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

AIMOVIG™ (erenumab-aooe) injection, for subcutaneous use
Initial U.S. Approval: 2018

----------INDICATIONS AND USAGE----------

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

----------DOSAGE AND ADMINISTRATION----------

- For subcutaneous use only (2.1, 2.2)
- Recommended dosage is 70 mg once monthly; some patients may benefit from a dosage of 140 mg once monthly (2.1)
- The 140 mg dose is administered once monthly as two consecutive injections of 70 mg each (2.1)
- The needle shield within the white cap of the prefilled autoinjector and the gray needle cap of the prefilled syringe contain dry natural rubber (a derivative of latex), which may cause allergic reactions in individuals sensitive to latex (2.2)
- Administer in the abdomen, thigh, or upper arm subcutaneously (2.2)
- See Dosage and Administration for important administration instructions (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

- Injection: 70 mg/mL solution in a single-dose prefilled SureClick® autoinjector (3)
- Injection: 70 mg/mL solution in a single-dose prefilled syringe (3)

----------CONTRAINDICATIONS----------

None (4)

----------ADVERSE REACTIONS----------

The most common adverse reactions in AIMOVIG clinical studies (occurring in at least 3% of treated patients and more often than placebo) are injection site reactions and constipation (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Amgen Medical Information at 1-800-77-AMGEN (1-800-772-6436) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Patient Labeling.

Revised: 5/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

The recommended dosage of AIMOVIG is 70 mg injected subcutaneously once monthly. Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly, which is administered as two consecutive subcutaneous injections of 70 mg each.

If a dose of AIMOVIG is missed, administer as soon as possible. Thereafter, AIMOVIG can be scheduled monthly from the date of the last dose.

2.2 Important Administration Instructions

AIMOVIG is for subcutaneous use only.

The needle shield within the white cap of the AIMOVIG prefilled autoinjector and gray needle cap of the AIMOVIG prefilled syringe contain dry natural rubber (a derivative of latex), which may cause allergic reactions in individuals sensitive to latex.

AIMOVIG is intended for patient self-administration. Prior to use, provide proper training to patients and/or caregivers on how to prepare and administer AIMOVIG using the single-dose prefilled autoinjector or single-dose prefilled syringe, including aseptic technique *[see Instructions for Use]*:

- Prior to subcutaneous administration, allow AIMOVIG to sit at room temperature for at least 30 minutes protected from direct sunlight *[see How Supplied/Storage and Handling (16.2)]*. Do not warm by using a heat source such as hot water or a microwave.
- Do not shake the product.
- Inspect visually for particulate matter and discoloration prior to administration *[see Dosage Forms and Strengths (3)]*. Do not use if the solution is cloudy or discolored or contains flakes or particles.
- Administer AIMOVIG in the abdomen, thigh, or upper arm subcutaneously. Do not inject into areas where the skin is tender, bruised, red, or hard.
- Both prefilled autoinjector and prefilled syringe are single-dose and deliver the entire contents.

3 DOSAGE FORMS AND STRENGTHS

AIMOVIG is a sterile, clear to opalescent, colorless to light yellow solution available as follows:

- Injection: 70 mg/mL in a single-dose prefilled SureClick® autoinjector
- Injection: 70 mg/mL in a single-dose prefilled syringe

4 CONTRAINDICATIONS

None.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

The safety of AIMOVIG has been evaluated in 2,537 patients with migraine who received at least one dose of AIMOVIG, representing 2,310 patient-years of exposure. Of these, 2,057 patients were exposed to 70 mg or 140 mg once monthly for at least 6 months, 1,198 patients were exposed for at least 12 months, and 287 patients were exposed for at least 18 months.

In placebo-controlled clinical studies (Studies 1, 2, and 3) of 2,184 patients, 787 patients received at least one dose of AIMOVIG 70 mg once monthly, 507 patients received at least one dose of AIMOVIG 140 mg once monthly, and 890 patients received placebo during 3 months or 6 months of double-blind treatment *[see Clinical Studies (14)]*. Approximately 84% were female, 91% were white, and the mean age was 42 years at study entry.

The most common adverse reactions (incidence ≥ 3% and more often than placebo) in the migraine studies were injection site reactions and constipation. Table 1 summarizes the adverse reactions that occurred during the first 3 months in the migraine studies (Studies 1, 2, and 3).

Table 1: Adverse Reactions Occurring with an Incidence of at Least 2% for Either Dose of AIMOVIG and at Least 2% Greater than Placebo During the First 3 Months in Studies 1, 2, and 3

Adverse Reaction	AIMOVIG 70 mg Once Monthly N = 787 %	AIMOVIG 140 mg Once Monthly N = 507 %	Placebo N = 890 %
Injection site reactions[a]	6	5	3
Constipation	1	3	1
Cramps, muscle spasms	< 1	2	< 1

[a]Injection site reactions include multiple adverse reactions related terms, such as injection site pain and injection site erythema.

In Studies 1, 2, and 3, 1.3% of patients treated with AIMOVIG discontinued double-blind treatment because of adverse events. The most frequent injection site reactions were injection site pain, injection site erythema, and injection site pruritus.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation, including neutralizing antibodies, is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to erenumab-aooe in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

The immunogenicity of AIMOVIG has been evaluated using an immunoassay for the detection of binding anti-erenumab-aooe antibodies. For patients whose sera tested positive in the screening immunoassay, an *in vitro* biological assay was performed to detect neutralizing antibodies.

In controlled studies with AIMOVIG, the incidence of anti-erenumab-aooe antibody development was 6.2% (48/778) in patients receiving AIMOVIG 70 mg once monthly (2 of whom had *in vitro* neutralizing activity) and 2.6% (13/504) in patients receiving AIMOVIG 140 mg once monthly (none of whom had *in vitro* neutralizing activity). The neutralizing anti-erenumab-aooe antibody positive rate may be underestimated because of limitations of the assay. Although these data do not demonstrate an impact of anti-erenumab-aooe antibody development on the efficacy or safety of AIMOVIG in these patients, the available data are too limited to make definitive conclusions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of AIMOVIG in pregnant women. No adverse effects on offspring were observed when pregnant monkeys were administered erenumab-aooe throughout gestation *(see Data).* Serum erenumab-aooe exposures in pregnant monkeys were greater than those in humans at clinical doses.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively. The estimated rate of major birth defects (2.2%-2.9%) and miscarriage (17%) among deliveries to women with migraine are similar to rates reported in women without migraine.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Published data have suggested that women with migraine may be at increased risk of preeclampsia during pregnancy.

Data

Animal Data

In a study in which female monkeys were administered erenumab-aooe (0 or 50 mg/kg) twice weekly by subcutaneous injection throughout pregnancy (gestation day 20-22 to parturition), no adverse effects on offspring were observed. Serum erenumab-aooe exposures (AUC) in pregnant monkeys were approximately 20 times that in humans at a dose of 140 mg once monthly.

8.2 Lactation

Risk Summary

There are no data on the presence of erenumab-aooe in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AIMOVIG and any potential adverse effects on the breastfed infant from AIMOVIG or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of AIMOVIG did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

11 DESCRIPTION

Erenumab-aooe is a human immunoglobulin G2 (IgG2) monoclonal antibody that has high affinity binding to the calcitonin gene-related peptide receptor. Erenumab-aooe is produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells. It is composed of 2 heavy chains, each containing 456 amino acids, and 2 light chains of the lambda subclass, each containing 216 amino acids, with an approximate molecular weight of 150 kDa.

AIMOVIG (erenumab-aooe) injection is supplied as a sterile, preservative-free, clear to opalescent, colorless to light yellow solution for subcutaneous administration. Each 1 mL single-dose prefilled autoinjector and single-dose prefilled glass syringe contains 70 mg erenumab-aooe, acetate (1.5 mg), polysorbate 80 (0.10 mg), and sucrose (73 mg). Enclosed within the autoinjector is a single-dose, prefilled glass syringe. The solution of AIMOVIG has a pH of 5.2.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Erenumab-aooe is a human monoclonal antibody that binds to the calcitonin gene-related peptide (CGRP) receptor and antagonizes CGRP receptor function.

12.2 Pharmacodynamics

In a randomized, double-blind, placebo-controlled study in healthy volunteers, concomitant administration of erenumab-aooe (140 mg intravenous, single-dose) with sumatriptan (12 mg subcutaneous, given as two 6 mg doses separated by one hour) had no effect on resting blood pressure compared with sumatriptan alone. AIMOVIG is for subcutaneous use only.

12.3 Pharmacokinetics

Erenumab-aooe exhibits non-linear kinetics as a result of binding to the CGRP receptor. The C_{max} mean and AUC_{last} mean following subcutaneous administration of a 70 mg once monthly and a 140 mg once monthly dose in healthy volunteers or migraine patients are included in Table 2.

Less than 2-fold accumulation was observed in trough serum concentrations (C_{min}) for episodic and chronic migraine patients following subcutaneous administration of 70 mg once monthly and 140 mg once monthly doses (see Table 2). Serum trough concentrations approached steady state by 3 months of dosing. The effective half-life of erenumab-aooe is 28 days.

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