HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PONTEVIA safely and effectively. See full prescribing information for PONTEVIA.
PONTEVIA (galcanezumab) injection, for subcutaneous use --------

---------- INDICATIONS AND USAGE ----------
PONTEVIA is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month. (1.1)

----------DOSAGE AND ADMINISTRATION----------
- For subcutaneous use only. (2.1, 2.2, 2.3)
- The recommended dose is 120 mg galcanezumab injected subcutaneously once monthly, with a 240 mg loading dose as the initial dose. (2.1)
- Administer in the abdomen, thigh, back of the upper arm, or buttocks subcutaneously. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
- Injection: 120 mg/mL solution in a single-dose prefilled pen (3)
- Injection: 120 mg/mL solution in a single-dose prefilled syringe (3)

---------- CONTRAINDICATIONS ----------
PONTEVIA is contraindicated in patients with serious hypersensitivity to galcanezumab or to any of the excipients. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Hypersensitivity Reactions: Serious hypersensitivity reactions including cases of anaphylaxis, angioedema and urticaria have been reported (see section 6.3). If a serious hypersensitivity reaction occurs, administration of galcanezumab should be discontinued immediately and appropriate therapy initiated (see section 4). Patients should be informed on the possibility of a delayed onset hypersensitivity reaction and instructed to contact their physician. (5.1)
- Hypertension: New-onset or worsening of pre-existing hypertension may occur. (5.2)
- Raynaud's Phenomenon: New-onset or worsening of pre-existing Raynaud's phenomenon may occur. (5.3)

---------- ADVERSE REACTIONS----------
The most common adverse reactions (incidence ≥2% and at least 2% greater than placebo) in PONTEVIA clinical studies were injection site reactions. (6.1)

Revised: 03 Sep 2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Migraine

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

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing for Migraine

The recommended dose is 120 mg galcanezumab injected subcutaneously once monthly, with a 240 mg loading dose as the initial dose.

Patients should be instructed to inject a missed dose as soon as possible and then resume monthly dosing.

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.

Elderly (≥ 65 years)

There is limited information in subjects aged ≥ 65 years. No dose adjustment is required as the pharmacokinetics of galcanezumab are not affected by age.

Renal impairment/hepatic impairment

No dose adjustment is required in patients with mild to moderate renal impairment or hepatic impairment.

Paediatric population

The safety and efficacy of galcanezumab in children aged 6 to 18 years have not yet been established. No data are available.

There is no relevant use of galcanezumab in children below the age of 6 years for the prevention of migraine.

1.1 Important Administration Instructions

PONTEVIA is for subcutaneous use only.

PONTEVIA is intended for patient self-administration. Prior to use, provide proper training to patients and/or caregivers on how to prepare and administer PONTEVIA using the single-dose prefilled pen or single-dose prefilled syringe, including aseptic technique *[see How Supplied/Storage and Handling (16) and Instructions for Use]*:

- Protect PONTEVIA from direct sunlight.
- Prior to subcutaneous administration, allow PONTEVIA to sit at room temperature for 30 minutes. Do not warm by using a heat source such as hot water or a microwave.
- Do not shake the product.
- Inspect PONTEVIA visually for particulate matter and discoloration prior to administration, whenever solution and container permit *[see Dosage Forms and Strengths (3) and How Supplied/Storage and Handling (16)]*. Do not use PONTEVIA if it is cloudy or there are visible particles.
- Administer PONTEVIA in the abdomen, thigh, back of the upper arm, or buttocks subcutaneously. Do not inject into areas where the skin is tender, bruised, red, or hard.
- Both the prefilled pen and prefilled syringe are single-dose and deliver the entire contents.

2.2 Overdose

Doses up to 600 mg have been administered subcutaneously to humans without dose-limiting toxicity. In case of an overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and

appropriate symptomatic treatment be instituted immediately.

3 DOSAGE FORMS AND STRENGTHS

PONTEVIA is a sterile clear to opalescent, colorless to slightly yellow to slightly brown solution available as follows:

- Injection: 120 mg/mL in a single-dose prefilled pen
- Injection: 120 mg/mL in a single-dose prefilled syringe

4 CONTRAINDICATIONS

PONTEVIA is contraindicated in patients with serious hypersensitivity to galcanezumab or to any of the excipients *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Serious hypersensitivity reactions including cases of anaphylaxis, angioedema and urticaria have been reported (see section 6.3). Serious hypersensitivity reactions may occur within 1 day after galcanezumab administration, however cases with a delayed onset (ranging from more than 1 day to 4 weeks after administration) have been reported. In some cases, hypersensitivity reactions had a prolonged duration. If a serious hypersensitivity reaction occurs, administration of galcanezumab should be discontinued immediately and appropriate therapy initiated (see section 4). Patients should be informed on the possibility of a delayed onset hypersensitivity reaction and instructed to contact their physician.

5.2 Hypertension

Development of hypertension and worsening of pre-existing hypertension have been reported following the use of CGRP antagonists, including PONTEVIA, in the postmarketing setting. Some of the patients who developed new-onset hypertension had risk factors for hypertension. There were cases requiring initiation of pharmacological treatment for hypertension and, in some cases, hospitalization. Hypertension may occur at any time during treatment but was most frequently reported within 7 days of therapy initiation. PONTEVIA was discontinued in many of the reported cases.

Monitor patients treated with PONTEVIA for new-onset hypertension or worsening of pre-existing hypertension, and consider whether discontinuation of PONTEVIA is warranted if evaluation fails to establish an alternative etiology or blood pressure is inadequately controlled.

5.3 Raynaud’s Phenomenon

Development of Raynaud’s phenomenon and recurrence or worsening of pre-existing Raynaud’s phenomenon have been reported in the postmarketing setting following the use of CGRP antagonists, including PONTEVIA. In reported cases with monoclonal antibody CGRP antagonists, symptom onset occurred after a median of 71 days following dosing. Many of the cases reported serious outcomes, including hospitalizations and disability, generally related to debilitating pain. In most reported cases, discontinuation of the CGRP antagonist resulted in resolution of symptoms.

PONTEVIA should be discontinued if signs or symptoms of Raynaud’s phenomenon develop, and patients should be evaluated by a healthcare provider if symptoms do not resolve. Patients with a history of Raynaud’s phenomenon should be monitored for, and informed about the possibility of, worsening or recurrence of signs and symptoms.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Serious Hypersensitivity Reactions *[see Contraindications (4) and Warnings and Precautions (5.1)]*
- Hypertension *[see Warnings and Precautions (5.2)]*
- Raynaud's Phenomenon *[see Warnings and Precautions (5.3)]*

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 with rates in clinical trials of another drug and may not reflect the rates observed in clinical practice.

Migraine

The safety of PONTEVIA has been evaluated in 2586 patients with migraine who received at least one dose of PONTEVIA, representing 1487 patient-years of exposure. Of these, 1920 patients were exposed to PONTEVIA once monthly for at least 6 months, and 526 patients were exposed for 12 months.

In placebo-controlled clinical studies (Studies 1, 2, and 3), 705 patients received at least one dose of PONTEVIA 120 mg once monthly, and 1451 patients received placebo, during 3 months or 6 months of double-blind treatment *[see Clinical Studies (14.1)]*. Of the PONTEVIA-treated patients, approximately 85% were female, 77% were white, and the mean age was 41 years at study entry.

The most common adverse reaction was injection site reactions. In Studies 1, 2, and 3, 1.8% of patients discontinued double-blind treatment because of adverse events. Table 1 summarizes the adverse reactions that occurred within up to 6 months of treatment in the migraine studies.

Table 1: Adverse Reactions Occurring in Adults with Migraine with an Incidence of at least 2% for PONTEVIA and at least 2% Greater than Placebo (up to 6 Months of Treatment) in Studies 1, 2, and 3

Adverse Reaction	PONTEVIA 120 mg Monthly (N=705) %	Placebo Monthly (N=1451) %
Injection site reactions[a]	18	13

[a] Injection site reactions include multiple related adverse event terms, such as injection site pain, injection site reaction, 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 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 galcanezumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

The immunogenicity of PONTEVIA has been evaluated using an in vitro immunoassay for the detection of binding anti-galcanezumab antibodies. For patients whose sera tested positive in the screening immunoassay, an in vitro ligand-binding immunoassay was performed to detect neutralizing antibodies.

In controlled studies with PONTEVIA up to 6 months (Study 1, Study 2, and Study 3), the incidence of anti-galcanezumab antibody development was 4.8% (33/688) in patients receiving PONTEVIA once monthly (32 out of 33 of whom had *in vitro* neutralizing activity). With 12 months of treatment in an open-label study, up to 12.5% (16/128) of PONTEVIA- treated patients developed anti-galcanezumab antibodies, most of whom tested positive for neutralizing antibodies.

Although anti-galcanezumab antibody development was not found to affect the pharmacokinetics, safety or efficacy of PONTEVIA in these patients, the available data are too limited to make definitive conclusions.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of PONTEVIA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to PONTEVIA exposure.

Immune System Disorders — Anaphylaxis, angioedema *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Skin and Subcutaneous Tissue Disorders — rash, pruritis rash, urticaria

Ear and Labyrinth disorders — vertigo

Gastrointestinal disorders— constipation

Vascular Disorders — Hypertension *[see Warnings and Precautions (5.2)]*, Raynaud's phenomenon *[see Warnings and Precautions (5.3)]*

7 DRUG INTERACTION

No drug interaction studies were conducted. No pharmacokinetic drug interactions are expected based on the characteristics of galcanezumab.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of PONTEVIA in pregnant women. Administration of galcanezumab to rats and rabbits during the period of organogenesis or to rats throughout pregnancy and lactation at plasma exposures greater than that expected clinically did not result in adverse effects on development *(see Animal Data)*.

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

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

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

Data

Animal Data

When galcanezumab was administered to female rats by subcutaneous injection in two studies (0, 30, or 100 mg/kg; 0 or 250 mg/kg) prior to and during mating and continuing throughout organogenesis, no adverse effects on embryofetal development were observed. The highest dose tested (250 mg/kg) was associated with a plasma exposure ($C_{ave, ss}$) 38 times that in humans at the recommended human dose (RHD) for migraine (120 mg).

Administration of galcanezumab (0, 30, or 100 mg/kg) by subcutaneous injection to pregnant rabbits throughout the period of organogenesis produced no adverse effects on embryofetal development. The higher dose tested was associated with a plasma $C_{ave, ss}$ 64 times that in humans at 120 mg.

Administration of galcanezumab (0, 30, or 250 mg/kg) by subcutaneous injection to rats throughout pregnancy and lactation produced no adverse effects on pre- and postnatal development. The higher dose tested was associated with a plasma $C_{ave, ss}$ 34 times that in humans at 120 mg.

8.2 Lactation

Risk Summary

There are no data on the presence of galcanezumab 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 PONTEVIA and any potential adverse effects on the breastfed infant from PONTEVIA or from the underlying maternal condition.

8.3 Effects on ability to drive and use machines

Galcanezumab may have a minor influence on the ability to drive and use machines. Vertigo may occur following the administration of galcanezumab.

11 DESCRIPTION

Galcanezumab is a humanized IgG4 monoclonal antibody specific for calcitonin-gene related peptide (CGRP) ligand. Galcanezumab is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. Galcanezumab is composed of two identical immunoglobulin kappa light chains and two identical immunoglobulin gamma heavy chains and has an overall molecular weight of approximately 147 kDa.

PONTEVIA (galcanezumab) injection is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow to slightly brown solution, for subcutaneous use. PONTEVIA is supplied in a 1 mL single-dose prefilled pen to deliver 120 mg of galcanezumab or a 1 mL single-dose prefilled syringe to deliver 120 mg of galcanezumab. Each mL of solution contains 120 mg of galcanezumab; L-histidine (0.5 mg); L- histidine hydrochloride monohydrate (1.5 mg); Polysorbate 80 (0.5 mg); Sodium Chloride (8.8 mg); Water for Injection, USP. The pH range is 5.3 - 6.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

12.2 Pharmacodynamics

There are no relevant data on the pharmacodynamic effects of galcanezumab.

12.3 Pharmacokinetics

Galcanezumab exhibits linear pharmacokinetics and exposure increases proportionally with doses between 1 and 600 mg.

A loading dose of 240 mg achieved the serum galcanezumab steady-state concentration after the first dose. The time to maximum concentration is 5 days, and the elimination half-life is 27 days.

Absorption

Following a subcutaneous dose of galcanezumab, the time to maximum concentration was about 5 days. Injection site location did not significantly influence the absorption of galcanezumab.

Distribution

The apparent volume of distribution (V/F) of galcanezumab was 7.3 L (34% Inter Individual Variability [IIV]).

Metabolism and Elimination

Galcanezumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

The apparent clearance (CL/F) of galcanezumab was 0.008 L/h and the elimination half-life of galcanezumab was approximately 27 days.

Specific Populations

Age, Sex, Weight, Race, Ethnicity

The pharmacokinetics of galcanezumab were not affected by age, sex, race, subtypes of migraine spectrum, or headache diagnosis based on a population pharmacokinetics analysis. Body weight has no clinically relevant effect on the pharmacokinetics of galcanezumab.

Patients with Renal or Hepatic Impairment

Renal and hepatic impairment are not expected to affect the pharmacokinetics of galcanezumab. Population pharmacokinetic analysis of integrated data from the galcanezumab clinical studies revealed that creatinine clearance did not affect the pharmacokinetics of galcanezumab in patients with mild or moderate renal impairment. Patients with severe renal impairment (creatinine clearance <30 mL/min) have not been studied. Based on a population PK analysis, bilirubin concentration did not significantly influence the CL/F of galcanezumab.

No dedicated clinical studies were conducted to evaluate the effect of hepatic impairment or renal impairment on the pharmacokinetics of galcanezumab.

Drug Interaction Studies

P450 Enzymes

Galcanezumab is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

The carcinogenic potential of galcanezumab has not been assessed.

Mutagenesis

Genetic toxicology studies of galcanezumab have not been conducted.

Impairment of Fertility

When galcanezumab (0, 30, or 250 mg/kg) was administered to male rats by subcutaneous injection prior to and during mating, no adverse effects on fertility was observed. The higher dose tested was associated with a plasma exposure ($C_{ave, ss}$) 8 times that in humans at the recommended human dose (RHD) for migraine (120 mg). When galcanezumab was administered to female rats by subcutaneous injection in two studies (0, 30, or 100 mg/kg; 0 or 250 mg/kg) prior to and during mating and continuing throughout organogenesis, no adverse effects on fertility were observed. The highest dose tested (250 mg/kg) was associated with a plasma $C_{ave, ss}$ 38 times that in humans at 120 mg.

14 CLINICAL STUDIES

14.1 Migraine

The efficacy of PONTEVIA was evaluated as a preventive treatment of episodic or chronic migraine in three multicenter, randomized, double-blind, placebo-controlled studies: two 6-month studies in patients with episodic migraine (Studies 1 and 2) and one 3-month study in patients with chronic migraine (Study 3).

Episodic Migraine

Study 1 (NCT02614183) and Study 2 (NCT02614196) included adults with a history of episodic migraine (4 to 14 migraine days per month). All patients were randomized in a 1:1:2 ratio to receive once-monthly subcutaneous injections of PONTEVIA 120 mg, PONTEVIA 240 mg, or placebo. All patients in the 120 mg PONTEVIA group

received an initial 240 mg loading dose. Patients were allowed to use acute headache treatments, including migraine-specific medications (i.e., triptans, ergotamine derivatives), NSAIDs, and acetaminophen during the study.

The studies excluded patients on any other migraine preventive treatment, patients with medication overuse headache, patients with ECG abnormalities compatible with an acute cardiovascular event and patients with a history of stroke, myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass grafting, deep vein thrombosis, or pulmonary embolism within 6 months of screening.

The primary efficacy endpoint for Studies 1 and 2 was the mean change from baseline in the number of monthly migraine headache days over the 6-month treatment period. Key secondary endpoints included response rates (the mean percentages of patients reaching at least 50%, 75%, and 100% reduction from baseline in the number of monthly migraine headache days over the 6-month treatment period), the mean change from baseline in the number of monthly migraine headache days with use of any acute headache medication during the 6-month treatment period, and the impact of migraine on daily activities, as assessed by the mean change from baseline in the average Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1) Role Function-Restrictive domain score during the last 3 months of treatment (Months 4 to 6). Scores are scaled from 0 to 100, with higher scores indicating less impact of migraine on daily activities.

In Study 1, a total of 858 patients (718 females, 140 males) ranging in age from 18 to 65 years, were randomized. A total of 703 patients completed the 6-month double-blind phase. In Study 2, a total of 915 patients (781 female, 134 male) ranging in age from 18 to 65 years, were randomized. A total of 785 patients completed the 6-month double-blind phase. In Study 1 and Study 2, the mean migraine frequency at baseline was approximately 9 migraine days per month, and was similar across treatment groups.

PONTEVIA 120 mg demonstrated statistically significant improvements for efficacy endpoints compared to placebo over the 6-month period, as summarized in Table 2. PONTEVIA treatment with the 240 mg once-monthly dose showed no additional benefit over the PONTEVIA 120 mg once-monthly dose.

Table 2: Efficacy Endpoints in Studies 1 and 2

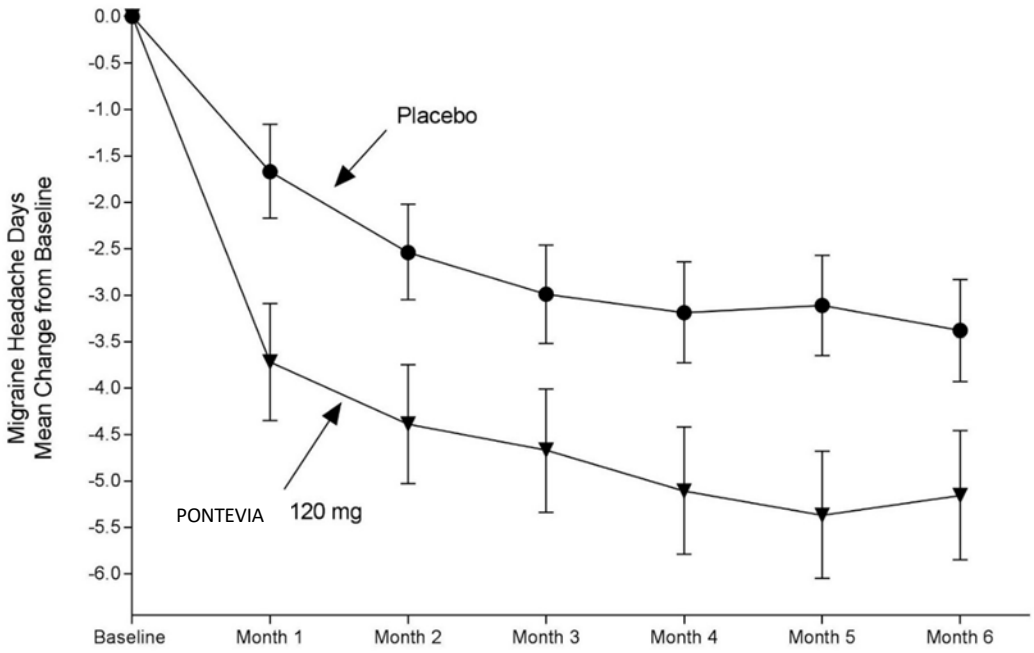
	Study 1		**Study 2**	
	PONTEVIA 120 mg N = 210	**Placebo N = 425**	**PONTEVIA 120 mg N = 226**	**Placebo N = 450**
Monthly Migraine Headache Days (over Months 1 to 6)				
Baseline migraine headache days	9.2	9.1	9.1	9.2
Mean change from baseline	-4.7	-2.8	-4.3	-2.3
Difference from placebo[a]	-1.9		-2.0	
≥50% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	62%	39%	59%	36%
≥75% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	39%	19%	34%	18%
100% Migraine Headache Days Responders (over Months 1 to 6)				
% Responders[a]	16%	6%	12%	6%
Monthly Migraine Headache Days that Acute Medication was Taken (over Months 1 to 6)				
Mean change from baseline (days)[a]	-4.0	-2.2	-3.7	-1.9
MSQ Role Function-Restrictive Domain Score (over Months 4 to 6)				
Baseline	51.4	52.9	52.5	51.4
Mean change from baseline[b]	32.4	24.7	28.5	19.7

Difference from placebo[a]	7.7		8.8	

[a] p<0.001

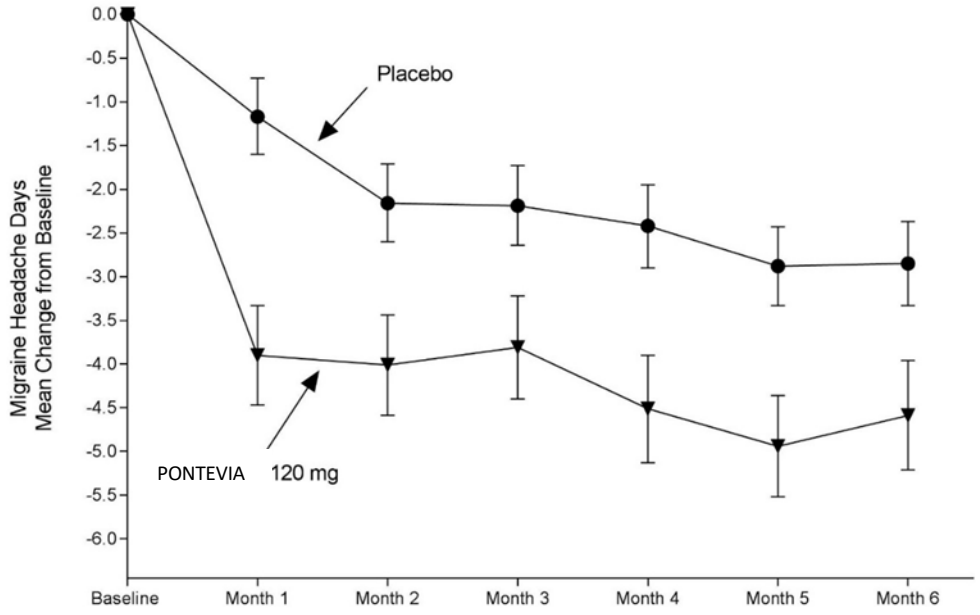
[b] N = 189 for PONTEVIA 120 mg and N = 377 for placebo in Study 1; N = 213 for PONTEVIA 120 mg and N = 396 for placebo in Study 2.

Figure 1: Change from Baseline in Monthly Migraine Headache Days in Study 1[a]



[a] Least-square means and 95% confidence intervals are presented.

Figure 2: Change from Baseline in Monthly Migraine Headache Days in Study 2[a]



[a] Least-square means and 95% confidence intervals are presented.

Figure 3 shows the distribution of change from baseline in the mean number of monthly migraine headache days in bins of 2 days, by treatment group, in Study 1. A treatment benefit over placebo for PONTEVIA is seen across a range of changes from baseline in monthly migraine headache days.

Figure 3: Distribution of Change from Baseline in Mean Monthly Migraine Headache Days over Months 1 to 6 by Treatment Group in Study 1

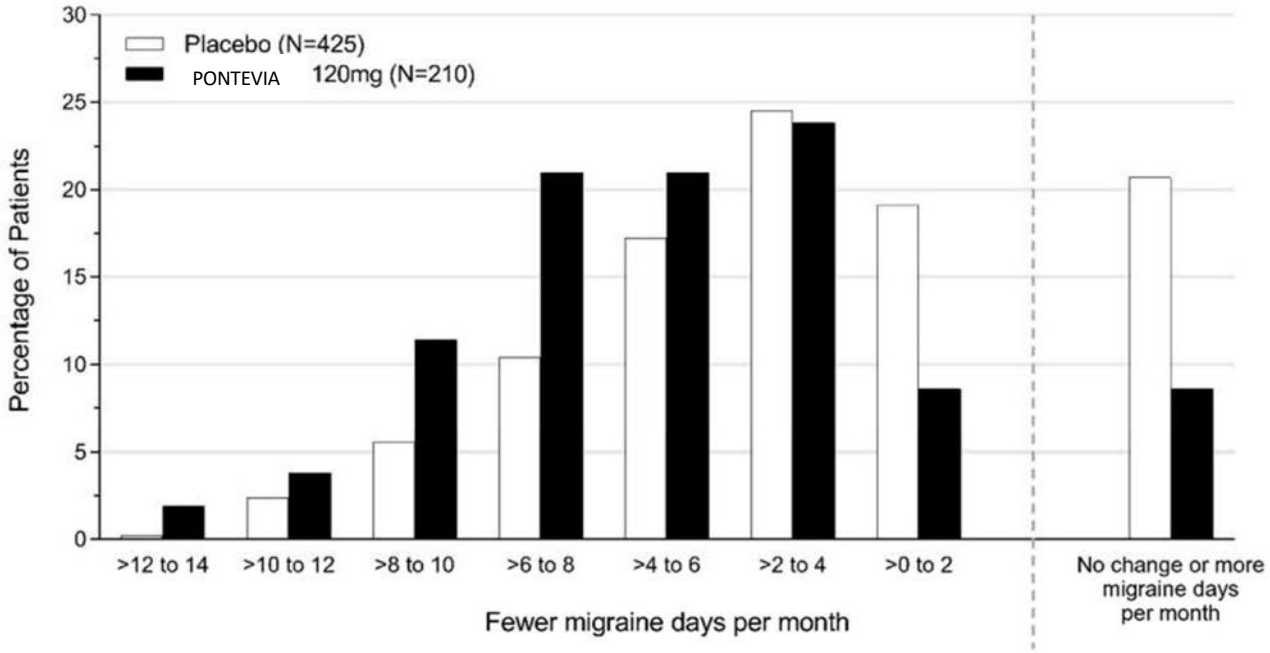
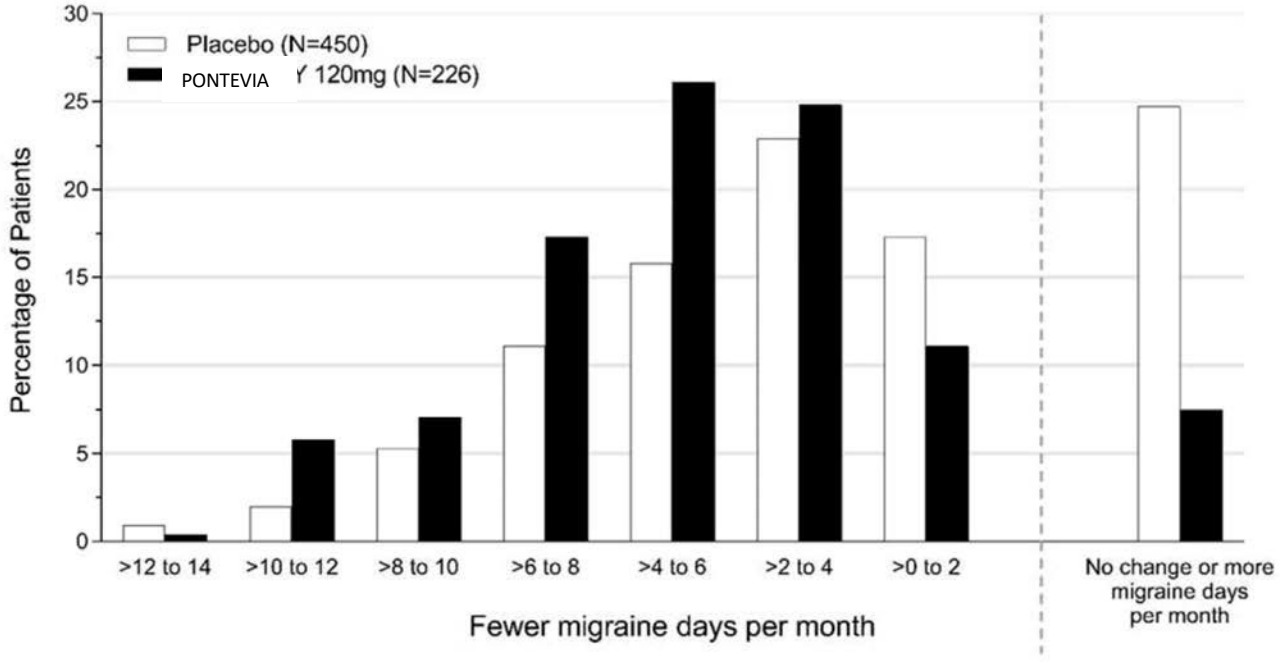


Figure 4 shows the distribution of change from baseline in the mean number of monthly migraine headache days in bins of 2 days, by treatment group, in Study 2. A treatment benefit over placebo for PONTEVIA is seen across a range of changes from baseline in monthly migraine headache days.

Figure 4: Distribution of Change from Baseline in Mean Monthly Migraine Headache Days over Months 1 to 6 by Treatment Group in Study 2



Chronic Migraine

Study 3 (NCT02614261) included adults with a history of chronic migraine (≥15 headache days per month with ≥8 migraine days per month). All patients were randomized in a 1:1:2 ratio to receive once-monthly subcutaneous injections of PONTEVIA 120 mg, PONTEVIA 240 mg, or placebo over a 3-month treatment period. All patients in the 120 mg PONTEVIA group received an initial 240 mg loading dose.

Patients were allowed to use acute headache treatments including migraine-specific medications (i.e., triptans, ergotamine derivatives), NSAIDs, and acetaminophen. A subset of patients (15%) was allowed to use one concomitant migraine preventive medication. Patients with medication overuse headache were allowed to enroll.

The study excluded patients with ECG abnormalities compatible with an acute cardiovascular event, and patients with a history of stroke, myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass grafting, deep vein thrombosis, or pulmonary embolism within 6 months of screening.

The primary endpoint was the mean change from baseline in the number of monthly migraine headache days over the 3- month treatment period. The secondary endpoints were response rates (the mean percentages of patients reaching at least 50%, 75% and 100% reduction from baseline in the number of monthly migraine headache days over the 3-month treatment period), the mean change from baseline in the number of monthly migraine headache days with use of any acute headache medication during the 3-month treatment period, and the impact of migraine on daily activities as assessed by the mean change from baseline in the MSQ v2.1 Role Function-Restrictive domain score at Month 3. Scores are scaled from 0 to 100, with higher scores indicating less impact of migraine on daily activities.

In Study 3, a total of 1113 patients (946 female, 167 male) ranging in age from 18 to 65 years, were randomized. A total of 1037 patients completed the 3-month double-blind phase. The mean number of monthly migraine headache days at baseline was approximately 19.

PONTEVIA 120 mg demonstrated statistically significant improvement for the mean change from baseline in the number of monthly migraine headache days over the 3-month treatment period, and in the mean percentage of patients reaching at least 50% reduction from baseline in the number of monthly migraine headache days over the 3-month treatment

period, as summarized in Table 3. PONTEVIA treatment with the 240 mg once-monthly dose showed no additional benefit over the PONTEVIA 120 mg once-monthly dose.

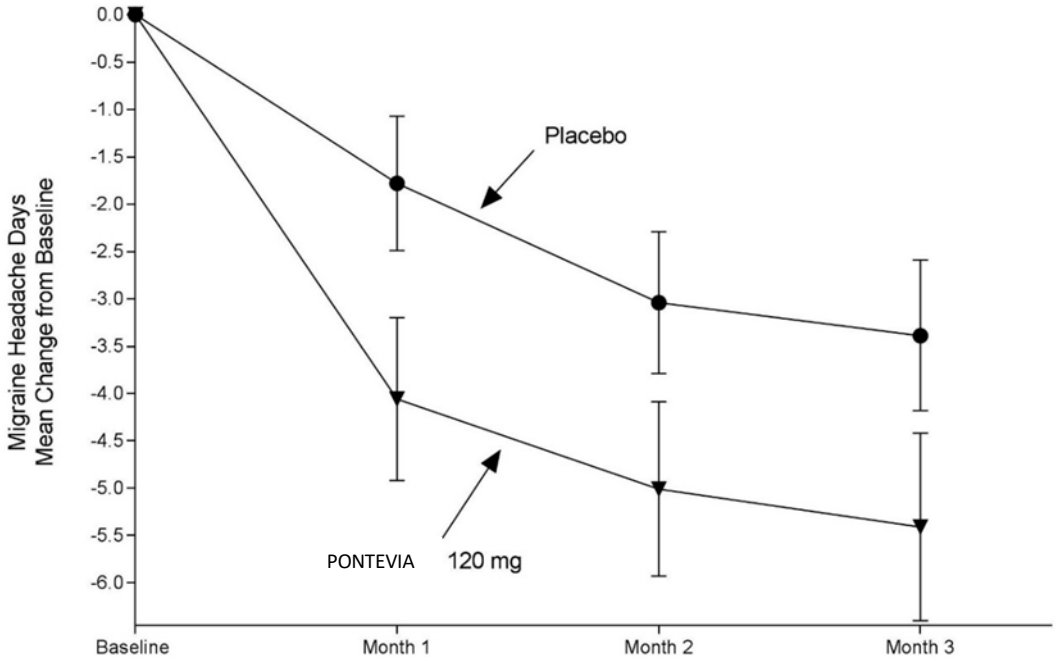
Table 3: Efficacy Endpoints in Study 3

	PONTEVIA 120 mg N = 273	**Placebo N =538**
Monthly Migraine Headache Days (over Months 1 to 3)		
Baseline migraine headache days	19.4	19.6
Mean change from baseline	-4.8	-2.7
Difference from placebo[a]	-2.1	
≥50% Migraine Headache Days Responders (over Months 1 to 3)		
% Responders[a]	28%	15%

[a] p<0.001

Study 3 utilized a sequential testing procedure to control the Type-I error rate for the multiple secondary endpoints. Once a secondary endpoint failed to reach the required level for statistical significance, formal hypothesis testing was terminated for subsequent endpoints, and p-values were considered nominal only. In Study 3, PONTEVIA 120 mg was not significantly better than placebo for the proportion of patients with ≥75% or 100% reduction in migraine headache days. Patients treated with PONTEVIA 120 mg showed a nominally greater reduction in the number of monthly migraine headache days that acute medication was taken (-4.7 for PONTEVIA 120 mg vs. -2.2 for placebo; nominal p-value <0.001), and the mean change from baseline in the MSQ Role Function-Restrictive Domain score at Month 3 was nominally greater in patients treated with PONTEVIA 120 mg than in patients on placebo (21.8 for PONTEVIA 120 mg vs. 16.8 for placebo; nominal p-value <0.001).

Figure 5: Change from Baseline in Monthly Migraine Headache Days in Study 3[a]

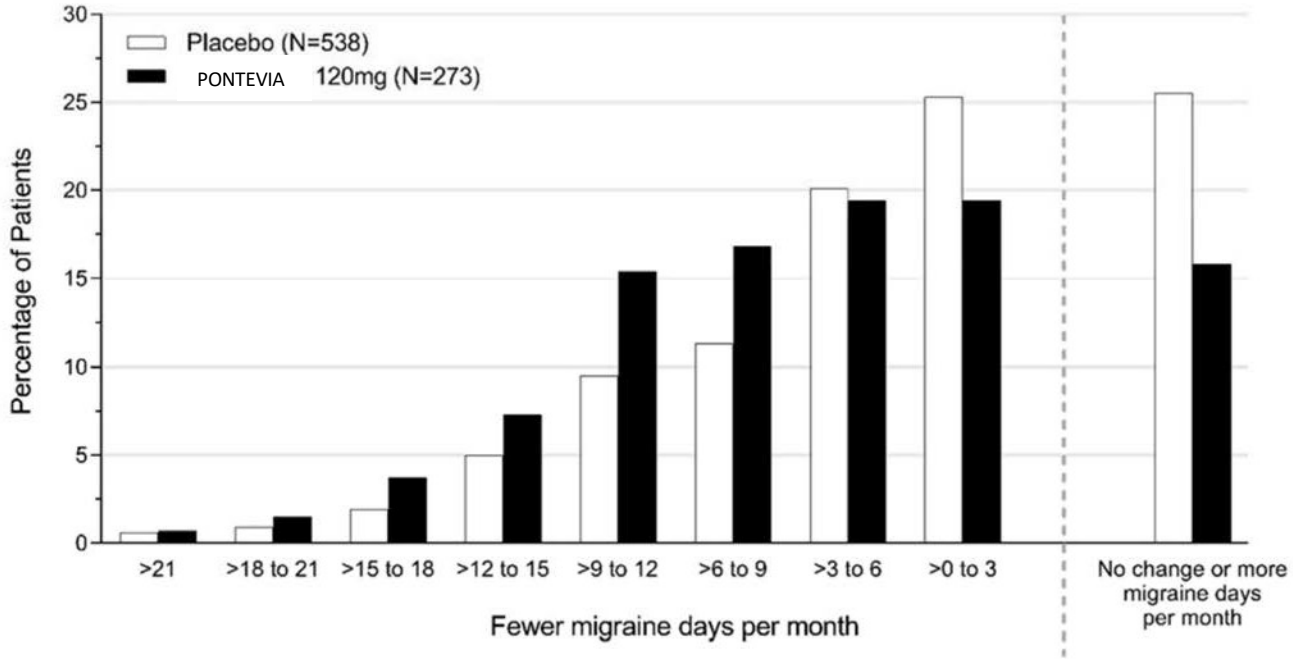


[a] Least-square means and 95% confidence intervals are presented.

Figure 6 shows the distribution of change from baseline in the mean number of monthly migraine headache days for

the 3-month study period in bins of 3 days by treatment group. A treatment benefit over placebo for PONTEVIA is seen across a range of changes from baseline in monthly migraine headache days.

Figure 6: Distribution of Change from Baseline in Mean Monthly Migraine Headache Days over Months 1 to 3 by Treatment Group in Study 3



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

PONTEVIA (galcanezumab) injection is a sterile, preservative-free, clear to opalescent, colorless to slightly yellow to slightly brown solution for subcutaneous administration.

PONTEVIA is not made with natural rubber latex.

PONTEVIA is supplied as follows:

Product	Pack Size
Prefilled pen: 120 mg/mL single-dose	Carton of 1
Prefilled syringe: 120 mg/mL single-dose	Carton of 1

16.2 Storage and Handling

- Store refrigerated at 2°C to 8°C in the original carton to protect PONTEVIA from light until use.
- Do not freeze.
- Do not shake.
- PONTEVIA may be stored out of refrigeration in the original carton at temperatures up to 30°C for up to 7 days. Once stored out of refrigeration, do not place back in the refrigerator.
- If these conditions are exceeded, PONTEVIA must be discarded.
- Discard the PONTEVIA single-dose prefilled pen or syringe after use in a puncture-resistant container.

17 PATIENT COUNSELING INFORMATION

Instructions on Self-Administration: Provide guidance to patients and/or caregivers on proper subcutaneous injection technique, including aseptic technique, and how to use the prefilled pen or prefilled syringe correctly *[see Instructions for Use]*. Instruct patients and/or caregivers to read and follow the Instructions for Use each time they use PONTEVIA.

Serious Hypersensitivity Reactions: Inform patients about the signs and symptoms of hypersensitivity reactions and that these reactions can occur with PONTEVIA. Advise patients to seek immediate medical attention if they experience any symptoms of serious or severe hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

Hypertension: Inform patients that hypertension can develop or pre-existing hypertension can worsen with PONTEVIA, and that they should contact their healthcare provider if they experience elevation in their blood pressure *[see Warnings and Precautions (5.2)]*.

Raynaud's Phenomenon: Inform patients that Raynaud's phenomenon can develop or worsen with PONTEVIA. Advise patients to discontinue PONTEVIA and contact their healthcare provider if they experience signs or symptoms of Raynaud's phenomenon *[see Warnings and Precautions (5.3)].*

18 MANUFACTURER

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana (IN)
46285, United States (USA)

Instructions for Use

Pontevia 120 mg Solution for Injection in Pre-filled Pen

Galcanezumab

For subcutaneous injection only.

Before you use the Pontevia pre-filled pen (Pen), read and carefully follow all the step-by-step instructions.

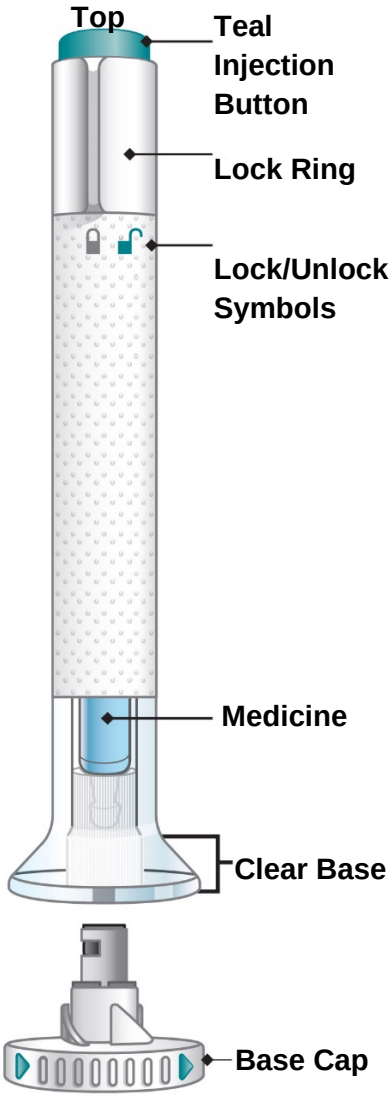
Important Information

- Your healthcare provider or nurse should show you how to prepare and inject Pontevia using the Pen. Do not inject yourself or someone else until you have been shown how to inject Pontevia.
- Keep these Instructions for Use and refer to them as needed.
- Each Pontevia Pen is for **one-time use only. Do not** share or reuse your Pontevia Pen. You may give or get an infection.
- The Pen contains glass parts. Handle it carefully. If you drop it on a hard surface, do not use it. Use a new Pen for your injection.
- Your healthcare provider may help you decide where on your body to inject your dose. You can also read the "**Choose your injection site**" section of these instructions to help you choose which area can work best for you.
- If you have vision or hearing problems, **do not** use Pontevia Pen without help from a caregiver.
- See "**Storage and Handling Information**" for important storage information.

INSTRUCTIONS FOR USE

Before you use the Pontevia Pen, read and carefully follow all the step-by-step instructions.

Parts of the Pontevia Pen



Bottom/Needle end

Before You Get Started

Take the Pen from the refrigerator

Put the original package with any unused Pens back in the refrigerator.

Leave the base cap on until you are ready to inject.
Do not shake**.**
Do not microwave the Pen, run hot water over it, or leave it in direct sunlight.
For a more comfortable injection, leave the Pen at room temperature for 30 minutes before injecting.

Gather Supplies

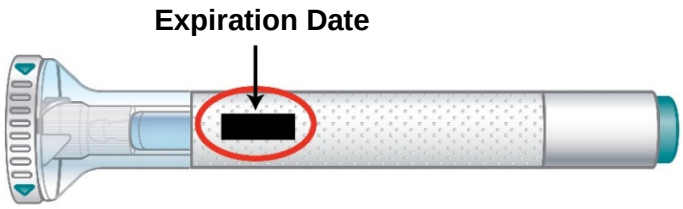
- 1 alcohol wipe
- 1 cotton ball or piece of gauze
- 1 sharps disposal container. See "After You Inject Your Medicine."

Inspect the Pen and the medicine

Make sure you have the right medicine. The medicine inside should be clear. Its color may be colorless to slightly yellow.

Do not use the Pen, and dispose of as directed by your healthcare provider or pharmacist if:

- it looks damaged
- the medicine is cloudy, is discolored, or has small particles
- the Expiration Date printed on the label has passed
- the medicine is frozen

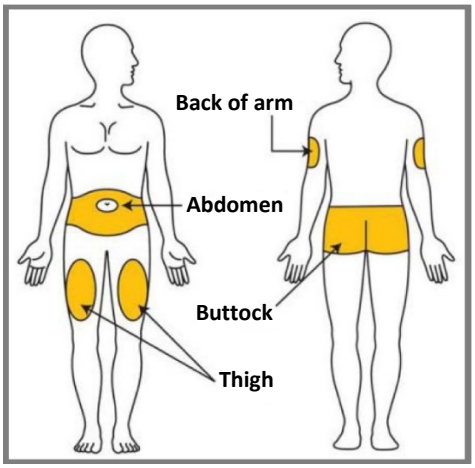


Prepare for injection

Wash your hands with soap and water before you inject your Pontevia. Make sure a sharps disposal container is close by.

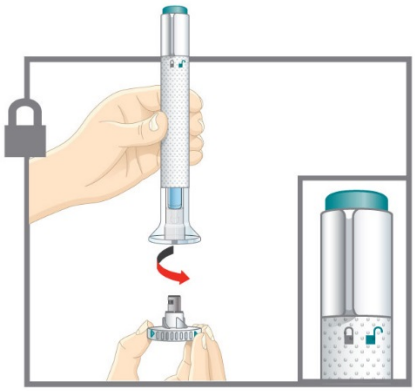
Choose your injection site

Your healthcare provider can help you choose the injection site that is best for you.



- **You** may inject the medicine into your stomach area (abdomen). Do not inject within 2 inches of the belly button (navel).
- **Another person** may give you the injection in the back of your upper arm, or buttocks.
- **Do not** inject in the exact same spot. For example, if your first injection was in your abdomen, your next injection could be in another area of your abdomen.
- **Clean and dry the injection site before you inject.**

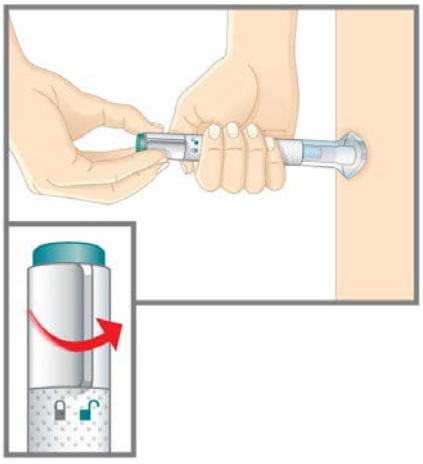
1 Uncap the Pen



Make sure the Pen is locked. Leave the base cap on until you are ready to inject.

- Twist off the base cap and throw it away in your household trash.
- **Do not** put the base cap back on – this could damage the needle.
- **Do not** touch the needle.

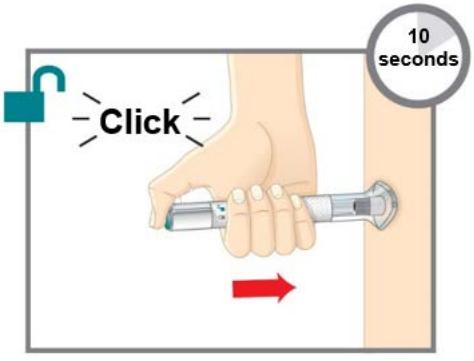
2 Place and Unlock



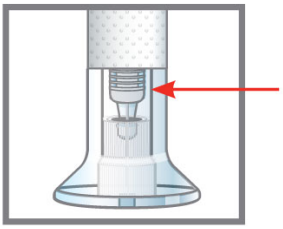
- Place and hold the clear base flat and firmly against your skin.

Turn the lock ring to the **unlock** position.

3 Press and Hold for 10 Seconds



- Press and hold the teal injection button; you will hear a loud click.
- **Keep holding the clear base firmly against your skin.** You will hear a second click in about 10 seconds after the first one. This second click tells you that your injection is complete.
- Remove the Pen from your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site. **Do not** rub the injection site.

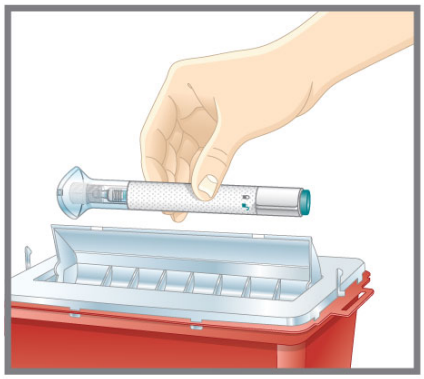


You will know your injection is complete when the gray plunger is visible.

After You Inject Your Medicine

Throw away the used Pen

- Put the used Pontevia Pen in a sharps disposal container right away after use. **Do not** throw away (dispose of) the Pontevia Pen in your household trash.



- If you do not have a sharps disposal container, ask your doctor, pharmacist or nurse where you can get one.
- When your sharps disposal container is almost full, dispose as directed by your doctor, pharmacist or nurse.
- **Do not** recycle your used sharps disposal container.

Commonly Asked Questions

Q. What if I see bubbles in the Pen?

A. It is normal to have air bubbles in the Pen. Pontevia is injected under your skin (subcutaneous injection), so these air bubbles will not harm you.

Q. What if there is a drop of liquid on the tip of the needle when I remove the base cap?
A. It is okay to see a drop of liquid on the tip of the needle.

Q. What if I unlocked the Pen and pressed the teal injection button before I twisted off the base cap?
A. Do not remove the base cap. Dispose of the Pen and get a new one.

Q. Do I need to hold the injection button down until the injection is complete?
A. This is not necessary, but it may help you keep the Pen steady and firm against your skin.

Q. What if the needle did not retract after my injection?
A. Do not touch the needle or replace the base cap. Store in a safe place to avoid an accidental needlestick and contact your doctor, pharmacist or nurse for instructions on how to return the Pen.

Q. What if there is a drop of liquid or blood on my skin after my injection?
A. This is normal. Press a cotton ball or gauze over the injection site. Do not rub the injection site.

Q. What if I heard more than 2 clicks during my injection – 2 loud clicks and a soft one. Did I get my complete injection?

A. Some patients may hear a soft click right before the second loud click. That is the normal operation of the Pen. Do not remove the Pen from your skin until you hear the second loud click.

Q. How can I tell if my injection is complete?

A. After you press the teal injection button, you will hear 2 loud clicks. The second click tells you that your injection is complete. You will also see the gray plunger at the top of the clear base.

If you have more questions about how to use the Pontevia Pen, contact your doctor, pharmacist or nurse.

Storage and Handling Information

- Store your Pen in the refrigerator between 2ºC to 8ºC.
- Your Pen may be stored outside of the refrigerator in the original carton at temperatures up to 30°C for up to 7 days. After storing out of the refrigerator, **do not** place Pontevia back in the refrigerator. **Do not** store above 30°C.
- **Do not** freeze your Pen.
- Keep your Pen in the carton it comes in to protect your Pen from light until time of use.
- **Do not** shake your Pen.
- Discard your Pen if any of the above conditions are not followed.
- **Keep your Pen and all medicines out of the reach of children.**

Read the full Prescribing Information for Pontevia inside this box to learn more about your medicine.

Date of Revision: 27 Aug 2020