the trigeminal ganglion. Erenumab potently and specifically competes with the binding of CGRP and inhibits its function at the CGRP receptor, and has no significant activity against other calcitonin family of receptors.

CGRP is a neuropeptide that modulates nociceptive signalling and a vasodilator that has been associated with migraine pathophysiology. In contrast with other neuropeptides, CGRP levels have been shown to increase significantly during migraine and return to normal with headache relief. Intravenous infusion of CGRP induces migraine-like headache in patients.

Inhibition of the effects of CGRP could theoretically attenuate compensatory vasodilation in ischaemic-related conditions. A study evaluated the effect of a single intravenous dose of 140 mg Aimovig in subjects with stable angina under controlled exercise conditions. Aimovig showed similar exercise duration compared to placebo and did not aggravate myocardial ischaemia in these patients.

Clinical efficacy and safety

Aimovig (erenumab) was evaluated for prophylaxis of migraine in two pivotal studies across the migraine spectrum in chronic and episodic migraine. In both studies, the patients enrolled had at least a 12-month history of migraine (with or without aura) according to the International Classification of Headache Disorders (ICHD-III) diagnostic criteria. Elderly patients (>65 years), patients with opioid overuse in study in chronic migraine, patients with medication overuse in study in episodic migraine, and also patients with pre-existing myocardial infarction, stroke, transient ischaemic attacks, unstable angina, coronary artery bypass surgery or other re-vascularisation procedures within 12 months prior to screening were excluded. Patients with poorly controlled hypertension or BMI >40 were excluded from Study 1.

Chronic migraine
Study 1
Aimovig (erenumab) was evaluated as monotherapy for prophylaxis of chronic migraine in a randomised, multicentre, 12-week, placebo-controlled, double-blind study in patients suffering from migraine with or without aura (≥15 headache days per month with ≥8 migraine days per month).

667 patients were randomised in a 3:2:2 ratio to receive placebo (n = 286) or 70 mg (n = 191) or 140 mg (n = 190) erenumab, stratified by the presence of acute medication overuse (present in 41% of overall patients). Patients were allowed to use acute headache treatments during the study.

Demographics and baseline disease characteristics were balanced and comparable between study arms. Patients had a median age of 43 years, 83% were female and 94% were white. The mean migraine frequency at baseline was approximately 18 migraine days per month. Overall, 68% had failed one or more previous prophylactic pharmacotherapies due to lack of efficacy or poor tolerability, and 49% had failed two or more previous prophylactic pharmacotherapies due to lack of efficacy or poor tolerability. A total of 366 (96%) patients in the erenumab arms and 265 (93%) patients in the placebo arm completed the study (i.e. completed Week 12 assessment).

Reduction in mean monthly migraine days from placebo was observed in a monthly analysis from Month 1 and in a follow-up weekly analysis an onset of erenumab effect was seen from the first week of administration.

Figure 1 Change from baseline in monthly migraine days over time in Study 1 (including primary endpoint at Month 3)

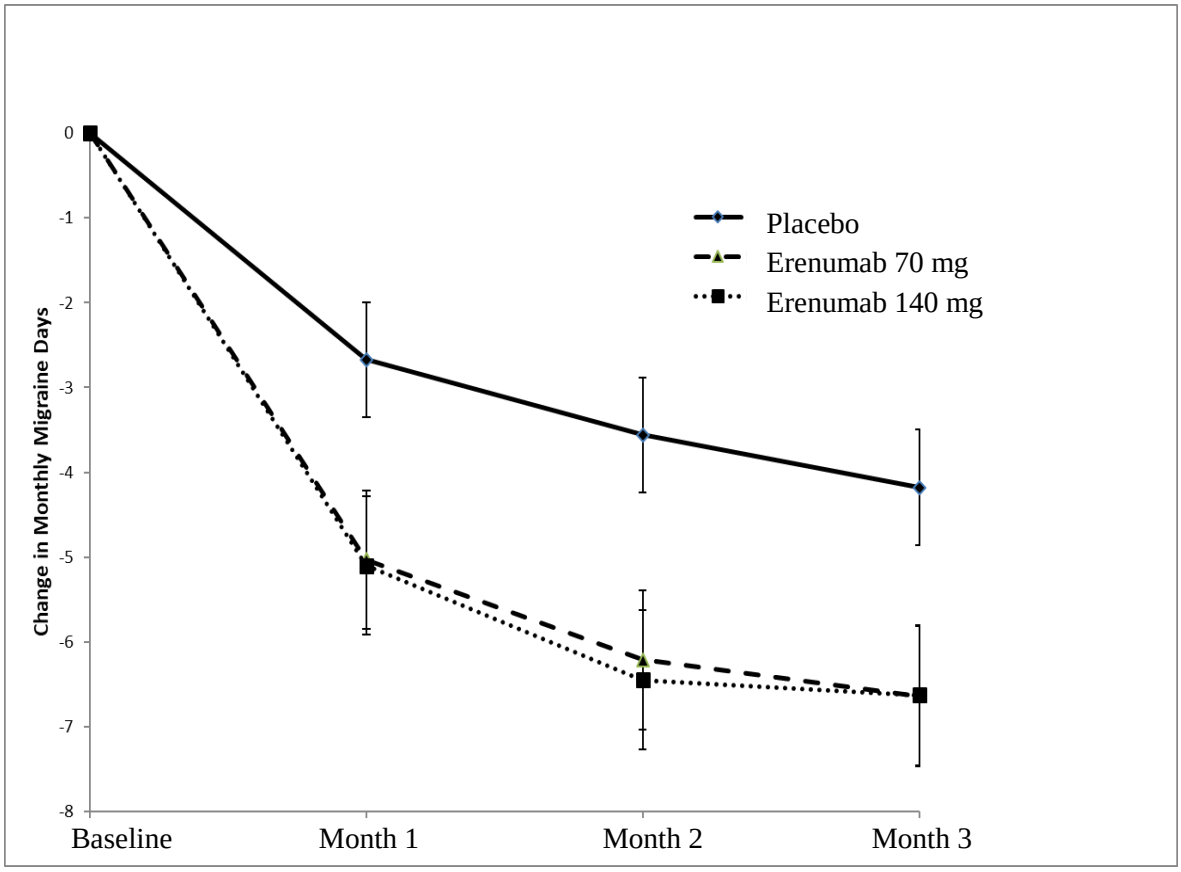

Table 2 Change from baseline in efficacy and patient-reported outcomes at Week 12 in Study 1

	Aimovig (erenumab) 140 mg (n = 187)	Aimovig (erenumab) 70 mg (n = 188)	Placebo (n = 281)	Treatment difference (95% CI)	p-value
Efficacy outcomes					
MMD					
Mean change (95% CI)	-6.6 (-7.5, -5.8)	-6.6 (-7.5; -5.8)	-4.2 (-4.9, -3.5)	Both -2.5 (-3.5, -1.4)	Both <0.001
Baseline (SD)	17.8 (4.7)	17.9 (4.4)	18.2 (4.7)		
≥50% MMD responders					
Percentage [%]	41.2%	39.9%	23.5%	n/a	Both <0.001[a,d]
≥75% MMD responders					
Percentage [%]	20.9%	17.0%	7.8%	n/a	n/a[b]
Monthly acute migraine-specific medication days					
Mean change (95% CI)	-4.1 (-4.7, -3.6)	-3.5 (-4.0, -2.9)	-1.6 (-2.1, -1.1)	70 mg: -1.9 (-2.6, -1.1) 140 mg: -2.6 (-3.3, -1.8)	Both <0.001[a]
Baseline (SD)	9.7 (7.0)	8.8 (7.2)	9.5 (7.6)		
Patient-reported outcome measures					
HIT-6					
Mean change[c] (95% CI)	-5.6 (-6.5, -4.6)	-5.6 (-6.5, -4.6)	-3.1 (-3.9, -2.3)	70 mg: -2.5 (-3.7, -1.2) 140 mg: -2.5 (-3.7, -1.2)	n/a[b]
MIDAS total					
Mean change[c] (95% CI)	-19.8 (-25.6, -14.0)	-19.4 (-25.2, -13.6)	-7.5 (-12.4, -2.7)	70 mg: -11.9 (-19.3, -4.4) 140 mg: -12.2 (-19.7, -4.8)	n/a[b]

CI = confidence interval; MMD = monthly migraine days; HIT-6 = Headache Impact Test; MIDAS = Migraine Disability Assessment

[a] For secondary endpoints, all p-values are reported as unadjusted p-values and are statistically significant after adjustment for multiple comparisons.

[b] For exploratory endpoints, no p-value is presented.

[c] For HIT-6: Change and reduction from baseline were evaluated in the last 4 weeks of the 12-week double-blind treatment phase. For MIDAS: Change and reduction from baseline were evaluated over 12 weeks. For data collection a recall period of 3 months has been used.

[d] p value was calculated based on the odds ratios.

In patients failing one or more prophylactic pharmacotherapies the treatment difference for the reduction of monthly migraine days (MMD) observed between erenumab 140 mg and placebo was -3.3 days (95% CI: -4.6, -2.1) and between erenumab 70 mg and placebo -2.5 days (95% CI: -3.8, -1.2). In patients failing two or more prophylactic pharmacotherapies the treatment difference was -4.3 days (95% CI: -5.8; -2.8) between 140 mg and placebo and -2.7 days (95% CI: -4.2, -1.2) between 70 mg and placebo. There was also a higher proportion of subjects treated with erenumab who achieved at least 50% reduction of MMD compared to placebo in the patients failing one or more prophylactic pharmacotherapies (40.8% for 140 mg, 34.7% for 70 mg versus 17.3% for placebo), with an odds ratio of 3.3 (95% CI: 2.0, 5.5) for 140 mg and 2.6 (95% CI: 1.6, 4.5) for 70 mg. In patients failing two or more prophylactic pharmacotherapies the proportion was 41.3% for 140 mg and 35.6% for 70 mg versus 14.2% for placebo with an odds ratio of 4.2 (95% CI: 2.2, 7.9) and 3.5 (95% CI: 1.8, 6.6), respectively.

Approximately 41% of patients in the study had medication overuse. The treatment difference observed between erenumab 140 mg and placebo and between erenumab 70 mg and placebo for the reduction of MMD in these patients was -3.1 days (95% CI: -4.8, -1.4) in both cases, and for the reduction of acute migraine-specific medication days was -2.8 (95% CI: -4.2, -1.4) for 140 mg and -3.3 (95% CI: -4.8, -1.9) for 70 mg. There was a higher proportion of patients in the erenumab group who achieved at least a 50% reduction of MMD compared to placebo (34.6% for 140 mg, 36.4% for 70 mg versus 17.7% for placebo), with an odds ratio of 2.5 (95% CI: 1.3, 4.9) and 2.7 (95% CI: 1.4, 5.2), respectively.

Efficacy was sustained for up to 1 year in the open-label extension of Study 1 in which patients received 70 mg and/or 140 mg erenumab. 74.1% of patients completed the 52-week extension. Pooled across the two doses, a reduction of -9.3 MMD was observed after 52 weeks relative to core study baseline. 59% of patients completing the study achieved a 50% response in the last month of the study.

Episodic migraine
Study 2
Aimovig (erenumab) was evaluated for prophylaxis of episodic migraine in a randomised, multicentre, 24-week, placebo-controlled, double-blind study in patients suffering from migraine with or without aura (4-14 migraine days per month).

955 patients were randomised in a 1:1:1 ratio to receive 140 mg (n = 319) or 70 mg (n = 317) erenumab or placebo (n = 319). Patients were allowed to use acute headache treatments during the study.

Demographics and baseline disease characteristics were balanced and comparable between study arms. Patients had a median age of 42 years, 85% were female and 89% were white. The mean migraine frequency at baseline was approximately 8 migraine days per month. Overall, 39% had failed one or more previous prophylactic pharmacotherapies due to lack of efficacy or poor tolerability. A total of 292 patients (92%) for 140 mg, 284 (90%) patients for 70 mg and 282 patients (88%) in the placebo arm completed the double-blind phase.

Patients treated with erenumab had a clinically relevant and statistically significant reduction from baseline in the frequency of migraine days from Months 4 to 6 (Figure 2) compared to patients receiving placebo. Differences from placebo were observed from Month 1.

Figure 2 Change from baseline in monthly migraine days over time in Study 2 (including primary endpoint over Months 4, 5 and 6)

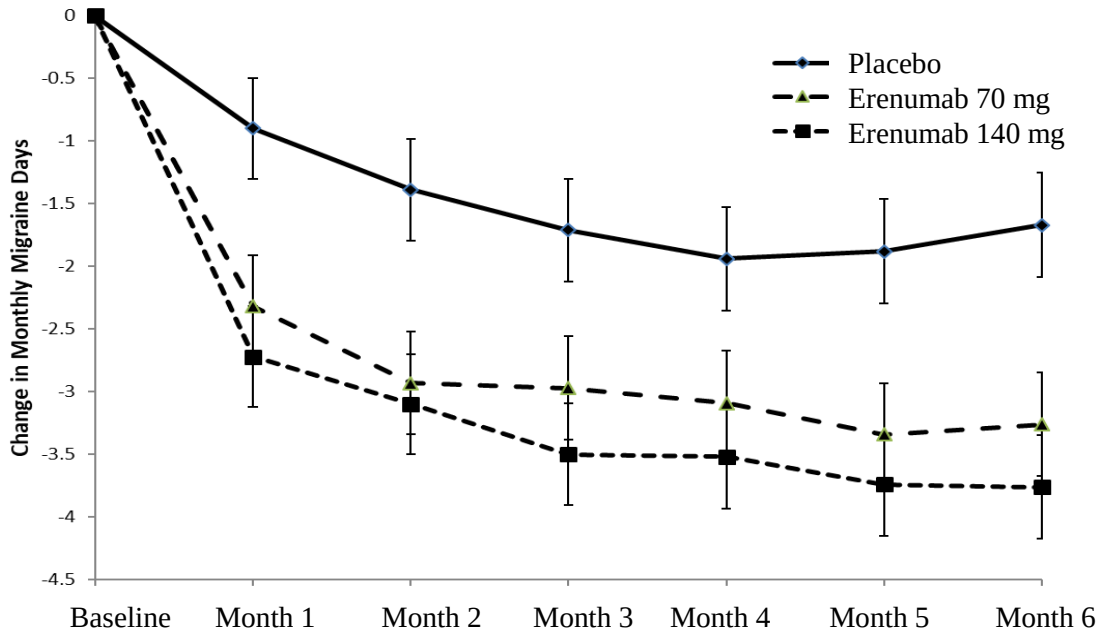

Table 3 Change from baseline in efficacy and patient-reported outcomes at Weeks 13-24 in Study 2

	Aimovig (erenumab) 140 mg (n = 318)	**Aimovig (erenumab) 70 mg** (n = 312)	**Placebo** (n = 316)	**Treatment difference** (95% CI)	**p-value**
Efficacy outcomes					
MMD					
Mean change (95% CI) Baseline (SD)	-3.7 (-4.0, -3.3) 8.3 (2.5)	-3.2 (-3.6, -2.9) 8.3 (2.5)	-1.8 (-2.2, -1.5) 8.2 (2.5)	70 mg: -1.4 (-1.9, -0.9) 140 mg: -1.9 (-2.3, -1.4)	Both <0.001[a]
≥50% MMD responders					
Percentage [%]	50.0%	43.3%	26.6%	n/a	Both <0.001[a,d]
≥75% MMD responders					
Percentage [%]	22.0%	20.8%	7.9%	n/a	n/a[b]
Monthly acute migraine-specific medication days					
Mean change (95% CI) Baseline (SD)	-1.6 (-1.8, -1.4) 3.4 (3.5)	-1.1 (-1.3, -0.9) 3.2 (3.4)	-0.2 (-0.4, 0.0) 3.4 (3.4)	70 mg: -0.9(-1.2, -0.6) 140 mg: -1.4 (-1.7, -1.1)	Both <0.001[a]
Patient-reported outcome measures					
HIT-6					
Mean change[c] (95% CI)	-6.9 (-7.6, -6.3)	-6.7 (-7.4, -6.0)	-4.6 (-5.3, -4.0)	70 mg: -2.1 (-3.0, -1.1) 140 mg: -2.3 (-3.2, -1.3)	n/a[b]
MIDAS (modified) total					n/a[b]
Mean change[c] (95% CI)	-7.5 (-8.3, -6.6)	-6.7 (-7.6, -5.9)	-4.6 (-5.5, -3.8)	70 mg: -2.1 (-3.3, -0.9) 140 mg: -2.8 (-4.0, -1.7)	

CI = confidence interval; MMD = monthly migraine days; HIT-6 = Headache Impact Test; MIDAS = Migraine Disability Assessment

[a] For the secondary endpoints, all p-values are reported as unadjusted p-values and are statistically significant after adjustment for multiple comparisons.

[b] For exploratory endpoints, no p-value was presented.

[c] For HIT-6: Change and reduction from baseline were evaluated in the last 4 weeks of the 12-week double-blind treatment phase. For MIDAS: Change and reduction from baseline were evaluated over 24 weeks. For data collection a recall period of 1 month has been used.

[d] p value is calculated based on the odds ratios.

In patients failing one or more prophylactic pharmacotherapies the treatment difference for the reduction of MMD observed between erenumab 140 mg and placebo was -2.5 (95% CI: -3.4, -1.7) and between erenumab 70 mg and placebo -2.0 (95% CI: -2.8, -1.2). There was also a higher proportion of subjects treated with erenumab who achieved at least 50% reduction of MMD compared to placebo (39.7% for 140 mg and 38.6% for 70 mg, with an odds ratio of 3.1 [95% CI: 1.7, 5.5] and 2.9 [95% CI: 1.6, 5.3], respectively).

Efficacy was sustained up to 1 year in the active re-randomisation part of Study 2. Patients were re-randomised in the active treatment phase (ATP) to 70 mg or 140 mg erenumab. 79.8% completed the entire study out to 52 weeks. The reduction in monthly migraine days from baseline to Week 52 was -4.22 in the 70 mg ATP group and -4.64 days in the 140 mg ATP group. At Week 52, the proportion of subjects who achieved a ≥50% reduction in MMD from baseline was 61.0% in the 70 mg ATP and 64.9% in the 140 mg ATP group.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Aimovig in prevention of migraine headaches in one or more subsets of the paediatric population (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Erenumab exhibits non-linear kinetics as a result of binding to the CGRP-R receptor. However, at therapeutically relevant doses, the pharmacokinetics of erenumab following subcutaneous dosing every 4 weeks are predominantly linear due to saturation of binding to CGRP-R. Subcutaneous administration of a 140 mg once monthly dose and a 70 mg once monthly dose in healthy volunteers resulted in a C_{max} mean (standard deviation [SD]) of 15.8 (4.8) µg/ml and 6.1 (2.1) µg/ml, respectively, and AUC_{last} mean (SD) of 505 (139) day*µg/ml and 159 (58) day*µg/ml, respectively.

Less than 2-fold accumulation was observed in trough serum concentrations following 140 mg doses administered subcutaneously every 4 weeks and serum trough concentrations approached steady state by 12 weeks of dosing.

Absorption

Following a single subcutaneous dose of 140 mg or 70 mg erenumab administered to healthy adults, median peak serum concentrations were attained in 4 to 6 days, and estimated absolute bioavailability was 82%.

Distribution

Following a single 140 mg intravenous dose, the mean (SD) volume of distribution during the terminal phase (Vz) was estimated to be 3.86 (0.77) l.

Biotransformation / Elimination

Two elimination phases were observed for erenumab. At low concentrations, the elimination is predominately through saturable binding to target (CGRP-R), while at higher concentrations the elimination of erenumab is largely through a non-specific proteolytic pathway. Throughout the dosing period erenumab is predominantly eliminated via a non-specific proteolytic pathway with the effective half-life of 28 days.

Special populations

Patients with renal impairment
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 Aimovig clinical studies did not reveal a difference in the pharmacokinetics of erenumab in patients with mild or moderate renal impairment relative to those with normal renal function (see section 4.2).

Patients with hepatic impairment
No studies have been performed in patients with hepatic impairment. Erenumab, as a human monoclonal antibody, is not metabolised by cytochrome P450 enzymes and hepatic clearance is not a major clearance pathway for erenumab (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.

Carcinogenicity studies have not been conducted with erenumab. Erenumab is not pharmacologically active in rodents. It has biological activity in cynomolgus monkeys, but this species is not an appropriate model for evaluation of tumorigenic risk. The mutagenic potential of erenumab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

In repeated-dose toxicology studies there were no adverse effects in sexually mature monkeys dosed up to 150 mg/kg subcutaneously twice weekly for up to 6 months at systemic exposures up to 123-fold and 246-fold higher than the clinical dose of 140 mg and 70 mg, respectively, every 4 weeks, based on serum AUC. There were also no adverse effects on surrogate markers of fertility (anatomical pathology or histopathology changes in reproductive organs) in these studies.

In a reproduction study in cynomolgus monkeys there were no effects on pregnancy, embryo-foetal or post-natal development (up to 6 months of age) when erenumab was dosed throughout pregnancy at exposure levels approximately 17-fold and 34-fold higher than those achieved in patients receiving erenumab 140 mg and 70 mg, respectively, every 4 weeks dosing regimen based on AUC. Measurable erenumab serum concentrations were observed in the infant monkeys at birth, confirming that erenumab, like other IgG antibodies, crosses the placental barrier.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Polysorbate 80
Sodium hydroxide (for pH adjustment)
Glacial acetic acid
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

2 years

6.4 Special precautions for storage

Pre-filled syringe

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
After removal from the refrigerator, Aimovig must be used within 14 days when stored at room temperature (up to 25°C), or discarded. If it is stored at a higher temperature or for a longer period it must be discarded.

Pre-filled pen

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.
After removal from the refrigerator, Aimovig must be used within 14 days when stored at room temperature (up to 25°C), or discarded. If it is stored at a higher temperature or for a longer period it must be discarded.

6.5 Nature and contents of container

Pre-filled syringe

Aimovig is supplied in a pre-filled syringe (1 ml, Type 1 glass) with a stainless steel needle and a needle cover (rubber containing latex).

Aimovig is available in packs containing 1 pre-filled syringe.

Pre-filled pen

Aimovig is supplied in a pre-filled pen (1 ml, Type 1 glass) with a stainless steel needle and a needle cover (rubber containing latex).

Aimovig is available in packs containing 1 pre-filled pen and in multipacks containing 3 (3x1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Before administration, the solution should be inspected visually. The solution should not be injected if it is cloudy, distinctly yellow or contains flakes or particles.

Pre-filled syringe

To avoid discomfort at the site of injection, the pre-filled syringe(s) should be left to stand at room temperature (up to 25°C) for at least 30 minutes before injecting. It should also be protected from direct sunlight. The entire contents of the pre-filled syringe(s) must be injected. The syringe(s) must not be warmed by using a heat source such as hot water or microwave and must not be shaken.

Pre-filled pen

To avoid discomfort at the site of injection, the pre-filled pen(s) should be left to stand at room temperature (up to 25°C) for at least 30 minutes before injecting. It should also be protected from direct sunlight. The entire contents of the pre-filled pen(s) must be injected. The pen(s) must not be warmed by using a heat source such as hot water or microwave and must not be shaken.

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

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1293/001-003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Amgen, Inc.
One Amgen Center Drive
Thousand Oaks
CA
91320
United States

Name and address of the manufacturer(s) responsible for batch release

Novartis Pharma GmbH
Roonstrasse 25
D-90429 Nuremberg
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Aimovig 70 mg solution for injection in pre-filled syringe
erenumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 70 mg erenumab.

3. LIST OF EXCIPIENTS

Also contains: sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.
Needle cap contains latex.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1293/003 Pack containing 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aimovig 70 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aimovig 70 mg injection
erenumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Aimovig 70 mg solution for injection in pre-filled pen
erenumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 70 mg erenumab.

3. LIST OF EXCIPIENTS

Also contains: sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.
Needle cap contains latex.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1293/001 Pack containing 1 pre-filled pen

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aimovig 70 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Aimovig 70 mg solution for injection in pre-filled pen
erenumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 70 mg erenumab.

3. LIST OF EXCIPIENTS

Also contains: sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.
Needle cap contains latex.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1293/002 Multipack containing 3 (3x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aimovig 70 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Aimovig 70 mg solution for injection in pre-filled pen
erenumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 70 mg erenumab.

3. LIST OF EXCIPIENTS

Also contains: sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.
Needle cap contains latex.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen
Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1293/002 Multipack containing 3 (3x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aimovig 70 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aimovig 70 mg injection
erenumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Aimovig 70 mg solution for injection in pre-filled syringe
erenumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Aimovig is and what it is used for

Aimovig contains the active substance erenumab. It belongs to a group of medicines called monoclonal antibodies.

Aimovig works by blocking the activity of the CGRP molecule, which has been linked to migraine (CGRP stands for calcitonin gene-related peptide).

Aimovig is used to prevent migraine in adults who have at least 4 migraine days per month when starting treatment with Aimovig.

2. What you need to know before you use Aimovig

Do not use Aimovig:
- if you are allergic to erenumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before using Aimovig:
- if you have ever had an allergic reaction to rubber latex. The container of this medicinal product contains latex rubber within the cap.
- if you suffer from a cardiovascular disease. Aimovig has not been studied in patients with certain cardiovascular diseases.

Children and adolescents
Do not give this medicine to children or adolescents (under 18 years old) because the use of Aimovig has not been studied in this age group.

Other medicines and Aimovig
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Pregnancy
Your doctor will decide whether you should stop using Aimovig during pregnancy.

Breast-feeding
Monoclonal antibodies like Aimovig are known to pass into breast milk during the first few days after birth, but after this first period Aimovig can be used. Talk to your doctor about using Aimovig while breast-feeding in order to help you decide whether you should stop breast-feeding or stop using Aimovig.

Driving and using machines
Aimovig is unlikely to affect your ability to drive and use machines.

Aimovig contains sodium
Aimovig contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Aimovig

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

If you have not noticed any treatment effect after 3 months, tell your doctor who will decide whether you should continue treatment.

If your doctor prescribes the 70 mg dose you should have one injection once every 4 weeks. If your doctor prescribes the 140 mg dose you should have two injections once every 4 weeks. The second injection must be given immediately after the first one at a different injection site. Make sure that you inject the entire contents of both syringes.

Aimovig is given as an injection under your skin (known as a subcutaneous injection). You or your caregiver can give the injection into your abdomen or your thigh. The outer area of your upper arm can also be used as an injection site, but only if someone else is giving you the injection. If you need 2 injections, they should be given in different sites to avoid hardening of the skin and should not be given into areas where the skin is tender, bruised, red or hard.

Your doctor or nurse will give you or your caregiver training in the right way to prepare and inject Aimovig. Do not try to inject Aimovig until this training has been given.

Aimovig syringes are for single use only.

For detailed instructions on how to inject Aimovig, see "Instructions for use of Aimovig pre-filled syringe" at the end of this leaflet.

If you use more Aimovig than you should
If you have received more Aimovig than you should or if the dose has been given earlier than it should have been, tell your doctor.

If you forget to use Aimovig
- If you forget an Aimovig dose, take it as soon as possible after you realise.
- Then contact your doctor, who will tell you when you should schedule your next dose. Follow the new schedule exactly as your doctor has told you.

If you stop using Aimovig
Do not stop using Aimovig without talking to your doctor first. Your symptoms may return if you stop the treatment.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Possible side effects are listed below. Most of these side effects are mild to moderate.

Common: may affect up to 1 in 10 people
- constipation
- itching
- muscle spasms
- injection site reactions, such as pain, redness and swelling where the injection is given.

Aimovig may cause skin reactions such as rash or itching which are usually mild.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aimovig

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Keep the syringe(s) in the outer carton in order to protect from light. Store in a refrigerator (2°C – 8°C). Do not freeze.

After Aimovig has been taken out of the refrigerator, it must be kept at room temperature (up to 25°C) in the outer carton and must be used within 14 days, or else discarded. Do not put Aimovig back in the refrigerator once it has been removed.

Do not use this medicine if you notice that the solution contains particles, is cloudy or is distinctly yellow.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aimovig contains
- The active substance is erenumab. Each pre-filled syringe contains 70 mg erenumab.
- The other ingredients are sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.

What Aimovig looks like and contents of the pack
Aimovig solution for injection is clear to opalescent, colourless to light yellow, and practically free from particles.

Each pack contains one single-use pre-filled syringe.

Marketing Authorisation Holder
Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

Manufacturer
Novartis Pharma GmbH
Roonstrasse 25
90429 Nuremberg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

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Novartis Bulgaria EOOD
Тел: +359 2 489 98 28

Česká republika
Novartis s.r.o.
Tel: +420 225 775 111

Danmark
Novartis Healthcare A/S
Tlf: +45 39 16 84 00

Deutschland
Novartis Pharma GmbH
Tel: +49 911 273 0

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Tel: +372 66 30 810

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Novartis Pharma N.V.
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Tlf: +47 23 05 20 00

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Tel: +43 1 86 6570

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Novartis Farmacéutica, S.A.
Tel: +34 93 306 42 00

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Tél: +33 1 55 47 66 00

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Novartis Hrvatska d.o.o.
Tel. +385 1 6274 220

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Novartis Ireland Limited
Tel: +353 1 260 12 55

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Sími: +354 535 7000

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Novartis Farma S.p.A.
Tel: +39 02 96 54 1

Κύπρος
Novartis Pharma Services Inc.
Τηλ: +357 22 690 690

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SIA "Novartis Baltics"
Tel: +371 67 887 070

Polska
Novartis Poland Sp. z o.o.
Tel.: +48 22 375 4888

Portugal
Novartis Farma - Produtos Farmacêuticos, S.A.
Tel: +351 21 000 8600

România
Novartis Pharma Services Romania SRL
Tel: +40 21 31299 01

Slovenija
Novartis Pharma Services Inc.
Tel: +386 1 300 75 50

Slovenská republika
Novartis Slovakia s.r.o.
Tel: +421 2 5542 5439

Suomi/Finland
Novartis Finland Oy
Puh/Tel: +358 (0)10 6133 200

Sverige
Novartis Sverige AB
Tel: +46 8 732 32 00

United Kingdom
Novartis Pharmaceuticals UK Ltd.
Tel: +44 1276 698370

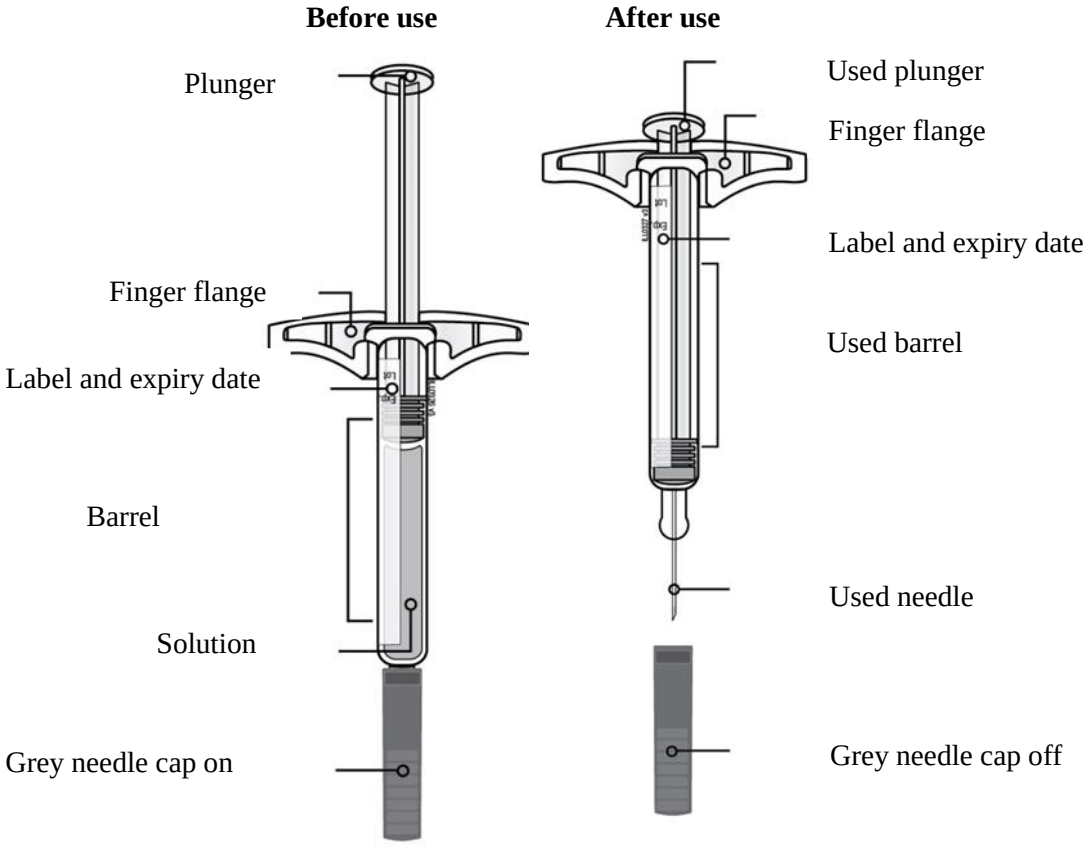
This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Aimovig pre-filled syringe

Illustration of the syringe



Note: Needle is inside.

General

Before you use the Aimovig pre-filled syringe, read this important information:

Step 1: Prepare
Note: The prescribed dose of Aimovig is either 70 mg or 140 mg. This means that for the 70 mg dose you must inject the contents of one 70 mg single-use syringe. For a dose of 140 mg you must inject the contents of two 70 mg single-use syringes, one after the other, to get your full dose of this medicine.

(**A)**

Remove Aimovig pre-filled syringe(s) from the carton by holding it/them at the barrel. You may need to use either one or two syringes based on your prescribed dose. Do not shake.

To avoid discomfort at the site of injection, leave the syringe(s) at room temperature for at least 30 minutes before injecting.

Note: Do not try to warm the syringe(s) by using a heat source such as hot water or microwave.

(B)

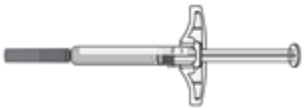
Inspect each syringe. Make sure the solution you see in the syringe is clear and colourless to light yellow.

Note:
- Do not use the syringe if any part of it appears cracked or broken.
- Do not use the syringe if it has been dropped.
- Do not use the syringe if the needle cap is missing or is not securely attached.

In all cases described above, use a new syringe, and if you are unsure contact your doctor or pharmacist.

(C)

Gather all materials needed for the injections:

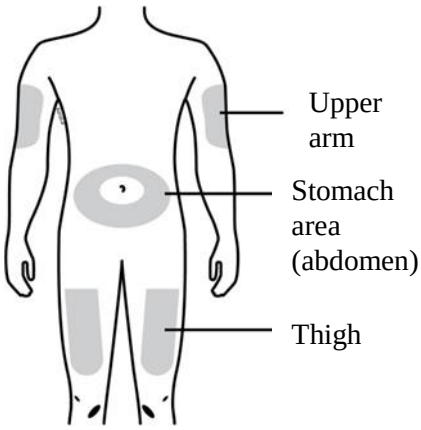


Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:
- New syringe
- Alcohol wipes
- Cotton balls or gauze pads
- Adhesive plasters
- Sharps disposal container

(D)

Prepare and clean the injection site(s).



You can use any of the following injection sites:
- Thigh
- Stomach area (abdomen) (except for a 5 cm area around the navel)
- Outer area of upper arm (only if someone else is giving you the injection)

Clean the injection site with an alcohol wipe and let the skin dry.

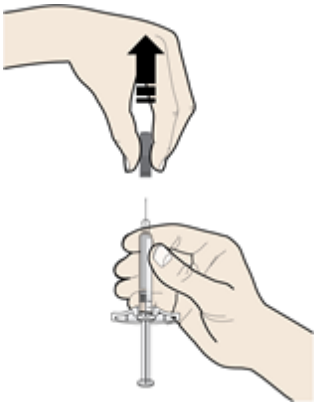
Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.

Note:
- After you have cleaned the area, do not touch it again before injecting.
- Do not choose an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Step 2: Get ready

(E)

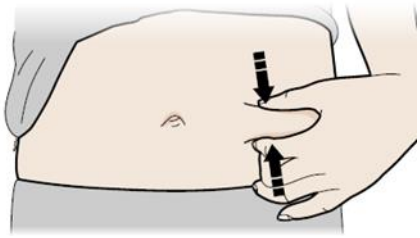
Pull the grey needle cap straight off and away from your body, only when you are ready to inject. The injection must be administered within 5 minutes. It is normal to see a drop of liquid at the end of the needle.



Note**:**
- Do not leave the grey needle cap off for more than 5 minutes. This can dry out the medicine.
- Do not twist or bend the grey needle cap.
- Do not put the grey needle cap back onto the syringe once it has been removed.

(F)

Firmly pinch the skin at the injection site.



Note: Keep skin pinched while injecting.

Step 3: Inject

(G)

While pinching, insert the syringe needle into the skin at an angle of 45 to 90 degrees.

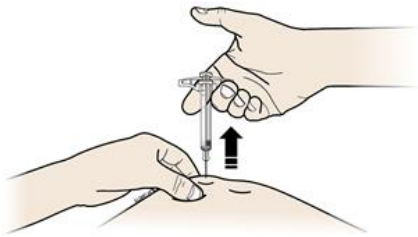
Do not place your finger on the plunger while inserting the needle.

(H)

Using slow and constant pressure, push the plunger rod all the way down until it stops moving.

(I)

When done, release your thumb, and gently lift the syringe off of the skin and then release the pinched skin.



Note: When you remove the syringe, if it looks like there is still medicine in the syringe barrel this means you have not received a full dose. Contact your doctor.

Step 4: Finish

(J)

Discard the used syringe and the grey needle cap.
Put the used syringe in a sharps disposal container immediately after use. Talk to your doctor or pharmacist about proper disposal. There may be local regulations for disposal.

Note:
- Do not reuse the syringe.
- Do not recycle the syringe or sharps disposal container, or throw them into household waste.

Always keep the sharps disposal container out of the reach of children.

(K)

Examine the injection site.
If there is any blood on the skin, press a cotton ball or gauze pad onto the injection site. Do not rub the injection site. Apply an adhesive plaster if needed.

In case your dose is 140 mg, repeat all steps with the second syringe to inject the full dose.

Package leaflet: Information for the user

Aimovig 70 mg solution for injection in pre-filled pen
erenumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Aimovig is and what it is used for

Aimovig contains the active substance erenumab. It belongs to a group of medicines called monoclonal antibodies.

Aimovig works by blocking the activity of the CGRP molecule, which has been linked to migraine (CGRP stands for calcitonin gene-related peptide).

Aimovig is used to prevent migraine in adults who have at least 4 migraine days per month when starting treatment with Aimovig.

2. What you need to know before you use Aimovig

Do not use Aimovig:
- if you are allergic to erenumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before using Aimovig:
- if you have ever had an allergic reaction to rubber latex. The container of this medicinal product contains latex rubber within the cap.
- if you suffer from a cardiovascular disease. Aimovig has not been studied in patients with certain cardiovascular diseases.

Children and adolescents
Do not give this medicine to children or adolescents (under 18 years old) because the use of Aimovig has not been studied in this age group.

Other medicines and Aimovig
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Pregnancy
Your doctor will decide whether you should stop using Aimovig during pregnancy.

Breast-feeding
Monoclonal antibodies like Aimovig are known to pass into breast milk during the first few days after birth, but after this first period Aimovig can be used. Talk to your doctor about using Aimovig while breast-feeding in order to help you decide whether you should stop breast-feeding or stop using Aimovig.

Driving and using machines
Aimovig is unlikely to affect your ability to drive and use machines.

Aimovig contains sodium
Aimovig contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Aimovig

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

If you have not noticed any treatment effect after 3 months, tell your doctor who will decide whether you should continue treatment.

If your doctor prescribes the 70 mg dose you should have one injection once every 4 weeks. If your doctor prescribes the 140 mg dose you should have two injections once every 4 weeks. The second injection must be given immediately after the first one at a different injection site. Make sure that you inject the entire contents of both pens.

Aimovig is given as an injection under your skin (known as a subcutaneous injection). You or your caregiver can give the injection into your abdomen or your thigh. The outer area of your upper arm can also be used as an injection site, but only if someone else is giving you the injection. If you need 2 injections, they should be given in different sites to avoid hardening of the skin and should not be given into areas where the skin is tender, bruised, red or hard.

Your doctor or nurse will give you or your caregiver training in the right way to prepare and inject Aimovig. Do not try to inject Aimovig until this training has been given.

Aimovig pens are for single use only.

For detailed instructions on how to inject Aimovig, see "Instructions for use of Aimovig pre-filled pen" at the end of this leaflet.

If you use more Aimovig than you should
If you have received more Aimovig than you should or if the dose has been given earlier than it should have been, tell your doctor.

If you forget to use Aimovig
- If you forget an Aimovig dose, take it as soon as possible after you realise.
- Then contact your doctor, who will tell you when you should schedule your next dose. Follow the new schedule exactly as your doctor has told you.

If you stop using Aimovig
Do not stop using Aimovig without talking to your doctor first. Your symptoms may return if you stop the treatment.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Possible side effects are listed below. Most of these side effects are mild to moderate.

Common: may affect up to 1 in 10 people
- constipation
- itching
- muscle spasms
- injection site reactions, such as pain, redness and swelling where the injection is given.

Aimovig may cause skin reactions such as rash or itching which are usually mild.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aimovig

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Keep the pen(s) in the outer carton in order to protect from light. Store in a refrigerator (2°C – 8°C). Do not freeze.

After Aimovig has been taken out of the refrigerator, it must be kept at room temperature (up to 25°C) in the outer carton and must be used within 14 days, or else discarded. Do not put Aimovig back in the refrigerator once it has been removed.

Do not use this medicine if you notice that the solution contains particles, is cloudy or is distinctly yellow.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aimovig contains
- The active substance is erenumab. Each pre-filled pen contains 70 mg erenumab.
- The other ingredients are sucrose, polysorbate 80, sodium hydroxide, glacial acetic acid, water for injections.

What Aimovig looks like and contents of the pack
Aimovig solution for injection is clear to opalescent, colourless to light yellow, and practically free from particles.

Aimovig is available in packs containing one single-use pre-filled pen and in multipacks containing 3 (3x1) pre-filled pens.

Not all pack sizes may be marketed.

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Manufacturer
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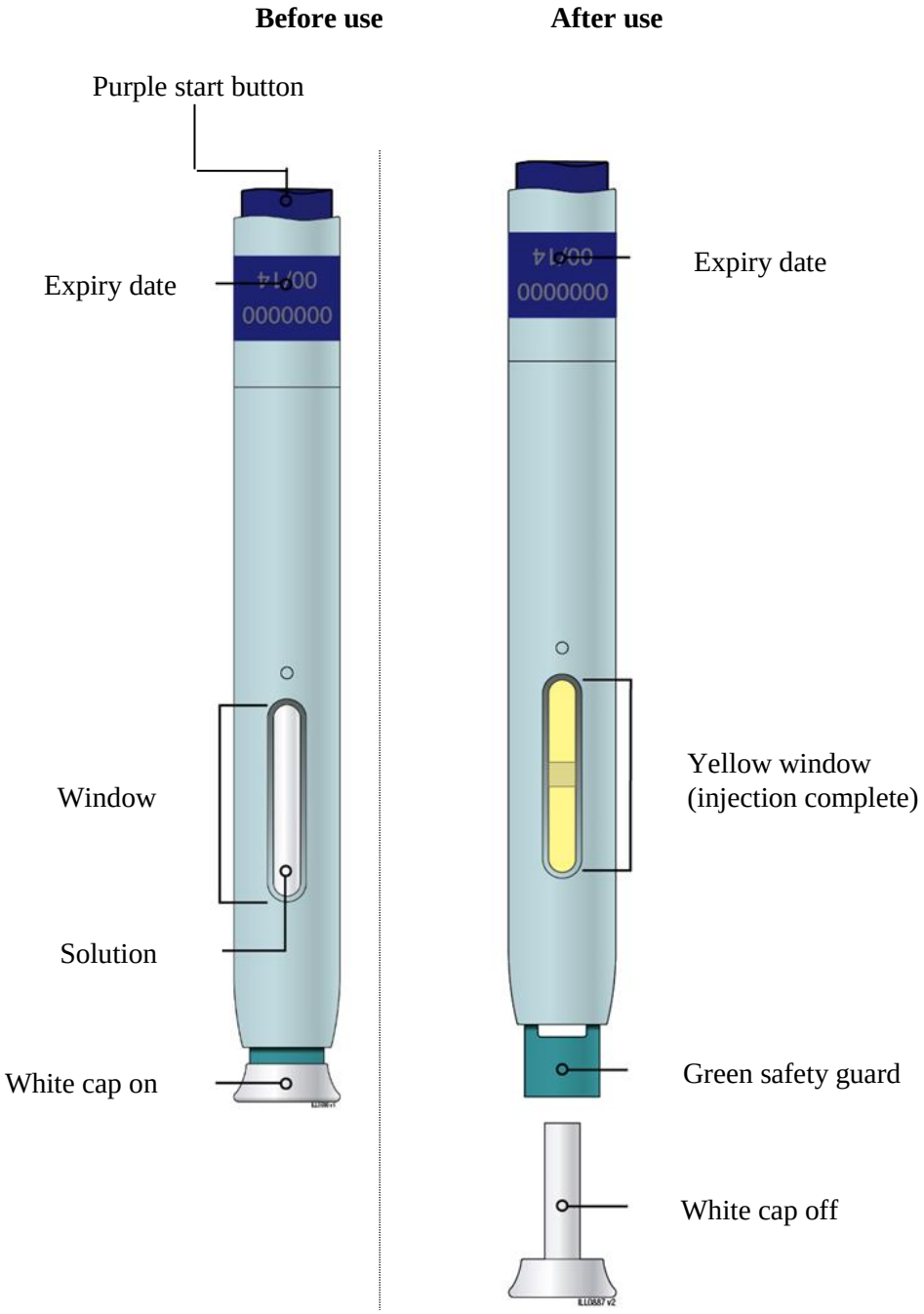
This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Aimovig pre-filled pen

Illustration of the pen



Note: Needle is inside the pen.

General

Before you use the Aimovig pre-filled pen, read this information.

Step 1: Prepare
Note: The prescribed dose of Aimovig is either 70 mg or 140 mg. This means that for the 70 mg dose you must inject the contents of one 70 mg single-use pen. For a dose of 140 mg you must inject the contents of two 70 mg single-use pens, one after the other, to get your full dose of this medicine.

(A)

Carefully lift Aimovig pre-filled pen out of the carton. You may need to use either one or two pens based on your prescribed dose. Do not shake.

To avoid discomfort at the site of injection, leave the pen(s) at room temperature for at least 30 minutes before injecting.

Note: Do not try to warm the pen(s) by using a heat source such as hot water or microwave.

(B)

Inspect each pen. Make sure the solution you see in the window is clear and colourless to light yellow.

Note:
- Do not use the pen if any part of it appears cracked or broken.
- Do not use the pen if it has been dropped.
- Do not use the pen if the white cap is missing or is not securely attached.

In all cases described above, use a new pen, and if you are unsure contact your doctor or pharmacist.

(C)

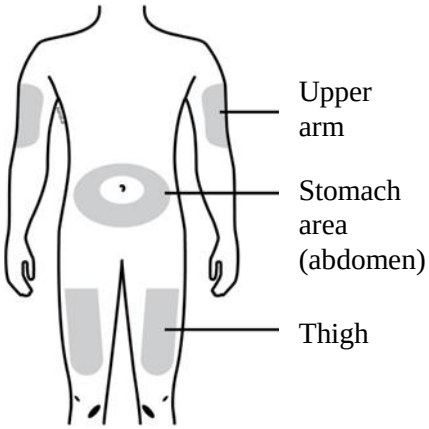
Gather all materials needed for the injections.

Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:
- New pen
- Alcohol wipes
- Cotton balls or gauze pads
- Adhesive plasters
- Sharps disposal container

(D)

Prepare and clean the injection site(s).



You can use any of the following injection sites:
- Thigh
- Stomach area (abdomen) (except for a 5 cm area around the navel)
- Outer area of upper arm (only if someone else is giving you the injection)

Clean the injection site with an alcohol wipe and let the skin dry.

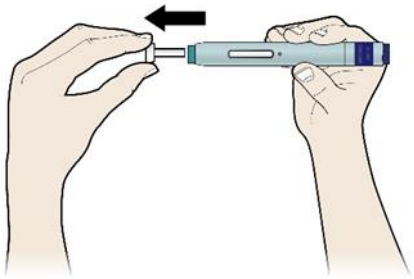
Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.

Note:
- After you have cleaned the area, do not touch it again before injecting.
- Do not choose an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Step 2: Get ready

(E)

Pull the white cap straight off, only when you are ready to inject. The injection must be administered within 5 minutes. It is normal to see a drop of liquid at the end of the needle or green safety guard.

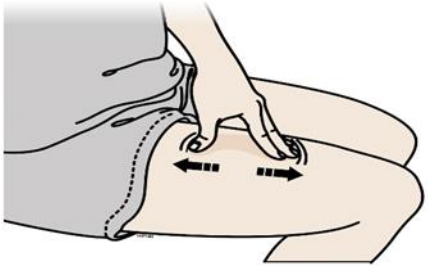


Note:
- Do not leave the white cap off for more than 5 minutes. This can dry out the medicine.
- Do not twist or bend the white cap.
- Do not put the white cap back onto the pen once it has been removed.

(F)

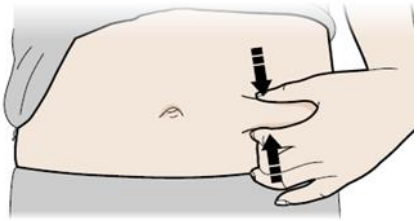
Stretch or pinch the injection site to create a firm surface.

Stretch method
Stretch skin firmly by moving your thumb and fingers in opposite directions, creating an area about **five** cm wide.



or

Pinch method
Pinch skin firmly between your thumb and fingers, creating an area about **five** cm wide.

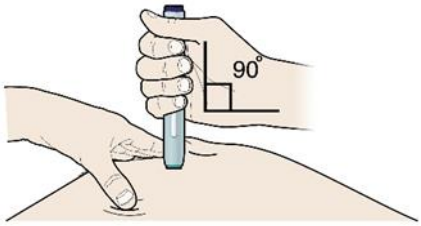


Note: Keep skin stretched or pinched while injecting.

Step 3: Inject

(G)

Keep holding the stretch or pinch. With the white cap off, place the pen on the skin at an angle of 90 degrees.

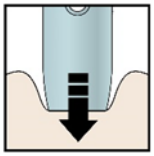


Note: Do not touch the purple start button yet.

(H)

Firmly push the pen down onto the skin until it stops moving.

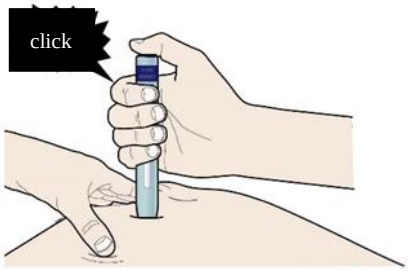
Push down



Note: You must push all the way down but do not touch the purple start button until you are ready to inject.

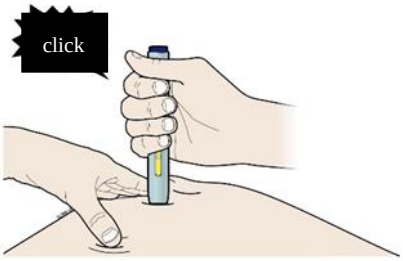
(I)

Press the purple start button. You will hear a click.

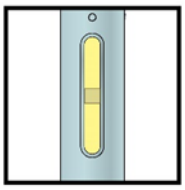


(J)

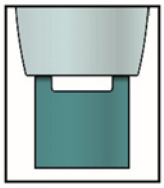
Remove your thumb from the button, but keep pushing down on the skin. The injection could take about 15 seconds.



15 seconds



Note: When the injection is completed, the window will turn yellow and you may hear a second click.



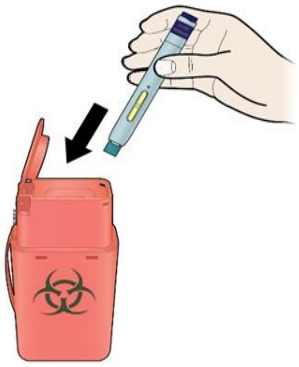
Note:

- After you remove the pen from the skin, the needle will automatically be covered by the green safety guard.
- When you remove the pen, if the window has not turned yellow, or if it looks like the medicine is still injecting, this means you have not received a full dose. Contact your doctor immediately.

Step 4: Finish

(K)

Discard the used pen and the white cap.
Put the used pen in a sharps disposal container immediately after use. Talk to your doctor or pharmacist about proper disposal. There may be local regulations for disposal.



Note:
- Do not reuse the pen.
- Do not recycle the pen or sharps disposal container, or throw them into household waste.
- Always keep the sharps disposal container out of the reach of children.

(L)

Examine the injection site.
If there is any blood on the skin, press a cotton ball or gauze pad onto the injection site. Do not rub the injection site. Apply an adhesive plaster if needed.

In case your dose is 140 mg, repeat all steps with the second pen to inject the full dose.