ZAVZPRET

Zavegepant

10 mg Nasal spray

Reference Market: US

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

ZAVZPRET™ (zavegepant) nasal spray

----------RECENT MAJOR CHANGES----------
Contraindications (4)
8/2025
Warnings and Precautions (5.1)
8/2025

Warnings and Precautions (5.2, 5.3)
3/2025

----------INDICATIONS AND USAGE----------
ZAVZPRET is a calcitonin gene-related peptide receptor antagonist indicated for the acute treatment of migraine with or without aura in adults. (1)

Limitations of Use
ZAVZPRET is not indicated for the preventive treatment of migraine. (1)

----------DOSAGE AND ADMINISTRATION----------
- The recommended dose is 10 mg given as a single spray in one nostril, as needed. (2.1)
- The maximum dose in a 24-hour period is 10 mg (one spray). (2.1)
- The safety of treating more than 8 migraines in a 30-day period has not been established. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Nasal spray: 10 mg (3)

----------CONTRAINDICATIONS----------
Patients with a history of hypersensitivity reaction to zavegepant or to any of the components of ZAVZPRET. (4)

----------WARNINGS AND PRECAUTIONS----------
Hypersensitivity Reactions: If a serious hypersensitivity reaction occurs, discontinue ZAVZPRET and initiate appropriate therapy. Hypersensitivity reactions including anaphylaxis, facial swelling and urticaria have occurred with ZAVZPRET. (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----------
Most common adverse reactions (at least 2% of patients treated with ZAVZPRET and greater than placebo) were taste disorders, nausea, nasal discomfort, and vomiting. (6.1)

----------DRUG INTERACTIONS----------
- Avoid use with drugs that inhibit OATP1B3 or NTCP transporters. (7.1)
- Avoid use with drugs that induce OATP1B3 or NTCP transporters. (7.2)
- Avoid use of intranasal decongestants; if unavoidable, administer intranasal decongestants at least 1 hour after ZAVZPRET administration. (7.3)

----------USE IN SPECIFIC POPULATIONS----------
- Avoid use in patients with severe hepatic impairment. (8.6)
- Avoid use in patients with CLcr < 30 mL/min. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and approved patient labeling.
Revised: 8/2025

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ZAVZPRET is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

ZAVZPRET is not indicated for the preventive treatment of migraine.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended dose of ZAVZPRET is 10 mg given as a single spray in one nostril, as needed.

The maximum dose that may be given in a 24-hour period is 10 mg (one spray). The safety of treating more than 8 migraines in a 30-day period has not been established.

3 DOSAGE FORMS AND STRENGTHS

Nasal spray: 10 mg of zavegepant per device. Each unit-dose nasal spray device delivers a single spray containing 10 mg of zavegepant.

4 CONTRAINDICATIONS

ZAVZPRET is contraindicated in patients with a history of hypersensitivity reaction to zavegepant or any of the components of ZAVZPRET. Reactions have included anaphylaxis *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, facial swelling and urticaria, have occurred in patients treated with ZAVZPRET. If a hypersensitivity reaction occurs, discontinue ZAVZPRET and initiate appropriate therapy *[see Contraindications (4) and Adverse Reactions (6.1, 6.2)]*.

5.2 Hypertension

Development of hypertension and worsening of pre-existing hypertension have been reported following the use of CGRP antagonists in the postmarketing setting.

Some of the patients receiving a CGRP antagonist 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. The CGRP antagonist was discontinued in many of the reported cases.

Monitor patients treated with ZAVZPRET for new-onset hypertension or worsening of pre-existing hypertension, and consider whether discontinuation of ZAVZPRET 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.

In reported cases with small molecule CGRP antagonists, symptom onset occurred a median of 1.5 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.

ZAVZPRET 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 discussed in greater detail in other sections of the labeling:

- Hypersensitivity Reactions *[see 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 to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of ZAVZPRET for the acute treatment of migraine in adults has been evaluated in two randomized, double-blind, placebo-controlled trials (Study 1 and Study 2) in patients with migraine who received one 10 mg dose of ZAVZPRET nasal spray (N=1023) or placebo (N=1056) *[see Clinical Studies (14)]*. Approximately 83% were female, 81% were White, 20% were Hispanic or Latino, and 15% were Black. The mean age at study entry was 41 years (range 18-79 years of age).

Adverse reactions in Study 1 and 2 are shown in Table 1.

Table 1: Adverse Reactions Occurring in At Least 2% of Patients Treated with ZAVZPRET and at a Frequency Greater than Placebo in Study 1 and 2

Adverse Reaction	ZAVZPRET N=1023 %	Placebo N=1056 %
Taste Disorders*	18	4
Nausea	4	1
Nasal Discomfort	3	1
Vomiting	2	<1

*Taste disorders includes dysgeusia and ageusia

Hypersensitivity, including facial swelling and urticaria, occurred in less than 1% of patients treated with ZAVZPRET *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Long-term safety was assessed in an open-label extension study. That study evaluated 603 patients, dosing intermittently for up to one year, including 360 patients who were exposed to ZAVZPRET 10 mg for at least 6 months, and 298 who were exposed for at least one year, all of whom treated an average of at least two migraine attacks per month.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of ZAVZPRET. 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 drug exposure.

Immune System Disorders: Hypersensitivity (e.g., anaphylaxis) [see Contraindications (4) and Warnings and Precautions (5.1)]

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

7 DRUG INTERACTIONS

7.1 OATP1B3 or NTCP Inhibitors

Concomitant administration of ZAVZPRET with inhibitors of the organic anion transporting polypeptide 1B3 (OATP1B3) or sodium taurocholate co-transporting polypeptide (NTCP) transporters may result in a significant increase in zavegepant exposure. Avoid concomitant administration of ZAVZPRET with drugs that inhibit OATP1B3 or NTCP transporters *[see Clinical Pharmacology (12.3)]*.

7.2 OATP1B3 or NTCP Inducers

Concomitant administration of ZAVZPRET with inducers of OATP1B3 or NTCP transporters may result in a decrease in zavegepant exposure. Avoid concomitant administration of ZAVZPRET with drugs that induce OATP1B3 or NTCP transporters *[see Clinical Pharmacology (12.3)]*.

7.3 Intranasal Decongestants

Concomitant administration of ZAVZPRET with intranasal decongestants may decrease the absorption of zavegepant. Avoid concomitant administration of intranasal decongestants with ZAVZPRET. When concomitant use is unavoidable, intranasal decongestants should be administered at least 1 hour after ZAVZPRET administration *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of ZAVZPRET in pregnant women. No adverse developmental effects were observed following subcutaneous administration of zavegepant to pregnant animals at doses associated with plasma exposures higher than those used clinically *(see Data)*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively. The estimated rate of major birth defects (2.2 to 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 and gestational hypertension during pregnancy.

Data

Animal Data

Subcutaneous administration of zavegepant to pregnant rats (0, 10, 20, or 40 mg/kg/day) or rabbits (0, 20, 40, or 60 mg/kg/day) during the period of organogenesis resulted in no adverse effects on embryofetal development. Plasma exposures (AUC) at the highest doses tested were approximately 4000 times that in humans at the maximum recommended human dose (MRHD) of 10 mg/day.

Subcutaneous administration of zavegepant (0, 5, 10, or 20 mg/kg/day) to rats throughout pregnancy and lactation resulted in no adverse effects on pre- and postnatal development. Plasma exposure (AUC) at the highest dose tested was approximately 2500 times that in humans at the MRHD.

8.2 Lactation

There are no data on the presence of zavegepant or its metabolites in human milk, the effects of zavegepant on the breastfed infant, or the effects of zavegepant on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for

ZAVZPRET and any potential adverse effects on the breastfed infant from ZAVZPRET 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 ZAVZPRET did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

In a limited number of patients 65 years of age and older, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects.

8.6 Hepatic Impairment

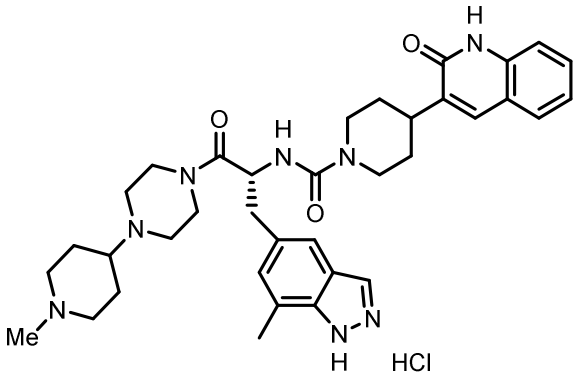
No dosage adjustment of ZAVZPRET is necessary in patients with mild hepatic impairment (Child-Pugh Class A) or moderate hepatic impairment (Child-Pugh Class B). ZAVZPRET has not been studied in patients with severe hepatic impairment (Child-Pugh Class C). Avoid use of ZAVZPRET in patients with severe hepatic impairment *[see Clinical Pharmacology (12.3)]*.

8.7 Renal Impairment

No dosage adjustment of ZAVZPRET is necessary in patients with estimated creatine clearance (CLcr) 30 mL/min or greater. Avoid use of ZAVZPRET in patients with CLcr less than 30 mL/min *[see Clinical Pharmacology (12.3)]*.

11 DESCRIPTION

ZAVZPRET (zavegepant) nasal spray contains zavegepant hydrochloride, a calcitonin gene-related peptide receptor antagonist. Zavegepant hydrochloride is described chemically as (R)-N-(3-(7-methyl-1H-indazol-5-yl)-1-(4-(1-methylpiperidin-4-yl) piperazin-1-yl)-1-oxopropan-2-yl)-4-(2-oxo-1,2-dihydroquinolin-3-yl) piperidine-1-carboxamide hydrochloride and its structural formula is:



Its molecular formula is $C_{36}H_{46}N_8O_3$.HCl, representing a molecular weight of 675. 28 g/mol. Zavegepant free base has a molecular weight of 638.82 g/mol. Zavegepant hydrochloride is a white to off-white powder, freely soluble in water, and has pKa values of 4.8 and 8.8.

Each unit-dose ZAVZPRET device for nasal administration delivers 10 mg of zavegepant (equivalent to 10.6 mg of zavegepant hydrochloride) in a buffered aqueous solution containing dextrose, hydrochloric acid, sodium hydroxide, and succinic acid in water for injection. The solution has a pH of 5.3 to 6.7.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Zavegepant is a calcitonin gene-related peptide (CGRP) receptor antagonist.

12.2 Pharmacodynamics

The relationship between pharmacodynamic activity and the mechanism by which zavegepant exerts its clinical effects is unknown.

No clinically relevant differences in resting blood pressure were observed when zavegepant was concomitantly administered with sumatriptan (12 mg subcutaneous, given as two 6 mg doses separated by one hour) compared with sumatriptan alone to healthy volunteers.

Cardiac Electrophysiology
At a dose up to 4 times the recommended daily dose, zavegepant does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

Absorption
Peak plasma concentration of zavegepant was observed at approximately 30 minutes after a single 10 mg dose of the nasal spray. After nasal spray administration of zavegepant, the absolute bioavailability is approximately 5%.

Zavegepant given as a single dose of the nasal spray displays slightly less than dose-proportional pharmacokinetics up to 40 mg (approximately 4 times the recommended dosage of 10 mg). Following once daily dosing of ZAVZPRET for 14 days there was no evidence of zavegepant accumulation.

Distribution
The mean apparent volume of distribution of intranasal zavegepant is approximately 1774 L. Plasma protein binding of zavegepant is approximately 90%.

Elimination
Metabolism
Zavegepant is primarily metabolized by CYP3A4 and to a lesser extent by CYP2D6, in vitro. After single IV dose of 5 mg [^{14}C]-zavegepant, unchanged zavegepant was the most prevalent (approximately 90%) circulating component in the human plasma. No major metabolites (i.e., greater than 10%) of zavegepant were detected in plasma.

Excretion
The effective half-life of zavegepant following a 10 mg dose of the nasal spray is 6.55 hours. The mean apparent clearance of intranasal zavegepant is 266 L/h. Zavegepant is excreted mostly via the biliary/fecal route, while the renal route is a minor route of elimination. Following a single intravenous dose of 5 mg [^{14}C]-zavegepant to healthy male subjects, approximately 80% and 11% of the dose was recovered as unchanged zavegepant in feces and urine, respectively.

Specific Populations

Patients with Hepatic Impairment

In a dedicated clinical study comparing the pharmacokinetics of zavegepant in subjects with moderate hepatic impairment (Child-Pugh B) to that of normal subjects (matched healthy controls), zavegepant C_{max} was 16% higher and AUC was 1.9-fold higher in patients with moderate hepatic impairment. These changes in exposures are not expected to be clinically significant, based on clinical safety experience and minimal accumulation of drug exposures. The impact of severe hepatic impairment (Child-Pugh C) on the pharmacokinetics of zavegepant was not studied *[see Use in Specific Populations (8.6)]*.

Patients with Renal Impairment

The renal route plays a minor role in the clearance of zavegepant. No clinically significant effect on the pharmacokinetics of zavegepant is expected in subjects with estimated creatinine clearance (CLcr) 30 mL/min or greater. In patients with CLcr 15 to 29 mL/min, accumulation of uremic solutes can cause an increase in zavegepant exposures by inhibiting OATP transporters. Zavegepant has not been studied in patients with CLcr less than 15 mL/min *[see Use in Specific Populations (8.7)]*.

Other Specific Populations

Age, sex, race, ethnicity, and body weight did not show clinically significant effects on the pharmacokinetics of zavegepant.

Drug Interaction Studies

In Vitro Studies

Enzymes

Zavegepant is a substrate of CYP3A4 and to a lesser extent CYP2D6. Zavegepant is not an inducer of CYP1A2, 2B6, or 3A4, or an inhibitor of CYP1A2, CYP2C9, 2C19, 2B6, 2D6, 2C8, and 3A4 at clinically relevant concentrations.

Transporters

Zavegepant is a substrate for OATP1B3 and NTCP (*see In Vivo studies)*.

Zavegepant is also a substrate for the transporters P-gp, MATE1, and MATE2-K. Considering the minor contribution of the renal pathway in the clearance of zavegepant, coadministration of zavegepant with inhibitors of P-gp, MATE1, and MATE2-K inhibitors is not expected to result in a clinically significant effect on zavegepant pharmacokinetics.

Zavegepant is not a substrate for BCRP, OATP1B1, OAT1, OAT3, OCT2, BSEP, MRP2, MRP3, and MRP4.

Zavegepant is an inhibitor of OCT2, MATE1, and MATE2-K, but drug interactions for ZAVZPRET are not expected at clinically relevant concentrations. Zavegepant is not an inhibitor of P-gp, BCRP, OAT1, OAT3, OATP1B1, and OATP1B3.

In Vivo Studies

CYP3A4 Inhibitors
Concomitant administration of a single dose of 10 mg ZAVZPRET with itraconazole (a strong CYP3A4 and P-gp inhibitor), at steady state did not result in a clinically relevant effect on the exposures of zavegepant.

OATP1B3 or NTCP Inhibitors
Concomitant administration of a single oral dose of 100 mg zavegepant with rifampin (an OATP1B3, NTCP inhibitor and a strong CYP3A inducer), at steady state resulted in increased zavegepant exposure (AUC by 2.3-fold and C_{max} by 2.2-fold). The observed change in zavegepant exposures is a composite effect of inhibition of OATP1B3 and NTCP transporters as well as induction of CYP3A enzymes. Concomitant administration of ZAVZPRET with inhibitors of OATP1B3 or NTCP transporters may result in a significant increase in zavegepant exposure *[see Drug Interactions (7.1)]*.

OATP1B3 or NTCP Inducers
Concomitant administration of ZAVZPRET with inducers of OATP1B3 or NTCP transporters has not been studied. However, since zavegepant is a substrate of OATP1B3 and NTCP, concomitant administration with inducers of these transporters may result in decreased zavegepant exposure *[see Drug Interactions (7.2)]*.

Intranasal Decongestants
The effect of concomitant intranasal decongestants on the pharmacokinetics of zavegepant nasal spray has not been evaluated. Concomitant administration of intranasal decongestants may decrease the systemic exposure of zavegepant and potentially the efficacy of zavegepant *[see Drug Interactions (7.3)]*.

Other Drugs
No significant pharmacokinetic interactions were observed when zavegepant was concomitantly administered with oral contraceptives (ethinyl estradiol) or sumatriptan *[see Clinical Pharmacology (12.2)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Intranasal administration of zavegepant (0, 0.3, 0.8, or 2.5 mg/day) to Tg.rasH2 mice for 26 weeks resulted in no evidence of drug-related tumors.

Intranasal administration of zavegepant (0, 2, 9, or 18.8 mg/kg/day) to rats for up to 96 weeks resulted in no evidence of drug-related tumors. Plasma exposure (AUC) at the highest dose tested was approximately 140 times that in humans at the maximum recommended human dose (MRHD) of 10 mg/day.

Mutagenesis
Zavegepant was negative in *in vitro* (bacterial reverse mutation, chromosomal aberration in Chinese hamster ovary cells) and *in vivo* (rat micronucleus) assays.

Impairment of Fertility
Subcutaneous administration of zavegepant (0, 5, 15, or 25 mg/kg/day) to male and female rats prior to and during mating and continuing in females to gestation day 7 resulted in no adverse effects on fertility

or reproductive performance. Plasma exposures (AUC) at the highest dose tested were approximately 2800 times that in humans at MRHD.

14 CLINICAL STUDIES

The efficacy of ZAVZPRET for the acute treatment of migraine with or without aura in adults was demonstrated in two randomized, double-blind, placebo-controlled trials (Study 1 and Study 2). In both studies, patients were instructed to treat a migraine of moderate to severe headache pain intensity. Rescue medication (i.e., NSAIDs, acetaminophen, and/or an antiemetic) was allowed 2 hours after the initial treatment. Other forms of rescue medication such as triptans were not allowed within 48 hours of initial treatment. In Study 1 and Study 2, 13.4% and 13.6% of patients were taking preventive medications for migraine at baseline, respectively. None of the patients were on concomitant preventive medication that act on the CGRP pathway.

In Study 1 (NCT04571060), patients were randomized to receive a single dose of ZAVZPRET 10 mg (N=623) or placebo (N=646). Efficacy was demonstrated with ZAVZPRET 10 mg by an effect on the coprimary endpoints of pain freedom and most bothersome symptom (MBS) freedom at 2 hours after a single dose, compared to placebo. Pain freedom was defined as a reduction of moderate or severe headache pain to no headache pain, and MBS freedom was defined as the absence of the self-identified MBS (i.e., photophobia, phonophobia, or nausea). The most common MBS reported before dosing was photophobia (55%), followed by nausea (28%), and phonophobia (16%).

In Study 1, the percentage of patients achieving headache pain freedom and MBS freedom 2 hours after a single dose was statistically significantly greater in patients who received ZAVZPRET compared to those who received placebo (Table 2).

Table 2: Efficacy Endpoints in Study 1

	ZAVZPRET 10 mg	**Placebo**
Pain Free at 2 hours		
n/N*	147/623	96/646
% Responders	23.6	14.9
Difference from placebo (%)	8.8	
p-value	<0.001	
MBS Free at 2 hours**		
n/N*	247/623	201/646
% Responders	39.6	31.1
Difference from placebo (%)	8.7	
p-value	0.001	

*n=number of responders/N=number of patients in that treatment group
**MBS = most bothersome symptoms of photophobia, phonophobia, or nausea.

Figures 1 and 2 present the percentage of patients achieving migraine pain freedom and MBS freedom within 2 hours following treatment in Study 1.

Figure 1: Percentage of Patients Achieving Pain Freedom within 2 Hours in Study 1

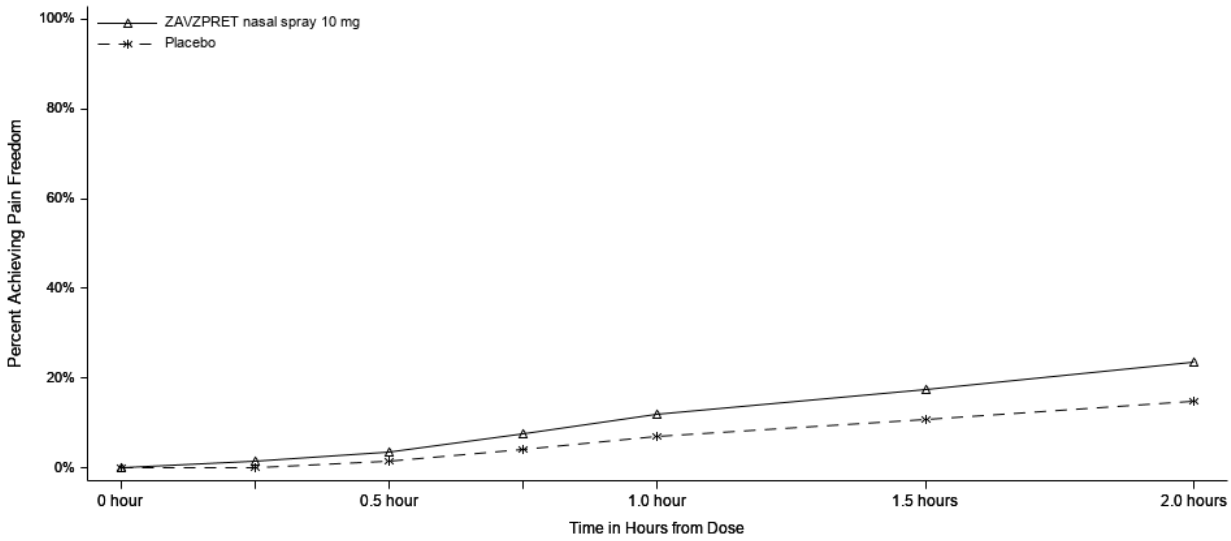
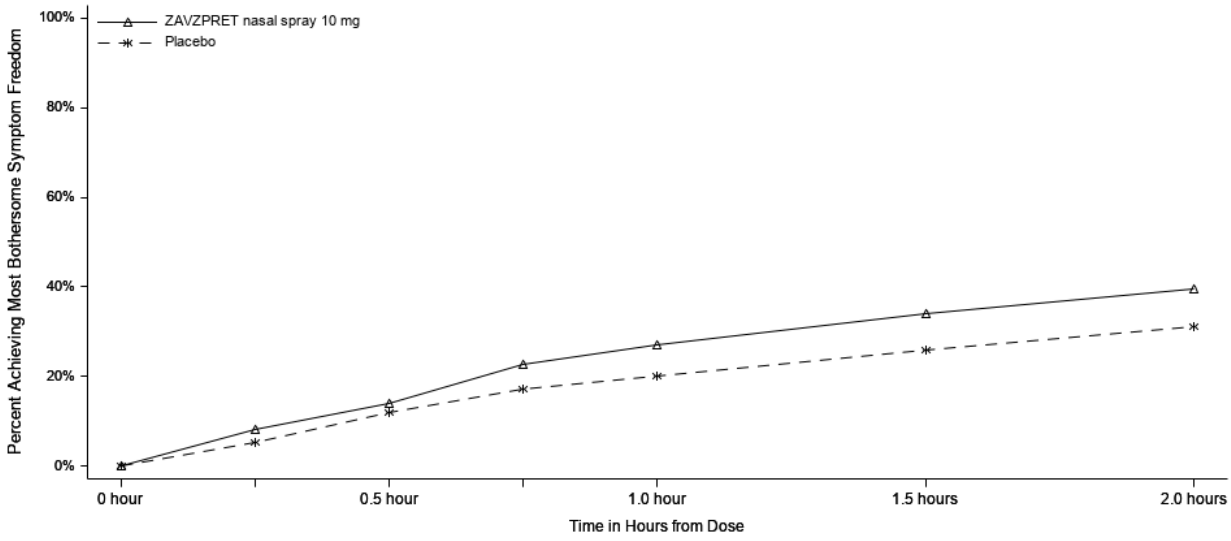


Figure 2: Percentage of Patients Achieving MBS Freedom within 2 Hours in Study 1



In Study 1, statistically significant effects of ZAVZPRET compared to placebo were demonstrated for the additional efficacy endpoints of pain relief at 2 hours post-dose, return to normal function at 2 hours post-dose, sustained pain freedom from 2 to 48 hours post-dose (Table 3), and phonophobia and photophobia freedom at 2 hours post-dose. Pain relief was defined as a reduction in migraine pain from moderate or severe severity to mild or none. The measurement of the percentage of patients reporting normal function at two hours after dosing was derived from a single item questionnaire, asking patients to select one response on a 4-point scale: normal function, mild impairment, severe impairment, or required bedrest.

Table 3: Additional Efficacy Endpoints in Study 1

	ZAVZPRET 10 mg	Placebo
Pain Relief at 2 hours		
n/N*	366/623	321/646
% Responders	58.7	49.7
Difference from placebo (%)	9.0	
p-value	0.001	
Percentage of Patients Reporting Normal Function at 2 hours**		
n/N*	204/570	152/593
% Responders	35.8	25.6
Difference from placebo (%)	10.2	
p-value	<0.001	
Sustained Pain Freedom from 2 to 48 hours		
n/N*	77/623	56/646
% Responders	12.4	8.7
Difference from placebo (%)	3.7	
p-value	0.031	

*n=number of responders/N=number of patients in that treatment group
**Includes patients with functional disability at time of dosing, according to the functional disability scale.

The incidence of photophobia and phonophobia was reduced following administration of ZAVZPRET 10 mg as compared to placebo.

In Study 2 (NCT03872453), patients were randomized to receive a single dose of ZAVZPRET 10 mg (n=391) or placebo (n=401).

In Study 2, statistically significant efficacy was demonstrated with ZAVZPRET 10 mg by an effect on the coprimary endpoints of pain freedom and most bothersome symptom (MBS) freedom at 2 hours after a single dose, compared to placebo. Pain freedom was observed in 22.5% of patients receiving ZAVZPRET and 15.5% of patients receiving placebo (p-value = 0.011). MBS freedom was observed in 41.9% of patients receiving ZAVZPRET and 33.7% of patients receiving placebo (p-value = 0.016). The most common MBS reported before dosing was photophobia (53%), followed by nausea (31%), and phonophobia (15%).

Table 4: Efficacy Endpoints in Study 2

	ZAVZPRET 10 mg	**Placebo**
Pain Free at 2 hours		
n/N*	88/391	62/401
% Responders	22.5	15.5
Difference from placebo (%)	7.0	
p-value	0.011	
MBS Free at 2 hours**		
n/N*	164/391	135/401
% Responders	41.9	33.7
Difference from placebo (%)	8.3	
p-value	0.016	

*n=number of responders/N=number of patients in that treatment group
**MBS = most bothersome symptoms of photophobia, phonophobia, or nausea.

Figure 3: Percentage of Patients Achieving Pain Freedom within 2 Hours in Study 2

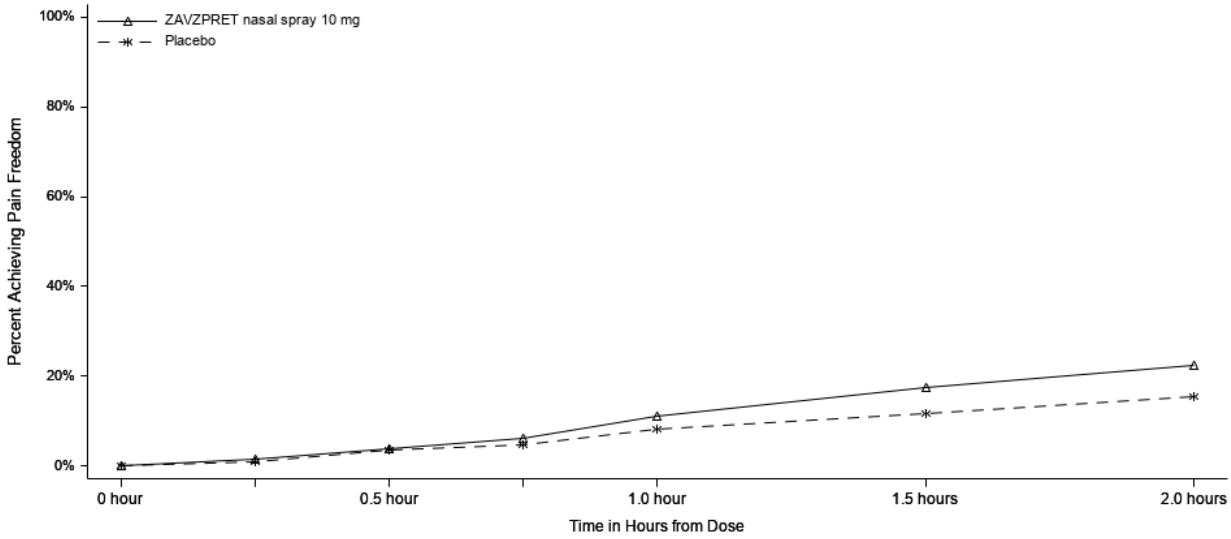
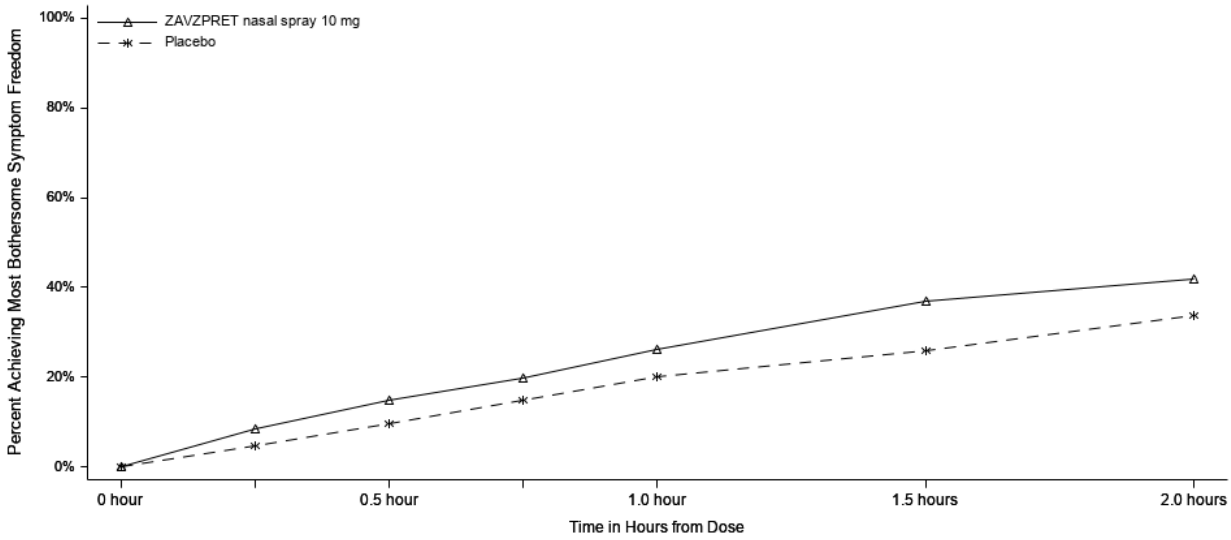


Figure 4: Percentage of Patients Achieving MBS Freedom within 2 Hours in Study 2



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ZAVZPRET nasal spray contains 10 mg zavegepant and is supplied as a ready-to-use, unit-dose disposable device.

Each carton contains 6 units and a Patient Information and Instructions for Use leaflet.

16.2 Storage and Handling

Store ZAVZPRET below 30C,

Do not freeze. Do not test spray, prime, or press the plunger before use.

Keep the device in the sealed blister package until time of use.

Warning: Keep out of reach of children

17 PATIENT COUNSELING INFORMATION

Advise patients to read the approved patient labeling (Patient Information and Instructions for Use).

Hypersensitivity Reactions
Inform patients about the signs and symptoms of hypersensitivity reactions, and that these reactions can occur after administration of ZAVZPRET. Advise patients to contact their healthcare provider immediately if signs or symptoms of hypersensitivity reactions occur *[see Warnings and Precautions (5.1)]*.

Hypertension
Inform patients that hypertension can develop or pre-existing hypertension can worsen with ZAVZPRET, 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 ZAVZPRET. Advise patients to discontinue ZAVZPRET and contact their healthcare provider if they experience signs or symptoms of Raynaud's phenomenon *[see Warnings and Precautions (5.3)]*.
Drug Interactions
Advise patients to speak with their healthcare provider about any prescription or over-the-counter medications or herbal supplements that they take or plan to take. Inform patients that if they need to use an intranasal decongestant it should be administered at least 1 hour after ZAVZPRET administration *[see Drug Interactions (7.3)]*.

MARKETING AUTHORISATION HOLDER
Pfizer Inc. , 66 Hudson Boulevard East, New York, NY 10001 United States of America

Manufacturer
Renaissance Lakewood LLC, 1200 Paco Way, Lakewood, NJ 08701 United States of America

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THIS IS A MEDICAMENT

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.

- Follow strictly the doctor's prescription, the method of use and the instructions of the Pharmacist who sold the medicament.
- The doctor and the Pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep all medicaments out of reach and sight of children

Council of Arab Health Ministers
Union of Arabic Pharmacists