テゼスパイア皮下注 210mg シリンジ
テゼスパイア皮下注 210mg ペン
に関する資料

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アストラゼネカ株式会社

第 1 部　申請書等行政情報及び添付文書に関する情報

一般名：テゼペルマブ（遺伝子組換え）

版番号：■

1.5　起原又は発見の経緯及び開発の経緯
テゼスパイア®皮下注 210mg シリンジ、同皮下注 210mg ペン

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1.5.1　起原又は発見の経緯

テゼペルマブ（以下、本剤）は、組換え DNA 技術によりチャイニーズハムスター卵巣細胞で産生されたヒト IgG2λモノクローナル抗体であり、直接ヒト胸腺間質性リンパ球新生因子（TSLP）に作用する。本剤の薬理学的作用機序及び開発根拠については第 2 部 2.5.1 項に示した。

1.5.2　開発の経緯

本剤の開発の経緯図は本文書の末尾に示した（図 1）。

1.5.2.1　品質に関する試験の概略

今回の申請にあたり、新たな品質に関する試験は実施していない。

1.5.2.2　非臨床試験

今回の申請にあたり、非臨床試験を新たに実施していない。

TSLP は、炎症誘発性刺激に反応して産生される上皮細胞由来サイトカインであり、主に樹状細胞、ILC-2 及び肥満細胞に作用してアレルギー性炎症反応を誘発する。テゼペルマブは、その TSLP に対するヒト型 IgG2λのモノクローナル抗体である。本剤の初回申請時に提出した非臨床薬理試験から、テゼペルマブは、ヒト TSLP に高い親和性で結合し、TSLP と TSLPR 複合体との相互作用を抑制することにより効果を示すことが明らかになった。

鼻茸を伴う慢性副鼻腔炎（CRSwNP）の病態生理には、喘息同様、Th2 及び ILC-2 を介した炎症性メディエーター放出経路が関与しており、鼻茸組織には好酸球の浸潤が認められている。CRSwNP 患者の鼻茸組織では、TSLP 及び TSLP 受容体が増加していることが免疫組織化学的検査を含めた様々な方法で確認されている（Boita et al 2011）。さらに、好酸球性 CRSwNP の患者では、健康被験者の対照群と比較して鼻粘膜液中に分泌された TSLP タンパク質のレベルが上昇しており、IL-5 及び IL-13 と相関していることが示されている（Chen et al 2024）。テゼペルマブは喘息患者及び鼻茸を伴う患者において、IL-5 や IL-13 等の ILC-2 及び Th2 のメディエーターを効果的に減少させると報告されている（Pham et al 2019、Diver et al 2021、Emson et al 2021）。テゼペルマブは CRSwNP への関与が知られている炎症カスケードで TSLP シグナル伝達を阻害することで、鼻茸を有する患者に利益をもたらす可能性がある。

以上のことから、テゼペルマブの TSLP によるアレルギー性炎症反応に対する効果は、気管支喘息の効能又は効果を取得した初回の承認申請時に提出した非臨床効薬理試験において裏付けられていること、また、本申請の用量は気管支喘息で承認された用量の範囲内であることから、今回の新効能・効果の申請に関して新たな非臨床薬理試験は必要ないと判断した。

1.5.2.3　臨床試験

本申請は、既承認医薬品であるテゼスパイア皮下注 210mg シリンジ及び同皮下注 210mg ペンに「鼻茸を伴う慢性副鼻腔炎（既存治療で効果不十分な患者に限る）」の効能又は効果を追加することを目標としている。本剤の製造販売承認申請に関連する臨床試験の概略は、第 2 部 2.5.1 項に示した。

図１　　本剤の開発の経緯図

	2021	2022	2023	2024
【臨床】				
第 III 相試験 D5242C00001	4 ←――――――

1.5.3　参考文献

Boita et al 2011

Boita M, Garzaro M, Raimondo L, Riva G, Mazibrada J Vizio B, et al. The expression of TSLP receptor in chronic rhinosinusitis with and without nasal polyps. Int J Immunopathol Pharmacol. 2011;24(3):761-8.

Chen et al 2024

Chen J, Hu L, Liu J, Zhang Q, Cheng F, Wang Y, et al. Association between preoperative nasal mucus thymic stromal lymphopoietin and decreased quality of life in chronic rhinosinusitis with nasal polyps. Clin Exp Allergy. 2024 Aug 15.

Diver et al 2021

Diver S, Khalfaoui L, Emson C, Wenzel SE, Menzies-Gow A, Wechsler ME, et al. Effect of tezepelumab on airway inflammatory cells, remodelling, and hyperresponsiveness in patients with moderate-to-severe uncontrolled asthma (CASCADE): a double-blind, randomised, placebo-controlled, phase 2 trial. Lancet Respir Med. 2021;9(11):1299-312.

Emson et al 2021

Emson C, Corren J, Salapa K, Hellqvist Å, Parnes JR, Colice G. Efficacy of tezepelumab in patients with severe, uncontrolled asthma with and without nasal polyposis: A post hoc analysis of the Phase 2b PATHWAY study. J Asthma Allergy. 2021;14:91-9.

Pham et al 2019

Pham T-H, Ren P, Parnes JR, Griffiths JM. Tezepelumab reduces multiple key inflammatory biomarkers in patients with severe, uncontrolled asthma in the phase 2b PATHWAY study. Am J Respir Crit Care Med. 2019;199:A2677.

第 1 部　申請書等行政情報及び添付文書に関する情報

一般名：テゼペルマブ（遺伝子組換え）

版番号：■

1.6　外国における使用状況等に関する資料
テゼスパイア®皮下注 210mg シリンジ、同皮下注 210mg ペン

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1.6.1　外国における使用状況

2025 年 11 月時点で、テゼスパイア皮下注 210mg シリンジは 30 以上の国又は地域で、同 210mg 皮下注ペンは 35 の国又は地域で喘息治療薬として承認されている。主要国での承認状況を表 1 に示した。「鼻茸を伴う慢性副鼻腔炎（既存治療で効果不十分な患者に限る）」の効能又は効果について米国及び欧州で承認されている。

表 1　主要国の承認状況

国名又は地域	販売名	承認年月日
米国	**TEZSPIRE® (tezepelumab-ekko) injection, for subcutaneous use**	2021 年 12 月 17 日
欧州	**Tezspire 210 mg solution for injection in pre-filled syringe** **Tezspire 210 mg solution for injection in pre-filled pen**	2022 年 9 月 19 日

1.6.2　主要国の添付文書の概要

テゼスパイアの米国及び欧州における添付文書の概要、原文、及び企業中核データシート（CDS）を添付する。

表 2　　米国添付文書の概要

	米国
販売名	**TEZSPIRE® (tezepelumab-ekko) injection, for subcutaneous use**
効能・効果	**1 効能・効果** **1.1 喘息** TEZSPIRE は、成人及び 12 歳以上の小児の重症喘息患者に対する追加維持治療を適応とする。 使用法の制限： TEZSPIRE は急性気管支痙攣又は喘息発作重積の緩和は適応としない。 **1.2 鼻茸を伴う慢性副鼻腔炎** TEZSPIRE は、コントロール不良な成人及び 12 歳以上の小児の鼻茸を伴う慢性副鼻腔炎（CRSwNP）患者に対する追加維持療法を適応とする。
用法・用量	**2 用法・用量** **2.1 推奨用量** TEZSPIRE の推奨される用法・用量は、210 mg を 4 週間毎に 1 回皮下投与である。 投与欠落について 予定どおりに投与をしなかった場合は、可能な限り速やかに投与すること。その後は、通常の投与日に投与を継続（再開）する。既に次の投与予定日になっている場合は、予定どおりに投与する。 **2.2 調製及び投与方法** TEZSPIRE のバイアル及びプレフィルドシリンジは医療従事者が投与する。 TEZSPIRE プレフィルドペンは患者／介護者又は医療従事者が投与できる。ただし、患者／介護者は、皮下注射方法について適切なトレーニングを受け、医療従事者よりその操作が適切であると判定されれば、TEZSPIRE プレフィルドペンを投与することができる。 各バイアル、プレフィルドシリンジ及びプレフィルドペンは 1 回投与用量の TEZSPIRE を含有する。

表 2　　米国添付文書の概要

	米国
	• 投与前に TEZSPIRE を冷蔵庫から取り出して室温に戻す。概ね 60 分間で室温に戻る。熱に曝さないこと、また撹拌しないこと。箱の開封防止シールが剥がれている場合は使用しないこと。一度室温に戻した TEZSPIRE は冷蔵庫に戻さないこと。 • 投与に先立ち、異物が混入していないか、変色していないか目視検査する。TEZSPIRE は澄明～やや不澄明な無色～淡黄色の溶液である。薬液が濁っている、変色している場合や、大きな粒子又は微粒子状異物が認められる場合は使用しないこと。バイアル、プレフィルドシリンジ又はプレフィルドペンを落としてしまった場合やそれらが破損している場合、あるいは有効期限を過ぎている場合も使用しないこと。 • TEZSPIRE 210 mg（以下に記載するバイアル 1 本、プレフィルドシリンジ 1 本又はプレフィルドペン 1 本の内容物）を大腿部又は腹部（臍の周囲 2 インチ［5 cm］を除く）に皮下注射する。医療従事者又は介護者が投与する場合は、上腕部の使用も可能である。なお、患者は上腕部に自己注射してはならない。皮膚の敏感な部位や、挫創、紅斑、又は硬化が認められる部位には注射しないこと。投与毎に注射部位をローテーションさせることが望ましい。 <u>単回使用プレフィルドシリンジによる投与方法</u> 投与手順で使用するプレフィルドシリンジの各構成要素は図 1 の通り。 手順の 2 で注射する準備ができるまで、針カバーは取り外さない。針ガードの安全性機能が早期に作動するのを防ぐため、針ガード作動クリップには触れないこと。

表 2　　米国添付文書の概要

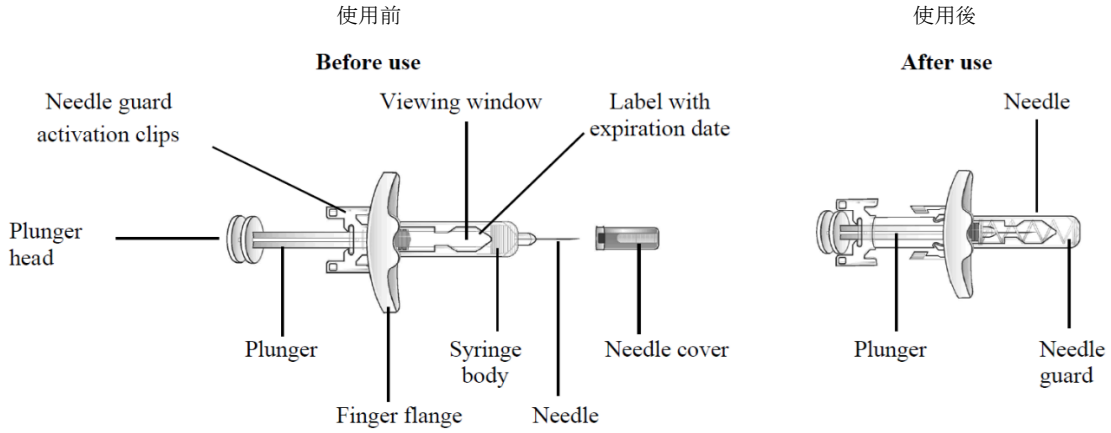
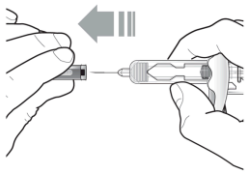
	米国
	図 1 TEZSPIRE プレフィルドシリンジの構成要素  Finger flange：フィンガーフランジ、Label with expiration date：有効期限ラベル、Needle：針、Needle cover：針カバー、Needle guard：針ガード、Needle guard activation clips：針ガード作動クリップ、Plunger：プランジャー、Plunger head:プランジャーヘッド、Syringe body：シリンジ本体、Viewing window：薬液確認窓 **1** シリンジ本体をしっかりとつかみ、カートンからプレフィルドシリンジを取り出す。プレフィルドシリンジのプランジャー部分をつかまないこと。 プレフィルドシリンジ内に少量の気泡がみられる場合があるが、問題はない。投与前に気泡を除こうとしないこと。 **2**  投与の準備ができるまで針カバーは取り外さないこと。シリンジ本体を片手で持ち、もう一方の手で針カバーをまっすぐ取り外す。針カバーを取り外す際、プランジャー又はプランジャーヘッドには触れないこと。針の先端に薬液の滴がみられることがあるが、問題はない。

表 2　　米国添付文書の概要

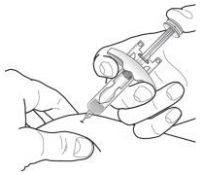
	米国
	3  皮膚を軽くつまみ、推奨注射部位（上腕部、大腿部又は腹部）の皮膚に対し約 45 度の角度で針を刺して皮下投与する。 **4**  プランジャーヘッドが針ガード作動クリップの間に完全に納まるまでプランジャーを押して、薬液全てを注射する。針ガードを作動させるには、プランジャーヘッドを最後まで押し切る必要がある。 **5**  注射し終えたならば、プランジャーヘッドを押し続けたままで皮膚から針を抜く。プランジャーヘッドを押している力を抜くと、針ガードが針を覆う。プレフィルドシリンジにキャップをはめなおさないこと。 **6** 使用済みのシリンジは鋭利医療器材廃棄容器（シャープスコンテナ）に廃棄する。

表 2　　米国添付文書の概要

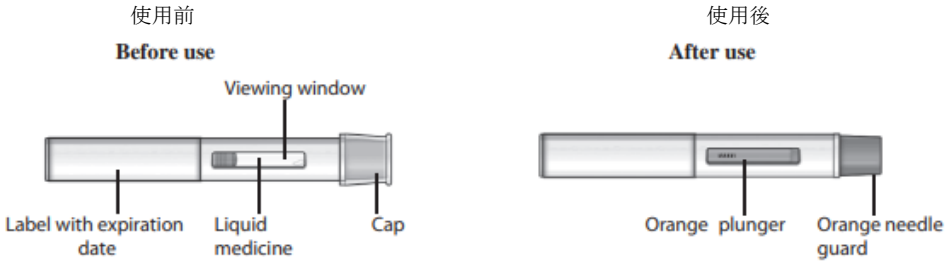
	米国
	単回使用プレフィルドペンによる投与時の注意 本項に記載する「投与時の注意」は医療従事者のみを対象とした内容である。患者及び介護者は、TEZSPIRE プレフィルドペンの調製及び投与に関する詳細な説明が必要な場合は、本剤の「使用説明書（投与方法）」を参照すること（「使用説明書（投与方法）」参照）。 患者／介護者は、皮下注射方法について適切なトレーニングを受け、医療従事者よりその操作が適切であると判定されれば、「使用説明書（投与方法）」に従って TEZSPIRE プレフィルドペンを投与することができる。 投与手順で使用するプレフィルドペンの各構成要素は図 2 の通り。 本剤を注射する準備ができるまで、キャップを外さないこと。 **図 2 TEZSPIRE プレフィルドペンの構成要素**  Viewing window：確認窓、Label with expiration date：有効期限表示ラベル、Liquid medicine：薬液、Cap：キャップ、Orange plunger：オレンジ色のプランジャー、Orange needle guard：オレンジ色の針ガード **1.** プレフィルドペン本体の中央部をつまんで、カートンからプレフィルドペンを取り出す。プレフィルドペン内に少量の気泡がみられる場合があるが、問題はない。投与前に気泡を除こうとしないこと。

表 2　　米国添付文書の概要

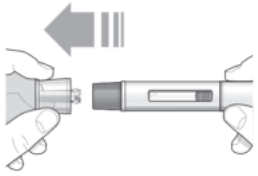
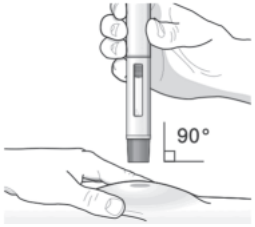
	米国
	2.  投与の準備ができるまでキャップは取り外さないこと。プレフィルドペン本体を片手で持ち、もう一方の手で慎重にキャップをまっすぐ取り外す。その際、針に触れたり、オレンジ色の針ガードを指で押したりしないこと。なお、キャップはプレフィルドペンの元の位置に戻さないこと。注入が早く起こりすぎたり、針を損傷させたりするおそれがある。 **3.** 注射部位の皮膚を軽くつまむか、又は皮膚をつままないで注射を行う。 手順に従って、推奨注射部位（上腕部、大腿部又は腹部）に TEZSPIRE を投与する。 注射の際には、最初にカチッと音がしたら、薬液の注入が始まる。2 回目のカチッという音が聞こえるまでプレフィルドペンを 15 秒間押し当てたままにする。注入が始まってからは、プレフィルドペンの位置を変えないこと。 **4.**  プレフィルドペンの位置を確認する。オレンジ色の針ガードを皮膚に対して 90 度の角度になるようにぴったり設置する。その際、確認窓が見えるようにしておくこと。

表 2　　米国添付文書の概要

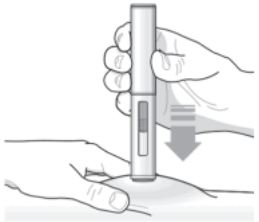
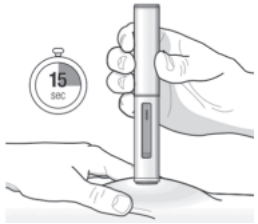
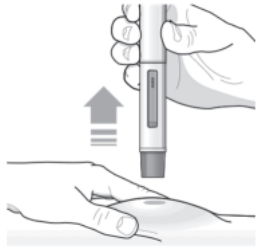
	米国
	5.  オレンジ色の針ガードが見えなくなるまで、ペンをしっかりと押し下げる。最初にカチッと音がすると、薬液の注入が始まる。薬液注入時には確認窓でオレンジ色のプランジャーが下に移動する。 **6.**  ペンを約 15 秒間、しっかりと押し当てたままにしておくこと。2 回目のカチッという音がしたら、薬液の注入は完了したことになる。確認窓はオレンジ色のプランジャーでいっぱいになる。 **7.**  注射が完了したら、プレフィルドペンを真っ直ぐ持ち上げる。オレンジ色の針ガードが下にスライドして針を覆った状態で固定される。

表 2　　米国添付文書の概要

	米国
	8. 使用済みのプレフィルドペンを鋭利医療器材廃棄容器（シャープスコンテナ）に廃棄する。
剤形及び含量	**3 剤形及び含量** 注射剤：澄明～やや不澄明な無色～淡黄色の溶液であり、以下の剤形が製造されている。 • 210 mg/1.91 mL（110 mg/mL）の注射液を含有する単回使用ガラスバイアル • 210 mg/1.91 mL（110 mg/mL）の注射液を含有する単回使用プレフィルドシリンジ • 210 mg/1.91 mL（110 mg/mL）の注射液を含有する単回使用プレフィルドペン
禁忌	**4 禁忌** Tezepelumab-ekko 又は添加物に対し過敏症の既往がある者には使用しないこと*［「警告及び使用上の注意」（5.1 項）参照］*。
警告及び使用上の注意	**5 警告及び使用上の注意** **5.1 過敏症反応** 臨床試験において、本剤投与後に過敏症反応（発疹、アレルギー性結膜炎等）が認められた。製造販売後にアナフィラキシーを発現した症例も報告されている*［「禁忌」（4 項）及び「副作用」（6 項）参照］*。過敏症反応は投与後数時間以内に発現しうるが、遅延性（数日後）に発現する場合もある。過敏症反応が認められた場合は、患者毎に個別にベネフィットとリスクを勘案して、本剤投与の継続又は中止を決定すること。 **5.2 急性喘息症状又は病状の悪化** 本剤は、急性喘息症状又は急性増悪の治療に使用すべきではない。急性気管支痙攣又は喘息発作重積の治療には本剤を使用しないこと。本剤による治療を開始しても喘息のコントロール不良状態が続いている又は喘息が悪化した場合は受診するよう患者に指導すること。 **5.3 ステロイド剤の突然の減量に伴うリスク** 本剤による治療開始時に、全身性ステロイド剤又は吸入ステロイド剤の投与を突然中止してはならない。ステロイド剤の減量が適切な場合は、医師の直接監視下で徐々に減量すること。ステロイド剤の減量に伴い全身性の離脱症状及び／又はそれまでステロイド療法により抑えられていた病態が露呈することがありうる。 **5.4 寄生虫（蠕虫）感染症**

表 2　　米国添付文書の概要

	米国
	一部の蠕虫感染症に対する免疫応答に胸腺間質性リンパ球新生因子（TSLP）が関与している可能性がある。蠕虫感染症が確認されている患者は臨床試験の対象から除外した。本剤が蠕虫感染症に対する患者の免疫応答に影響を及ぼすかどうかは不明である。 既に蠕虫感染症がある患者では、本剤による治療を開始する前に感染症を治療すること。本剤投与中に蠕虫に感染し、抗蠕虫療法に反応しない患者では、感染症が消失するまで本剤の投与を中止すること。 **5.5 弱毒生ワクチン** 本剤と弱毒生ワクチンの併用について検討されていない。本剤を投与されている患者では、弱毒生ワクチンを接種しないこと。
副作用	**6 副作用** 臨床的に重要な下記の副作用について、ラベルに記載しておく。 • 過敏症 *［「警告及び使用上の注意」（5.1 項）参照］* **6.1 臨床試験成績** 臨床試験は多様な条件下で実施しているため、ある薬剤の臨床試験での副作用発現率を別の薬剤の臨床試験での発現率と直接比較することはできず、また試験での発現率は臨床場面での発現率を反映していないこともありうる。 <u>成人及び 12 歳以上の小児の喘息患者における副作用</u> 本剤の安全性は、PATHWAY 試験及び NAVIGATOR 試験の併合安全性解析対象集団での結果に基づいている。同集団は、本剤 210 mg の 4 週間毎 1 回皮下投与を 1 回以上受けた成人及び 12 歳以上の小児の重症喘息患者 665 例で構成されている。この 2 件のプラセボ対照臨床試験の試験期間は 52 週間であった。更に、経口ステロイド剤の連日投与を必要とする重症喘息の成人患者 150 例を組み入れた試験でも、同様の安全性プロファイルが認められた *［「臨床試験」（14.1 項）参照］*。 併合安全性解析対象集団（PATHWAY 試験及び NAVIGATOR 試験）の TEZSPIRE 群で発現率が 3%以上であり、かつプラセボ群よりも発現率が高かった副作用を表 1 に示す。 **表 1** 重症喘息患者の併合安全性解析対象集団（PATHWAY 試験及び NAVIGATOR 試験）における TEZSPIRE 群で発現率が 3%以上であり、かつプラセボ群よりも発現率が高かった副作用

副作用	TEZSPIRE	プラセボ

表 2　　米国添付文書の概要

	米国

	N=665 %	N=669 %
咽頭炎*	4	3
関節痛	4	3
背部痛	4	3

* 咽頭炎（咽頭炎、細菌性咽頭炎、レンサ球菌性咽頭炎及びウイルス性咽頭炎を含む）

特定の副作用

心血管系イベント

NAVIGATOR 試験及びその追加試験から組み入れられた 12 歳以上の重症喘息患者を対象としたランダム化、二重盲検、長期継続投与試験*［「臨床試験」（14.1 項）参照］*において、本剤 210 mg 又はプラセボを 4 週間に 1 回、最長 104 週間にわたり皮下投与した。本試験で認められた重篤な心血管系有害事象の 100 患者年（patient-year：PY）あたりの発現率（IR）は TEZSPIRE 群で 1.08、プラセボ群で 0.21 となり、発現率の差（IRD）は 0.88（95%CI：0.24～1.53）であった。重篤な心血管系有害事象の種類は均一ではなかった。本試験で認められた、判定済み主要心血管イベント（MACE：心血管死、非致死性心筋梗塞、及び非致死性脳卒中と定義）の 100PY あたりの発現率は TEZSPIRE 群 0.60 及びプラセボ群 0.42 で、IRD は 0.18（95%CI：-0.51～0.75）であった。

注射部位反応

医療従事者がバイアルにて本剤又はプラセボを投与した併合安全性解析対象集団（PATHWAY 試験及び NAVIGATOR 試験）で認められた注射部位反応（注射部位紅斑、注射部位腫脹、注射部位疼痛等）の発現率はプラセボ群の 2.7%に対し、TEZSPIRE 群では 3.3%であった。

喘息患者 216 例を対象に医療従事者及び患者又は介護者がプレフィルドペン又はプレフィルドシリンジを用いて本剤を投与した非盲検試験において、注射部位反応（注射部位紅斑、注射部位腫脹、注射部位疼痛等）がプレフィルドペンを用いた患者の 5.7%で認められたが、プレフィルドシリンジを用いた患者では認められなかった。ただし、本試験はプレフィルドペンによる本剤投与例とプレフィルドシリンジによる本剤投与例とで注射部位反応を比較するようにデザインされた試験ではなかった。

成人の CRSwNP 患者における副作用

表 2　　米国添付文書の概要

	米国
	本剤のCRSwNPに対する安全性は、無作為化、二重盲検、並行群間比較、多施設共同、プラセボ対照、52週間のWAYPOINT試験の結果に基づいている。本剤 210 mg の 4 週間毎 1 回皮下投与を 1 回以上受けた 18 歳以上の CRSwNP に対する標準治療を受けている成人患者 203 例で構成されている*［「臨床試験」（14.2 項）参照］*。 安全性解析対象集団（WAYPOINT 試験）の TEZSPIRE 群で発現率が 3%以上であり、かつプラセボ群よりも発現率が高かった副作用を表 2 に示す。 **表 2** CRSwNP 患者の安全性解析対象集団（WAYPOINT 試験）における TEZSPIRE 群で発現率が 3%以上であり、かつプラセボ群よりも発現率が高かった副作用

副作用	TEZSPIRE N=203 %	プラセボ N=205 %
鼻咽頭炎	18	10
上気道感染*	12	8
鼻出血	6	3
咽頭炎†	5	1
背部痛	5	2
インフルエンザ	4	1
注射部位反応‡	4	2
関節痛	3	2

*上気道感染（上気道感染、ウイルス性上気道感染を含む）

†咽頭炎（咽頭炎、細菌性咽頭炎、レンサ球菌性咽頭炎及びウイルス性咽頭炎を含む）

‡注射部位反応（注射部位紅斑、注射部位腫脹、及び注射部位疼痛など）

6.2　市販後の使用経験

本剤の製造販売承認取得以降に以下の副作用が確認されている。これらの副作用は規模不明確な集団から自発報告されたものであるため、必ずしも確実に頻度を推定できる、又は本剤投与との因果関係を確立できるとは限らない。

過敏症反応：アナフィラキシー

表 2　　米国添付文書の概要

	米国
薬物相互作用	**7 薬物相互作用** 正式な薬物相互作用試験は実施していない。
特定の患者集団における使用	**8 特定の患者集団における使用** **8.1　妊婦** リスク概要 本剤投与に伴う主要な先天異常、流産、その他の母体又は胎児の転帰に対する有害作用のリスクを評価するための、妊婦における本剤使用データはない。Tezepelumab-ekko のようなモノクローナル抗体の胎盤通過は妊娠後期に多くなることから、胎児への影響は妊娠後期に大きくなる可能性がある。カニクイザルを用いた拡張型出生前及び出生後の発生（ePPND）試験では、tezepelumab-ekko の胎盤輸送が認められたものの、ヒトでの最大推奨臨床用量（MRHD）である 210 mg を皮下投与したときの 168 倍までの曝露量をもたらす用量で母動物に妊娠期間を通じて tezepelumab-ekko を静脈内投与しても、胎児に有害作用は認められなかった*［「データ」参照］*。 適応となる集団における主要な先天異常及び流産の推定背景リスク率は不明である。あらゆる妊娠例に、先天異常、胎児消失、その他の有害転帰の背景リスクがある。米国の一般集団では、臨床的に確認された妊娠例での主要な先天異常及び流産の推定背景リスク率はそれぞれ 2～4%及び 15～20%である。 臨床的禁忌 *疾患関連の母体及び／又は胚・胎児のリスク：* コントロール不良又は中等度にコントロールされている喘息の女性では、子癇前症、早産、低出生体重児及び妊娠期間に比して小さい新生児というリスクが上昇することが確認されている。妊婦では喘息のコントロール状況を綿密に監視し、最適な状態を維持できるよう、必要に応じて投与を調節すること。 *データ* *動物データ* ePPND 試験では、妊娠しているカニクイザルに tezepelumab-ekko を MRHD での曝露量の 168 倍までの曝露量になる用量で（AUC に基づき、最大 300 mg/kg/週）、妊娠 20 日～22 日（妊娠判明日により異なる）、器官形成期開始時点、その後は妊娠終了時まで 7 日毎に静脈内投与した。母動物の健康状態、妊娠の転帰、胚・胎児の発生、又は新生児の 6.5 ヵ月齢までの発育及び発達に、tezepelumab-ekko に関連する有害作用は認められなかった。Tezepelumab-ekko はカニクイザルの胎盤を通過し、乳児の血清中 tezepelumab-ekko 濃度は母動物での同濃度の 0.5～6.7 倍であった。

表 2　　米国添付文書の概要

	米国
	8.2 授乳婦 リスク概要 Tezepelumab-ekko のヒト母乳中への移行、母乳哺育児への影響、又は母乳分泌への影響に関する情報はない。ただし、tezepelumab-ekko はヒトモノクローナル抗体免疫グロブリン G2λ（IgG2λ）であり、免疫グロブリン G（IgG）はヒト母乳中に少量存在する。妊娠中に投与したカニクイザルの出産後の母乳中に tezepelumab-ekko が認められた*［「データ」参照］*。母乳哺育児の発育・発達及び健康に及ぼすベネフィットを、母親に対する本剤の必要性及び本剤又は母親の基礎疾患が母乳哺育児に及ぼしうる有害作用と併せて考慮すること。 *データ* *動物データ* カニクイザルを用いた出生前及び出生後の発生試験で、tezepelumab-ekko を最高 300 mg/kg/週（MRHD での AUC に基づく曝露量の 168 倍になる用量）で静脈内投与後、tezepelumab-ekko の母乳中濃度は母動物の血清中濃度の最大 0.5%であった。動物の母乳中 tezepelumab-ekko 濃度から、必ずしもヒト母乳中の薬物濃度を予測できるわけではない。 **8.4 小児への使用** 喘息 12 歳以上の小児患者における重症喘息の追加維持治療としての本剤の安全性及び有効性は確立されている*［「副作用」（6.1 項）及び「臨床試験」（14.1 項）参照］*。この適応に対する本剤の使用は、NAVIGATOR 試験に組み入れられて TEZSPIRE 210 mg の 4 週間毎皮下投与（41 例）又はプラセボ投与（41 例）を受けた 12～17 歳の小児患者 82 例から得られたデータが裏付けとなっている。TEZSPIRE 群ではプラセボ群と比較して年間喘息増悪率の改善（率比 0.70、95% CI：0.34～1.46）及び FEV_1 の改善（最小二乗平均値のプラセボ群との差 0.17 L、95% CI：−0.01～0.35）が認められた。小児患者での安全性プロファイル及び薬力学的反応は、試験の全体集団での結果と概ね類似していた。 12 歳未満の喘息患者における安全性及び有効性は確立されていない。 CRSwNP 12 歳以上のコントロール不良な CRSwNP 患者に対する追加維持療法としての本剤の安全性及び有効性は確立されている。この適応に対する本剤の使用は、適切にコントロールされた成人における臨床試験（WAYPOINT 試験）から得られたデータ*［「臨床試験」（14.2 項）参照］*及び下記のデータが裏付けとなっている： • 成人及び 12 歳以上の小児の重症喘息患者及び成人の CRSwNP からの薬物動態データ*［「薬物動態」（12.3 項）参照］*

表 2　　米国添付文書の概要

	米国
	• 12 歳以上の小児の重症喘息患者からの安全性データ *［「副作用」（6.1 項）参照］* 12 歳未満の CRSwNP 患者における安全性及び有効性は確立されていない。 **8.5　高齢者への使用** 喘息 臨床試験（PATHWAY 試験及び NAVIGATOR 試験）で TEZSPIRE を投与された重症喘息患者 665 例のうち、119 例（18%）が 65 歳以上であった。本剤の安全性又は有効性に、65 歳以上の患者とそれより若い患者との間で全般的に差は認められていない *［「副作用」（6.1 項）及び「臨床試験」（14.1 項）参照］*。 CRSwNP 臨床試験（WAYPOINT 試験）で TEZSPIRE を投与された CRSwNP 患者 203 例のうち、29 例（14%）が 65 歳以上であった。本剤の安全性又は有効性に、65 歳以上の患者とそれより若い患者との間で全般的に差は認められていない *［「副作用」（6.1 項）及び「臨床試験」（14.2 項）参照］*。

表 3　　欧州添付文書の概要

	欧州
販売名	**1. 販売名** Tezspire 210 mg solution for injection in pre-filled syringe Tezspire 210 mg solution for injection in pre-filled pen
成分及び組成	**2. 成分及び組成** プレフィルドシリンジ プレフィルドシリンジ 1 本につき、テゼペルマブ 210 mg を含有する注射液 1.91 mL（110 mg/mL）が充填されている。

表 3　　欧州添付文書の概要

	欧州
	プレフィルドペン プレフィルドペン 1 本につき、テゼペルマブ 210 mg を含有する注射液 1.91 mL（110 mg/mL）が充填されている。 テゼペルマブは、組換え DNA 技術により、チャイニーズハムスター卵巣（CHO）細胞で産生されたヒトモノクローナル抗体である。 既知の作用を有する添加剤 本剤 210 mg（1.91 mL）につき、L-プロリン 48 mg 及びポリソルベート 80 0.19 mg を含む。 6.1 項に全添加剤の一覧を示す。
剤形	**3. 剤形** 注射液（注射剤） 無色～淡黄色の澄明～やや不澄明な溶液
効能・効果	**4. 臨床特性** **4.1 効能・効果** 喘息 TEZSPIRE は、高用量の吸入ステロイド剤に加え別の喘息治療薬を維持投与しているにもかかわらずコントロール不良な重症喘息の成人及び 12 歳以上の青少年患者に対する追加維持療法を適応とする。 鼻茸を伴う慢性副鼻腔炎（CRSwNP）

表 3　　欧州添付文書の概要

	欧州
	TEZSPIRE は、全身性ステロイド薬及び/又は手術療法でコントロール不良な成人の重症 CRSwNP 患者に対する鼻噴霧用ステロイド薬への追加療法を適応とする。
用法・用量及び投与方法	**4.2 用法・用量及び投与方法** TEZSPIRE の適応症の診断及び治療の経験を有する医師が投与を開始すること（4.1 項参照）。 用法・用量 TEZSPIRE は長期使用を想定した薬剤である。少なくとも 1 年に 1 回、患者の疾患コントロールの程度に基づき、投与継続の有無について決定すること。 喘息 *成人及び青少年（12 歳以上）* 推奨される用法・用量は、テゼペルマブ 210 mg の 4 週間毎の皮下投与である。 CRSwNP 成人患者に推奨される用法・用量は、テゼペルマブ 210 mg の 4 週間毎の皮下投与である。 *投与欠落について* 予定どおりに投与をしなかった場合は、可能な限り速やかに投与すること。その後は、通常の投与予定日に投与を継続（再開）する。既に次の投与予定日になっている場合は、予定どおりの投与とし、2 回分の用量を投与してはならない。 特定の患者集団 *高齢者（65 歳以上）*

表 3　　欧州添付文書の概要

	欧州
	高齢者に対する用量調節は不要である（5.2 項参照）。 *腎機能障害患者及び肝機能障害患者* 腎機能障害又は肝機能障害の患者に対する用量調節は不要である（5.2 項参照）。 *小児* 12 歳未満の小児における喘息の治療について、TEZSPIRE の安全性及び有効性についてはデータがなく、確立されていない。 18 歳未満の小児における CRSwNP の治療について、TEZSPIRE の安全性及び有効性についてはデータがなく、確立されていない。 <u>投与方法</u> TEZSPIRE は皮下注射剤である。 本剤は、患者又は患者の介護者が皮下注射手技についてトレーニングを受けた後は、自己注射又は患者への投与が可能である。使用前に、「使用説明書」に基づき TEZSPIRE の調製及び投与について、患者及び/又は介護者に適切なトレーニングを行うこと。 TEZSPIRE は、大腿部又は腹部（臍の周囲 5 cm を除く）に皮下注射する。医療従事者又は介護者が投与する場合は、上腕部に投与してもよい。患者による自己注射の場合は、腕に投与しないこと。皮膚の敏感な部位や、挫傷、紅斑、硬化のある場所には注射しないこと。投与回毎に注射部位をローテーションさせることが推奨される。 プレフィルドシリンジ又はプレフィルドペンによる投与の詳細は、「使用説明書」を参照のこと。
禁忌	**4.3 禁忌** 本剤の有効成分又は 6.1 項に示す添加物に対し過敏症の既往がある者には使用しないこと。

表 3　　欧州添付文書の概要

	欧州
警告及び使用上の注意	**4.4 警告及び使用上の注意** トレーサビリティ 生物製剤のトレーサビリティを高める目的で、処方した薬剤の製品名及びロット番号を明確に記録しておくこと。 喘息の急性増悪 TEZSPIRE は、喘息の急性増悪の治療に使用すべきではない。 投与中に喘息に関連した症状又は増悪が発現する可能性がある。本剤による治療を開始しても喘息のコントロール不良状態が続いている又は喘息が悪化した場合は受診するよう患者に指導すること。 ステロイド剤 本剤による治療開始時に、ステロイド剤の投与を突然中止してはならない。ステロイド剤の減量が適切な場合は、医師の直接監視下で徐々に減量すること。 過敏症反応 テゼペルマブの投与後に過敏症反応（アナフィラキシー、発疹等）が発現する可能性がある（4.8 項参照）。過敏症反応は投与後数時間以内に発現しうるが、遅発性に（数日後に）発現することもある。 テゼペルマブと関連性のないアナフィラキシーの既往歴が、TEZSPIRE 投与後のアナフィラキシーのリスク因子となる可能性がある。医療慣行に基づき、TEZSPIRE 投与後から適切な時間、患者を観察すること。 重篤な過敏症反応（アナフィラキシー等）が発現した場合は、テゼペルマブの投与を即座に中止し、臨床的に必要とされる適切な治療を開始すること。 重篤な感染症 胸腺間質性リンパ球新生因子（TSLP）阻害により、理論的には重篤な感染症リスクが増加する可能性があるが、プラセボ対照試験においてテゼペルマブ投与例における重篤な感染症の増加はみられなかった。

表 3　　欧州添付文書の概要

	欧州
	既に重篤な感染症がある患者では、テゼペルマブによる治療を開始する前に感染症を治療すること。テゼペルマブの投与中に重篤な感染症を発現した場合は、感染症が消失するまでテゼペルマブの投与を中止すること。 重篤な心イベント 長期の臨床試験において、テゼペルマブ投与例とプラセボ投与例とで、重篤な有害事象の心イベントの発現に数値的な不均衡が認められた。これらのイベントとテゼペルマブとの間に因果関係は確立しておらず、当該イベントの高リスク患者集団も特定されていない。 心イベントが疑われる徴候や症状（胸痛、呼吸困難、倦怠感、ふらつき、失神等）について患者に説明し、該当する症状が発現した場合は速やかに医療機関を受診するよう患者に指導すること。テゼペルマブ投与中に重篤な心イベントが発現した場合は、当該の急性イベントが安定するまで投与を中止すること。 現時点で、重篤な心イベント又は重篤な感染症を発現した患者に再投与したデータはない。 寄生虫（蠕虫）感染症 一部の蠕虫感染症に対する免疫応答に TSLP が関与している可能性がある。蠕虫感染症が確認されている患者は臨床試験の対象から除外した。テゼペルマブが蠕虫感染症に対する患者の免疫応答に影響を及ぼすかどうかは不明である。 既に蠕虫感染症がある患者では、テゼペルマブによる治療を開始する前に感染症を治療すること。テゼペルマブ投与中に蠕虫に感染し、抗蠕虫療法に反応しない患者では、感染症が消失するまで投与を中止すること。 既知の作用を有する添加剤 本剤の 1 回投与量 210 mg あたりのナトリウム含有量は 1 mmol（23 mg）未満である。すなわち、実質的には「ナトリウムを含有していない」といえる。

表 3　　欧州添付文書の概要

	欧州
	本剤の 1 回投与量 210 mg（1.91 mL）あたりの L-プロリン含有量は 48 mg である。L-プロリンは高プロリン血症患者に有害である可能性がある。 本剤の 1 回投与量 210 mg（1.91 mL）あたりのポリソルベート 80 含有量は 0.19 mg である。ポリソルベート 80 はアレルギー反応を起こす可能性がある。
他剤との相互作用及びその他の相互作用	**4.5 他剤との相互作用及びその他の相互作用** 相互作用試験は実施していない。 テゼペルマブを投与されている患者では、弱毒生ワクチンを接種しないこと。 12 歳から 21 歳までの中等症から重症喘息患者 70 例を対象としたランダム化二重盲検並行群間比較試験において、テゼペルマブは 4 価季節性インフルエンザワクチンによる液性抗体反応に影響しないと考えられた。 喘息治療薬と併用した場合、テゼペルマブは当該薬剤の薬物動態に臨床的に重要な影響を与えないと考えられる。また、母集団薬物動態解析において、一般的に併用される喘息治療薬（ロイコトリエン受容体拮抗薬、テオフィリン/アミノフィリン、及び経口ステロイド等）はテゼペルマブのクリアランスに影響しなかった。
生殖能、妊娠、及び授乳	**4.6 生殖能、妊娠、及び授乳** 妊婦 テゼペルマブを妊婦に使用したデータはないか、若しくはあっても限られている（妊娠転帰のデータは 300 例に満たない）。また、動物試験において、生殖毒性に関する直接的又は間接的な有害作用は認められていない（5.3 項参照）。 テゼペルマブのようなヒト IgG 抗体は胎盤関門を通過して移行する。したがって、TEZSPIRE は母体から発育中の胎児に移行する可能性がある。 母体に対する治療上の有益性が胎児で予測される危険性を上回ると判断されない限り、 予防的措置として、妊娠期間中は TEZSPIRE の使用を避けることが望ましい。 授乳婦

表 3　　欧州添付文書の概要

	欧州
	テゼペルマブのヒト乳汁移行の有無は不明である。ヒト IgG は、出生後最初の数日は母乳中に移行することが知られているが、その後速やかに濃度が低下する。すなわち、この短期間においては、母乳哺育児におけるリスクを排除することはできない。 上記の期間中は、乳児に授乳するベネフィットと母親にテゼペルマブを投与するベネフィットとを考慮したうえで、投与中止/投与回避について決定すること。 その後の期間は、臨床的に必要であれば、授乳中のテゼペルマブの投与は可能である。 テゼペルマブの動物（カニクイザル）における乳汁移行については 5.3 項を参照すること。 生殖能 ヒト生殖能に関するデータはない。動物試験において、テゼペルマブの生殖能に対する有害作用は示されていない（5.3 項参照）。
運転及び機械操作能力に対する影響	**4.7 運転及び機械操作能力に対する影響** 運転及び機械操作能力に対する TEZSPIRE の影響はないか、若しくはあっても無視できる程度である。
副作用	**4.8 副作用** 安全性プロファイルの要約 投与中に最もよくみられた副作用は、喘息患者では関節痛（3.8%）及び咽頭炎（4.1%）、CRSwNP 患者では咽頭炎（5.4%）であった。 副作用一覧表 表 1 に、重症喘息患者及び CRSwNP 患者に TEZSPIRE を 1 回以上投与した 52 週間の臨床試験及び市販後の使用経験において認められた副作用を示す。

表 3　　欧州添付文書の概要

	欧州
	副作用の頻度を、極めて高頻度（10%以上）、高頻度（1%以上 10%未満）、低頻度（0.1%以上 1%未満）、まれ（0.01%以上 0.1%未満）、極めてまれ（0.01%未満）、不明（既存データから推測不能）、と定義する。各頻度内で重篤度の高い順に副作用を示す。 **表 1　副作用一覧** **器官別大分類** / **副作用** / **頻度** 感染症および寄生虫症 / 咽頭炎 [a] / 高頻度 免疫系障害 / 過敏症（アナフィラキシー反応含む） / 不明 皮膚および皮下組織障害 / 発疹 [b] / 高頻度 筋骨格系および結合組織障害 / 関節痛 / 高頻度 一般・全身障害および投与部位の状態 / 注射部位反応 [c] / 高頻度 [a] 咽頭炎は次の基本語からなるグループ化事象と定義した：咽頭炎、細菌性咽頭炎、レンサ球菌性咽頭炎、ウイルス性咽頭炎。 [b] 発疹は次の基本語からなるグループ化事象と定義した：発疹、そう痒性皮疹、紅斑性皮疹、斑状丘疹状皮疹、斑状皮疹。 [c]「主な副作用の説明」参照 主な副作用の説明 *注射部位反応* PATHWAY 試験及び NAVIGATOR 試験の併合安全性データにおいて、テゼペルマブ 210 mg を 4 週間毎（Q4W）に皮下投与した患者における注射部位反応（注射部位紅斑、注射部位腫脹、注射部位疼痛等）の発現率は、3.8%であった。 小児

表 3　　欧州添付文書の概要

	欧州
	52 週間の第 III 相試験である NAVIGATOR 試験には、12～17 歳のコントロール不良の青少年重症喘息患者が合計 82 例組み入られた（5.1 項参照）。青少年患者における安全性プロファイルは、試験の全体集団における安全性プロファイルと概ね類似していた。 副作用疑いの報告 承認後における副作用疑いの報告は、本剤のベネフィット・リスクバランスについて継続的な観察を可能とするものであり、重要である。医療従事者は、全ての副作用疑いについて、Appendix V に示す各国の報告システムを通して報告することが求められる。
過量投与	**4.9 過量投与** 臨床試験では喘息患者を対象として、最大 280 mg までを 2 週間毎（Q2W）に皮下投与及び 700 mg までを 4 週間毎（Q4W）に静脈内投与したが、用量依存性の毒性を示すエビデンスは認められなかった。 テゼペルマブの過量投与に対する治療は特にない。過量投与した場合は、対症療法を行い、必要に応じて適切に患者を観察すること。
廃棄及びその他の取り扱いに関する注意喚起	**6.6 廃棄及びその他の取り扱いに関する注意喚起** 本剤は単回使用製剤である。 投与前に薬剤の箱を冷蔵庫から取り出して TEZESPIRE を室温に戻す。概ね 60 分間で室温に戻る。 投与に先立ち、異物が混入していないか、変色していないか目視検査する。TEZSPIRE は澄明～やや不澄明な無色～淡黄色の溶液である。薬液が濁っている、変色している、又は大きな粒子若しくは微粒子状異物が認められる場合は使用しないこと。 TEZESPIRE のプレフィルドシリンジ製剤又はプレフィルドペン製剤の調製及び投与に関する詳細及び説明は、添付文書及び「使用説明書」を参照すること。 本剤の未使用分若しくは残余分は、各国の規制に従って廃棄すること。

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.

Revised: 10/2025

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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.

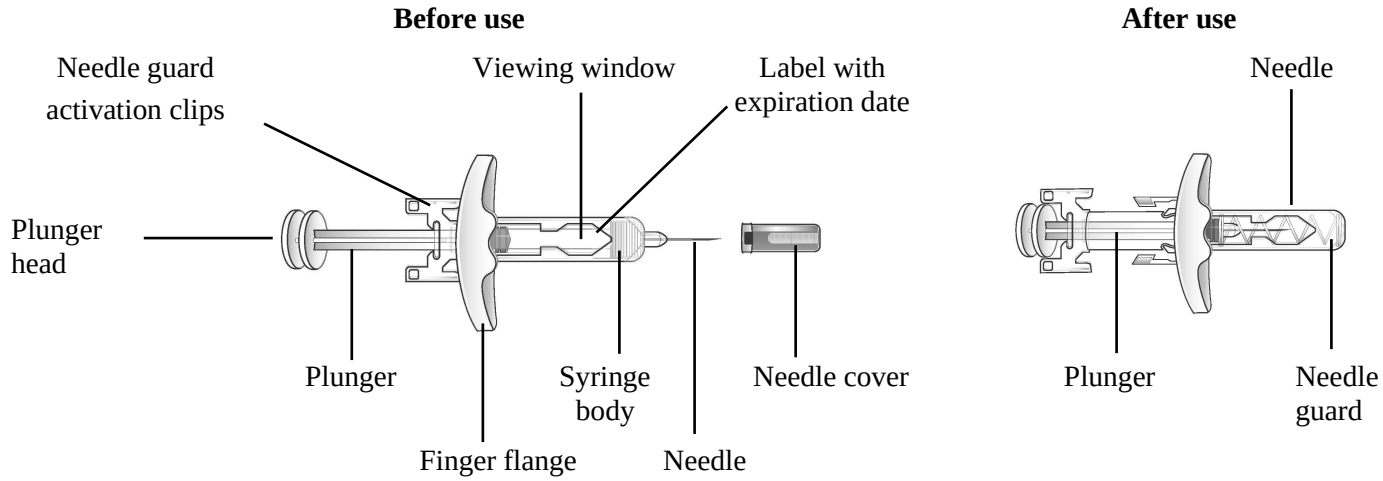
- Prior to administration, remove TEZSPIRE from the refrigerator and allow it to reach room temperature. This generally takes 60 minutes. Do not expose to heat and do not shake. Do not use if the security seal on the carton has been broken. Do not put back in the refrigerator once TEZSPIRE has reached 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.

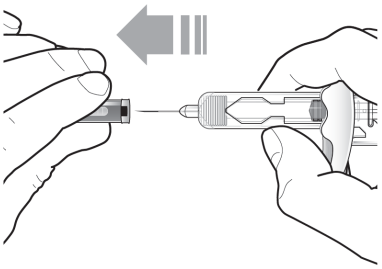
Do not remove the needle cover until Step 2 of these instructions when you are ready to inject TEZSPIRE. Do not touch the needle guard activation clips to prevent premature activation of the needle safety guard.

Figure 1 TEZSPIRE Pre-filled Syringe Components

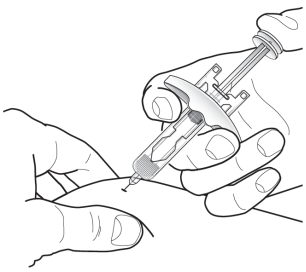


1. Grasp the syringe body to remove the pre-filled syringe from its carton. Do not grab the pre-filled syringe by the plunger.

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

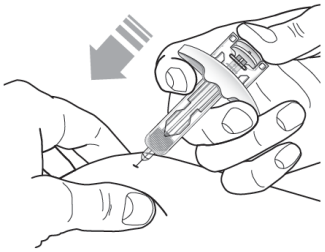
2. 

   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.

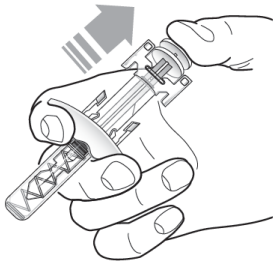
3. 

   Gently pinch the skin and administer subcutaneously at approximately 45º 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

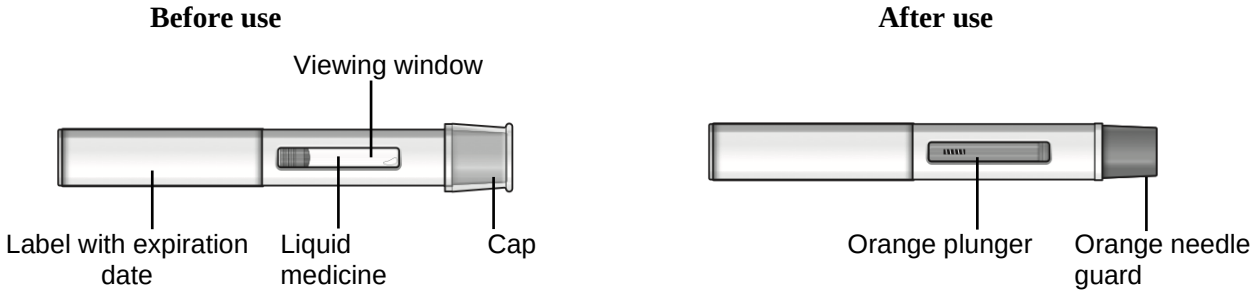
These administration instructions are intended for healthcare providers use only. Patients and caregivers should refer to the TEZSPIRE pre-filled pen 'Instructions for Use' for more detailed instructions on the preparation and administration of TEZSPIRE pre-filled pen *[See Instructions for Use]*.

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.

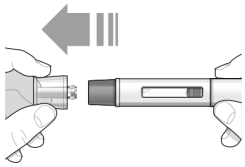
Do not remove the cap until you are ready to inject TEZSPIRE.

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.

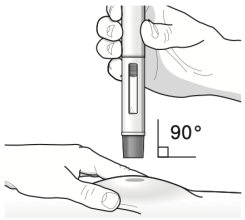
2. 

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.

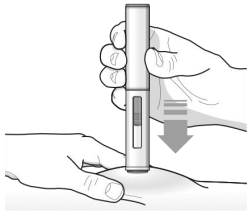
3. Gently pinch the skin at the injection site or give the injection without pinching the skin.

   Inject TEZSPIRE by following the steps into the recommended injection site (i.e., upper arm, thigh, or abdomen).

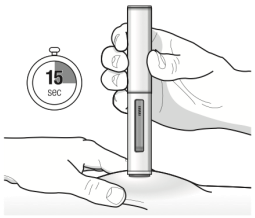
   When injecting, you will hear the first click that tells you the injection has started. Press and hold the pre-filled pen for 15 seconds until you hear the second click. Do not change the position of the pre-filled pen after the injection has started.

4. 

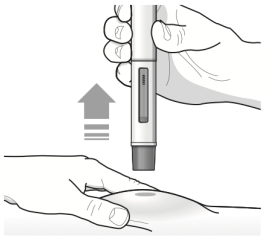
Position the pre-filled pen. Place the orange needle guard flat against the skin (90-degree angle). Make sure you can see the viewing window.

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 FEV_1 (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 (FEV_1) 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 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.

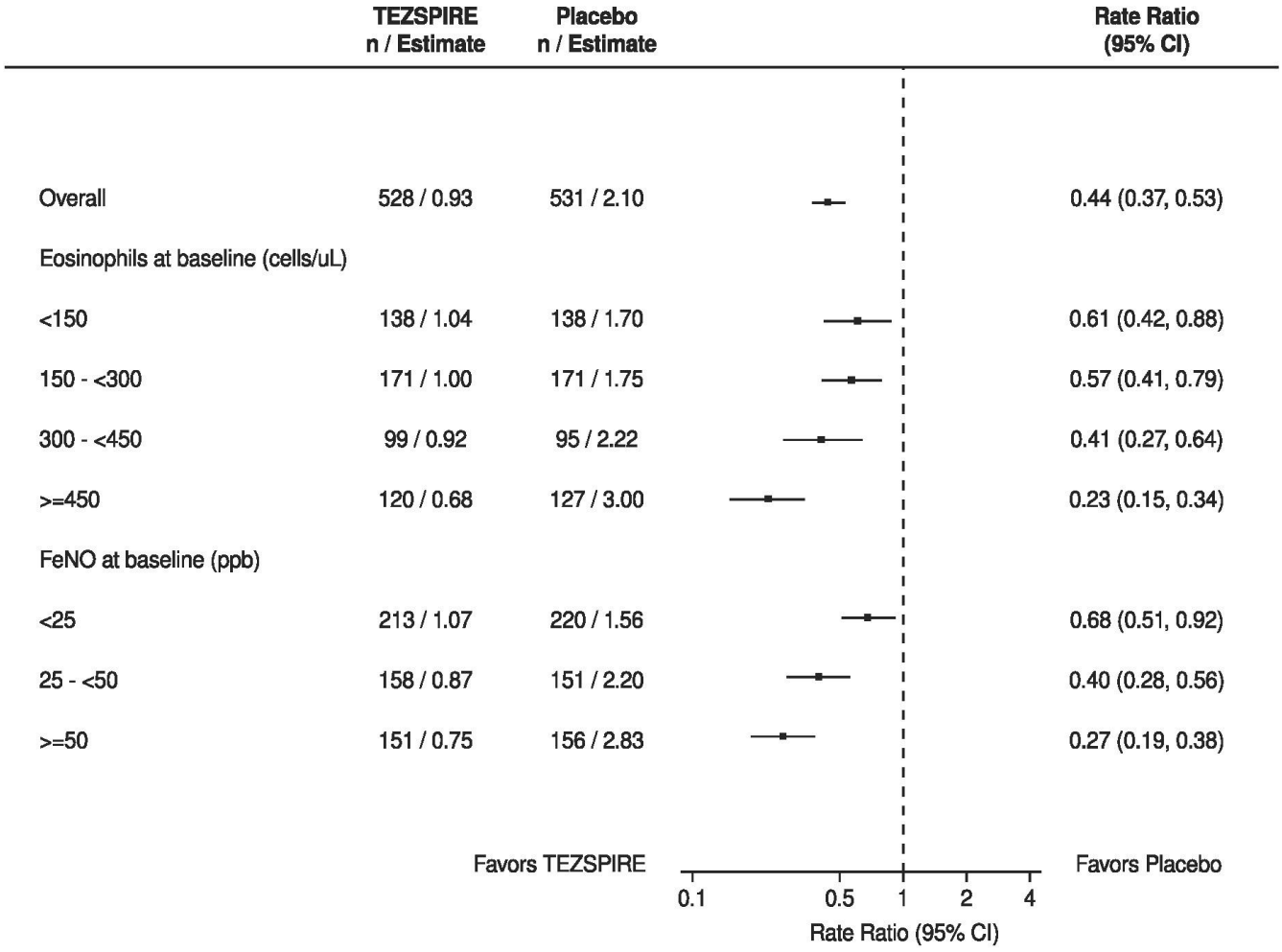
In both PATHWAY and NAVIGATOR, patients receiving TEZSPIRE had significant reductions in the annualized rate of asthma exacerbations compared to placebo. There were also fewer exacerbations requiring emergency room visits and/or hospitalization in patients treated with TEZSPIRE compared with placebo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

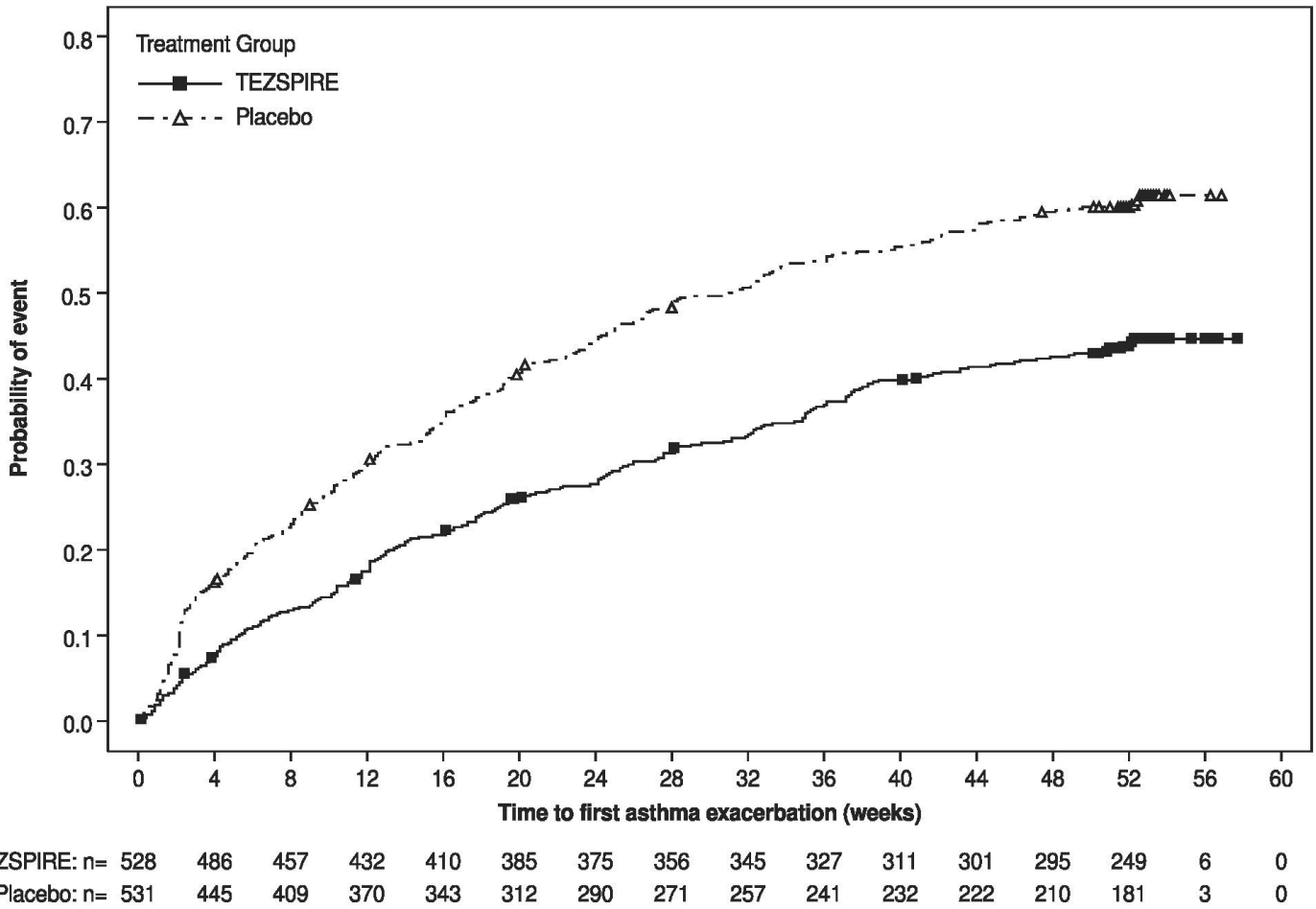
In NAVIGATOR, patients receiving TEZSPIRE experienced fewer exacerbations than those receiving placebo regardless of baseline levels of blood eosinophils or FeNO (Figure 3). Similar results were seen in PATHWAY.

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).

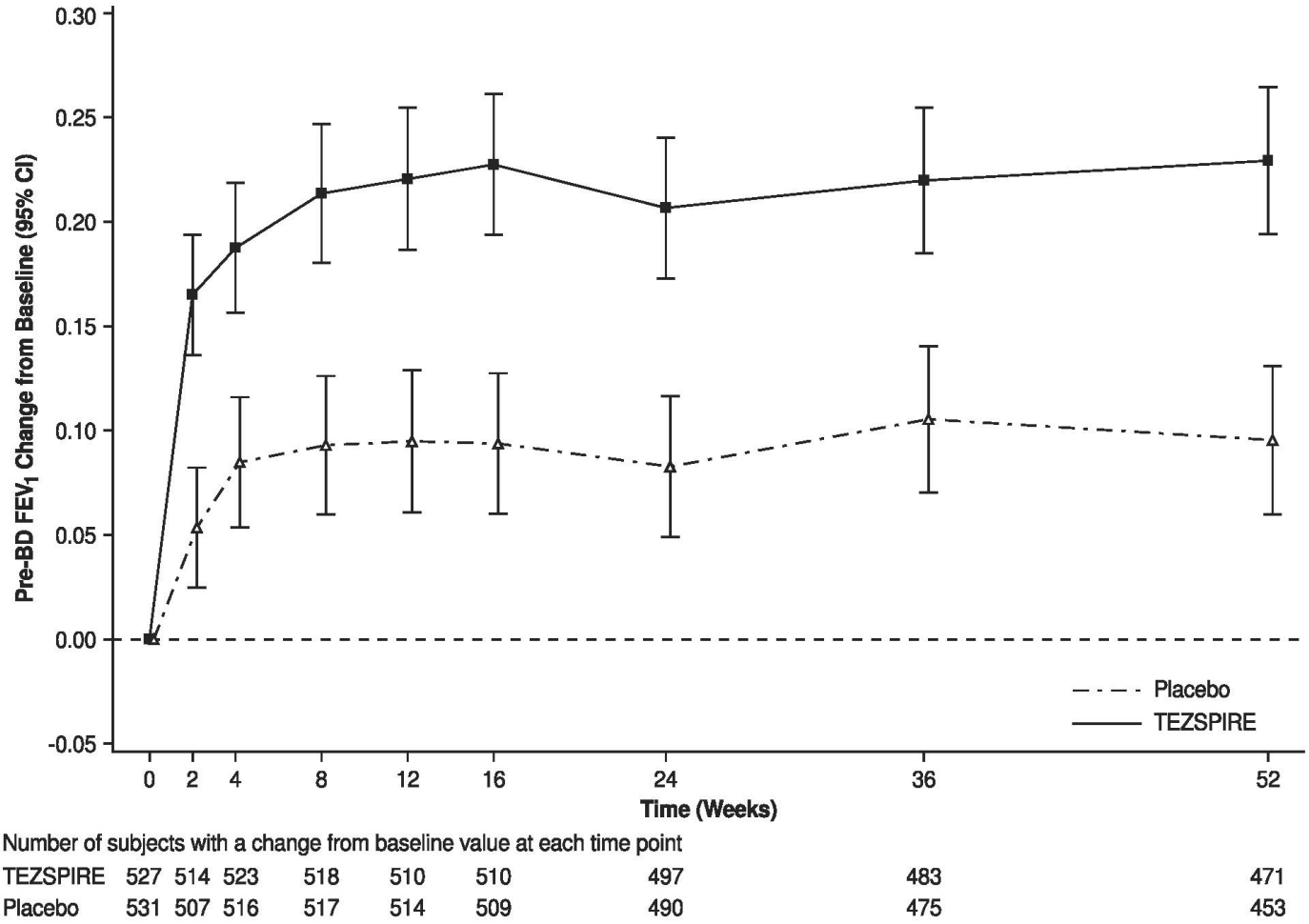
Table 5 Mean Change from Baseline in Pre-Bronchodilator FEV_1 at End of Trial in PATHWAY and NAVIGATOR*

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 FEV_1 (L) in NAVIGATOR



Number of subjects with a change from baseline value at each time point

TEZSPIRE	527	514	523	518	510	510	497	483	471
Placebo	531	507	516	517	514	509	490	475	453

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)

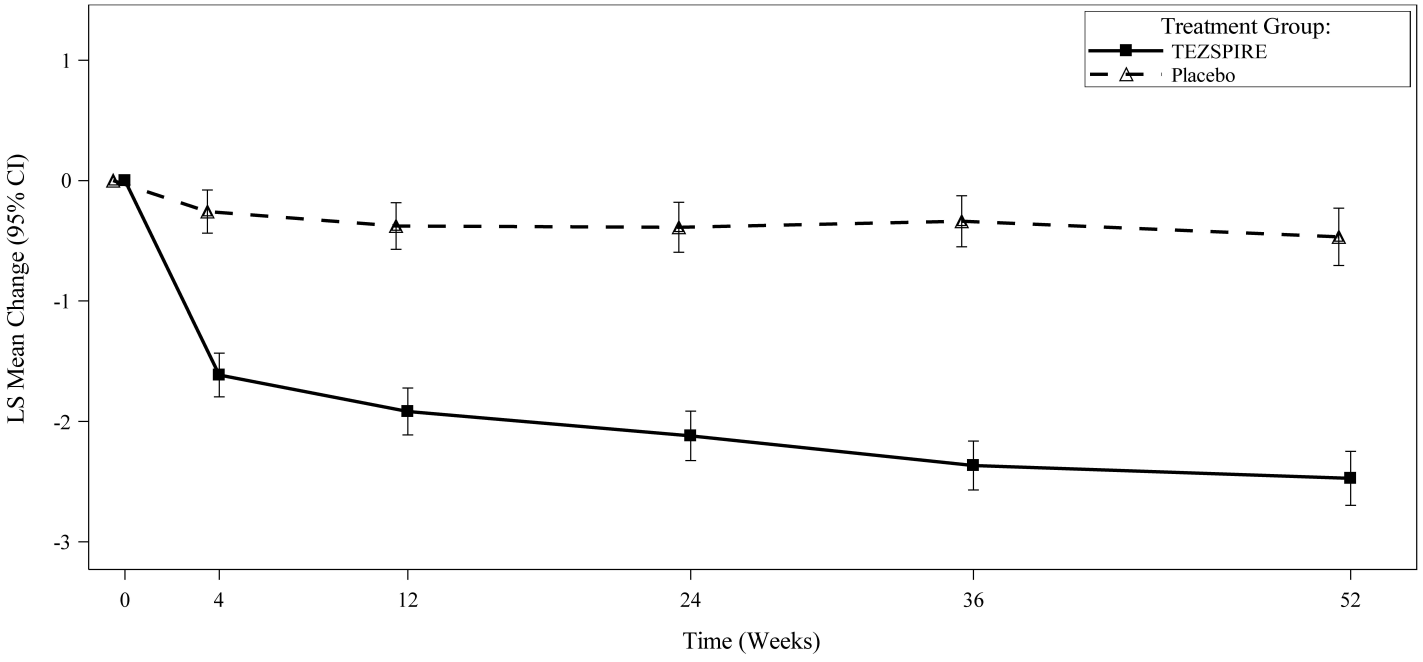
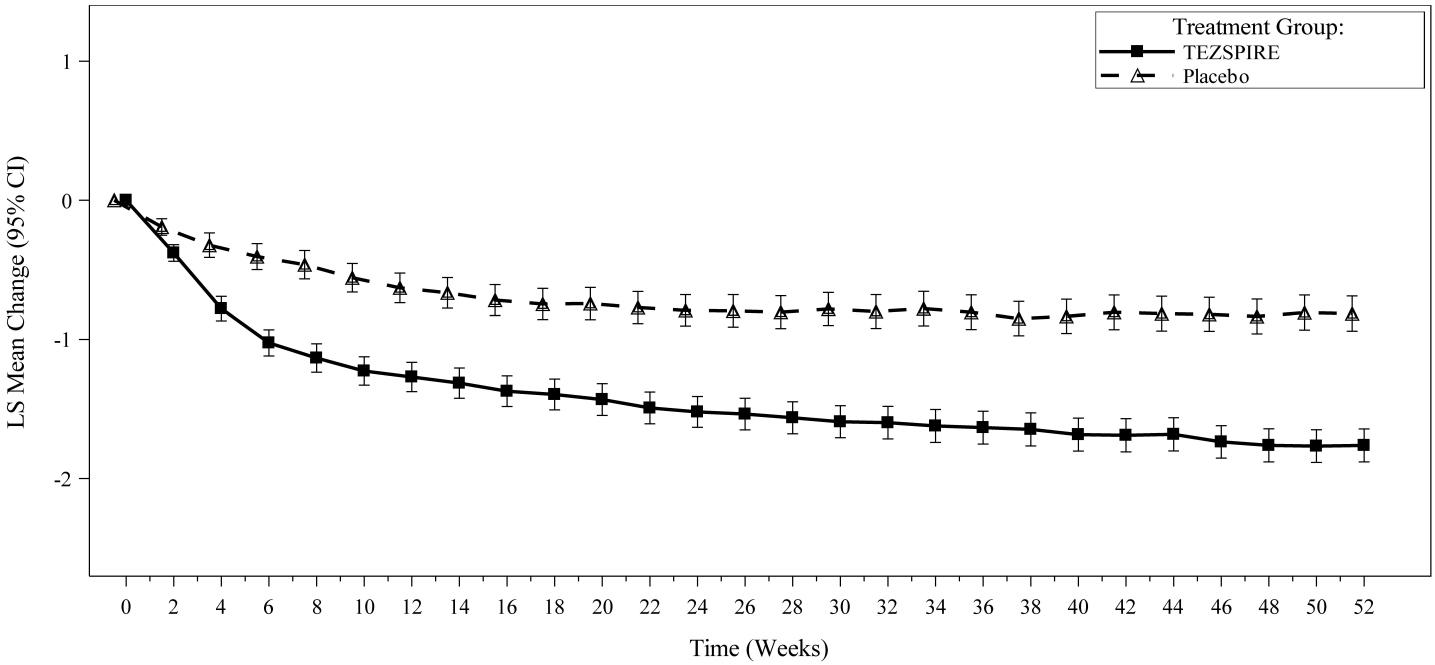


Figure 7 demonstrates the time course of improvement in the bi-weekly mean change from baseline in NCS.

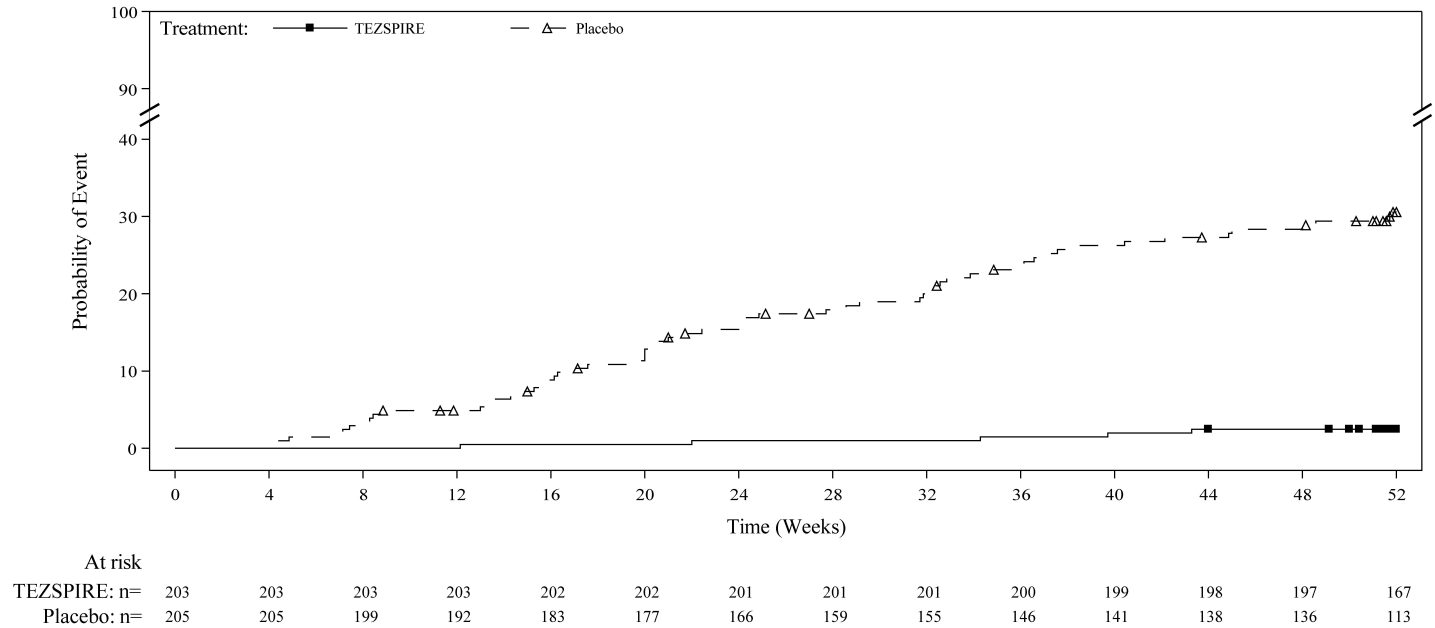
Figure 7 **LS Mean Change from Baseline in Bi-weekly Mean Nasal Congestion Score up to Week 52 in Adults (WAYPOINT)**



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

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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
- swelling of your face, mouth, and tongue
- breathing problems
- red, itchy, swollen, or inflamed eyes
- 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
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TEZSPIRE is a trademark of Amgen Inc. and AstraZeneca.
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.

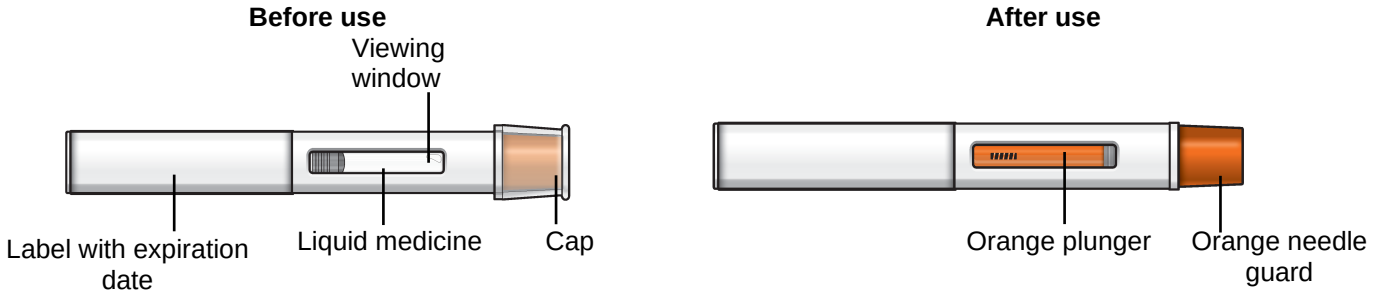
Each TEZSPIRE pre-filled pen contains 1 dose of TEZSPIRE that can only be used 1 time.

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.



Pre-filled pen



Alcohol wipe



Cotton ball or gauze



Bandage



Sharps disposal container

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.

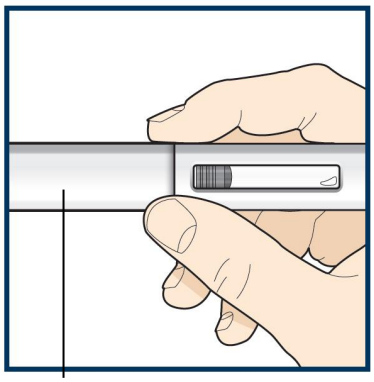
Check the pre-filled pen for damage. Do not use the pre-filled pen if the pre-filled pen is damaged.

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

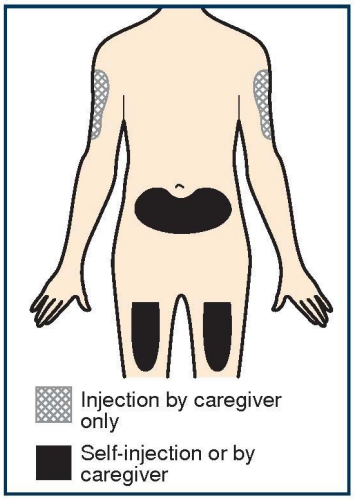
If you are giving yourself the injection, the **recommended injection site** is the front of your thigh or the lower part of your stomach (abdomen). **Do not** inject yourself in the arm.

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

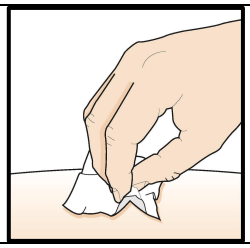
Wash your hands well with soap and water.

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.

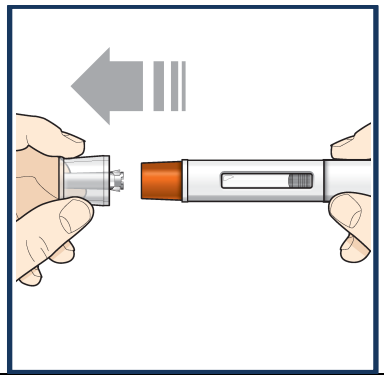
Hold the pre-filled pen body with 1 hand, and carefully pull the cap straight off with your other hand.

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.



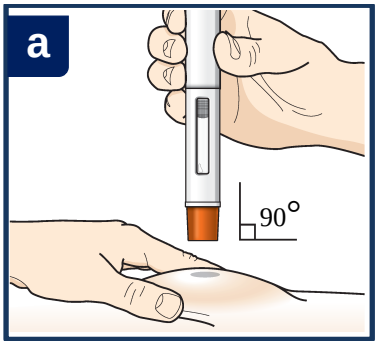
Step 7 – Inject TEZSPIRE

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**.

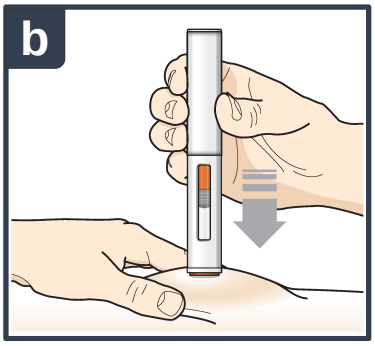
When injecting, you will hear the first click that tells you the injection has started. Press and hold the pre-filled pen for 15 seconds until you hear the **second click.**

Do not change the position of the pre-filled pen after the injection has started.



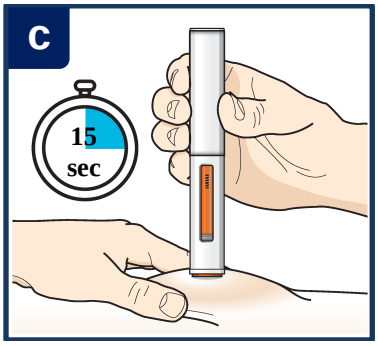
Position the pre-filled pen.

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



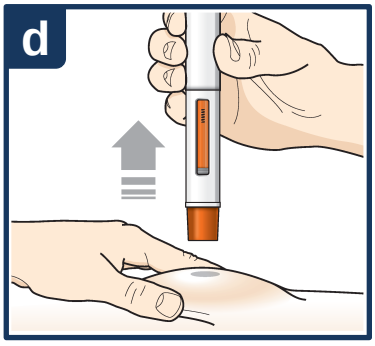
Press down firmly until you cannot see the orange needle guard.

- 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.

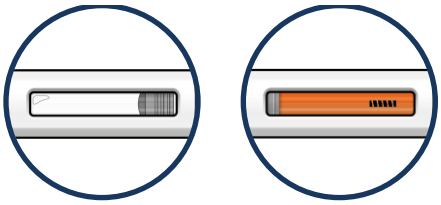
Step 8 – Check the viewing window

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

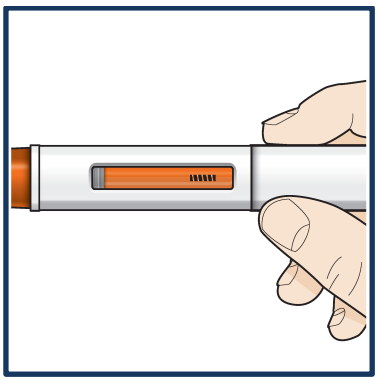
If the orange plunger rod does not fill the viewing window, you may not have received the full dose.

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

Before injection



After injection

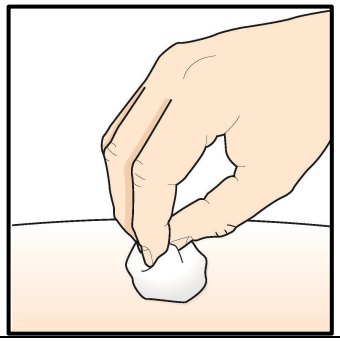


Step 9 – Check the injection site

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.



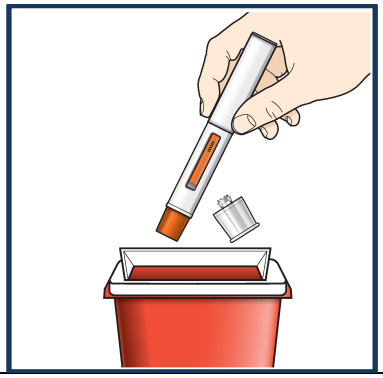
Disposing of TEZSPIRE

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.

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AstraZeneca AB, Södertälje, Sweden SE-15185
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This Instructions for Use has been approved by the U.S. Food and Drug Administration. Revised: October 2025

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled syringe
Tezspire 210 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pre-filled syringe
Each pre-filled syringe contains 210 mg tezepelumab in 1.91 mL solution (110 mg/mL).

Pre-filled pen
Each pre-filled pen contains 210 mg tezepelumab in 1.91 mL (110 mg/mL).

Tezepelumab is a human monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

Excipients with known effect
This medicine contains 48 mg of L-proline and 0.19 mg of polysorbate 80 in each 210 mg dose (1.91 mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Clear to opalescent, colourless to light yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Asthma

Tezspire is indicated as an add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids plus another medicinal product for maintenance treatment.

Chronic rhinosinusitis with nasal polyps (CRSwNP)

Tezspire is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids, and/or surgery do not provide adequate disease control.

4.2 Posology and method of administration

Treatment should be initiated by physicians experienced in the diagnosis and treatment of conditions for which Tezspire is indicated (see section 4.1).

Posology

Tezspire is intended for long-term treatment. A decision to continue the therapy should be made at least annually based on the patient's level of disease control.

Asthma
Adults and adolescents (aged 12 years and older)
The recommended dose is 210 mg of tezepelumab by subcutaneous injection every 4 weeks.

CRSwNP
The recommended dose for adult patients is 210 mg of tezepelumab by subcutaneous injection every 4 weeks.

Missed dose
If a dose is missed, the dose should be administered as soon as possible. Thereafter, the patient can resume dosing on the scheduled day of administration. If the next dose is already due, then administer as planned. A double dose must not be administered.

Special populations

Elderly (≥65 years of age)
No dose adjustment is required for elderly patients (see section 5.2).

Renal and hepatic impairment
No dose adjustment is required for patients with renal or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of Tezspire in children under 12 years of age for the treatment of asthma have not been established. No data are available.

The safety and efficacy of Tezspire in children under 18 years of age for the treatment of CRSwNP have not been established. No data are available.

Method of administration

Tezspire is administered as a subcutaneous injection.

A patient may self-inject or the patient's caregiver may administer this medicinal product after training in subcutaneous injection technique. Proper training should be provided to patients and/or caregivers on the preparation and administration of Tezspire prior to use according to the "Instructions for Use".

Tezspire should be injected into the thigh or abdomen, except for the 5 cm around the navel. If a healthcare professional or caregiver administers the injection, the upper arm can also be used. A patient should not self-inject in the arm. It 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.

Comprehensive instructions for administration using the pre-filled syringe or pre-filled pen is provided in the "Instructions for Use".

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Acute asthma exacerbations

Tezspire should not be used to treat acute asthma exacerbations.

Asthma-related symptoms or exacerbations may occur during treatment. Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment.

Corticosteroids

Abrupt discontinuation of corticosteroids after initiation of therapy is not recommended. Reduction in corticosteroid doses, if appropriate, should be gradual and performed under the supervision of a physician.

Hypersensitivity reactions

Hypersensitivity reactions (e.g. anaphylaxis, rash) may occur following administration of tezepelumab (see section 4.8). These reactions may occur within hours of administration, but in some instances have a delayed onset (i.e. days).

A history of anaphylaxis unrelated to tezepelumab may be a risk factor for anaphylaxis following Tezspire administration. In line with clinical practice, patients should be monitored for an appropriate time after administration of Tezspire.

In the event of a serious hypersensitivity reaction (e.g. anaphylaxis), administration of tezepelumab should be discontinued immediately and appropriate treatment as clinically indicated should be initiated.

Serious infections

Blocking thymic stromal lymphopoietin (TSLP) may theoretically increase the risk of serious infections. In placebo-controlled studies, no increase in serious infections was observed with tezepelumab.

Patients with pre-existing serious infections should be treated before initiating therapy with tezepelumab. If patients develop a serious infection while receiving tezepelumab treatment, therapy with tezepelumab should be discontinued until the serious infection resolves.

Serious cardiac events

In a long-term clinical study, a numerical imbalance in serious cardiac adverse events was observed in patients treated with tezepelumab compared to placebo. No causal relationship between tezepelumab and these events has been established, nor has a patient population at risk of these events been identified.

Patients should be advised of signs or symptoms suggestive of a cardiac event (for example, chest pain, dyspnoea, malaise, feeling lightheaded or faint) and to seek immediate medical attention if such symptoms occur. If patients develop a serious cardiac event while receiving tezepelumab treatment, therapy with tezepelumab should be discontinued until the acute event stabilises.

There is currently no data on re-treatment of patients who develop a serious cardiac event or serious infection.

Parasitic (helminth) infection

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 tezepelumab may influence a patient's response against helminth infections.

Patients with pre-existing helminth infections should be treated before initiating therapy with tezepelumab. If patients become infected while receiving treatment and do not respond to anti-helminth treatment, therapy with tezepelumab should be discontinued until infection resolves.

Excipients with known effect

This medicinal product contains less than 1 mmol sodium (23 mg) per 210 mg dose, that is to say essentially 'sodium-free'.

This medicinal product contains 48 mg of L-proline in each 210 mg dose (1.91 mL). L-proline may be harmful for patients with hyperprolinaemia.

This medicinal product contains 0.19 mg of polysorbate 80 in each 210 mg dose (1.91 mL). Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

The use of live attenuated vaccines should be avoided in patients receiving tezepelumab.

In a randomised, double blind, parallel group study of 70 patients aged between 12 and 21 years with moderate to severe asthma, tezepelumab treatment did not appear to affect the humoral antibody responses induced by seasonal quadrivalent influenza vaccination.

A clinically relevant effect of tezepelumab on the pharmacokinetics of co-administered asthma medicinal products is not expected. Based on the population pharmacokinetic analysis, commonly co-administered asthma medicinal products (including leukotriene receptor antagonists, theophylline/aminophylline and oral corticosteroids) had no effect on tezepelumab clearance.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of tezepelumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Human IgG antibodies, such as tezepelumab, are transported across the placenta barrier; therefore, Tezspire may be transmitted from the mother to the developing foetus.

As a precautionary measure, it is preferable to avoid the use of Tezspire during pregnancy unless the expected benefit to the pregnant mother is greater than any possible risk to the foetus.

Breast-feeding

It is unknown whether tezepelumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed child cannot be excluded during this short period.

For this specific period, a decision should be made whether to discontinue/abstain from tezepelumab therapy, taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Afterwards, tezepelumab could be used during breast-feeding if clinically needed.

See section 5.3 for information on the excretion of tezepelumab in animal (cynomolgus monkey) milk.

Fertility

There are no fertility data in humans. Animal studies showed no adverse effects of tezepelumab treatment on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Tezspire has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions during treatment for asthma are arthralgia (3.8%) and pharyngitis (4.1%) and during treatment for CRSwNP is pharyngitis (5.4%).

Tabulated list of adverse reactions

Table 1 presents the adverse reactions from clinical studies in patients with severe asthma and CRSwNP who received at least one dose of Tezspire in trials of 52 weeks duration, and from post-marketing experience.

The frequency of adverse reactions is defined using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 List of adverse reactions

System organ class	Adverse reactions	Frequency
Infections and infestations	Pharyngitis[a]	Common
Immune system disorders	Hypersensitivity (including anaphylactic reaction)	Not known
Skin and subcutaneous tissue disorders	Rash[b]	Common
Musculoskeletal and connective tissue disorders	Arthralgia	Common
General disorders and administration site conditions	Injection site reaction[c]	Common

[a] Pharyngitis was defined by the following grouped preferred terms: pharyngitis, pharyngitis bacterial, pharyngitis streptococcal and viral pharyngitis.

[b] Rash was defined by the following grouped preferred terms: rash, rash pruritic, rash erythematous, rash maculo-papular, rash macular.
[c] See 'Description of selected adverse reactions'.

Description of selected adverse reactions

Injection site reactions
In the pooled safety data from PATHWAY and NAVIGATOR, injection site reactions (e.g. injection site erythema, injection site swelling, injection site pain) occurred at a rate of 3.8% in patients treated with tezepelumab 210 mg subcutaneous every 4 weeks (Q4W).

Paediatric population

A total of 82 adolescents aged 12 to 17 with severe, uncontrolled asthma were enrolled in the 52-week Phase 3 NAVIGATOR study (see section 5.1). The safety profile in adolescents was generally similar to the overall study population.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In clinical trials, doses of up to 280 mg were administered subcutaneously every 2 weeks (Q2W) and doses of up to 700 mg were administered intravenously every 4 weeks (Q4W) to patients with asthma without evidence of dose-related toxicities.

There is no specific treatment for an overdose with tezepelumab. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for obstructive airway diseases, other systemic drugs for obstructive airway diseases, ATC code: R03DX11

Mechanism of action

Tezepelumab is a monoclonal antibody (IgG2λ) directed against thymic stromal lymphopoietin (TSLP), preventing its interaction with the heterodimeric TSLP receptor. In asthma and CRSwNP, both allergic and non-allergic triggers induce TSLP production. Blocking TSLP with tezepelumab reduces a broad spectrum of biomarkers and cytokines associated with airway and mucosal inflammation in asthma and CRSwNP (e.g. blood eosinophils, airway submucosal eosinophils, IgE, FeNO, IL-5, and IL-13); however, the mechanism of action of tezepelumab in asthma and CRSwNP has not been definitively established.

Pharmacodynamic effects

Effect on blood eosinophils and inflammatory biomarkers and cytokines
In asthma clinical trials, administration of tezepelumab 210 mg subcutaneously every 4 weeks reduced blood eosinophils counts, FeNO, IL-5 concentration, IL-13 concentration and serum IgE concentration from baseline compared with placebo. These markers were near maximal suppression after 2 weeks of

treatment, except for IgE which declined more slowly. These effects were sustained throughout treatment.

In a CRSwNP clinical trial, administration of tezepelumab 210 mg subcutaneously every 4 weeks resulted in reductions of inflammatory biomarkers (blood eosinophils, FeNO [in participants with co-morbid asthma] and serum IgE).

Effect on eosinophils in the airway submucosa
In a clinical trial, administration of tezepelumab 210 mg subcutaneously every 4 weeks reduced submucosal eosinophil counts by 89% compared with a 25% reduction with placebo. Reduction was consistent regardless of baseline inflammatory biomarkers.

Immunogenicity

In patients with asthma (NAVIGATOR), anti-drug antibodies (ADA) were detected at any time in 26 (4.9%) out of 527 patients who received tezepelumab at the recommended dosing regimen during the 52-week study period. Of these 26 patients, 10 patients (1.9% of patients treated with tezepelumab) developed treatment-emergent ADA and 1 patient (0.2% of patients treated with tezepelumab) developed neutralising antibodies. ADA titres 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 6 (4%) out of 164 patients treated with tezepelumab 210 mg subcutaneously every 4 weeks during the 52-week treatment period. Neutralising antibody activity was detected in 1 of the ADA positive patients. While there was no apparent 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.

Clinical efficacy

Asthma

The efficacy of tezepelumab was evaluated in two randomised, double-blind, parallel group, placebo-controlled clinical trials (PATHWAY and NAVIGATOR) of 52 weeks in duration involving a total of 1609 patients aged 12 years and older with severe asthma. In both trials, patients were enrolled without requiring a minimum baseline level of blood eosinophils or other inflammatory biomarkers (e.g. FeNO or IgE).

PATHWAY was a 52-week exacerbation trial which enrolled 550 patients (18 years of age and older) with severe, uncontrolled asthma to receive treatment with tezepelumab 70 mg subcutaneous Q4W, tezepelumab 210 mg subcutaneous Q4W, tezepelumab 280 mg subcutaneous Q2W or placebo. Patients were required to have a history of 2 or more asthma exacerbations requiring oral or systemic corticosteroid treatment or 1 asthma exacerbation resulting in hospitalisation in the past 12 months.

NAVIGATOR was a 52-week exacerbation trial which enrolled a total of 1061 patients (adults and adolescents 12 years of age and older) with severe, uncontrolled asthma to receive treatment with tezepelumab 210 mg subcutaneous Q4W or placebo. Patients were required to have a history of 2 or more asthma exacerbations requiring oral or systemic corticosteroid treatment or resulting in hospitalisation 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 FEV_1 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 control therapy with or without oral corticosteroids (OCS). High ICS dose was defined as > 500 mcg fluticasone propionate or equivalent per day. Medium ICS dose was defined as > 250 to 500 mcg fluticasone propionate or equivalent per

day in PATHWAY and as 500 mcg fluticasone propionate or equivalent per day in NAVIGATOR. Patients continued background asthma therapy throughout the duration of the trials.

The demographics and baseline characteristics of these two trials are provided in Table 2 below.

Table 2 Demographics and baseline characteristics of asthma trials

	PATHWAY N=550	**NAVIGATOR N=1059**
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
Mean duration of asthma, (years) (SD)	17 (12)	22 (16)
Never smoked (%)	81	80
High-dose ICS use (%)	49	75
OCS use (%)	9	9
Mean number of exacerbations in previous year (SD)	2.4 (1.2)	2.8 (1.4)
Mean baseline % predicted FEV_1 (SD)	60 (13)	63 (18)
Mean pre-bronchodilator FEV_1 (L) (SD)	1.9 (0.6)	1.8 (0.7)
Mean post-bronchodilator FEV_1 reversibility (%) (SD)	23 (20)	15 (15)
Mean baseline blood EOS count (cells/µL) (SD)	371 (353)	340 (403)
Blood EOS count ≥ 150 cells/µL (%)	76	74
Positive allergic status (%)[a]	46	64
Mean FeNO (ppb) (SD)	35 (39)	44 (41)
FeNO ≥ 25 ppb (%)	44	59
Mean ACQ-6 (SD)	2.7 (0.8)	2.8 (0.8)
Blood EOS count ≥ 150 cells/µL and FeNO ≥ 25 ppb (%)	38	47

[a] Positive allergic status as defined by a positive serum IgE result specific to any perennial aeroallergen in the FEIA panel.
ACQ-6, Asthma Control Questionnaire 6; 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 summarised below are for the recommended tezepelumab 210 mg subcutaneous Q4W dosing regimen.

Exacerbations

The primary endpoint for PATHWAY and NAVIGATOR was the rate of severe asthma exacerbations measured over 52 weeks. Severe asthma exacerbations were defined as worsening of asthma requiring the use of or increase in oral or systemic corticosteroids for at least 3 days or a single depo-injection of

corticosteroids, and/or emergency department visits requiring use of oral or systemic corticosteroids and/or hospitalisation.

In both PATHWAY and NAVIGATOR, patients receiving tezepelumab had significant reductions in the annualised rate of severe asthma exacerbations compared with placebo (Table 3 and Table 4). There were also fewer exacerbations requiring emergency room visits and/or hospitalisation in patients treated with tezepelumab compared with placebo. In PATHWAY and NAVIGATOR, severe asthma exacerbations requiring emergency room visits and/or hospitalisation were reduced by 85% and 79% with tezepelumab 210 mg subcutaneous Q4W, respectively.

Table 3 Rate of severe exacerbations at week 52 in NAVIGATOR[a]

	Tezepelumab (N=528)	**Placebo (N=531)**
Annualised severe asthma exacerbation rate		
Rate	0.93	2.10
Rate ratio (95% CI)	0.44 (0.37, 0.53)	
p-value	<0.001	

[a] Time at risk is defined as the total duration of time in which a new exacerbation can occur (i.e. total follow-up time minus time during exacerbation and 7 days after).
CI, Confidence interval

Table 4 Rate of severe exacerbations at week 52 in PATHWAY[a]

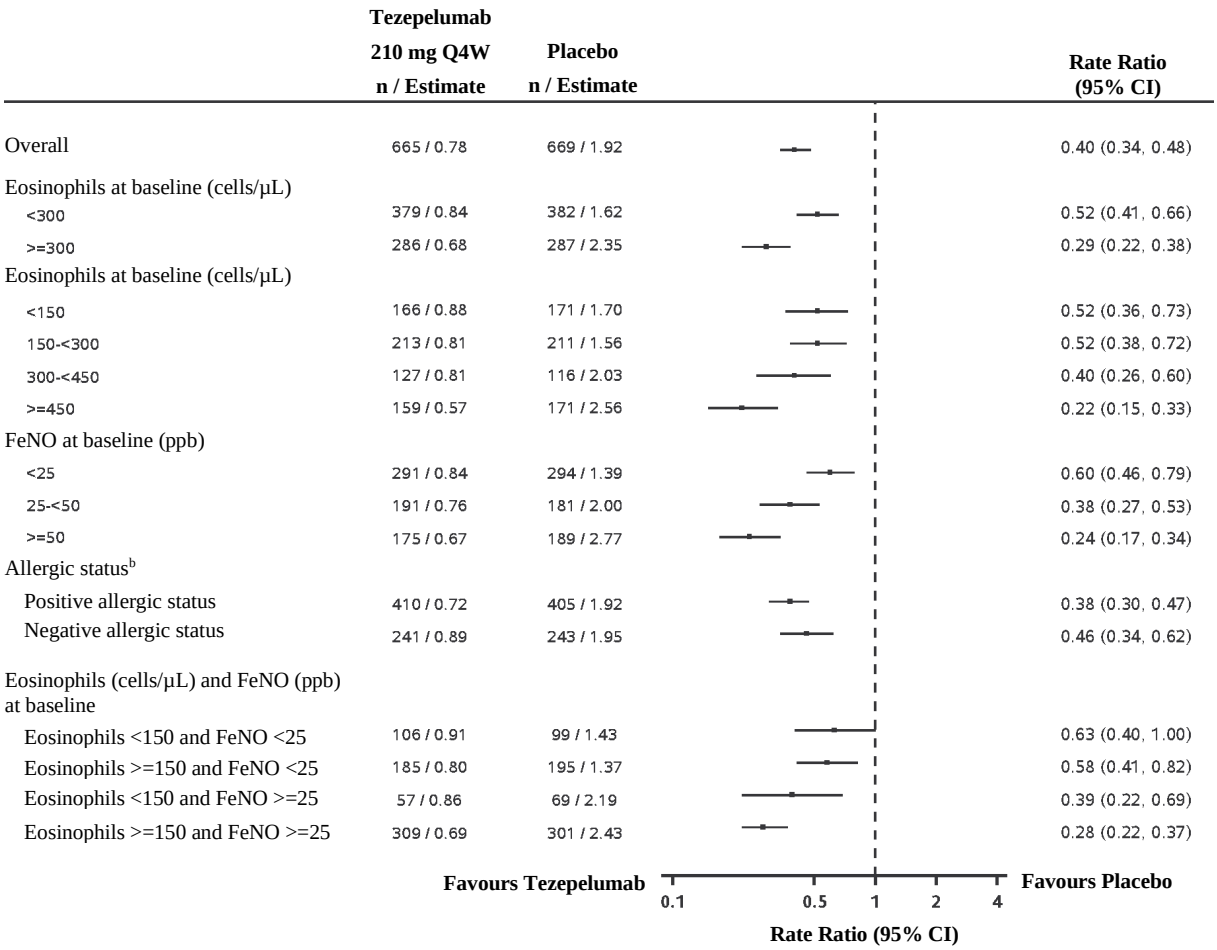
	Tezepelumab (N=137)	**Placebo (N=138)**
Annualised severe asthma exacerbation rate		
Rate	0.20	0.72
Rate ratio (95% CI)	0.29 (0.16, 0.51)	
p-value	<0.001	

[a] Time at risk is defined as the total follow-up time.
CI, Confidence interval

Subgroup analysis
In NAVIGATOR, tezepelumab demonstrated a reduction in the rate of severe asthma exacerbations regardless of the baseline levels of blood eosinophils, FeNO, as well as allergic status (determined by a perennial aeroallergen specific IgE). Similar results were seen in PATHWAY. See Figure 1.

In NAVIGATOR, reductions in the rate of severe asthma exacerbations were greater with increasing baseline blood eosinophil counts and FeNO values (rate ratio = 0.79 [95% CI: 0.48, 1.28] for patients with both baseline blood eosinophil count < 150 cells/µL and baseline FeNO < 25 ppb; rate ratio = 0.30 [95% CI: 0.23, 0.40] for patients with both baseline blood eosinophil count ≥ 150 cells/µL and baseline FeNO ≥ 25 ppb).

Figure 1 **Annualised severe asthma exacerbation rate ratio over 52 weeks across different baseline biomarkers for the Full Analysis Set (pooled NAVIGATOR and PATHWAY)[a]**



[a] Time at risk is defined as the total duration of time in which a new exacerbation can occur (i.e. total follow-up time minus time during exacerbation and 7 days after).
[b] Allergic status as defined by a serum IgE result specific to any perennial aeroallergen in the FEIA panel.

Lung function

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

Patient reported outcomes

Changes from baseline in ACQ-6, Standardised Asthma Quality of Life Questionnaire for ages 12 and older [AQLQ(S)+12] and weekly mean Asthma Symptom Diary (ASD) scores were assessed as secondary endpoints in NAVIGATOR. Severity of wheezing, shortness of breath, cough, and chest tightness were assessed twice daily (morning and evening). Night-time awakening and activity were assessed on a daily basis. The total ASD score was calculated as the mean of 10 items (Table 5).

Improvements in ACQ-6 and AQLQ(S)+12 were seen as early as 2 weeks and 4 weeks after administration of tezepelumab, respectively, and sustained through week 52 in both trials.

Table 5 Results of key secondary endpoints at week 52 in NAVIGATOR[a]

	Tezepelumab	Placebo
Pre-bronchodilator FEV_1		
N	527	531
LS Mean Change from Baseline (L)	0.23	0.10
LS Mean Difference from Placebo (L) (95% CI)	0.13 (0.08, 0.18)	
p-value	<0.001	
AQLQ(S)+12 total score		
N	525	526
LS Mean Change from Baseline	1.48	1.14
Difference from Placebo (95% CI)	0.33 (0.20, 0.47)	
p-value	<0.001	
ACQ-6 score		
N	527	531
LS Mean Change from Baseline	-1.53	-1.20
Difference from Placebo (95% CI)	-0.33 (-0.46, -0.20)	
p-value	<0.001	
ASD		
N	525	531
LS Mean Change from Baseline	-0.70	-0.59
Difference from Placebo (95% CI)	-0.11 (-0.19, -0.04)	
p-value	0.004	

[a] Estimates are derived from a Mixed Model for Repeated Measures (MMRM) using all available data from patients with at least 1 change from baseline value, including data post-discontinuation.
ACQ-6, Asthma Control Questionnaire 6; AQLQ(S)+12, Standardised Asthma Quality of Life Questionnaire for 12 years and older; ASD Asthma Symptom Diary; CI, Confidence interval; FEV_1, Forced expiratory volume in one second; LS, Least square; N, Number of patients contributing to the analysis (FA) with at least 1 change from baseline value

Elderly patients (≥ 65 years of age)
Of the 665 patients with asthma exposed to tezepelumab 210 mg subcutaneous Q4W in PATHWAY and NAVIGATOR, a total of 119 patients were 65 years of age or older, of which 32 patients were 75 years of age or older. Safety in these age groups were similar to the overall study population. Efficacy in these age groups were similar to the overall study population in NAVIGATOR. PATHWAY did not include sufficient numbers of patients aged 65 and over to determine efficacy in this age group.

Chronic rhinosinusitis with nasal polyps (CRSwNP)

The efficacy of tezepelumab was evaluated in a randomised, double-blind, parallel group, multicentre, placebo-controlled trial (WAYPOINT) 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 systemic corticosteroids within the past 12 months and/or any history of sino-nasal surgery, or contraindications/intolerance to either.

Patients received tezepelumab 210 mg or placebo subcutaneously Q4W for 52 weeks in addition to intranasal corticosteroid treatment (e.g. mometasone furoate nasal spray) for CRSwNP.

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

Table 6 Demographics and baseline characteristics of WAYPOINT

	WAYPOINT N=408[a]
Mean age (years) (SD)	50 (14)
Male (%)	65
Mean CRSwNP duration (years) (SD)	13 (10)
Patients with ≥1 prior surgery (%)	71
Patients with systemic corticosteriod use for CRSwNP in the previous year (%)	58
Mean total NPS[b] (SD), range 0-8	6.1 (1.2)
Mean bi-weekly NCS[b, c] (SD), range 0-3	2.6 (0.5)
Mean LMK sinus CT total score[b] (SD), range 0-24	19 (4)
Mean bi-weekly loss of smell[b, d] (SD), range 0-3	2.9 (0.4)
Mean SNOT-22 total score[b] (SD), range 0-110	69 (18)
Mean blood eosinophils (cells/µL) (SD)	360 (235)
Mean total IgE IU/mL (SD)	176 (285)
Asthma/NSAID-ERD/AERD[e] (%)	61
NSAID-ERD/AERD (%)	17
Allergic rhinitis (%)	14

[a] 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.
[b] Higher scores indicate greater disease severity or symptom severity.
[c] Evaluated as part of the Nasal Polyposis Symptom Diary (NPSD).
[d] Evaluated via difficulty with sense of smell score in the NPSD.
[e] 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; SNOT-22, 22-item Sino-Nasal Outcome Test

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 as part of the Nasal Polyposis Symptom Diary (NPSD) at week 52. Total NPS was graded on a categorical scale (0-8). Nasal congestion was rated daily by the patients on a 0 to 3 categorical severity scale. Unadjusted p-values are presented for WAYPOINT.

Patients who received tezepelumab had statistically significant improvements in total NPS and bi-weekly mean NCS at week 52 compared with placebo (see Table 7).

The results for the co-primary and key secondary endpoints in WAYPOINT are presented in Table 7.

Table 7 Results of co-primary and key secondary endpoints in WAYPOINT

	Tezepelumab (N=203)	Placebo (N=205)	p-value[a]
Co-primary endpoints			
NPS at week 52			
Baseline Mean	6.1	6.1	
LS Mean Change	-2.46	-0.38	
LS Mean Difference vs. Placebo (95% CI)	-2.08 (-2.40, -1.76)		<0.0001
NCS at week 52			
Baseline Mean	2.59	2.55	
LS Mean Change	-1.74	-0.70	
LS Mean Difference vs. Placebo (95% CI)	-1.04 (-1.21, -0.87)		<0.0001
Key secondary endpoints			
Loss of smell[b] at week 52			
Baseline Mean	2.9	2.8	
LS Mean Change	-1.26	-0.26	
LS Mean Difference vs. Placebo (95% CI)	-1.01 (-1.18, -0.83)		<0.0001
SNOT-22 at week 52			
Baseline Mean	68.2	69.2	
LS Mean Change	-45.02	-17.58	
LS Mean Difference vs. Placebo (95% CI)	-27.44 (-32.51, -22.37)		<0.0001
Lund Mackay score (LMK) at week 52			
Baseline Mean	18.9	18.5	
LS Mean Change	-6.27	-0.57	
LS Mean Difference vs. Placebo (95% CI)	-5.70 (-6.37, -5.03)		<0.0001
Time to first sino-nasal surgery decision and/or SCS for CRSwNP up to week 52			
Proportion of Patients (%)[c]	5.7	31.4	
% Reduction vs. Placebo [Hazard ratio (95% CI)]	92% [0.08 (0.03, 0.16)]		<0.0001
Time to first sino-nasal surgery decision up to week 52			
Proportion of Patients (%)[c]	0.5	22.0	
% Reduction vs. Placebo [Hazard ratio (95% CI)]	98% [0.02 (0.00, 0.09)]		<0.0001
Time to first SCS use for CRSwNP up to week 52			
Proportion of Patients (%)[c]	5.2	19.3	
% Reduction vs. Placebo [Hazard ratio (95% CI)]	89% [0.11 (0.04, 0.25)]		<0.0001
Total Symptom Score (TSS) at week 52			
Baseline Mean	16.3	16.4	
LS Mean Change	-10.39	-3.43	
LS Mean Difference vs. Placebo (95% CI)	-6.96 (-8.09, -5.83)		<0.0001

[a] Unadjusted p-values are presented. Statistically significant after multiplicity adjustment.
[b] Change from baseline in loss of smell evaluated as bi-weekly mean difficulty with sense of smell item score in the NPSD.
[c] Kaplan–Meier estimates for the proportion of patients with events.
CRSwNP, Chronic rhinosinusitis with nasal polyps; CI, Confidence interval; LS mean change, Least squared mean change from baseline; reduction in score indicates improvement; NCS, Nasal congestion score; NPS, Nasal polyp score; SCS, Systemic corticosteroids; SD, Standard deviation; SNOT-22, 22-item Sino-Nasal Outcome Test.

Figure 2 LS mean change from baseline in total nasal polyp score (NPS) and bi-weekly mean nasal congestion score (NCS) up to week 52

Figure 2a. Total NPS

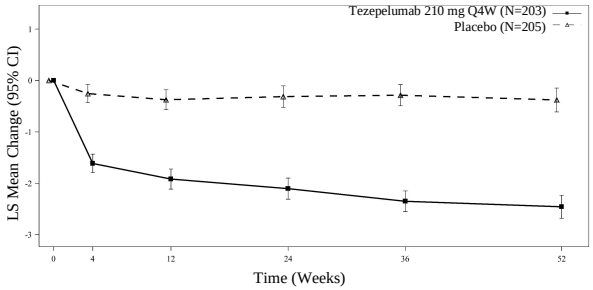
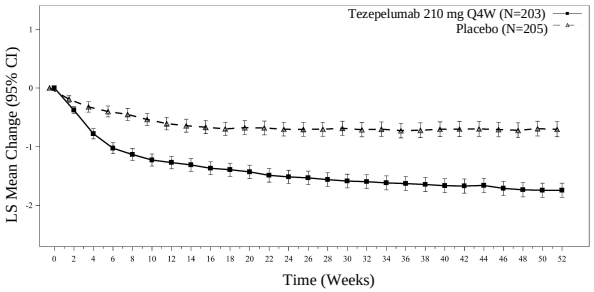


Figure 2b. Bi-weekly mean NCS



Improvement in loss of smell in patients treated with tezepelumab compared with those treated with placebo was seen as early as the first assessment at 2 weeks.

Paediatric population

Asthma

A total of 82 adolescents aged 12 to 17 with severe, uncontrolled asthma were enrolled in NAVIGATOR and received treatment with tezepelumab (n=41) or placebo (n=41). Of the 41 adolescents receiving treatment with tezepelumab, 15 were taking high-dose ICS at baseline. The annualised asthma exacerbation rate observed in adolescents treated with tezepelumab was 0.68 versus 0.97 for placebo (rate ratio 0.70; 95% CI 0.34, 1.46). The LS mean change from baseline for FEV_1 observed in adolescents treated with tezepelumab was 0.44 L versus 0.27 L for placebo (LS mean difference 0.17 L; 95% CI -0.01, 0.35). The pharmacodynamic responses in adolescents were generally similar to the overall study population.

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

CRSwNP

The European Medicines Agency has waived the obligation to submit the results of studies with Tezspire in all subsets of the paediatric population in CRSwNP (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

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

The pharmacokinetics of tezepelumab were dose-proportional following subcutaneous administration over a dose range of 2.1 mg to 420 mg.

Absorption

Following a single 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 were 3.9 L and 2.2 L, respectively, for a 70 kg individual.

Metabolism

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

Elimination

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

Special populations

Age, gender, race
Based on population pharmacokinetic analysis, age, gender and race had no clinically meaningful effects on the pharmacokinetics of tezepelumab.

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.

Paediatric patients
Based on the population pharmacokinetic analysis, there was no clinically meaningful age-related difference in the pharmacokinetics of tezepelumab between adults and adolescents aged 12 to 17 years with asthma. Tezepelumab has not been studied in children under 12 years of age for the treatment of asthma or in children under 18 years of age for the treatment of CRSwNP (see section 4.2).

Elderly patients (≥65 years of age)
Based on population pharmacokinetic analysis, there was no clinically meaningful difference in the pharmacokinetics of tezepelumab between patients 65 years of age or older and younger patients.

Renal impairment
No formal clinical studies have been conducted to investigate the effect of renal impairment on tezepelumab. Based on population pharmacokinetic analysis, tezepelumab clearance was similar in patients with mild renal impairment (creatinine clearance 60 to < 90 mL/min), moderate renal impairment (creatinine clearance 30 to < 60 mL/min) and those with normal renal function (creatinine clearance ≥ 90 mL/min). Tezepelumab has not been studied in patients with severe renal impairment (creatinine clearance < 30 mL/min); however, tezepelumab is not cleared renally.

Hepatic impairment
No formal clinical studies have been conducted to investigate the effect of hepatic impairment on tezepelumab. IgG monoclonal antibodies are not primarily cleared via hepatic pathway; change in hepatic function is not expected to influence tezepelumab clearance. Based on population

pharmacokinetic analysis, baseline hepatic function biomarkers (ALT, AST, and bilirubin) had no effect on tezepelumab clearance.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on repeated dose toxicity studies including safety pharmacology and fertility evaluations, and an ePPND (enhanced Pre- and Post-Natal Development) reproductive toxicity study in cynomolgus monkeys at doses of up to 300 mg/kg/week (producing exposures of greater than 100-times the clinical exposure at maximum recommended human dose [MRHD]).

Tezepelumab is excreted in milk in monkeys, although at low concentrations (< 1%).

Tezepelumab is a monoclonal antibody, as such genotoxicity and carcinogenicity studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid (E 260)
L-proline
Polysorbate 80 (E 433)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

Tezspire may be kept at room temperature (20°C - 25°C) for a maximum of 30 days. After removal from the refrigerator, Tezspire must be used within 30 days or discarded.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). For storage after removal from refrigeration, see section 6.3.
Keep the pre-filled syringe or pre-filled pen in the outer carton in order to protect from light.
Do not freeze. Do not shake. Do not expose to heat.

6.5 Nature and contents of container

<u>Pre-filled syringe</u>

1.91 mL solution in a siliconised Type I glass pre-filled syringe subassembly consisting of a 27-gauge ½-inch (12.7 mm) stainless steel special thin wall needle covered with a rigid needle cover and bromobutyl plunger-stopper. The pre-filled syringe subassembly is assembled with a needle guard and an extended finger flange.

Pack sizes:
Pack containing 1 pre-filled syringe.
Multipack containing 3 (3 packs of 1) pre-filled syringes.

Pre-filled pen

1.91 mL solution in a siliconised Type I glass pre-filled syringe subassembly consisting of a 27-gauge ½-inch (12.7 mm) stainless steel special thin wall needle covered with a needle cover and plunger-stopper. The pre-filled pen consists of the pre-filled syringe subassembly and handheld, mechanical (spring-based) injection device.

Pack sizes:
Pack containing 1 pre-filled pen.
Multipack containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product is for single-use only.

Prior to administration, remove carton from refrigerator and allow Tezspire to reach room temperature. This generally takes 60 minutes.

Visually inspect Tezspire for particulate matter and discolouration prior to administration. Tezspire is clear to opalescent, colourless to light yellow. Do not use this medicinal product if liquid is cloudy, discoloured, or if it contains large particles or foreign particulate matter.

Additional information and instructions for the preparation and administration of Tezspire using the pre-filled syringe or pre-filled pen are given in the package leaflet and 'Instructions for Use'.

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

7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/001	1 pre-filled syringe
EU/1/22/1677/002	Multipack: 3 (3 packs of 1) pre-filled syringes
EU/1/22/1677/003	1 pre-filled pen
EU/1/22/1677/004	Multipack 3 (3 packs of 1) pre-filled pens

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 September 2022

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Amgen Inc. (Amgen Thousand Oaks or ATO)
One Amgen Centre Drive
Thousand Oaks
California 91320
United States

Immunex Rhode Island Corporation (referred to as Amgen Rhode Island or ARI)
40 Technology Way
West Greenwich
Rhode Island 02817
United States

Name and address of the manufacturer responsible for batch release

AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

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

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

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

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

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

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;

- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled syringe
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/001 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR PRE-FILLED SYRINGE MULTIPACK – WITH BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled syringe
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
Multipack: 3 (3 packs of 1) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/002 Multipack: 3 (3 packs of 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON FOR PRE-FILLED SYRINGE MULTIPACK – WITHOUT BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled syringe
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/002 Multipack: 3 (3 packs of 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

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

Tezspire 210 mg injection
tezepelumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.91 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled pen
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/003 1 pre-filled pen

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR PRE-FILLED PEN MULTIPACK – WITH BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled pen
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
Multipack 3 (3 packs of 1) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/004 Multipack 3 (3 packs of 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON FOR PRE-FILLED PEN MULTIPACK – WITHOUT BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Tezspire 210 mg solution for injection in pre-filled pen
tezepelumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 210 mg of tezepelumab in 1.91 mL solution (110 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: acetic acid, L-proline, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled pen. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Open Here
For single use only

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1677/004 Multipack 3 (3 packs of 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

tezspire 210 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

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

Tezspire 210 mg injection
tezepelumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.91 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Tezspire 210 mg solution for injection in pre-filled syringe
tezepelumab

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

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

What is in this leaflet

1. What Tezspire is and what it is used for
2. What you need to know before you use Tezspire
3. How to use Tezspire
4. Possible side effects
5. How to store Tezspire
6. Contents of the pack and other information

1. What Tezspire is and what it is used for

What Tezspire is and how it works
Tezspire contains the active substance tezepelumab, which is a monoclonal antibody. Antibodies are proteins that recognise and bind to a specific target substance in the body, which in the case of tezepelumab is a protein called *thymic stromal lymphopoietin* (TSLP). TSLP plays a key role in causing the inflammation in your airways that leads to the signs and symptoms of asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). By blocking the action of TSLP, this medicine helps to reduce inflammation and symptoms of asthma and CRSwNP.

What Tezspire is used for
Asthma
Tezspire is used with other asthma medicines to treat severe asthma in adults and adolescents (12 years of age and older) when the disease is not controlled with their current asthma medicines.

CRSwNP
Tezspire is also used with other medicines to treat CRSwNP in adults.

How Tezspire can help
Asthma
Tezspire may reduce the number of asthma attacks you experience, improve your breathing and reduce your asthma symptoms.

CRSwNP
Tezspire may reduce the size of your polyps and improves symptoms including nasal congestion and loss of smell. Tezspire may also reduce the need for oral corticosteroids and surgery.

2. What you need to know before you use Tezspire

Do not use Tezspire

- **if you are allergic** to tezepelumab or any of the other ingredients of this medicine (listed in section 6). If this applies to you, or if you are not sure, **check with your doctor, pharmacist or nurse**.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Tezspire.

- Tezspire is **not a rescue medicine.** Do not use it to treat a sudden asthma attack.

- **If your asthma is not getting any better, or it gets worse** during treatment with this medicine, **talk to a doctor or nurse**.

- **Look out for signs of allergic reactions.** Medicines like Tezspire can potentially cause serious allergic reactions in some people. The signs of these reactions may vary, but can include swelling of your face, tongue or mouth, breathing problems, fast heartbeat, fainting, dizziness, feeling lightheaded, hives and rash. If you notice any of these signs, **speak to a doctor or nurse immediately**.

  Talk to your doctor about how to recognise early signs of allergy, and how to manage reactions if they occur.

- **Look out for any signs of a possible serious infection** while you are taking Tezspire such as:
  - fever, flu-like symptoms, night sweats;
  - cough which will not go away;
  - warm, red and painful skin, or a painful skin rash with blisters.

  If you notice any of these signs, **speak to a doctor or nurse immediately.**

  If you already have a serious infection, talk to your doctor before taking Tezspire.

- **Look out for any symptoms of a heart problem**, such as:
  - chest pain;
  - shortness of breath;
  - a general feeling of discomfort, illness, or lack of well-being;
  - feeling lightheaded or faint.

  If you notice any of these symptoms, **speak to a doctor or nurse immediately**.

- **If you have a parasitic infection** or if you live in (or travel to) an area where parasitic infections are common, **talk to your doctor**. Tezspire may weaken your body's ability to fight certain types of parasitic infections.

Each time you get a new pack of Tezspire

- Write down the name and the Lot number shown on the outer carton and the label of the pre-filled syringe, and keep this information in a safe place. You may be asked for this information in the future.

Children

Asthma

Do not give this medicine to children under 12 years of age for the treatment of asthma because the safety and benefits of this medicine are not known in children in this age group.

CRSwNP
Do not give this medicine to children under 18 years of age for the treatment of CRSwNP because the safety and benefits of this medicine are not known in children in this age group.

Other medicines for asthma
- **Do not suddenly stop taking** your other asthma medicines when you start Tezspire. This is especially important if you take steroids (also called corticosteroids). These medicines must be stopped gradually, under the supervision of your doctor and based on your response to Tezspire.

Other medicines and Tezspire
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might use any other medicines.
- if you have recently had or are due to have a vaccination.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
- Do not use Tezspire during pregnancy unless your doctor advises it. It is not known if Tezspire can harm your unborn baby.
- Tezspire may pass into breast milk. If you are breast-feeding or plan to breast-feed, talk to your doctor.

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

Tezspire contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 210 mg dose, that is to say essentially 'sodium-free'.

Tezspire contains L-proline
This medicine contains 48 mg of L-proline per 210 mg dose which is equivalent to 25 mg/mL. L-proline may be harmful for patients with hyperprolinaemia, a rare genetic disorder in which L-proline builds up in the body. Tell your doctor if you or your child have hyperprolinaemia, and do not use this medicine unless your doctor has recommended it.

Tezspire contains polysorbate
This medicine contains 0.19 mg of polysorbate 80 per 210 mg dose, which is equivalent to 0.1 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you or your child has any known allergies.

3. How to use Tezspire

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

Tezspire is given as an injection under the skin (subcutaneously).

Asthma
Adults and adolescents aged 12 years and over:
- **The recommended dose** is 210 mg (1 injection) every 4 weeks.

CRSwNP
Adults aged 18 years and over:
- **The recommended dose** is 210 mg (1 injection) every 4 weeks.

Your doctor or nurse will decide if you can inject yourself or if your caregiver can do that for you. If so, you or your caregiver will receive training on the right way to prepare and inject Tezspire.

Before injecting Tezspire yourself, carefully read the 'Instructions for Use' for Tezspire pre-filled syringe. Do this each time you get another injection. There may be new information.

Do not share Tezspire pre-filled syringes or use a syringe more than one time.

If you forget to use Tezspire
- If you have forgotten to inject a dose, inject a dose as soon as possible. Then have your next injection on your next scheduled injection day.
- If you did not notice that you missed a dose until it is time for your next dose, simply inject the next dose as scheduled. **Do not inject a double dose to make up for a forgotten dose.**
- If you are not sure when to inject Tezspire, ask your doctor, pharmacist or nurse.

If you stop using Tezspire
- Do not stop using Tezspire without speaking first to your doctor, pharmacist or nurse. Interrupting or stopping the treatment with Tezspire may cause your symptoms or attacks to come back.

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

4. Possible side effects

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

Serious allergic reactions

Seek medical attention immediately if you think you may be having an allergic reaction. Such reactions may happen within hours or days after the injection.

Not known (the frequency cannot be estimated from the available data)
- allergic reactions, including serious allergic reaction (anaphylaxis)
  symptoms usually include:
  - swelling of your face, tongue, or mouth
  - breathing problems, fast heartbeat
  - fainting, dizziness, feeling lightheaded

Other side effects

Common (these may affect up to 1 in 10 people)
- sore throat
- rash
- joint pain
- injection site reaction (such as redness, swelling, and pain)

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

5. How to store Tezspire

- Keep this medicine out of the sight and reach of children.
- Do not use after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C).
- Keep the pre-filled syringe in the outer carton in order to protect from light.
- Tezspire may be kept at room temperature (20°C to 25°C) in the outer carton for a maximum of 30 days. Once Tezspire has reached room temperature, do not put it back in the refrigerator. Tezspire that has been stored at room temperature for more than 30 days should be safely disposed of.
- Do not shake, freeze or expose to heat.
- Do not use this medicine if it has been dropped or damaged, or if the security seal on the carton has been broken.

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

6. Contents of the pack and other information

What Tezspire contains
- The active substance is tezepelumab.
- The other ingredients are acetic acid (E 260), L-proline, polysorbate 80 (E 433), sodium hydroxide, and water for injections.

What Tezspire looks like and contents of the pack
Tezspire is a clear to opalescent, colourless to light yellow solution.

Tezspire is available in a pack containing 1 single-use pre-filled syringe or in a multipack containing 3 (3 packs of 1) pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
AstraZeneca AB
SE-151 85 Södertälje
Sweden

Manufacturer
AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

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

België/Belgique/Belgien	**Lietuva**
AstraZeneca S.A./N.V.	UAB AstraZeneca Lietuva

Tel: +32 2 370 48 11

България
АстраЗенека България ЕООД
Тел.: +359 24455000

Česká republika
AstraZeneca Czech Republic s.r.o.
Tel: +420 222 807 111

Danmark
AstraZeneca A/S
Tlf.: +45 43 66 64 62

Deutschland
AstraZeneca GmbH
Tel: +49 40 809034100

Eesti
AstraZeneca
Tel: +372 6549 600

Ελλάδα
AstraZeneca A.E.
Τηλ: +30 210 6871500

España
AstraZeneca Farmacéutica Spain, S.A.
Tel: +34 91 301 91 00

France
AstraZeneca
Tél: +33 1 41 29 40 00

Hrvatska
AstraZeneca d.o.o.
Tel: +385 1 4628 000

Ireland
AstraZeneca Pharmaceuticals (Ireland) DAC
Tel: +353 1609 7100

Ísland
Vistor
Sími: +354 535 7000

Italia
AstraZeneca S.p.A.
Tel: +39 02 00704500

Κύπρος
Αλέκτωρ Φαρμακευτική Λτδ
Τηλ: +357 22490305

Latvija
SIA AstraZeneca Latvija
Tel: +370 5 2660550

Luxembourg/Luxemburg
AstraZeneca S.A./N.V.
Tél/Tel: +32 2 370 48 11

Magyarország
AstraZeneca Kft.
Tel.: +36 1 883 6500

Malta
Associated Drug Co. Ltd
Tel: +356 2277 8000

Nederland
AstraZeneca BV
Tel: +31 85 808 9900

Norge
AstraZeneca AS
Tlf: +47 21 00 64 00

Österreich
AstraZeneca Österreich GmbH
Tel: +43 1 711 31 0

Polska
AstraZeneca Pharma Poland Sp. z o.o.
Tel.: +48 22 245 73 00

Portugal
AstraZeneca Produtos Farmacêuticos, Lda.
Tel: +351 21 434 61 00

România
AstraZeneca Pharma SRL
Tel: +40 21 317 60 41

Slovenija
AstraZeneca UK Limited
Tel: +386 1 51 35 600

Slovenská republika
AstraZeneca AB, o.z.
Tel: +421 2 5737 7777

Suomi/Finland
AstraZeneca Oy
Puh/Tel: +358 10 23 010

Sverige
AstraZeneca AB
Tel: +46 8 553 26 000

Tel: +371 67377100

This leaflet was last revised in

Other sources of information

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

Instructions for Use

Tezspire 210 mg solution for injection in pre-filled syringe
tezepelumab

This 'Instructions for Use' contains information on how to inject Tezspire.
Before you use your Tezspire pre-filled syringe, 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 syringe and each time you get another injection. 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 2°C to 8°C in its outer carton until you are ready to use it. Tezspire may be kept at room temperature between 20°C to 25°C in the outer carton for a maximum of 30 days.
Once 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 (see Step 10).

Do not use your Tezspire pre-filled syringe if:

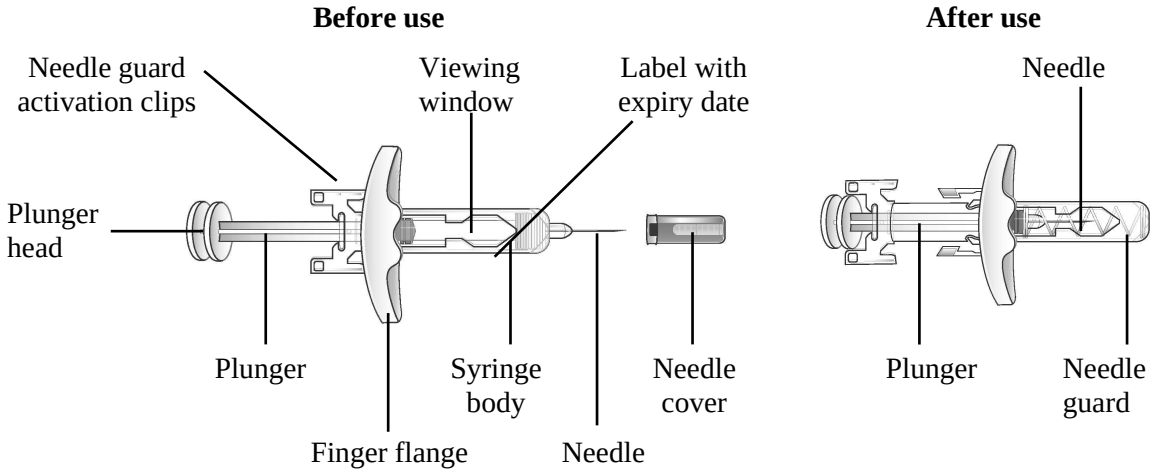
- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiry date (EXP) has passed

Do not shake your pre-filled syringe.
Do not share your pre-filled syringe or use it more than 1 time.
Do not expose your Tezspire pre-filled syringe to heat.

If any of the above happens, throw away the syringe in a puncture-resistant (sharps) container and use a new Tezspire pre-filled syringe.
Each Tezspire pre-filled syringe contains 1 dose of Tezspire that can only be used 1 time.
Keep Tezspire pre-filled syringe and all medicines out of the sight and reach of children.
Tezspire is given only as an injection under the skin (subcutaneous).

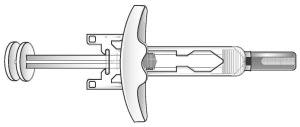
Your Tezspire pre-filled syringe

Do not remove the needle cover until Step 7 of these instructions when you are ready to inject Tezspire.
Do not touch the needle guard activation clips. This will keep you from activating the safety device (needle guard) too soon.



Preparing to inject Tezspire
Step 1 – Gather supplies

- 1 Tezspire pre-filled syringe 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 syringe safely.



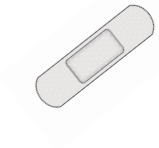
Pre-filled syringe



Alcohol wipe



Cotton ball or gauze



Bandage



Sharps disposal container

Step 2 – Prepare to use your Tezspire pre-filled syringe

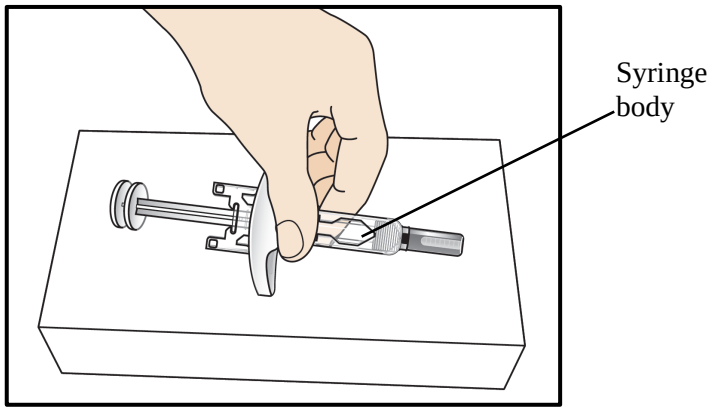
Let Tezspire come to room temperature between 20°C to 25°C for about 60 minutes or longer (up to a maximum of 30 days) before giving the injection.
Keep the pre-filled syringe in the outer carton in order to protect from light.
Do not warm the pre-filled syringe in any other way. For example, **do not** warm it in a microwave or hot water, in direct sunlight, or near other heat sources.



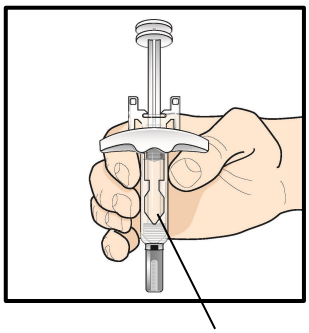
Do not put Tezspire back in the refrigerator after it has reached room temperature. Throw away (dispose of) Tezspire that has been stored at room temperature for more than 30 days.
Do not remove the needle cover until Step 7.

Step 3 – Remove pre-filled syringe

Grab the syringe body to remove the pre-filled syringe from its carton. **Do not** grab the pre-filled syringe by the plunger.

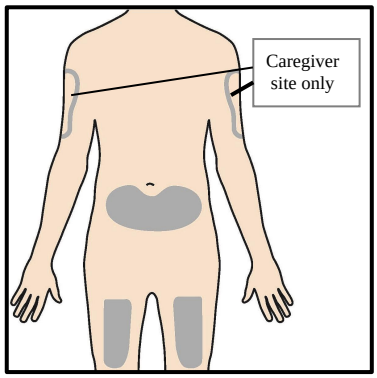


Step 4 – Check the pre-filled syringe



Check the pre-filled syringe for damage. Do not use the pre-filled syringe if the pre-filled syringe is damaged.
Check the expiry date on the pre-filled syringe. **Do not** use the pre-filled syringe if the expiry date has passed.
Look at the liquid through the viewing window. The liquid should be clear and colourless to light yellow.
Do not inject Tezspire if the liquid is cloudy, discoloured, 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 5 – Choose an injection site

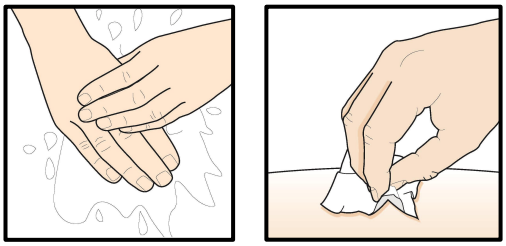


If you are giving yourself the injection, the **recommended injection site** is the front of your thigh or the lower part of your stomach (abdomen). **Do not** inject yourself in the arm.
A caregiver may inject you in the upper arm, thigh, or abdomen.
For each injection, choose a different site that is at least 3 cm away from where you last injected.
Do not inject:

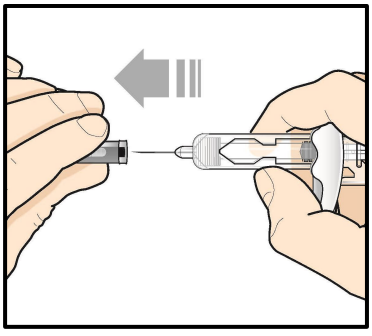
- into the 5 cm area around your belly button
- where the skin is tender, bruised, scaly or hard
- into scars or damaged skin
- through clothing

Step 6 – 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.



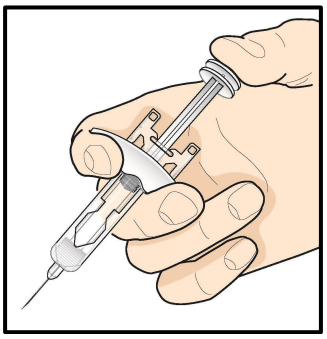
Step 7 – Pull off the needle cover

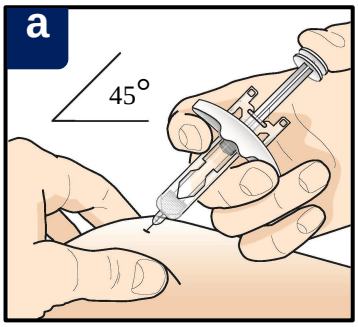


Do not remove the needle cover until you are ready to inject.
Hold the syringe body with 1 hand, and carefully pull the needle cover straight off with your other hand.
Do not hold the plunger or plunger head while removing the needle cover.
Put the needle cover to the side and throw it away later.
You may see a drop of liquid at the end of the needle. This is normal.
Do not touch the needle or let it touch any surface.
Do not put the needle cover back on the syringe.

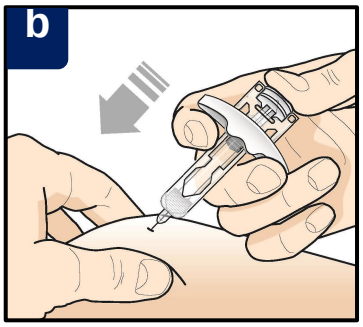
Step 8 – Inject Tezspire

Hold the pre-filled syringe in 1 hand as shown.
Use your other hand to gently pinch and hold the area of skin where you want to inject. This will make the skin firmer.
Do not press down on the plunger head until the needle is inserted into the skin.
Do not pull back on the plunger head at any time.
Inject Tezspire by following the steps in figures **a**, **b** and **c**.

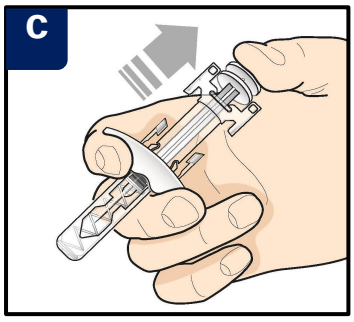




Using a 45 degree angle, fully insert the needle into the pinched skin.
Do not try to change the position of the pre-filled syringe after you insert it into the skin.



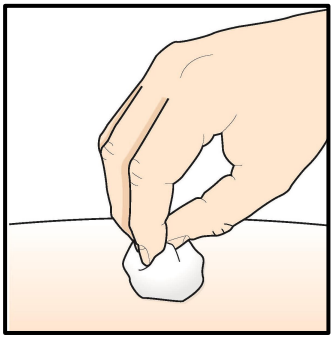
Use your thumb to push down on the plunger head.
Keep pushing until it is down as far as it will go to make sure you inject all of the medicine.



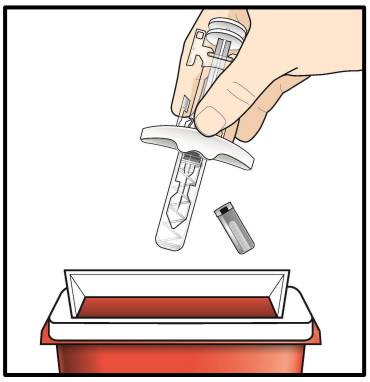
Keep your thumb pressed down on the plunger head as you take the needle out of the skin.
Slowly let go of the plunger until the needle guard covers the needle.

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 syringe safely



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

Disposal guidelines

Dispose of the full container as instructed by your healthcare provider or pharmacist.

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.

Package leaflet: Information for the patient

Tezspire 210 mg solution for injection in pre-filled pen
tezepelumab

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

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

What is in this leaflet

1. What Tezspire is and what it is used for
2. What you need to know before you use Tezspire
3. How to use Tezspire
4. Possible side effects
5. How to store Tezspire
6. Contents of the pack and other information

1. What Tezspire is and what it is used for

What Tezspire is and how it works
Tezspire contains the active substance tezepelumab, which is a monoclonal antibody. Antibodies are proteins that recognise and bind to a specific target substance in the body, which in the case of tezepelumab is a protein called *thymic stromal lymphopoietin* (TSLP). TSLP plays a key role in causing the inflammation in your airways that leads to the signs and symptoms of asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). By blocking the action of TSLP, this medicine helps to reduce inflammation and symptoms of asthma and CRSwNP.

What Tezspire is used for
Asthma
Tezspire is used with other asthma medicines to treat severe asthma in adults and adolescents (12 years of age and older) when the disease is not controlled with their current asthma medicines.

CRSwNP
Tezspire is also used with other medicines to treat CRSwNP in adults.

How Tezspire can help
Asthma
Tezspire may reduce the number of asthma attacks you experience, improve your breathing and reduce your asthma symptoms.

CRSwNP
Tezspire may reduce the size of your polyps and improves symptoms including nasal congestion and loss of smell. Tezspire may also reduce the need for oral corticosteroids and surgery.

2. What you need to know before you use Tezspire

Do not use Tezspire

- **if you are allergic** to tezepelumab or any of the other ingredients of this medicine (listed in section 6). If this applies to you, or if you are not sure, **check with your doctor, pharmacist or nurse**.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Tezspire.

- Tezspire is **not a rescue medicine.** Do not use it to treat a sudden asthma attack.

- **If your asthma is not getting any better, or it gets worse** during treatment with this medicine, **talk to a doctor or nurse**.

- **Look out for signs of allergic reactions.** Medicines like Tezspire can potentially cause serious allergic reactions in some people. The signs of these reactions may vary, but can include swelling of your face, tongue, or mouth, breathing problems, fast heartbeat, fainting, dizziness, feeling lightheaded, hives and rash. If you notice any of these signs, **speak to a doctor or nurse immediately**.

  Talk to your doctor about how to recognise early signs of allergy, and how to manage reactions if they occur.

- **Look out for any signs of a possible serious infection** while you are taking Tezspire such as:
  - fever, flu-like symptoms, night sweats;
  - cough which will not go away;
  - warm, red and painful skin, or a painful skin rash with blisters.

  If you notice any of these signs, **speak to a doctor or nurse immediately.**

  If you already have a serious infection, talk to your doctor before taking Tezspire.

- **Look out for any symptoms of a heart problem**, such as:
  - chest pain;
  - shortness of breath;
  - a general feeling of discomfort, illness, or lack of well-being;
  - feeling lightheaded or faint.

  If you notice any of these symptoms, **speak to a doctor or nurse immediately**.

- **If you have a parasitic infection** or if you live in (or travel to) an area where parasitic infections are common, **talk to your doctor**. Tezspire may weaken your body's ability to fight certain types of parasitic infections.

Each time you get a new pack of Tezspire

- Write down the name and the Lot number shown on the outer carton and the label of the pre-filled pen, and keep this information in a safe place. You may be asked for this information in the future.

Children

Asthma

Do not give this medicine to children under 12 years of age for the treatment of asthma because the safety and benefits of this medicine are not known in children in this age group.

CRSwNP
Do not give this medicine to children under 18 years of age for the treatment of CRSwNP because the safety and benefits of this medicine are not known in children in this age group.

Other medicines for asthma
- **Do not suddenly stop taking** your other asthma medicines when you start Tezspire. This is especially important if you take steroids (also called corticosteroids). These medicines must be stopped gradually, under the supervision of your doctor and based on your response to Tezspire.

Other medicines and Tezspire
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might use any other medicines.
- if you have recently had or are due to have a vaccination.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
- Do not use Tezspire during pregnancy unless your doctor advises it. It is not known if Tezspire can harm your unborn baby.
- Tezspire may pass into breast milk. If you are breast-feeding or plan to breast-feed, talk to your doctor.

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

Tezspire contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 210 mg dose, that is to say essentially 'sodium-free'.

Tezspire contains L-proline
This medicine contains 48 mg of L-proline per 210 mg dose which is equivalent to 25 mg/mL. L-proline may be harmful for patients with hyperprolinaemia, a rare genetic disorder in which L-proline builds up in the body. Tell your doctor if you or your child have hyperprolinaemia, and do not use this medicine unless your doctor has recommended it.

Tezspire contains polysorbate
This medicine contains 0.19 mg of polysorbate 80 per 210 mg dose, which is equivalent to 0.1 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you or your child has any known allergies.

3. How to use Tezspire

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

Tezspire is given as an injection under the skin (subcutaneously).

Asthma
Adults and adolescents aged 12 years and over:
- **The recommended dose** is 210 mg (1 injection) every 4 weeks.

CRSwNP
Adults aged 18 years and over:
- **The recommended dose** is 210 mg (1 injection) every 4 weeks.

Your doctor or nurse will decide if you can inject yourself or if your caregiver can do that for you. If so, you or your caregiver will receive training on the right way to prepare and inject Tezspire.

Before injecting Tezspire yourself, carefully read the 'Instructions for Use' for Tezspire pre-filled pen. Do this each time you get another injection. There may be new information.

Do not share Tezspire pre-filled pen or use a pen more than one time.

If you forget to use Tezspire
- If you have forgotten to inject a dose, inject a dose as soon as possible. Then have your next injection on your next scheduled injection day.
- If you did not notice that you missed a dose until it is time for your next dose, simply inject the next dose as scheduled. **Do not inject a double dose to make up for a forgotten dose.**
- If you are not sure when to inject Tezspire, ask your doctor, pharmacist or nurse.

If you stop using Tezspire
- Do not stop using Tezspire without speaking first to your doctor, pharmacist or nurse. Interrupting or stopping the treatment with Tezspire may cause your symptoms or attacks to come back.

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

4. Possible side effects

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

Serious allergic reactions

Seek medical attention immediately if you think you may be having an allergic reaction. Such reactions may happen within hours or days after the injection.

Not known (the frequency cannot be estimated from the available data)
- allergic reactions, including serious allergic reaction (anaphylaxis)
  symptoms usually include:
  - swelling of your face, tongue, or mouth
  - breathing problems, fast heartbeat
  - fainting, dizziness, feeling lightheaded

Other side effects

Common (these may affect up to 1 in 10 people)
- sore throat
- rash
- joint pain
- injection site reaction (such as redness, swelling, and pain)

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

5. How to store Tezspire

- Keep this medicine out of the sight and reach of children.
- Do not use after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C).
- Keep the pre-filled pen in the outer carton in order to protect from light.
- Tezspire may be kept at room temperature (20°C to 25°C) in the outer carton for a maximum of 30 days. Once Tezspire has reached room temperature, do not put it back in the refrigerator. Tezspire that has been stored at room temperature for more than 30 days should be safely disposed of.
- Do not shake, freeze or expose to heat.
- Do not use this medicine if it has been dropped or damaged, or if the security seal on the carton has been broken.

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

6. Contents of the pack and other information

What Tezspire contains
- The active substance is tezepelumab.
- The other ingredients are acetic acid (E 260), L-proline, polysorbate 80 (E 433), sodium hydroxide, and water for injections.

What Tezspire looks like and contents of the pack
Tezspire is a clear to opalescent, colourless to light yellow solution.

Tezspire is available in a pack containing 1 single-use pre-filled pen or in a multipack containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
AstraZeneca AB
SE-151 85 Södertälje
Sweden

Manufacturer
AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

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

België/Belgique/Belgien	**Lietuva**
AstraZeneca S.A./N.V.	UAB AstraZeneca Lietuva

Tel: +32 2 370 48 11

България
АстраЗенека България ЕООД
Тел.: +359 24455000

Česká republika
AstraZeneca Czech Republic s.r.o.
Tel: +420 222 807 111

Danmark
AstraZeneca A/S
Tlf.: +45 43 66 64 62

Deutschland
AstraZeneca GmbH
Tel: +49 40 809034100

Eesti
AstraZeneca
Tel: +372 6549 600

Ελλάδα
AstraZeneca A.E.
Τηλ: +30 210 6871500

España
AstraZeneca Farmacéutica Spain, S.A.
Tel: +34 91 301 91 00

France
AstraZeneca
Tél: +33 1 41 29 40 00

Hrvatska
AstraZeneca d.o.o.
Tel: +385 1 4628 000

Ireland
AstraZeneca Pharmaceuticals (Ireland) DAC
Tel: +353 1609 7100

Ísland
Vistor
Sími: +354 535 7000

Italia
AstraZeneca S.p.A.
Tel: +39 02 00704500

Κύπρος
Αλέκτωρ Φαρμακευτική Λτδ
Τηλ: +357 22490305

Latvija
SIA AstraZeneca Latvija
Tel: +370 5 2660550

Luxembourg/Luxemburg
AstraZeneca S.A./N.V.
Tél/Tel: +32 2 370 48 11

Magyarország
AstraZeneca Kft.
Tel.: +36 1 883 6500

Malta
Associated Drug Co. Ltd
Tel: +356 2277 8000

Nederland
AstraZeneca BV
Tel: +31 85 808 9900

Norge
AstraZeneca AS
Tlf: +47 21 00 64 00

Österreich
AstraZeneca Österreich GmbH
Tel: +43 1 711 31 0

Polska
AstraZeneca Pharma Poland Sp. z o.o.
Tel.: +48 22 245 73 00

Portugal
AstraZeneca Produtos Farmacêuticos, Lda.
Tel: +351 21 434 61 00

România
AstraZeneca Pharma SRL
Tel: +40 21 317 60 41

Slovenija
AstraZeneca UK Limited
Tel: +386 1 51 35 600

Slovenská republika
AstraZeneca AB, o.z.
Tel: +421 2 5737 7777

Suomi/Finland
AstraZeneca Oy
Puh/Tel: +358 10 23 010

Sverige
AstraZeneca AB
Tel: +46 8 553 26 000

Tel: +371 67377100

This leaflet was last revised in

Other sources of information

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

Instructions for Use

Tezspire 210 mg solution for injection in pre-filled pen
tezepelumab

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 another injection. 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 2°C to 8°C in its outer carton until you are ready to use it. Tezspire may be kept at room temperature between 20°C to 25°C in the outer carton for a maximum of 30 days.
Once 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 (see Step 10).

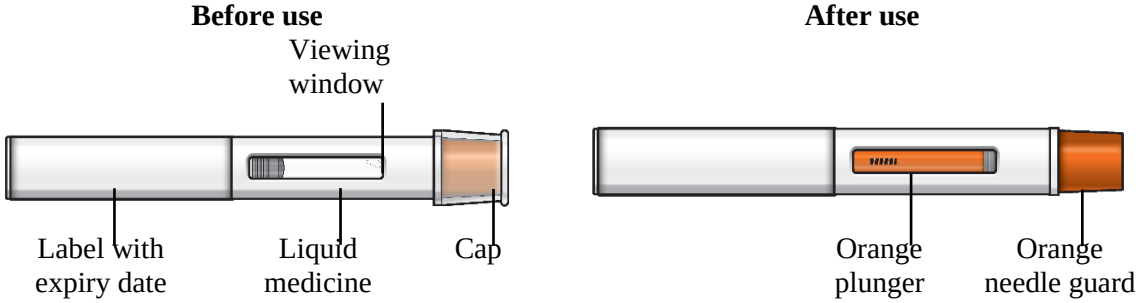
Do not use your Tezspire pre-filled pen if:
- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiry date (EXP) has passed

Do not shake your pre-filled pen.
Do not share your pre-filled pen or use it more than 1 time.
Do not expose your Tezspire pre-filled pen to heat.

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.
Keep Tezspire pre-filled pen and all medicines out of the sight and reach of children.
Tezspire is given only as an injection under the skin (subcutaneous).

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.



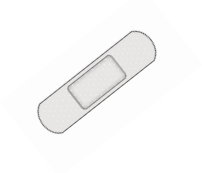
Pre-filled pen



Alcohol wipe



Cotton ball or gauze



Bandage



Sharps disposal container

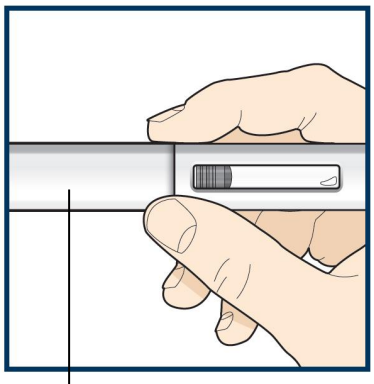
Step 2 – Prepare to use your Tezspire pre-filled pen



Let Tezspire come to room temperature between 20°C to 25°C for about 60 minutes or longer (up to a maximum of 30 days) before giving the injection.
Keep the pre-filled pen in the outer carton in order to protect 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

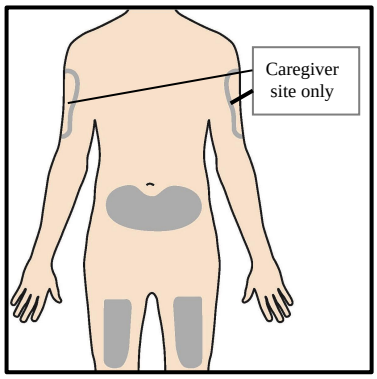
Grab the middle of the pre-filled pen body to remove the pre-filled pen from its carton.
Check the pre-filled pen for damage. Do not use the pre-filled pen if the pre-filled pen is damaged.
Check the expiry date on the pre-filled pen. **Do not** use the pre-filled pen if the expiry date has passed.
Look at the liquid through the viewing window. The liquid should be clear and colourless to light yellow.
Do not inject Tezspire if the liquid is cloudy, discoloured, 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

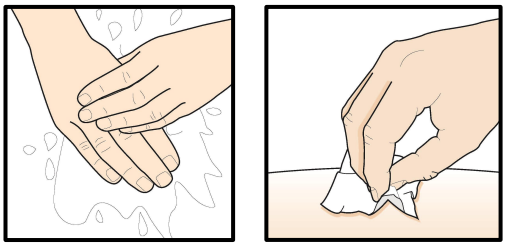
If you are giving yourself the injection, the **recommended injection site** is the front of your thigh or the lower part of your stomach (abdomen). **Do not** inject yourself in the arm.
A caregiver may inject you in the upper arm, thigh, or abdomen.
For each injection, choose a different site that is at least 3 cm away from where you last injected.
Do not inject:

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



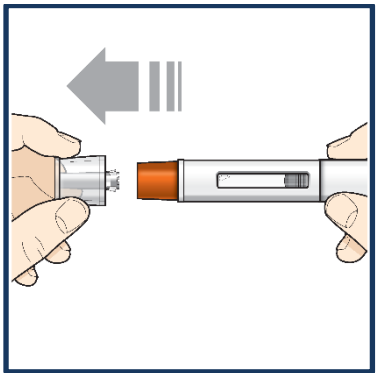
Step 5 – Wash your hands and clean the injection site

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.



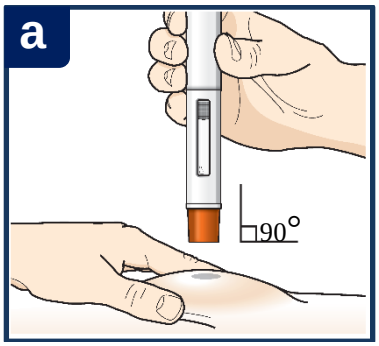
Step 6 – Pull off the cap

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.



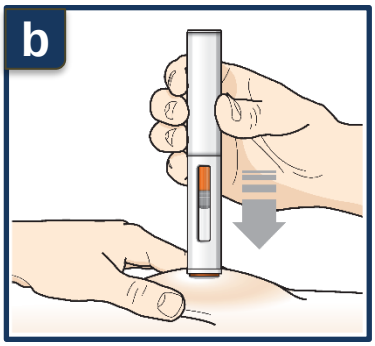
Step 7 – Inject Tezspire

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.



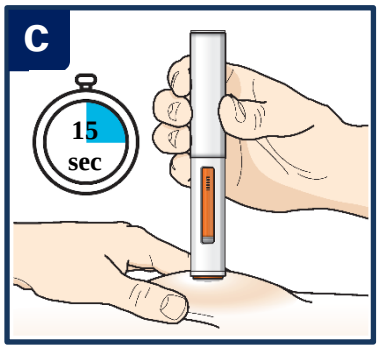
Position the pre-filled pen.

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



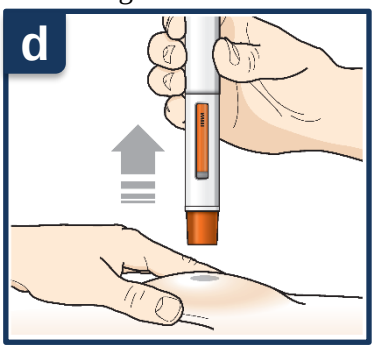
Press down firmly until you cannot see the orange needle guard.

- 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.



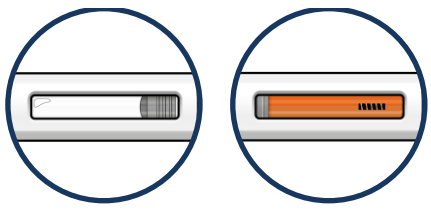
After you have completed your injection, lift the pre-filled pen straight up.

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

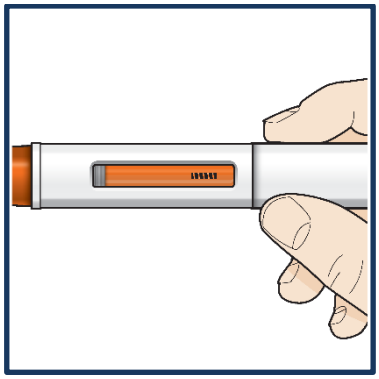
Step 8 – Check the viewing window

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.

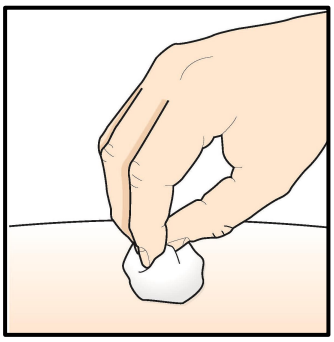
Before injection



After injection

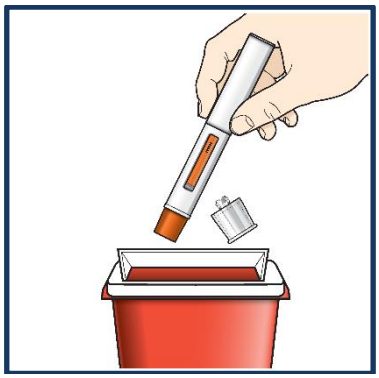


Step 9 – Check the injection site



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.

Disposal guidelines

Dispose of the full container as instructed by your healthcare provider or pharmacist.

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.

CDS

Drug Substance	Tezepelumab
Document Number	[redacted]
Version	[redacted]
Date	[redacted] 20[redacted]
Supersedes	Version [redacted] / [redacted] 20[redacted]

Core Data Sheet
TEZSPIRE, Solution for Injection, 110 mg/mL

[redacted]

[redacted]

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