TEZSPIRE- tezepelumab-ekko injection, solution
Amgen Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TEZSPIRE safely and effectively. See full prescribing information for TEZSPIRE.
TEZSPIRE® (tezepelumab-ekko) injection, for subcutaneous use
Initial U.S. Approval: 2021

RECENT MAJOR CHANGES

Indications and Usage (1.2)	10/2025

INDICATIONS AND USAGE

TEZSPIRE is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody (IgG2λ), indicated:

- for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. (1.1)
  Limitations of Use:
  Not for relief of acute bronchospasm or status asthmaticus. (1.1)
- for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP). (1.2)

DOSAGE AND ADMINISTRATION

Recommended dosage is 210 mg administered once every 4 weeks. (2.1)

- Administer by subcutaneous injection. (2.1)
- See full prescribing information for preparation and administration instructions. (2.2)

DOSAGE FORMS AND STRENGTHS

Injection:

- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose glass vial. (3)
- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled syringe. (3)
- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled pen. (3)

CONTRAINDICATIONS

Known hypersensitivity to tezepelumab-ekko or excipients. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Hypersensitivity reactions have been observed in the clinical trials (e.g., rash, allergic conjunctivitis) following the administration of TEZSPIRE. Postmarketing cases of anaphylaxis have been reported. Initiate appropriate treatment as clinically indicated in the event of a hypersensitivity reaction. (5.1)
- Risk Associated with Abrupt Reduction in Corticosteroid Dosage: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with TEZSPIRE. Decrease corticosteroids gradually, if appropriate. (5.3)
- Parasitic (Helminth) Infection: Treat patients with pre-existing helminth infections before therapy with TEZSPIRE. If patients become infected while receiving TEZSPIRE and do not respond to anti-helminth treatment, discontinue TEZSPIRE until the parasitic infection resolves. (5.4)
- Vaccination: Avoid use of live attenuated vaccines. (5.5)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 3%) are:

- Asthma: pharyngitis, arthralgia, and back pain. (6.1)
- Chronic rhinosinusitis with nasal polyps: nasopharyngitis, upper respiratory tract infection, epistaxis, pharyngitis, back pain, influenza, injection site reaction and arthralgia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
1.1 Asthma
1.2 Chronic Rhinosinusitis with Nasal Polyps
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosage
2.2 Preparation and Administration Instructions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions
5.2 Acute Asthma Symptoms or Deteriorating Disease
5.3 Risk Associated with Abrupt Reduction of Corticosteroid Dosage
5.4 Parasitic (Helminth) Infection
5.5 Live Attenuated Vaccines
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.6 Immunogenicity
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
14.1 Clinical Studies in Patients with Asthma
14.2 Clinical Studies in Patients with Chronic Rhinosinusitis with Nasal Polyps
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Asthma

TEZSPIRE is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.

Limitations of Use:

TEZSPIRE is not indicated for the relief of acute bronchospasm or status asthmaticus.

1.2 Chronic Rhinosinusitis with Nasal Polyps

TEZSPIRE is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of TEZSPIRE is 210 mg administered subcutaneously once every 4 weeks.

Missed Dose Information

If a dose is missed, administer the dose as soon as possible. Thereafter, the patient can continue (resume) dosing on the usual day of administration. If the next dose is already due, then administer as planned.

2.2 Preparation and Administration Instructions

TEZSPIRE vial and pre-filled syringe are intended for administration by a healthcare provider.

TEZSPIRE pre-filled pen can be administered by patients/caregivers or healthcare providers. Patients/caregivers may administer TEZSPIRE pre-filled pen after proper training in subcutaneous injection technique and after the healthcare provider determines it is appropriate.

Each vial, pre-filled syringe and pre-filled pen contain a single dose of TEZSPIRE.

- Prior to administration, remove TEZSPIRE from the refrigerator and allow it to reach room temperature. This generally takes 60 minutes. Do not expose to heat and do not shake. Do not use if the security seal on the carton has been broken. Do not put back in the refrigerator once TEZSPIRE has reached room temperature.
- Visually inspect TEZSPIRE for particulate matter and discoloration prior to administration. TEZSPIRE is a clear to opalescent, colorless to light yellow solution. Do not use TEZSPIRE if liquid is cloudy, discolored, or if it contains large particles or foreign particulate matter. Do not use if the vial, pre-filled syringe or pre-filled pen has been dropped or damaged or if the expiration date has passed.
- Inject TEZSPIRE 210 mg (contents of one vial, one pre-filled syringe or one pre-filled pen as described below) subcutaneously into the thigh or abdomen, except for the

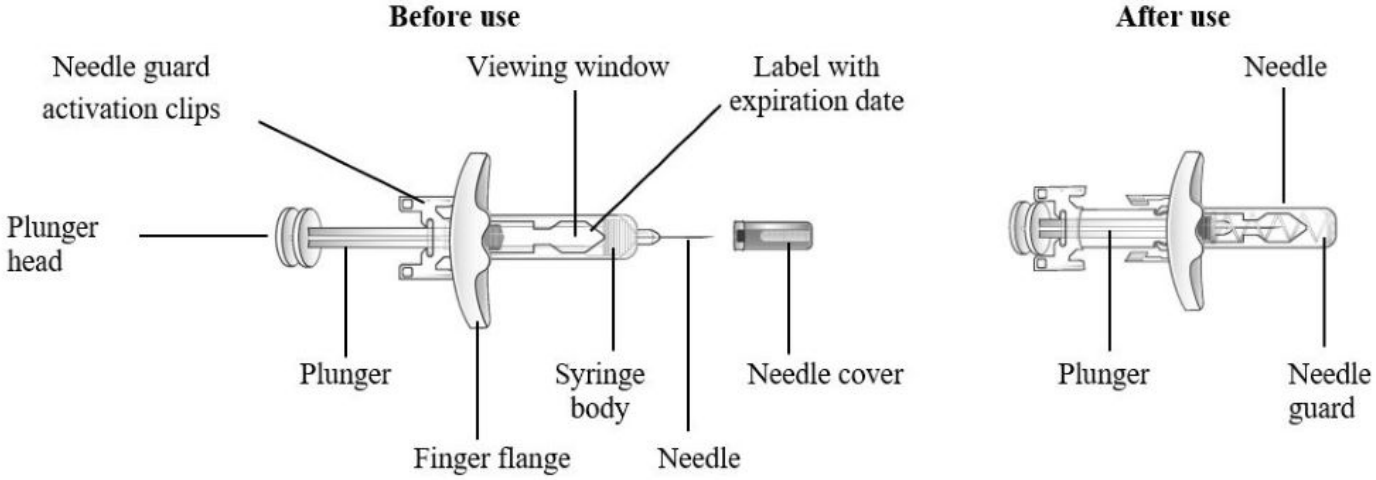
2 inches (5 cm) around the navel. If a healthcare provider or caregiver administers the injection, the upper arm can also be used. A patient should not self-inject in the upper arm. TEZSPIRE should not be injected into areas where the skin is tender, bruised, erythematous, or hardened. It is recommended to rotate the injection site with each injection.

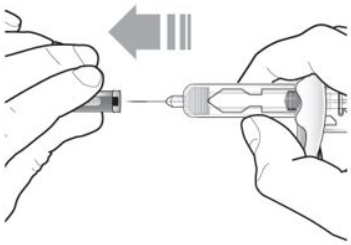
Administration Instructions for Single-Dose Pre-filled Syringe

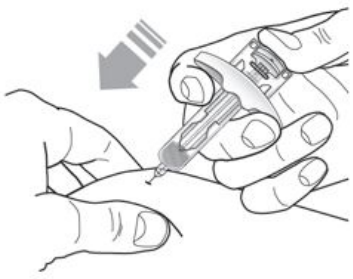
Refer to Figure 1 to identify the pre-filled syringe components for use in the administration steps.

Do not remove the needle cover until Step 2 of these instructions when you are ready to inject TEZSPIRE. Do not touch the needle guard activation clips to prevent premature activation of the needle safety guard.

Figure 1 TEZSPIRE Pre-filled Syringe Components



1. Grasp the syringe body to remove the pre-filled syringe from its carton. Do not grab the pre-filled syringe by the plunger.
   The pre-filled syringe may contain small air bubbles; this is normal. Do not expel the air bubbles prior to administration.
2. 
   Do not remove the needle cover until ready to inject. Hold the syringe body and remove the needle cover by pulling straight off. Do not hold the plunger or plunger head while removing the needle cover. You may see a drop of liquid at the end of the needle. This is normal.
3. 
   Gently pinch the skin and administer subcutaneously at approximately 45° angle into the recommended injection site (i.e., upper arm, thigh, or abdomen).

4. 
Inject all of the medication by pushing in the plunger all the way until the plunger head is completely between the needle guard activation clips. This is necessary to activate the needle guard.

5. 
After injection, maintain pressure on the plunger head and remove the needle from the skin. Release pressure on the plunger head to allow the needle guard to cover the needle. Do not re-cap the pre-filled syringe.

6. Discard the used syringe into a sharps container.

Administration Instructions for Single-Dose Pre-filled Pen

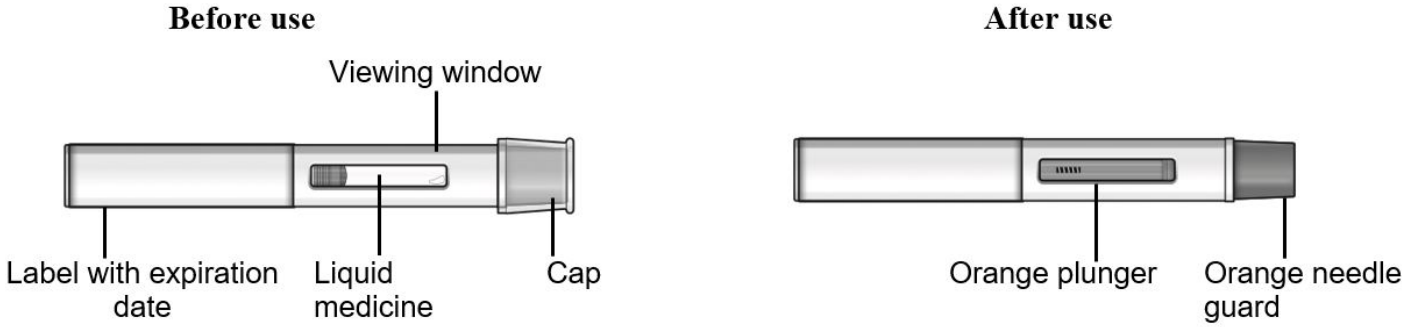
These administration instructions are intended for healthcare providers use only. Patients and caregivers should refer to the TEZSPIRE pre-filled pen 'Instructions for Use' for more detailed instructions on the preparation and administration of TEZSPIRE pre-filled pen *[See Instructions for Use]*.

Patients/caregivers may inject after proper training in subcutaneous injection technique according to the 'Instructions for Use', and after the healthcare provider determines it is appropriate.

Refer to Figure 2 to identify the pre-filled pen components for use in the administration steps.

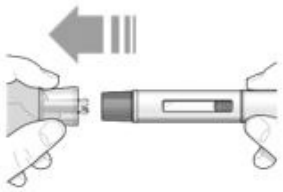
Do not remove the cap until you are ready to inject TEZSPIRE.

Figure 2 TEZSPIRE Pre-filled Pen Components



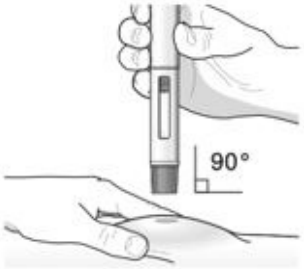
1. Grab the middle of the pre-filled pen body to remove the pre-filled pen from its carton.

The pre-filled pen may contain small air bubbles; this is normal. Do not expel the air bubbles prior to administration.

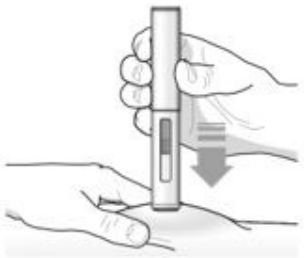
2. 

Do not remove the cap until ready to inject. Hold the pre-filled pen body with 1 hand and carefully pull the cap straight off with your other hand. Do not touch the needle or push the orange needle guard with your finger. Do not put the cap back on the pre-filled pen. You could cause the injection to happen too soon or damage the needle.

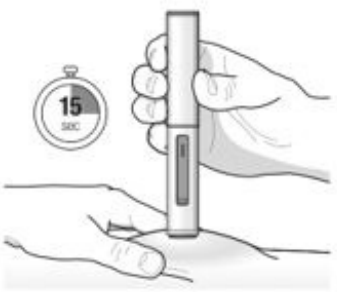
3. Gently pinch the skin at the injection site or give the injection without pinching the skin.
Inject TEZSPIRE by following the steps into the recommended injection site (i.e., upper arm, thigh, or abdomen).
When injecting, you will hear the first click that tells you the injection has started. Press and hold the pre-filled pen for 15 seconds until you hear the second click. Do not change the position of the pre-filled pen after the injection has started.

4. 

Position the pre-filled pen. Place the orange needle guard flat against the skin (90-degree angle). Make sure you can see the viewing window.

5. 

Press down firmly until you cannot see the orange needle guard. You will hear the first ‘click’, this tells you the injection has started. The orange plunger will move down in the viewing window during the injection.

6. 

Hold down firmly for about 15 seconds. You will hear a second ‘click’, this tells you the injection has finished. The orange plunger will fill the viewing window.

7. 

After you have completed the injection, lift the pre-filled pen straight up. The orange needle guard will slide down and lock into place over the needle.

8. Discard the used pre-filled pen into a sharps container.

3 DOSAGE FORMS AND STRENGTHS

Injection: a clear to opalescent, colorless to light yellow solution available as:

- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose glass vial.
- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled syringe.
- 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled pen.

4 CONTRAINDICATIONS

TEZSPIRE is contraindicated in patients who have known hypersensitivity to tezepelumab-ekko or any of its excipients *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions were observed in the clinical trials (e.g., rash and allergic conjunctivitis) following the administration of TEZSPIRE. Postmarketing cases of anaphylaxis have also been reported *[see Contraindications (4) and Adverse Reactions (6.2)]*. These reactions can occur within hours of administration, but in some instances have a delayed onset (i.e., days). In the event of a hypersensitivity reaction, consider the benefits and risks for the individual patient to determine whether to continue or discontinue treatment with TEZSPIRE.

5.2 Acute Asthma Symptoms or Deteriorating Disease

TEZSPIRE should not be used to treat acute asthma symptoms or acute exacerbations. Do not use TEZSPIRE to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with TEZSPIRE.

5.3 Risk Associated with Abrupt Reduction of Corticosteroid Dosage

Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with TEZSPIRE. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.4 Parasitic (Helminth) Infection

Thymic stromal lymphopoietin (TSLP) may be involved in the immunological response to some helminth infections. Patients with known helminth infections were excluded from participation in clinical trials. It is unknown if TEZSPIRE will influence a patient’s response against helminth infections.

Treat patients with pre-existing helminth infections before initiating therapy with TEZSPIRE. If patients become infected while receiving treatment with TEZSPIRE and do not respond to anti-helminth treatment, discontinue treatment with TEZSPIRE until

infection resolves.

5.5 Live Attenuated Vaccines

The concomitant use of TEZSPIRE and live attenuated vaccines has not been evaluated. The use of live attenuated vaccines should be avoided in patients receiving TEZSPIRE.

6 ADVERSE REACTIONS

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

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*

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 practice.

Adverse Reactions in Adult and Pediatric Patients 12 Years of Age and Older with Asthma

The safety of TEZSPIRE in asthma was based on the pooled safety population from PATHWAY and NAVIGATOR, which consists of 665 adult and pediatric patients 12 years of age and older with severe asthma who received at least one dose of TEZSPIRE 210 mg subcutaneously once every 4 weeks. The two placebo-controlled clinical trials were of 52 weeks duration. In addition, a similar safety profile was seen in a trial that enrolled 150 adult patients with severe asthma who required treatment with daily oral corticosteroids *[see Clinical Studies (14.1)]*.

Adverse reactions that occurred at an incidence greater than or equal to 3% and more common than in the placebo group from the pooled safety population (PATHWAY and NAVIGATOR) are shown in Table 1.

Table 1 Adverse Reactions with TEZSPIRE with Incidence Greater than or Equal to 3% and More Common than Placebo in Patients with Severe Asthma in the Pooled Safety Population (PATHWAY and NAVIGATOR)

Adverse Reaction	TEZSPIRE N=665 %	Placebo N=669 %
Pharyngitis*	4	3
Arthralgia	4	3
Back pain	4	3

* Pharyngitis (including Pharyngitis, Pharyngitis bacterial, Pharyngitis streptococcal and Viral pharyngitis)

Specific Adverse Reactions

Cardiovascular Events

In a randomized, double-blind, long term extension trial, patients 12 years and older with

severe asthma from trials NAVIGATOR and the additional trial *[see Clinical Studies (14.1)]* received TEZSPIRE 210 mg subcutaneously every 4 weeks or placebo for up to 104 weeks. In the trial, the incidence rates (IR) per 100 patient-years (PY) for serious cardiac adverse events in patients treated with TEZSPIRE or placebo were 1.08 and 0.21, respectively, with an incidence rate difference (IRD) of 0.88 (95% CI: 0.24, 1.53). The types of serious cardiac adverse events were heterogeneous. In the trial, the IR per 100 PY for adjudicated major adverse cardiovascular events (MACE, defined as cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) in patients treated with TEZSPIRE or placebo were 0.60 and 0.42, respectively, with an IRD of 0.18 (95% CI: -0.51, 0.75).

Injection Site Reactions

In the pooled safety population (PATHWAY and NAVIGATOR), in which TEZSPIRE or placebo was administered using the vial by a healthcare provider, injection site reactions (e.g., injection site erythema, injection site swelling, injection site pain) occurred at a rate of 3.3% in patients treated with TEZSPIRE compared with 2.7% in patients treated with placebo.

In an open-label trial of 216 patients with asthma in which TEZSPIRE was administered by healthcare providers and patients or caregivers using either the pre-filled pen or pre-filled syringe, injection site reactions (e.g., injection site erythema, injection site swelling, injection site pain) were observed in 5.7% patients using the pre-filled pen and 0% using the pre-filled syringe. However, the trial was not designed to compare injection site reactions between patients who received TEZSPIRE by the pre-filled pen versus pre-filled syringe.

Adverse Reactions in Adult Patients with Chronic Rhinosinusitis with Nasal Polyps

The safety of TEZSPIRE in CRSwNP was based on WAYPOINT, a randomized, double-blind, parallel group, multicenter, placebo-controlled trial of 52 weeks duration, which consisted of 203 adult patients aged 18 years and older on standard of care treatment for CRSwNP who received at least one dose of TEZSPIRE 210 mg subcutaneously once every 4 weeks *[see Clinical Studies (14.2)]*.

Adverse reactions that occurred at an incidence greater than or equal to 3% and more common than in the placebo group from the safety population (WAYPOINT) are shown in Table 2.

Table 2 Adverse Reactions with TEZSPIRE with Incidence Greater than or Equal to 3% and More Common than Placebo in Patients with CRSwNP (WAYPOINT)

Adverse Reaction	TEZSPIRE N=203 %	Placebo N=205 %
Nasopharyngitis	18	10
Upper respiratory tract infection*	12	8
Epistaxis	6	3
Pharyngitis†	5	1
Back pain	5	2

Influenza	4	1
Injection site reaction‡	4	2
Arthralgia	3	2

* Upper respiratory tract infection (including Upper respiratory tract infection and Viral upper respiratory tract infection)
† Pharyngitis (including Pharyngitis, Pharyngitis bacterial, Pharyngitis streptococcal and Viral pharyngitis)
‡ Injection site reaction (e.g., Injection site erythema, Injection site swelling and Injection site pain)

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of TEZSPIRE. 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.

Hypersensitivity reactions: anaphylaxis

7 DRUG INTERACTIONS

No formal drug interaction studies have been performed with TEZSPIRE.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on TEZSPIRE use in pregnant women to evaluate for any drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Placental transfer of monoclonal antibodies such as tezepelumab-ekko is greater during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy. In an enhanced pre- and post-natal development (ePPND) study conducted in cynomolgus monkeys, placental transport of tezepelumab-ekko was observed but there was no evidence of fetal harm following intravenous administration of tezepelumab-ekko throughout pregnancy at doses that produced maternal exposures up to 168 times the exposure at the maximum recommended human dose (MRHD) of 210 mg administered subcutaneously *(see Data)*.

The estimated background risk of major birth defects and miscarriages for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk:

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should

be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Data

Animal Data

In the ePPND study, pregnant cynomolgus monkeys received tezepelumab-ekko from GD20 to GD22 (dependent on pregnancy determination), at the beginning of organogenesis, and once every 7 days until the end of gestation at doses that produced exposures up to 168 times that achieved with the MRHD (on an AUC basis with maternal intravenous doses up to 300 mg/kg/week). There were no tezepelumab-ekko related adverse effects on maternal health, pregnancy outcome, embryo-fetal development, or neonatal growth and development up to 6.5 months of age. Tezepelumab-ekko crossed the placenta in cynomolgus monkeys and tezepelumab-ekko serum concentrations were 0.5- to 6.7-fold higher in infants relative to maternal animals.

8.2 Lactation

Risk Summary

There is no information regarding the presence of tezepelumab-ekko in human milk, its effects on the breastfed infant, or its effects on milk production. However, tezepelumab-ekko is a human monoclonal antibody immunoglobulin G2λ (IgG2λ), and immunoglobulin G (IgG) is present in human milk in small amounts. Tezepelumab-ekko was present in the milk of cynomolgus monkeys postpartum following dosing during pregnancy *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TEZSPIRE and any potential adverse effects on the breastfed infant from TEZSPIRE or from the underlying maternal condition.

Data

Animal Data

In a prenatal and postnatal development study in cynomolgus monkeys, tezepelumab-ekko concentrations in milk were up to 0.5% of the maternal serum concentrations after intravenous administration of tezepelumab-ekko up to 300 mg/kg/week (168 times the exposures based on AUC achieved at MRHD). The concentration of tezepelumab-ekko in animal milk does not necessarily predict the concentration of drug in human milk.

8.4 Pediatric Use

Asthma

The safety and effectiveness of TEZSPIRE for the add-on maintenance treatment of severe asthma have been established in pediatric patients aged 12 years and older *[see Adverse Reactions (6.1) and Clinical Studies (14.1)]*. Use of TEZSPIRE for this indication is supported by evidence from a total of 82 pediatric patients aged 12 to 17 years enrolled in NAVIGATOR and received treatment with TEZSPIRE 210 mg subcutaneously every 4 weeks (n=41) or placebo (n=41). Compared with placebo, improvements in annualized asthma exacerbation (rate ratio 0.70; 95% CI 0.34, 1.46) and FEV1 (LS mean change versus placebo 0.17 L; 95% CI -0.01, 0.35) were observed in pediatric patients treated with TEZSPIRE. The safety profile and pharmacodynamic responses in pediatric patients were generally similar to the overall study population.

The safety and effectiveness of TEZSPIRE have not been established in patients younger than 12 years of age with asthma.

CRSwNP

The safety and effectiveness of TEZSPIRE for the add-on maintenance treatment of inadequately controlled CRSwNP have been established in pediatric patients aged 12 years and older. Use of TEZSPIRE for this indication is supported by evidence from the adequate and well-controlled study of TEZSPIRE in adults (WAYPOINT) *[see Clinical Studies (14.2)]* with the following additional data:

- Pharmacokinetic (PK) data from adult and pediatric patients aged 12 years and older with severe asthma and adult patients with CRSwNP *[see Clinical Pharmacology (12.3)]*.
- Safety data in pediatric patients aged 12 years and older with severe asthma *[see Adverse Reactions (6.1)]*.

The safety and effectiveness of TEZSPIRE have not been established in patients younger than 12 years of age with CRSwNP.

8.5 Geriatric Use

Asthma

Of the 665 patients with asthma treated with TEZSPIRE in clinical trials (PATHWAY and NAVIGATOR) for severe asthma, 119 patients (18%) were 65 years or older. No overall differences in safety or effectiveness of TEZSPIRE have been observed between patients 65 years of age and older and younger patients *[see Adverse Reactions (6.1) and Clinical Studies (14.1)]*.

CRSwNP

Of the 203 patients with CRSwNP treated with TEZSPIRE in a clinical trial (WAYPOINT) for CRSwNP, 29 patients (14%) were 65 years or older. No overall differences in safety or effectiveness of TEZSPIRE have been observed between patients 65 years of age and older and younger adult patients *[see Adverse Reactions (6.1) and Clinical Studies (14.2)]*.

11 DESCRIPTION

Tezepelumab-ekko, a thymic stromal lymphopoietin (TSLP) blocker, is a human monoclonal antibody immunoglobulin G2λ (IgG2λ) produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. Tezepelumab-ekko has a molecular weight of approximately 147 kDa.

TEZSPIRE (tezepelumab-ekko) injection is a sterile, preservative-free, clear to opalescent, colorless to light yellow solution for subcutaneous injection supplied in a single-dose vial, single-dose pre-filled syringe or single-dose pre-filled pen.

Each single-dose vial, pre-filled syringe or pre-filled pen delivers 1.91 mL containing 210 mg tezepelumab-ekko, glacial acetic acid (2.8 mg), L-proline (48 mg), polysorbate 80 (0.19 mg), sodium hydroxide, and water for injection. The pH is 5.2.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tezepelumab-ekko is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody IgG2λ that binds to human TSLP with a dissociation constant of 15.8 pM and blocks its interaction with the heterodimeric TSLP receptor. TSLP is a cytokine mainly derived from epithelial cells and occupies an upstream position in inflammatory cascades.

Airway and mucosal inflammation are important components of the pathogenesis of asthma and CRSwNP. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes, ILC2 cells) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in airway and mucosal inflammation. Increased levels of TSLP mRNA and protein are found in the airways of patients with asthma as well as in nasal polyp tissue. Blocking TSLP with tezepelumab-ekko reduces biomarkers and cytokines associated with inflammation including blood eosinophils, airway submucosal eosinophils, IgE, FeNO, IL-5, and IL-13; however, the mechanism of tezepelumab-ekko action in asthma and CRSwNP has not been definitively established.

12.2 Pharmacodynamics

In NAVIGATOR, administration of TEZSPIRE 210 mg subcutaneously every 4 weeks (n=528) reduced blood eosinophils counts, FeNO, IL-5 concentration and IL-13 concentration from baseline compared with placebo (n=531) with an onset of effect 2 weeks after initiation of treatment and sustained reduction on treatment to 52 weeks. TEZSPIRE caused a slow but progressive reduction in serum total IgE concentration throughout 52 weeks of treatment. Similar effects were seen in PATHWAY.

In WAYPOINT, administration of TEZSPIRE 210 mg subcutaneously every 4 weeks (n=203) resulted in reductions from baseline of blood eosinophils, FeNO (in participants with co-morbid asthma [about 60% of patients]) and serum IgE as compared to placebo (n=205). Blood eosinophils were reduced beginning at Week 4, the first observed timepoint, with reductions maintained through Week 52. Reductions in FeNO and serum IgE were observed during the treatment period at Weeks 24 and 52.

12.3 Pharmacokinetics

The pharmacokinetics of tezepelumab-ekko is similar in patients with asthma and CRSwNP.

The pharmacokinetics of tezepelumab-ekko were dose-proportional following administration of a single subcutaneous dose over a dose range from 0.01 to 2 times the recommended dose. With an every 4 weeks dosing regimen, tezepelumab-ekko achieves steady-state after 12 weeks and the accumulation ratio for C_{trough} is 1.86-fold.

Absorption

Following subcutaneous administration, the maximum serum concentration was reached in approximately 3 to 10 days. Based on population pharmacokinetic analysis, the estimated absolute bioavailability was approximately 77%. There was no clinically relevant difference in bioavailability when administered to different injection sites (abdomen, thigh, or upper arm).

Distribution

Based on population pharmacokinetic analysis, central and peripheral volume of distribution of tezepelumab-ekko were 3.9 L and 2.2 L, respectively, for a 70 kg individual.

Elimination

As a human monoclonal antibody, tezepelumab-ekko is eliminated by intracellular catabolism and there is no evidence of target-mediated clearance within the studied dose range. Based on population pharmacokinetic analysis, the estimated clearance for tezepelumab-ekko was 0.17 L/d for a 70 kg individual. The elimination half-life was approximately 26 days.

Metabolism

Tezepelumab-ekko is a human monoclonal antibody (IgG2λ) that is degraded by proteolytic enzymes widely distributed in the body and not metabolized by hepatic enzymes.

Specific Populations

Age, Sex, Race

Based on population pharmacokinetic analysis, age (12 to 80 years), sex and race (White, Black, Asian, Other) had no clinically meaningful effects on the pharmacokinetics of tezepelumab-ekko.

Body Weight

Based on population pharmacokinetic analysis, higher body weight was associated with lower exposure. However, the effect of body weight on exposure had no meaningful impact on efficacy or safety and does not require dose adjustment.

Pediatric Patients

CRSwNP

Clinical studies have not been conducted in pediatric patients aged 12 years and older with CRSwNP. Tezepelumab-ekko exposures are expected to be comparable between adults and pediatric patients aged 12 years and older at the recommended subcutaneous dosage (210 mg every 4 weeks) for CRSwNP.

Patients with Renal impairment

No formal clinical studies have been conducted to investigate the effect of renal impairment on tezepelumab-ekko. The population pharmacokinetic analysis included 320 (23%) subjects with mild renal impairment and 38 (3%) subjects with moderate renal impairment. Tezepelumab-ekko clearance was similar in patients with mild renal impairment (estimated creatinine clearance 60 to 89 mL/min), moderate renal impairment (estimated creatinine clearance 30 to 59 mL/min) and those with normal renal function (estimated creatinine clearance ≥ 90 mL/min). Tezepelumab-ekko has not been studied in patients with severe renal impairment (estimated creatinine clearance < 30 mL/min).

Patients with Hepatic impairment

No formal clinical studies have been conducted to investigate the effect of hepatic

impairment on tezepelumab-ekko. Since tezepelumab-ekko is degraded by proteolytic enzymes widely distributed in the body and not metabolized by hepatic-specific enzymes, change in hepatic function is not expected to influence tezepelumab-ekko clearance.

Drug Interaction Studies

No formal drug interaction studies have been conducted with tezepelumab-ekko. Based on the population pharmacokinetic analysis, commonly co-administered asthma medications (leukotriene receptor antagonist, theophylline/aminophylline, oral and inhaled corticosteroid) had no clinically meaningful effect on tezepelumab-ekko clearance.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of tezepelumab-ekko or of other tezepelumab products.

In patients with asthma (NAVIGATOR and an additional trial), anti-drug antibodies (ADA) were detected at any time in 29 (5%) out of 601 patients who received TEZSPIRE at the recommended dosing regimen during the 48 to 52-week study period. Of these 29 patients, 11 patients (2% of patients treated with TEZSPIRE) developed treatment-emergent antibodies and 1 patient (<1% of patients treated with TEZSPIRE) developed neutralizing antibodies. ADA titers were generally low and often transient. No evidence of ADA impact on pharmacokinetics, pharmacodynamics, efficacy, or safety was observed.

In patients with CRSwNP (WAYPOINT), a treatment-emergent ADA response developed in 5 (3%) out of 164 patients treated with TEZSPIRE at the recommended dosage regimen during the 52-week treatment period. Neutralizing antibodies were detected in 1 of the ADA positive patients. While there was no observed impact of ADA on pharmacokinetics, pharmacodynamics, efficacy, or safety, there were insufficient numbers of patients with treatment-emergent ADA to make a formal assessment in CRSwNP.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic potential of tezepelumab-ekko. The malignancy risk in humans from an antibody that blocks TSLP ligand, such as tezepelumab-ekko, is currently unknown.

Male and female fertility was unaffected based upon no observed adverse histopathological findings in the reproductive organs and no changes in menstrual cycle or semen analysis in sexually mature cynomolgus monkeys that received tezepelumab-ekko for 26 weeks at subcutaneous doses up to 300 mg/kg/week (approximately 134 times the MRHD on an AUC basis).

14 CLINICAL STUDIES

14.1 Clinical Studies in Patients with Asthma

The efficacy of TEZSPIRE for add-on maintenance treatment of severe asthma was evaluated in two randomized, double-blind, parallel group, placebo-controlled clinical trials (PATHWAY [NCT02054130] and NAVIGATOR [NCT03347279]) of 52 weeks duration. The two trials enrolled a total of 1,609 patients 12 years of age and older with severe asthma.

PATHWAY was a 52-week dose-ranging exacerbation trial that enrolled 550 adult patients with severe asthma who received treatment with tezepelumab-ekko 70 mg subcutaneously every 4 weeks, TEZSPIRE 210 mg subcutaneously every 4 weeks, tezepelumab-ekko 280 mg subcutaneously every 2 weeks, or placebo subcutaneously. Patients were required to have a history of 2 or more asthma exacerbations requiring oral or injectable corticosteroid treatment or 1 asthma exacerbation resulting in hospitalization in the past 12 months.

NAVIGATOR was a 52-week exacerbation trial that enrolled 1,061 patients (adult and pediatric patients 12 years of age and older) with severe asthma who received treatment with TEZSPIRE 210 mg subcutaneously every 4 weeks or placebo subcutaneously every 4 weeks. Patients were required to have a history of 2 or more asthma exacerbations requiring oral or injectable corticosteroid treatment or resulting in hospitalization in the past 12 months.

In both PATHWAY and NAVIGATOR, patients were required to have an Asthma Control Questionnaire 6 (ACQ-6) score of 1.5 or more at screening and reduced lung function at baseline [pre-bronchodilator forced expiratory volume in 1 second (FEV1) below 80% predicted in adults, and below 90% predicted in adolescents]. Patients were required to have been on regular treatment with medium or high-dose inhaled corticosteroids (ICS) and at least one additional asthma controller, with or without oral corticosteroids (OCS). Patients continued background asthma therapy throughout the duration of the trials. In both trials, patients were enrolled without requiring a minimum baseline level of blood eosinophils or FeNO.

The demographics and baseline characteristics of PATHWAY and NAVIGATOR are provided in Table 3 below.

Table 3 Demographics and Baseline Characteristics of Patients in PATHWAY and NAVIGATOR

	PATHWAY N=550	**NAVIGATOR N=1,059**
Mean age (year) (SD)	52 (12)	50 (16)
Female (%)	66	64
White (%)	92	62
Black or African American (%)	3	6
Asian (%)	3	28
Hispanic or Latino (%)	1	15
Never smoked (%)	81	80
High-dose ICS use (%)	49	75
OCS use (%)	9	9
Mean number of exacerbations in	2.4 (1.2)	2.8 (1.4)

previous year (SD)	2.4 (1.2)	2.8 (1.4)
Mean duration of asthma (years) (SD)	17 (12)	22 (16)
Mean baseline % predicted FEV_1 (SD)	60 (13)	63 (18)
Mean post-bronchodilator FEV_1 reversibility (%) (SD)	23 (20)	15 (15)
Mean baseline blood EOS count (cells/µL) (SD)	371 (353)	340 (403)
Positive serum specific IgE to any perennial allergen (%)*	46	64
Mean FeNO (ppb) (SD)	35 (39)	44 (41)

* In the FEIA panel

EOS, Eosinophils; FEIA, Fluorescent enzyme immunoassay; FeNO, Fractional exhaled nitric oxide; FEV_1, Forced expiratory volume in one second; ICS, Inhaled corticosteroid, IgE, Immunoglobulin E; OCS, Oral corticosteroid; ppb, Parts per billion; SD, Standard deviation

The results summarized below are for the recommended TEZSPIRE 210 mg subcutaneously every 4 weeks dosing regimen.

Exacerbations

The primary endpoint for PATHWAY and NAVIGATOR was the rate of clinically significant asthma exacerbations measured over 52 weeks. Clinically significant asthma exacerbations were defined as worsening of asthma requiring the use of or increase in oral or injectable corticosteroids for at least 3 days, or a single depo-injection of corticosteroids, and/or emergency department visits requiring use of oral or injectable corticosteroids and/or hospitalization.

In both PATHWAY and NAVIGATOR, patients receiving TEZSPIRE had significant reductions in the annualized rate of asthma exacerbations compared to placebo. There were also fewer exacerbations requiring emergency room visits and/or hospitalization in patients treated with TEZSPIRE compared with placebo (Table 4).

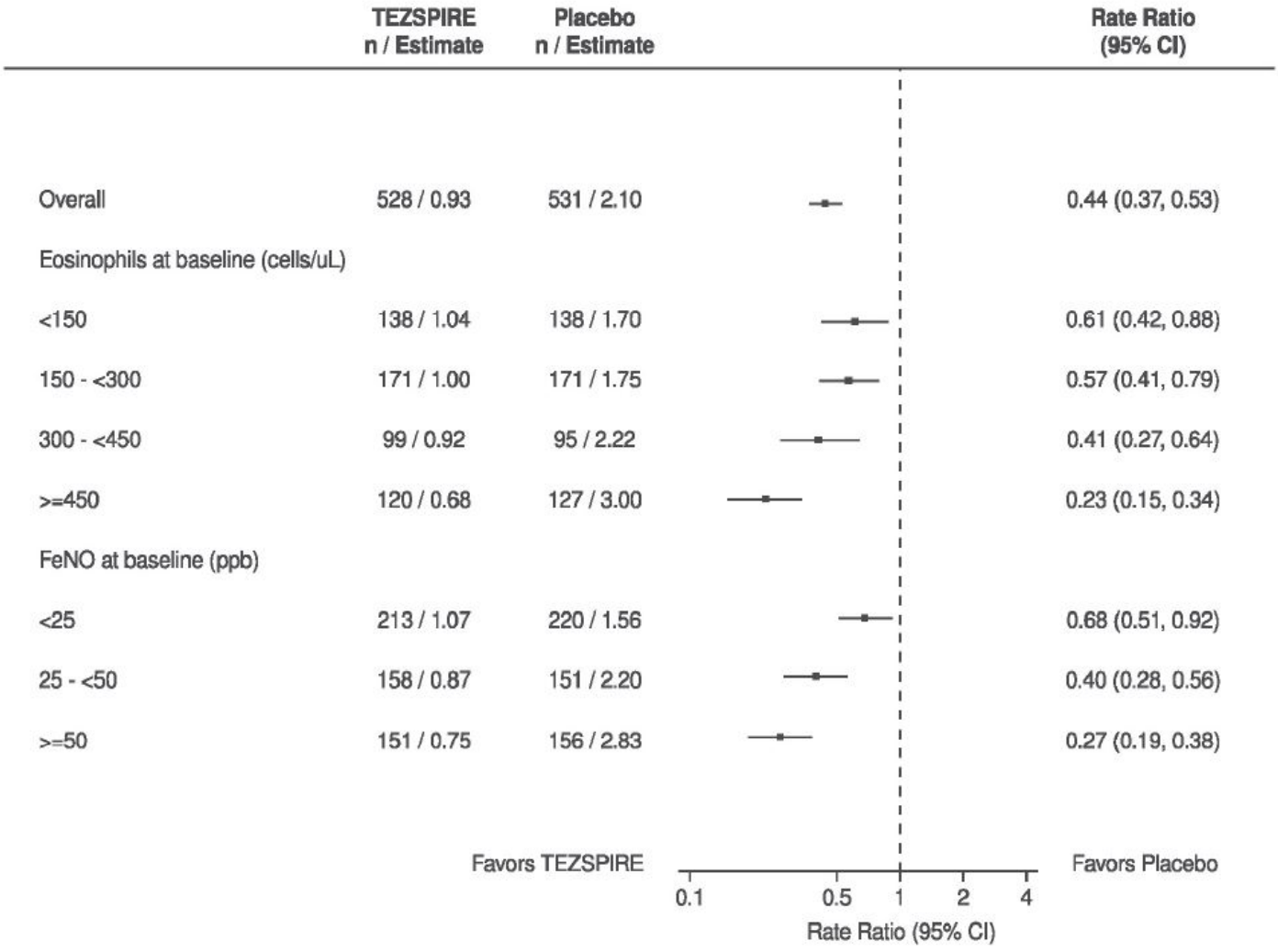
Table 4 Rate of Clinically Significant Exacerbations Over 52 Weeks in PATHWAY and NAVIGATOR

Trial	Treatment	Exacerbations per year	
		Rate	Rate Ratio (95% CI)
Annualized Asthma Exacerbation Rate			
PATHWAY	TEZSPIRE (N=137)	0.20	0.29 (0.16, 0.51)
	Placebo (N=138)	0.72	
NAVIGATOR	TEZSPIRE (N=528)	0.93	0.44 (0.37, 0.53)
	Placebo (N=531)	2.10	
Exacerbations requiring emergency room visit/hospitalization			
PATHWAY	TEZSPIRE (N=137)	0.03	0.15 (0.04, 0.58)
	Placebo (N=138)	0.18	
NAVIGATOR	TEZSPIRE (N=528)	0.06	0.21 (0.12, 0.37)

	Placebo (N=531)	0.28	0.21 (0.12, 0.37)
Exacerbations requiring hospitalization			
PATHWAY	TEZSPIRE (N=137)	0.02	0.14 (0.03, 0.71)
	Placebo (N=138)	0.14	
NAVIGATOR	TEZSPIRE (N=528)	0.03	0.15 (0.07, 0.22)
	Placebo (N=531)	0.19	

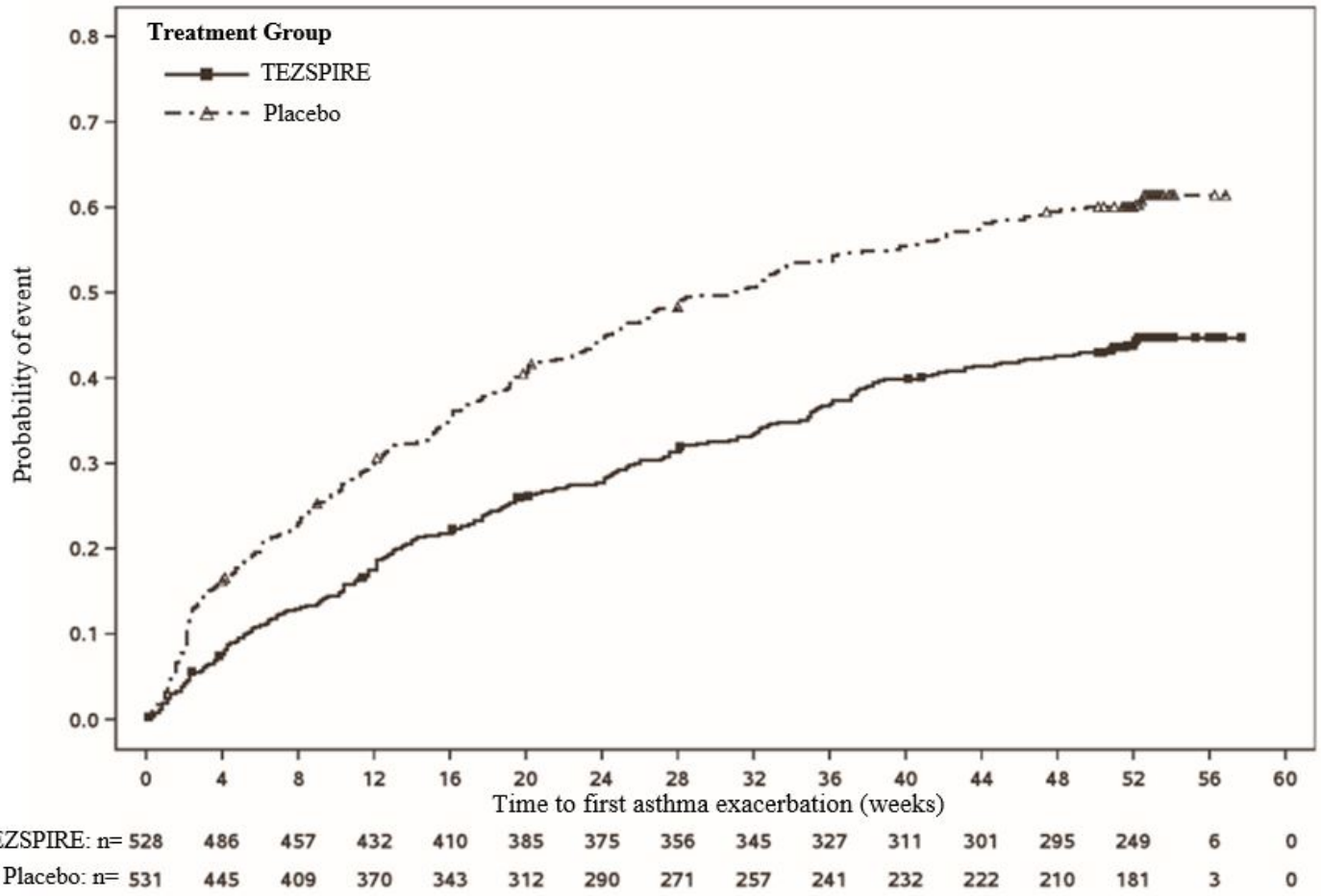
In NAVIGATOR, patients receiving TEZSPIRE experienced fewer exacerbations than those receiving placebo regardless of baseline levels of blood eosinophils or FeNO (Figure 3). Similar results were seen in PATHWAY.

Figure 3 Annualized Asthma Exacerbation Rate Ratio Over 52 Weeks Across Different Baseline Biomarkers in NAVIGATOR



The time to first exacerbation was longer for the patients receiving TEZSPIRE compared with placebo in NAVIGATOR (Figure 4). Similar findings were seen in PATHWAY.

Figure 4 Kaplan-Meier Cumulative Incidence Curves for Time to First Exacerbation in NAVIGATOR



Lung Function

Change from baseline in FEV_1 was assessed as a secondary endpoint in PATHWAY and NAVIGATOR. Compared with placebo, TEZSPIRE provided clinically meaningful improvements in the mean change from baseline in FEV_1 in both trials (Table 5).

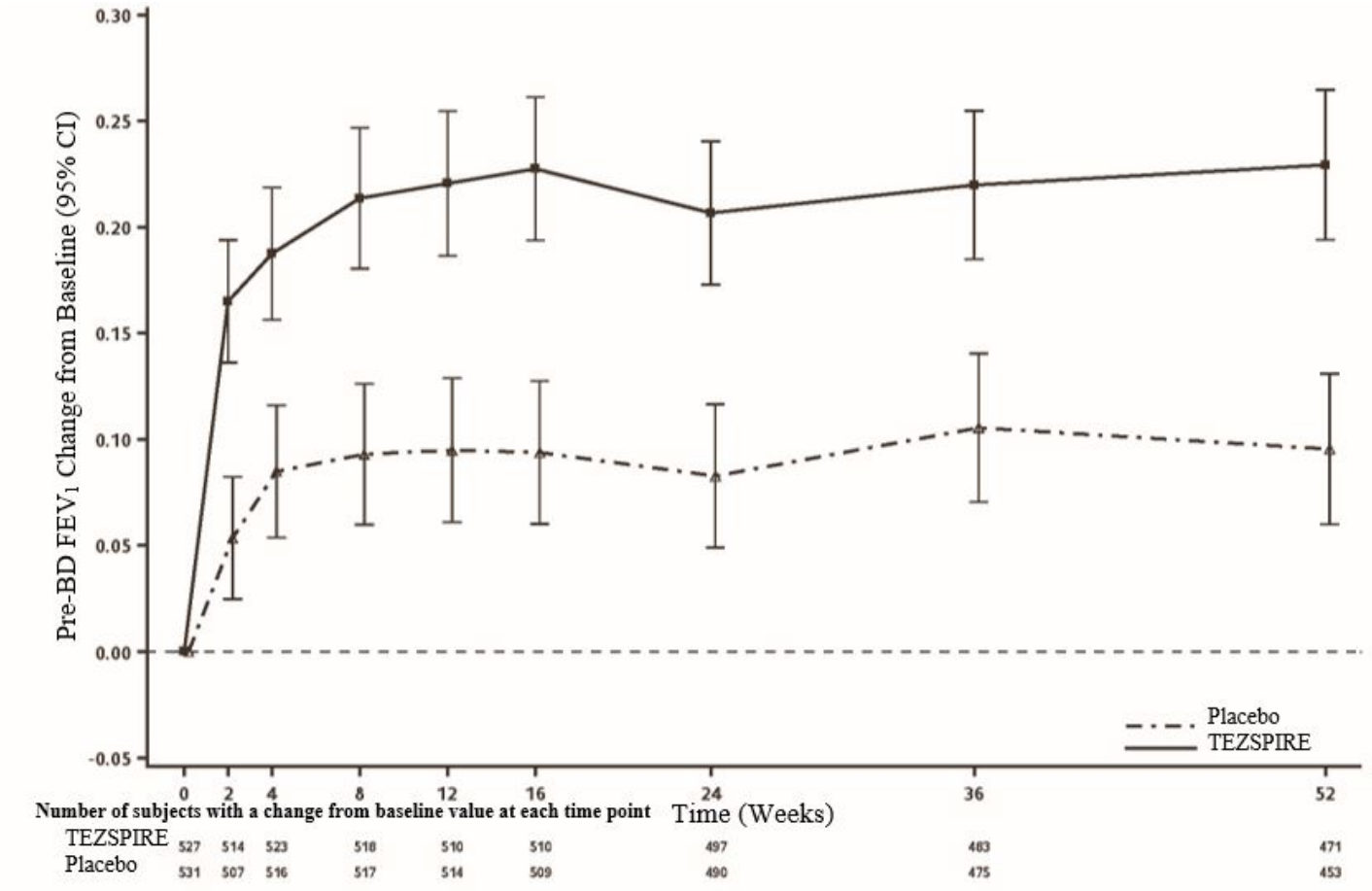
Table 5 Mean Change from Baseline in Pre-Bronchodilator FEV1 at End of Trial in PATHWAY and NAVIGATOR*

Trial	Treatment	LS Mean Change from Baseline (L)	Difference from Placebo (95% CI)
PATHWAY	TEZSPIRE (N=133)†	0.08	0.13 (0.03, 0.23)
	Placebo (N=138)†	-0.06	
NAVIGATOR	TEZSPIRE (N=527)†	0.23	0.13 (0.08, 0.18)
	Placebo (N=531)†	0.10	

* Week 52 in PATHWAY, Week 52 in NAVIGATOR
† Number of patients contributing to the full analysis (FA) with at least 1 change from baseline value

In NAVIGATOR, improvement in FEV_1 was seen as early as 2 weeks after initiation of treatment and was sustained through week 52 (Figure 5).

Figure 5 Mean Change (95% CI) from Baseline in Pre-Bronchodilator FEV1 (L) in NAVIGATOR



Patient Reported Outcomes

Changes from baseline in Asthma Control Questionnaire 6 (ACQ-6) and Standardized Asthma Quality of Life Questionnaire for ages 12 and older [AQLQ(S)+12] were also assessed as secondary endpoints in PATHWAY and NAVIGATOR. In both trials, more patients treated with TEZSPIRE compared to placebo had a clinically meaningful improvement in ACQ-6 and AQLQ(S)+12. Clinically meaningful improvement (responder rate) for both measures was defined as improvement in score of 0.5 or more at end of trial. In NAVIGATOR, the ACQ-6 responder rate for TEZSPIRE was 86% compared with 77% for placebo (OR=1.99; 95% CI 1.43, 2.76) and the AQLQ(S)+12 responder rate for TEZSPIRE was 78% compared with 72% for placebo (OR=1.36; 95% CI 1.02, 1.82). Similar findings were seen in PATHWAY.

Additional Trial

In a randomized, double-blind, parallel group, placebo-controlled clinical trial, the effect of TEZSPIRE (210 mg subcutaneously every 4 weeks) on reducing the use of maintenance OCS was evaluated. The trial enrolled 150 adult patients with severe asthma who required treatment with daily OCS (7.5 mg to 30 mg per day) in addition to regular use of high-dose ICS and a long-acting beta-agonist with or without additional controller(s). The primary endpoint was categorized percent reduction from baseline of the final OCS dose at Week 48 (≥90% reduction, ≥75% to <90% reduction, ≥50% to <75% reduction, >0% to <50% reduction, and no change or any increase in OCS), while maintaining asthma control. TEZSPIRE did not demonstrate a statistically significant

reduction in maintenance OCS dose compared with placebo (cumulative OR=1.28; 95% CI 0.69, 2.35).

14.2 Clinical Studies in Patients with Chronic Rhinosinusitis with Nasal Polyps

The efficacy of TEZSPIRE for add-on maintenance treatment of inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP) was evaluated in a randomized, double-blind, parallel group, multicenter, placebo-controlled trial (WAYPOINT [NCT04851964]) of 52 weeks treatment duration conducted in 408 patients aged 18 years and older on standard of care treatment for CRSwNP. This study included patients with symptomatic CRSwNP despite treatment with nasal corticosteroids, and who had systemic corticosteroids within the past 12 months and/or any history of sino-nasal surgery, or with contraindications and/or intolerance to either.

Patients received TEZSPIRE 210 mg or placebo subcutaneously every 4 weeks for 52 weeks in addition to nasal corticosteroid treatment for CRSwNP.

The demographics and baseline characteristics of patients enrolled in WAYPOINT are provided in Table 6.

Table 6 Demographics and Baseline Characteristics of Adult Patients in WAYPOINT

	WAYPOINT N=408*
Mean age (years) (SD)	50 (14)
Male (%)	65
Mean CRSwNP duration (years) (SD)	13 (10)
Patients with ≥1 prior surgery (%)	71
Patients with systemic corticosteroid use for CRSwNP in the previous year (%)	58
Mean total NPS† (SD), range 0-8	6.1 (1.2)
Mean bi-weekly NCS† (SD), range 0-3	2.6 (0.5)
Mean LMK sinus CT total score† (SD), range 0-24	19 (4)
Mean bi-weekly loss of smell† (SD), range 0-3	2.9 (0.4)
Mean blood eosinophils (cells/µL) (SD)	358 (238)
Mean total IgE IU/mL (SD)	176 (285)
Asthma‡ (%)	61
NSAID-ERD/AERD (%)	17

* Number of patients (N) =407 for mean total NPS; N=406 for mean bi-weekly NCS and mean bi-weekly loss of smell; N=404 for mean LMK sinus CT total score and mean blood eosinophils; N=389 for mean total IgE.
† Higher scores indicate greater disease severity or symptom severity.
‡ Includes patients with asthma or AERD or NSAID-ERD. All but 3 patients with AERD or NSAID-ERD included in this subgroup also had a diagnosis of asthma reported.

AERD, Aspirin exacerbated respiratory disease; CRSwNP, Chronic rhinosinusitis with nasal polyps; CT, Computed tomography; IgE, Immunoglobulin E; IU, International units; LMK, Lund-Mackay; NCS, Nasal congestion score; NPS, Nasal polyp score; NSAID-ERD,

Nonsteroidal anti-inflammatory drug exacerbated respiratory disease; SD, Standard deviation

The co-primary efficacy endpoints were change from baseline in total nasal polyp score (NPS) evaluated by nasal endoscopy at Week 52 as graded by independent blinded assessors, and change from baseline in bi-weekly mean nasal congestion score (NCS) evaluated at Week 52. For total NPS, polyps on each side of the nose were graded on a categorical scale (0=no polyps, 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate, 2=polyps reaching below the lower border of the middle turbinate, 3=polyps reaching the lower border of the inferior turbinate or a middle meatal polyp with a score of 2 with any additional polyp medial to the middle turbinate, 4=large polyps causing complete or near complete obstruction of the inferior nasal cavity [i.e. touching the floor of the nose]) for a total score of 0 to 8. Nasal congestion was rated daily by the patients on a 0 to 3 categorical severity scale (0=none, 1=mild, 2=moderate, 3=severe).

Statistically significant efficacy was observed in WAYPOINT for the co-primary endpoints of improvement in total NPS and in bi-weekly mean NCS at Week 52 (Table 7).

Table 7 Results of Change from Baseline in Total Nasal Polyp Score and Bi-weekly Mean Nasal Congestion Score at Week 52 in Adults with CRSwNP (WAYPOINT)

	TEZSPIRE 210 mg Q4W (N=203)		**Placebo (N=205)**		**LS mean difference vs. placebo (95% CI)**
Scores	Baseline mean	LS mean change	Baseline mean	LS mean change	
NPS	6.1	-2.47	6.1	-0.47	-2.01 (-2.33, -1.68)
NCS	2.59	-1.76	2.55	-0.81	-0.95 (-1.12, -0.78)

LS mean change, Least squared mean change from baseline; reduction in score indicates improvement; NCS, Nasal congestion score; NPS, Nasal polyp score

Figure 6 demonstrates the time course of improvement in the mean change from baseline in NPS.

Figure 6 LS Mean Change from Baseline in Total Nasal Polyp Score up to Week 52 in Adults (WAYPOINT)

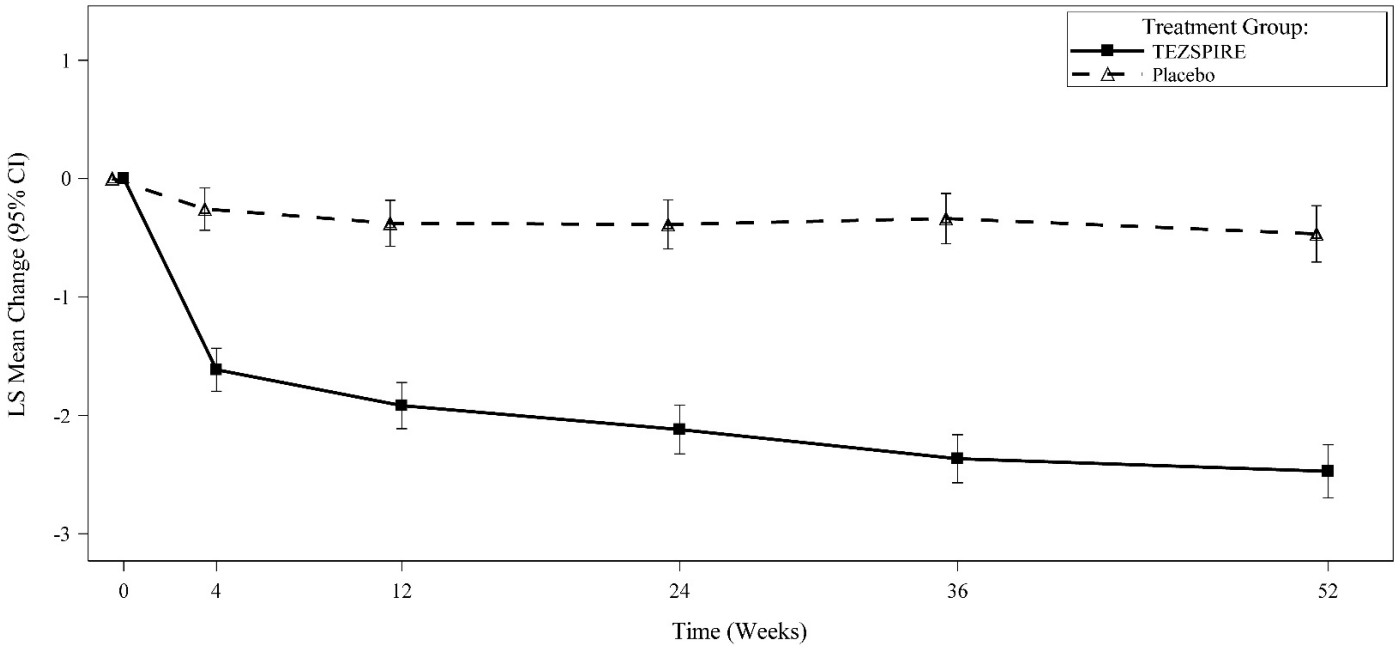
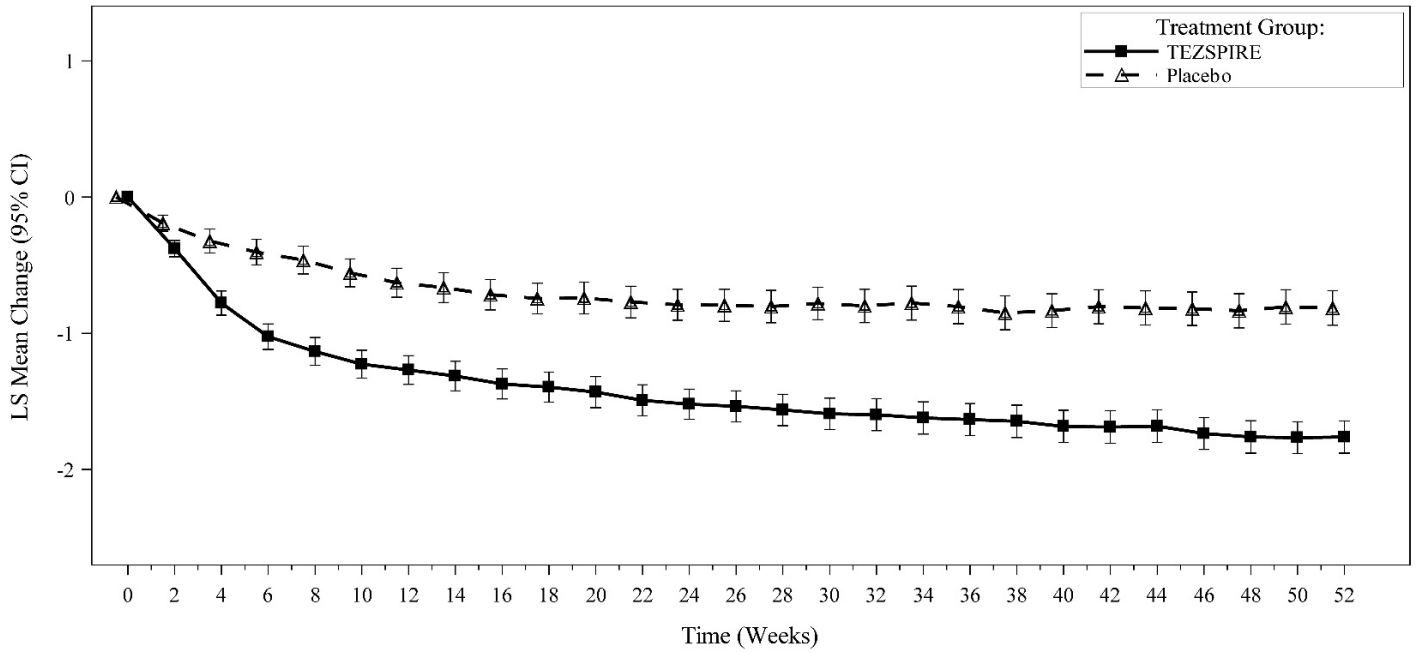


Figure 7 demonstrates the time course of improvement in the bi-weekly mean change from baseline in NCS.

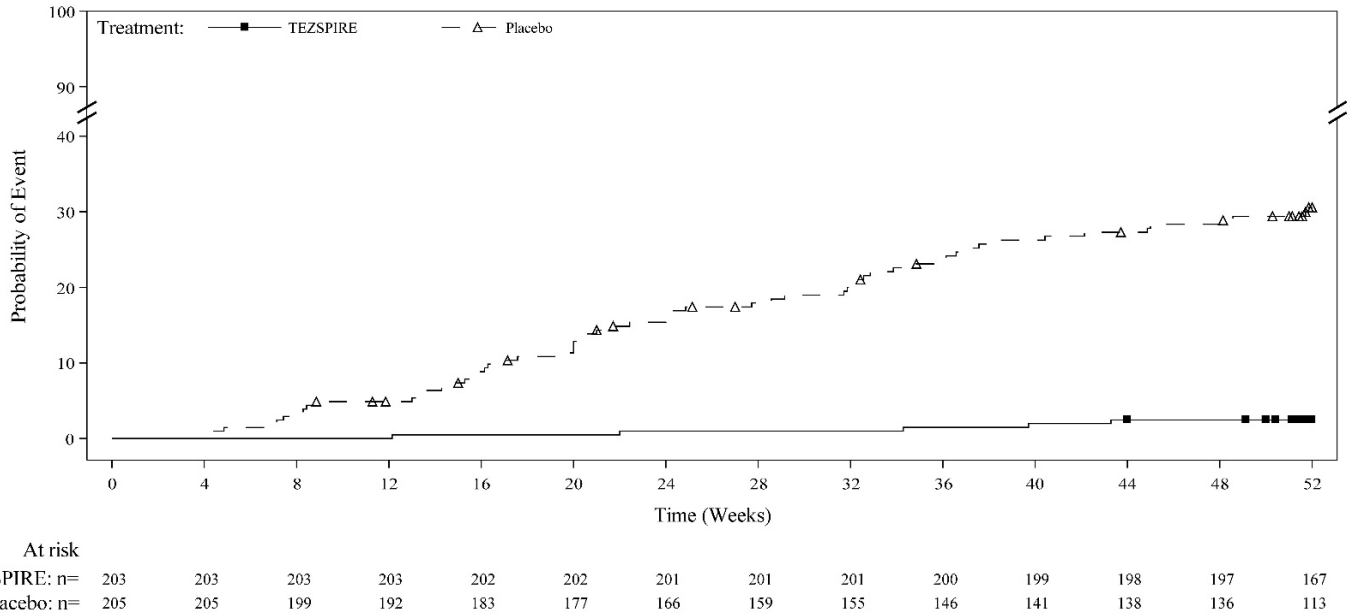
Figure 7 LS Mean Change from Baseline in Bi-weekly Mean Nasal Congestion Score up to Week 52 in Adults (WAYPOINT)



Key secondary endpoints at Week 52 included time to surgery decision and/or systemic corticosteroid use for nasal polyps, change from baseline in loss of smell, and change from baseline in Lund-Mackay (LMK) sinus CT scan score.

TEZSPIRE significantly reduced the proportion of patients with need for sino-nasal surgery or systemic corticosteroids by 92% compared to placebo over 52 weeks (Hazard Ratio: 0.08; 95% CI: 0.03, 0.17) (Figure 8).

Figure 8 Kaplan Meier Curve for Time to First Systemic Corticosteroid Use and/or Sino-Nasal Surgery Decision Over 52 Weeks in Adults (WAYPOINT)



TEZSPIRE significantly reduced the proportion of patients requiring sino-nasal surgery by 98% compared to placebo over 52 weeks (Hazard Ratio: 0.02; 95% CI: 0.00, 0.09) and significantly reduced the proportion of patients requiring systemic corticosteroids for CRSwNP by 88% compared to placebo over 52 weeks (Hazard Ratio: 0.12; 95% CI: 0.04, 0.27).

The loss of smell score was based on a subject's daily rating of the severity of their worst difficulty with sense of smell over the past 24 hours on a 0 to 3 scale (0=none, 1=mild, 2=moderate, 3=severe). The loss of smell score was calculated every 2 weeks as the bi-weekly mean. TEZSPIRE significantly improved the loss of smell compared to placebo. The LS mean difference for loss of smell at Week 52 in the TEZSPIRE group versus placebo was -1.01 [95% CI: -1.18, -0.83].

The LMK sinus CT scan score evaluated the opacification of each sinus at baseline and Week 52 using a 0 to 2 scale (0=no abnormality; 1=partial opacification, 2=total opacification) deriving a maximum score of 12 per side and a total maximum score of 24 (higher scores indicate more opacification). A significant decrease in the LMK sinus CT scan score was observed. The LS mean difference for LMK sinus CT scan score at Week 52 in the TEZSPIRE group versus placebo was -5.76 [95% CI: -6.45, -5.07].

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

TEZSPIRE (tezepelumab-ekko) injection is a sterile, preservative-free, clear to opalescent, colorless to light yellow solution supplied as a single-dose vial, single-dose pre-filled syringe with a fixed 27-gauge ½ inch needle with a needle cover or single-dose pre-filled pen with a fixed 27-gauge ½ inch needle with a needle cover. The vial, pre-filled syringe and pre-filled pen, including the needle cover and stopper, are not made with natural

rubber latex.

TEZSPIRE is available as:

- Single-Dose Vial: Carton contains one 210 mg/1.91 mL (110 mg/mL) glass vial (NDC 55513-100-01)
- Single-Dose Pre-filled Syringe: Carton contains one 210 mg/1.91 mL (110 mg/mL) pre-filled syringe (NDC 55513-112-01)
- Single-Dose Pre-filled Pen: Carton contains one 210 mg/1.91 mL (110 mg/mL) pre-filled pen (NDC 55513-123-01)

Storage and Handling

Store refrigerated between 36°F to 46°F (2°C to 8°C). If necessary, TEZSPIRE may be kept at room temperature between 68°F to 77˚F (20°C to 25°C) for a maximum of 30 days. Do not put back in the refrigerator once TEZSPIRE has reached room temperature. After removal from the refrigerator, TEZSPIRE must be used within 30 days or discarded.

Store TEZSPIRE in original carton to protect from light until time of use.

Do not freeze. Do not shake. Do not expose to heat.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Hypersensitivity Reactions

Inform patients that hypersensitivity reactions (e.g., anaphylaxis, rash and allergic conjunctivitis) can occur following administration of TEZSPIRE *[see Contraindications (4) and Adverse Reactions (6)]*. These reactions can occur within hours of administration, but in some instances have a delayed onset (i.e., days). Instruct patients to contact their healthcare provider if they experience symptoms of an allergic reaction *[see Warnings and Precautions (5.1)]*.

Not for Acute Symptoms or Deteriorating Disease

Inform patients that TEZSPIRE does not treat acute asthma symptoms or acute exacerbations. Inform patients to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with *TEZSPIRE [see Warnings and Precautions (5.2)]*.

Risk Associated with Abrupt Reduction of Corticosteroid Dosage

Inform patients to not discontinue systemic or inhaled corticosteroids except under the direct supervision of a healthcare provider. Inform patients that reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy *[see Warnings and Precautions (5.3)]*.

Administration of Vaccines

Instruct patients to inform the healthcare provider that they are taking TEZSPIRE prior to a potential vaccination *[see Warnings and Precautions (5.5)]*.

Proper Storage and Disposal

Advise patients to refrigerate TEZSPIRE at 36°F to 46°F (2°C to 8°C). TEZSPIRE may be kept at room temperature between 68°F to 77˚F (20°C to 25°C) for a maximum of 30 days *[see How Supplied/Storage and Handling (16)]*. Inform patients and caregivers of the need for proper disposal of the pre-filled pen after use, including the use of a sharps disposal container.

Manufactured by: AstraZeneca AB, Södertälje, Sweden SE-15185

US License No. 2059

At: Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA 91320-1799

Marketed by: Amgen Inc. and AstraZeneca AB

PATIENT INFORMATION
TEZSPIRE® (TEZ-SPY-ER)
(tezepelumab-ekko)
injection, for subcutaneous use

What is TEZSPIRE?
TEZSPIRE is a prescription medicine used:

- with other asthma medicines for the maintenance treatment of severe asthma in people 12 years of age and older whose asthma is not controlled with their current asthma medicine.
- with other medicines for the maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in people 12 years of age and older whose CRSwNP is not controlled with their current CRSwNP medicine.

TEZSPIRE helps:

- prevent severe asthma attacks (exacerbations) and can improve your breathing.
- reduce the size of your polyps, improve symptoms i.e. nasal congestion and loss of smell, and reduce the need for oral corticosteroids and surgery for your nasal polyps.

TEZSPIRE is not used to treat sudden breathing problems. Tell your healthcare provider if your asthma does not get better or if it gets worse after you start treatment with TEZSPIRE.
It is not known if TEZSPIRE is safe and effective in children under 12 years of age for the treatment of asthma.
It is not known if TEZSPIRE is safe and effective in children under 12 years of age for the treatment of CRSwNP.

Do not use TEZSPIRE if you:

- are allergic to tezepelumab-ekko or any of the ingredients in TEZSPIRE. See the end of this Patient Information leaflet for a complete list of ingredients in TEZSPIRE.

Before using TEZSPIRE, tell your healthcare provider about all of your medical conditions, including if you:

- have ever had a severe allergic reaction (hypersensitivity).
- have a parasitic (helminth) infection.
- have recently received or are scheduled to receive any live attenuated vaccinations. People who receive TEZSPIRE should not receive live attenuated vaccines.
- are pregnant, think you may be pregnant, or plan to become pregnant. It is not known if TEZSPIRE may harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if TEZSPIRE passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you use TEZSPIRE.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. **Do not** change or stop your other medicines, including corticosteroid medicines or other asthma medicines unless your healthcare provider tells you to. This may cause other symptoms that were controlled by those medicines to come back.

How should I use TEZSPIRE?

- **See the detailed Instructions for Use that comes with TEZSPIRE pre-filled pen for information on how to prepare and inject TEZSPIRE.**
- Use TEZSPIRE exactly as prescribed by your healthcare provider.
- TEZSPIRE is injected under your skin (subcutaneously) 1 time every 4 weeks.
- TEZSPIRE comes in a single-dose vial, in a single-dose pre-filled syringe, and in a single-dose pre-filled pen.
- Your healthcare provider can inject you with TEZSPIRE in a healthcare setting.
- If your healthcare provider decides that you or a caregiver can give the injections of TEZSPIRE, you or your caregiver should receive training on the right way to prepare and inject the TEZSPIRE single dose pre-filled pen.
- **Do not** try to inject TEZSPIRE until you or your caregiver have been shown the right way by your healthcare provider.
- If you miss a dose, inject a dose as soon as possible. After that, you can continue to use TEZSPIRE on your usual injection day. If you did not notice that you missed a dose until it is time for your next scheduled dose, skip the missed dose and inject the next scheduled dose as planned. **Do not** inject more than one dose in a day. If you have questions about when to inject TEZSPIRE, contact your healthcare provider.

What are the possible side effects of TEZSPIRE?
TEZSPIRE may cause serious side effects, including:

- **allergic (hypersensitivity) reactions, including anaphylaxis.** Serious allergic reactions can happen after you get your TEZSPIRE injection. Allergic reactions can sometimes happen hours or days after you get a dose of TEZSPIRE. Call your healthcare provider or get emergency medical care if you get any of the following symptoms of allergic reaction:

  - rash
  - hives
  - breathing problems
  - red, itchy, swollen, or inflamed eyes

- swelling of your face, mouth, and tongue
- fainting, dizziness, feeling lightheaded

The most common side effects of TEZSPIRE include:

- sore throat (pharyngitis)
- common cold symptoms (nasopharyngitis)
- flu
- joint pain (arthralgia)
- upper respiratory tract infections
- injection site reactions
- back pain
- nose bleeds

These are not all of the possible side effects of TEZSPIRE.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of TEZSPIRE
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use TEZSPIRE for a condition for which it was not prescribed. Do not give TEZSPIRE to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about TEZSPIRE that is written for health professionals.

What are the ingredients in TEZSPIRE?
Active ingredient: tezepelumab-ekko.
Inactive ingredients: glacial acetic acid, L-proline, polysorbate 80, sodium hydroxide, and water for injection.
Manufactured by:
AstraZeneca AB, Södertälje, Sweden SE-15185
US License No. 2059
At: Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA 91320-1799
Marketed by: Amgen Inc. and AstraZeneca AB

For more information, go to https://www.TEZSPIRE.com or call 1-800-236-9933.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: October 2025

INSTRUCTIONS FOR USE
TEZSPIRE® (TEZ-SPY-ER)
(tezepelumab-ekko)
injection, for subcutaneous use
Single-dose Pre-filled pen

This Instructions for Use contains information on how to inject TEZSPIRE.
Before using your TEZSPIRE pre-filled pen, your healthcare provider should show you or your caregiver how to use it the right way.
Read this Instructions for Use before you start using your TEZSPIRE pre-filled pen and each time you get a refill. There may be new information. This information should not replace talking to your healthcare provider about your medical condition and your treatment.
If you or your caregiver have any questions, talk to your healthcare provider.

Important information you need to know before injecting TEZSPIRE

Store TEZSPIRE in a refrigerator between 36°F to 46°F (2°C to 8°C) in its original carton until you are ready to use it.

TEZSPIRE may be kept at room temperature between 68°F to 77˚F (20°C to 25°C) for a maximum of 30 days.

Store TEZSPIRE in the original carton to protect it from light.

When TEZSPIRE has reached room temperature, **do not** put it back in the refrigerator.

Throw away (dispose of) TEZSPIRE that has been stored at room temperature for more than 30 days.

Do not use your TEZSPIRE pre-filled pen if:

- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiration date (EXP) has passed

Do not:

- freeze your pre-filled pen or expose it to heat
- shake your pre-filled pen
- share, or use your pre-filled pen more than 1 time

If any of the above happens, throw away the pre-filled pen in a puncture-resistant (sharps) container and use a new TEZSPIRE pre-filled pen.

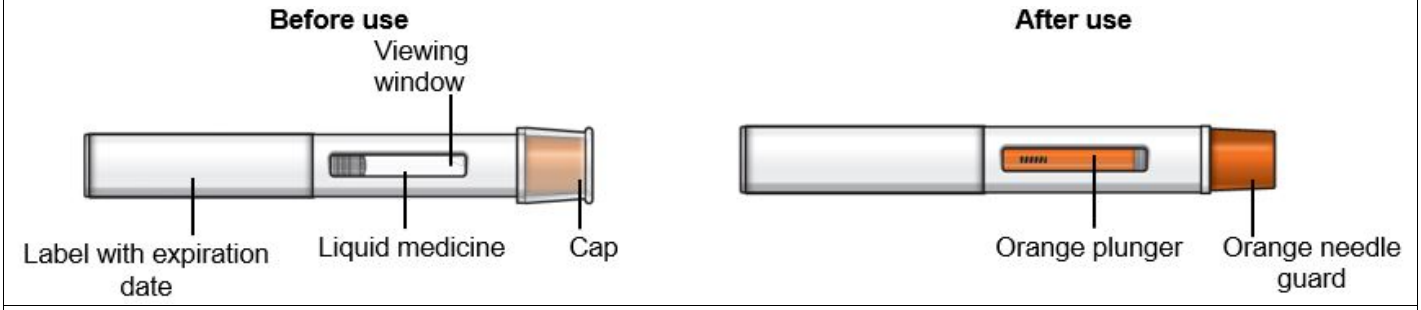
Each TEZSPIRE pre-filled pen contains 1 dose of TEZSPIRE that can only be used 1 time.

TEZSPIRE is given only as an injection under the skin (subcutaneous).

Keep the TEZSPIRE pre-filled pen and all medicines out of the sight and reach of children.

Your TEZSPIRE pre-filled pen

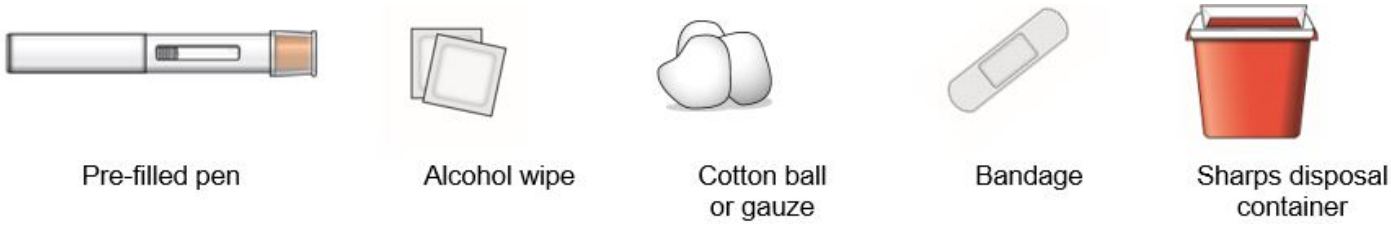
Do not remove the cap until Step 6 of these instructions when you are ready to inject TEZSPIRE.



Preparing to inject TEZSPIRE

Step 1 – Gather supplies

- 1 TEZSPIRE pre-filled pen from the refrigerator
- 1 alcohol wipe
- 1 cotton ball or gauze
- 1 small bandage (optional)
- 1 puncture-resistant (sharps) disposal container. See Step 10 for instructions on how to throw away (dispose of) the used TEZSPIRE pre-filled pen safely.



Step 2 – Prepare to use your TEZSPIRE pre-filled pen

Let TEZSPIRE come to room temperature between 68°F to 77˚F (20°C to 25°C) for about 60 minutes before giving the injection.

Keep the pre-filled pen in its original carton to protect it from light.

Do not warm the pre-filled pen in any other way. For example, **do not** warm it in a microwave or hot water, in direct sunlight, or near other heat sources.

Do not put TEZSPIRE back in the refrigerator after it has reached room temperature. Throw away (dispose of) TEZSPIRE that has been stored at room temperature for more than 30 days.

Do not remove the cap until Step 6.

Step 3 – Remove and check the pre-filled pen

Grab the middle of the pre-filled pen body to remove the pre-filled pen from its carton.

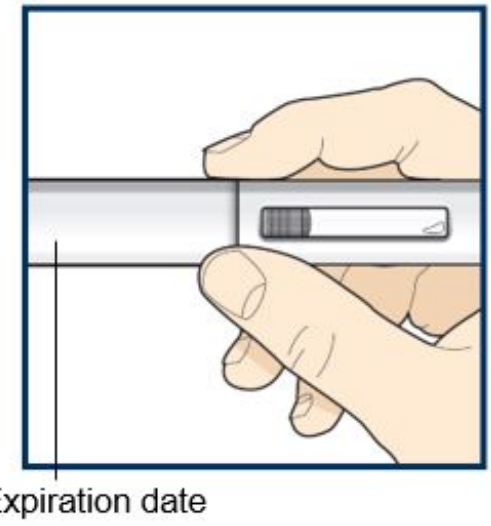
Check the pre-filled pen for damage. Do not use the pre-filled pen if the pre-filled pen is damaged.

Check the expiration date on the pre-filled pen. **Do not** use the pre-filled pen if the expiration date has passed.

Look at the liquid through the viewing window. The liquid should be clear and colorless to light yellow.

Do not inject TEZSPIRE if the liquid is cloudy, discolored, or contains large particles.

You may see small air bubbles in the liquid. This is normal. You do not need to do anything about it.



Injecting TEZSPIRE

Step 4 – Choose an injection site

If you are giving yourself the injection, the **recommended injection site** is the front of your thigh or the lower part of your stomach (abdomen).

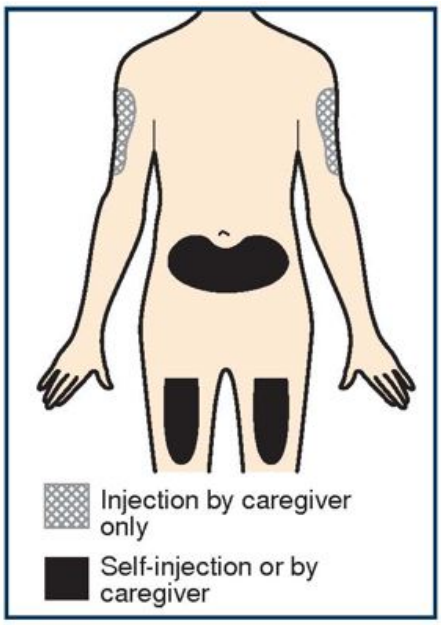
Do not inject yourself in the arm.

A caregiver may inject you in the upper arm, thigh, or abdomen.

For each injection, choose a different site that is at least 1 inch (3 cm) away from where you last injected.

Do not inject:

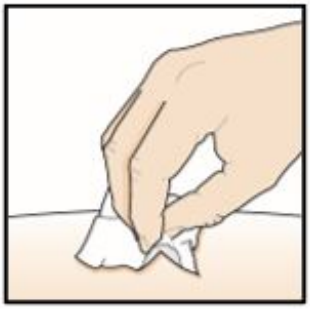
- into the 2-inch (5 cm) area around your belly button
- where the skin is tender, bruised, scaly or hard
- into scars or damaged skin
- through clothing



Step 5 – Wash your hands and clean the injection site

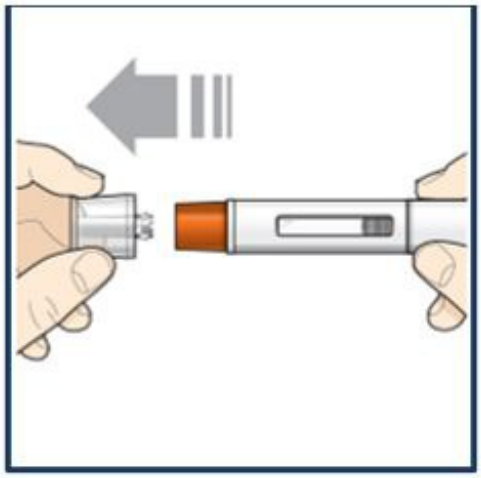
Wash your hands well with soap and water.

Clean the injection site with an alcohol wipe in a circular motion. Let it air dry.
Do not touch the cleaned area before injecting.
Do not fan or blow on the cleaned area.



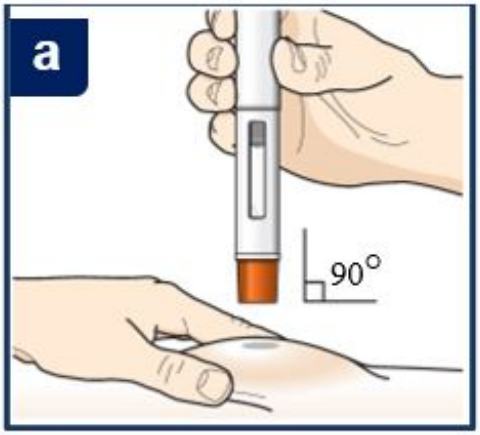
Step 6 – Pull off the cap

Do not remove the cap until you are ready to inject.
Hold the pre-filled pen body with 1 hand, and carefully pull the cap straight off with your other hand.
Put the cap to the side and throw it away later.
The orange needle guard is now exposed. The orange needle guard is there to prevent you from touching the needle.
Do not touch the needle or push on the orange needle guard with your finger.
Do not put the cap back on the pre-filled pen. You could cause the injection to happen too soon or damage the needle.



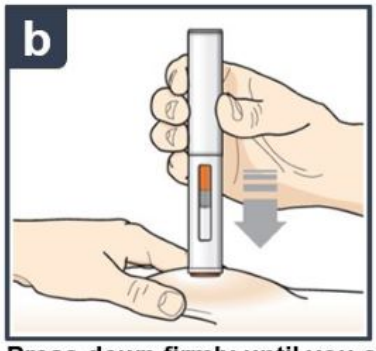
Step 7 – Inject TEZSPIRE

Follow your healthcare provider's instruction on how to inject. You can either gently pinch the skin at the injection site or give the injection without pinching the skin.
Inject TEZSPIRE by following the steps in figures **a, b, c** and **d**.
When injecting, you will hear the first click that tells you the injection has started. Press and hold the pre-filled pen for 15 seconds until you hear the **second click**.
Do not change the position of the pre-filled pen after the injection has started.



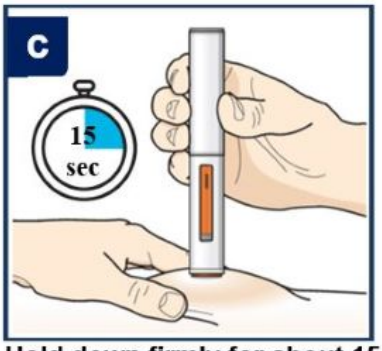
Position the pre-filled pen.

- Place the orange needle guard flat against your skin (90-degree angle).
- Make sure you can see the viewing window.



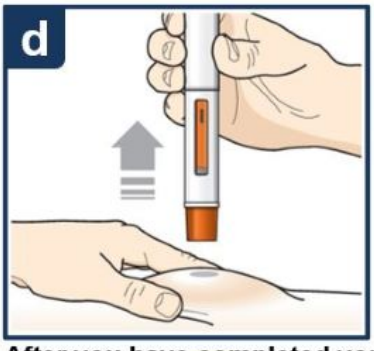
Press down firmly until you cannot see the orange needle guard.

- You will hear the **first 'click'**, this tells you the injection has started.
- The orange plunger will move down in the viewing window during the injection.



Hold down firmly for about 15 seconds.

- You will hear a **second 'click'**, this tells you the injection has finished.
- The orange plunger will fill the viewing window.



After you have completed your injection, lift the pre-filled pen straight up.

- The orange needle guard will slide down and lock into place over the needle.

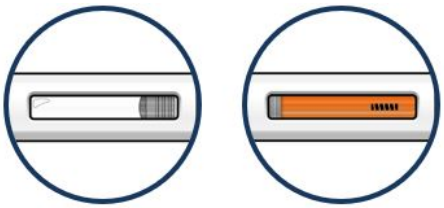
Step 8 – Check the viewing window

Check the viewing window to make sure all the medicine has been injected.

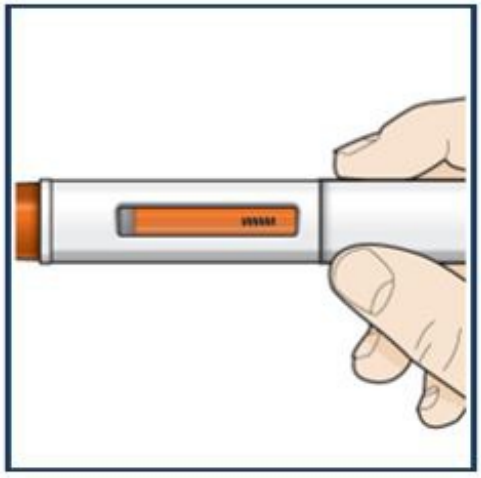
If the orange plunger rod does not fill the viewing window, you may not have received the full dose.

If this happens or if you have any other concerns, contact your healthcare provider.

Before injection



After injection

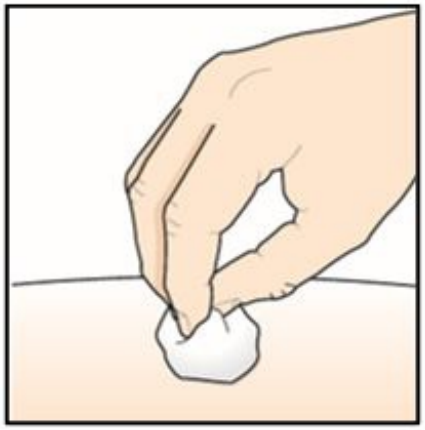


Step 9 – Check the injection site

There may be a small amount of blood or liquid where you injected. This is normal.

Gently hold pressure over your skin with a cotton ball or gauze until the bleeding stops.

Do not rub the injection site. If needed, cover the injection site with a small bandage.



Disposing of TEZSPIRE

Step 10 – Dispose of the used pre-filled pen safely

Each pre-filled pen contains a single dose of TEZSPIRE and **cannot be used again**. **Do not** put the cap back on the pre-filled pen.
Put your used pre-filled pen and cap in a **sharps disposal container** right away after use. Put other used supplies in your household trash.
Do not throw away the pre-filled pen in your household trash.

Throw away (Disposal) guidelines
If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the area that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.
Do not recycle your used sharps disposal container.
Manufactured by:
AstraZeneca AB, Södertälje, Sweden SE-15185
US License No. 2059
At: Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA 91320-1799
Marketed by: Amgen Inc. and AstraZeneca AB

For more information, go to https://www.TEZSPIRE.com or call 1-800-236-9933.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Revised: October 2025

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 55513-100-01 Rx only

TEZSPIRE™

(tezepelumab-ekko)

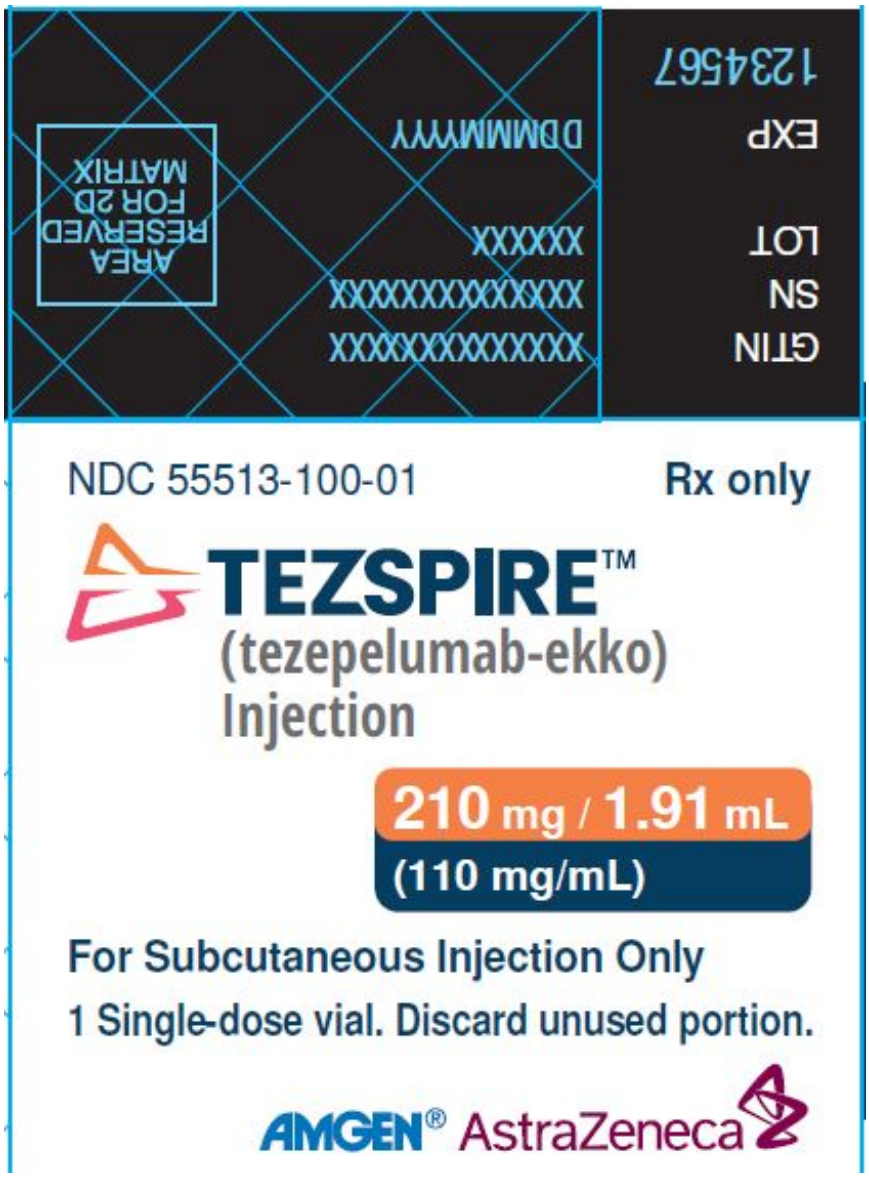
Injection

210 mg/1.91 mL (110 mg/mL)

For Subcutaneous Injection Only

1 singe-dose vial. Discard unused portion.

AMGEN® AstraZeneca



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 55513-112-01

TEZSPIRE™ (tezepelumab-ekko) Injection

210 mg/1.91 mL (110 mg/mL)

Rx Only

For Subcutaneous Injection Only

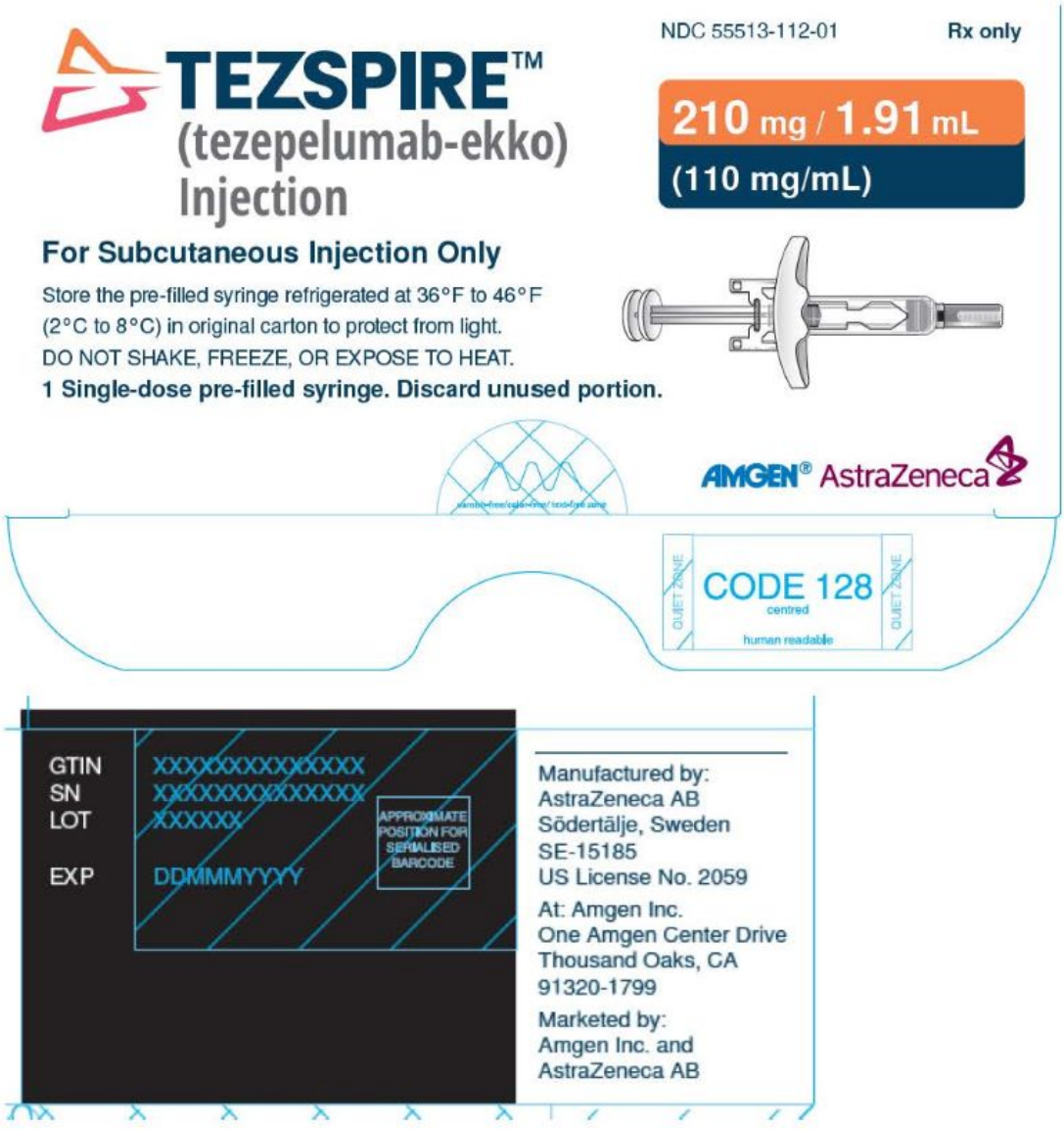
Store the pre-filled syringe refrigerated at 36° F to 46° F

(2° C to 8° C) in original carton to protect from light.

DO NOT SHAKE, FREEEZE, OR EXPOSE TO HEAT.

1 Singe-dose pre-filled syringe. Discard unused portion

AMGEN® AstraZeneca



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 55513-123-01 Rx only

TEZSPIRE®

(tezepelumab-ekko)

Injection

210 mg/1.91 mL (110 mg/mL)

For Subcutaneous Injection Only

Store the pre-filled pen refrigerated at 36°F to 46°F

(2°C to 8°C) in original carton to protect from light.

DO NOT SHAKE FREEZE OR EXPOSE TO HEAT.

1 Single-dose pre-filled pen.

Discard unused portion.

ATTENTION: Follow enclosed “Instructions for Use”

to prepare and deliver your dose.

AMGEN® AstraZeneca

TEZSPIRE

tezepelumab-ekko injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:55513-100
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TEZEPELUMAB (UNII: RJ1IW3B4QX) (TEZEPELUMAB - UNII:RJ1IW3B4QX)	TEZEPELUMAB	210 mg in 1.9 mL

Inactive Ingredients	
Ingredient Name	**Strength**
PROLINE (UNII: 9DLQ4CIU6V)	
ACETIC ACID (UNII: Q40Q9N063P)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:55513-100-01	1 in 1 CARTON	12/17/2021	12/18/2021
1		1.91 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:55513-100-96	1 in 1 CARTON	12/17/2021	12/18/2021
2		1.91 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
3	NDC:55513-100-99	1.91 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	12/17/2021	12/18/2021

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761224	12/17/2021	12/18/2021

TEZSPIRE

tezepelumab-ekko injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:55513-112
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TEZEPELUMAB (UNII: RJ1IW3B4QX) (TEZEPELUMAB - UNII:RJ1IW3B4QX)	TEZEPELUMAB	210 mg in 1.9 mL

Inactive Ingredients	
Ingredient Name	**Strength**
PROLINE (UNII: 9DLQ4CIU6V)	
ACETIC ACID (UNII: Q40Q9N063P)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:55513-112-01	1 in 1 CARTON	12/17/2021	
1		1.91 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		
2	NDC:55513-112-96	1 in 1 CARTON	12/17/2021	
2		1.91 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		
3	NDC:55513-112-99	1.91 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)	12/17/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761224	12/17/2021	

TEZSPIRE

tezepelumab-ekko injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:55513-123
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TEZEPELUMAB (UNII: RJ1IW3B4QX) (TEZEPELUMAB - UNII:RJ1IW3B4QX)	TEZEPELUMAB	210 mg in 1.9 mL

Inactive Ingredients

Ingredient Name	Strength
PROLINE (UNII: 9DLQ4CIU6V)	
ACETIC ACID (UNII: Q40Q9N063P)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55513-123-01	1 in 1 CARTON	02/14/2023	
1		1.91 mL in 1 CARTRIDGE; Type 0: Not a Combination Product		
2	NDC:55513-123-96	1 in 1 CARTON	02/20/2024	
2		1.91 mL in 1 CARTRIDGE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761224	12/17/2021	

Labeler - Amgen Inc (039976196)

Registrant - AstraZeneca PLC (230790719)

Revised: 10/2025 Amgen Inc