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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe (injection)

Clear to opalescent, colourless to light yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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.

4.2 Posology and method of administration

Treatment should be initiated by physicians experienced in the diagnosis and treatment of severe asthma.

Posology

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

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 asthma control.

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 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 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.

Sodium content

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

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.

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 are arthralgia (3.8%) and pharyngitis (4.1%).

Tabulated list of adverse reactions

In clinical studies in patients with severe asthma, a total of 665 patients received at least one dose of Tezspire in trials of 52 weeks duration.

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
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, both allergic and non-allergic triggers induce TSLP production. Blocking TSLP with tezepelumab reduces a broad spectrum of biomarkers and cytokines associated with airway inflammation (e.g. blood eosinophils, airway submucosal eosinophils, IgE, FeNO, IL-5, and IL-13); however, the mechanism of action of tezepelumab in asthma has not been definitively established.

Pharmacodynamic effects

Effect on blood eosinophils and inflammatory biomarkers and cytokines
In 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.

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 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.

Clinical efficacy

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]

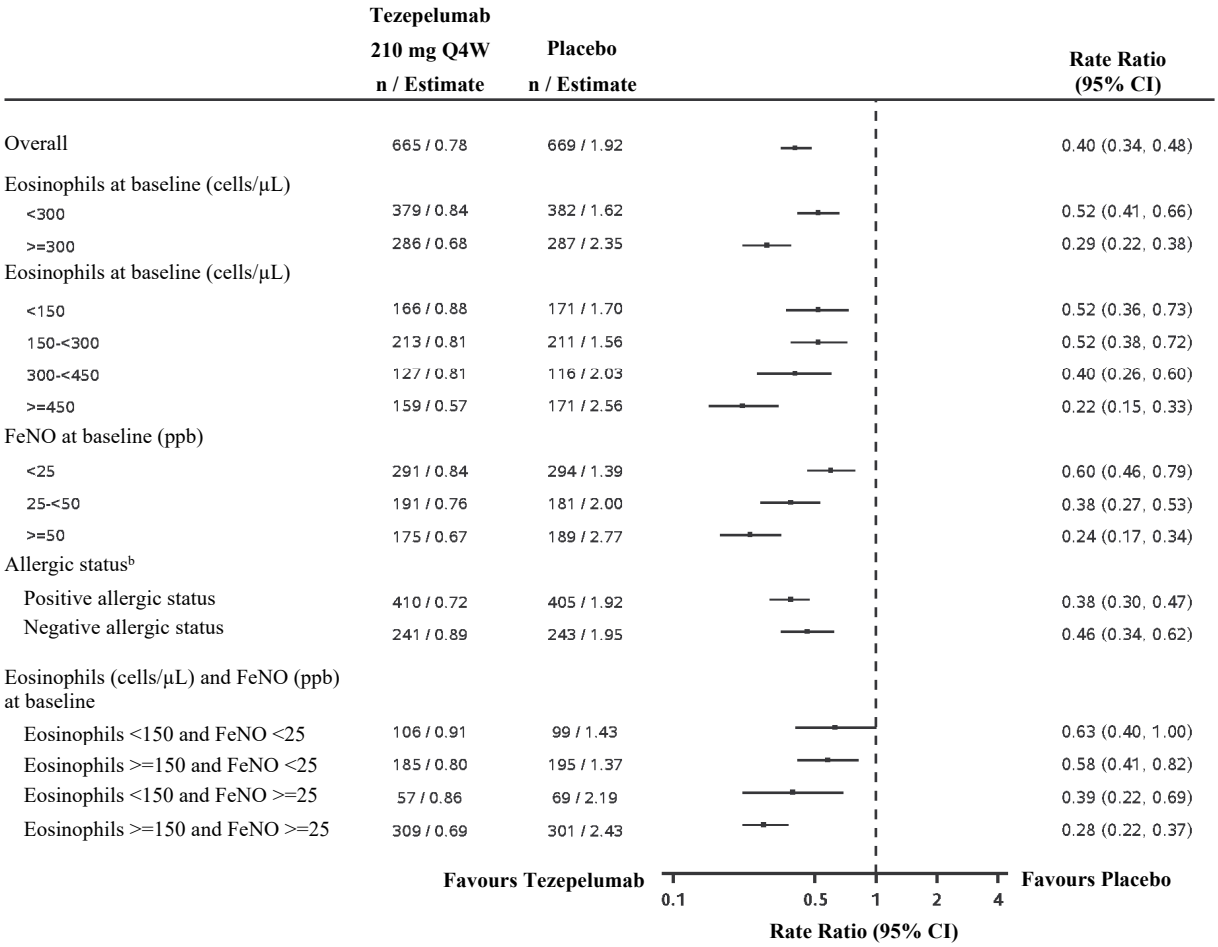
	Tezepelumab (N=137)	**Placebo (N=138)**
Annualised severe asthma exacerbation rate		
Rate	0.20	0.72
Rate ratio (95% CI)	0.29 (0.16, 0.51)	
p-value	<0.001	

[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 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.

Paediatric population

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).

5.2 Pharmacokinetic properties

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. Tezepelumab has not been studied in children under 12 years of age (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
L-proline
Polysorbate 80
Sodium hydroxide
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 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

1.91 mL solution in a siliconized 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

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 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

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 http://www.ema.europa.eu.

ANNEX II

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

Name and address of the manufacturer of the biological active substance

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

Name and address of the manufacturer responsible for batch release

AstraZeneca AB
Gärtunavägen
SE-151 85 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

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

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. By blocking the action of TSLP, this medicine helps to reduce inflammation and asthma symptoms.

What Tezspire is used for
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.

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

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 allergic reactions in some people. The signs of these reactions may vary, but can include breathing problems, 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.

Children
Do not give this medicine to children under 12 years of age 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'.

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.

Adults and adolescents aged 12 years and over:
- **The recommended dose** is 210 mg (1 injection) every 4 weeks. Tezspire is given as an injection under the skin (subcutaneously).

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 asthma symptoms and 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.

Common side effects (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, L-proline, polysorbate 80, 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-151 85 Södertälje
Sweden

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

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AstraZeneca S.A./N.V.	UAB AstraZeneca Lietuva

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://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:

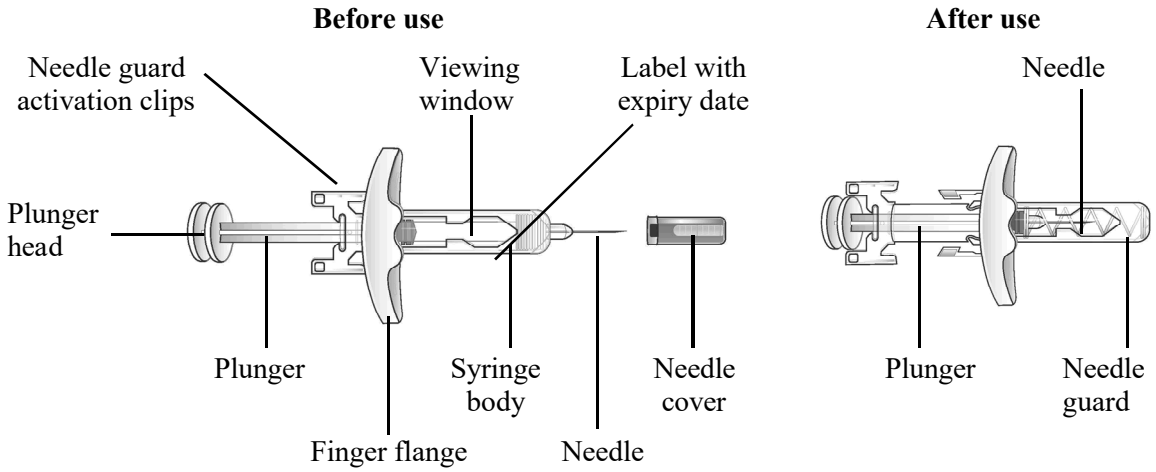
- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiry date (EXP) has passed

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).

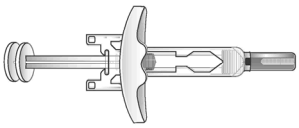
Your Tezspire pre-filled syringe

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

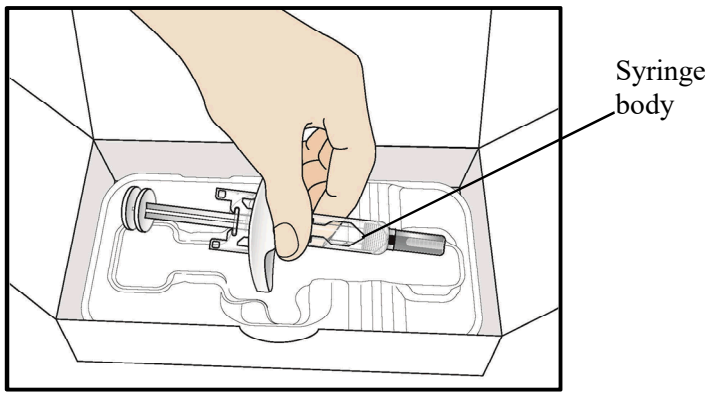
Step 2 – Prepare to use your Tezspire pre-filled syringe

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.

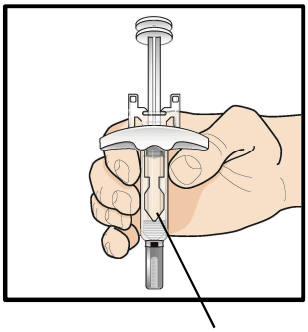
Step 3 – Remove pre-filled syringe

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



Step 4 – Check the pre-filled syringe

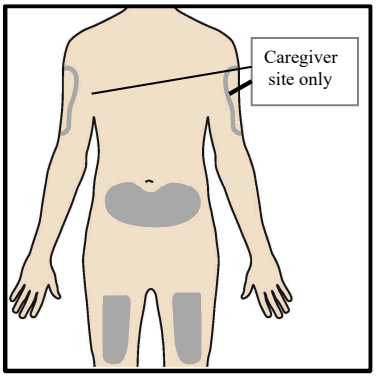
Check the pre-filled syringe for damage. Do not use the pre-filled syringe if the pre-filled syringe is damaged.
Check the expiry date on the pre-filled syringe. **Do not** use the pre-filled syringe if the expiry date has passed.
Look at the liquid through the viewing window. The liquid should be clear 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

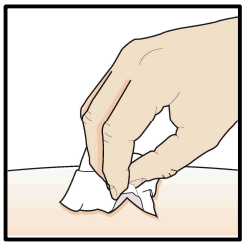
If you are giving yourself the injection, the **recommended injection site** is the front of your thigh or the lower part of your stomach (abdomen). **Do not** inject yourself in the arm.
A caregiver may inject you in the upper arm, thigh, or abdomen.
For each injection, choose a different site that 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



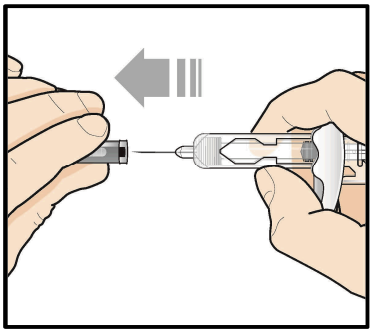
Step 6 – Wash your hands and clean the injection site

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.

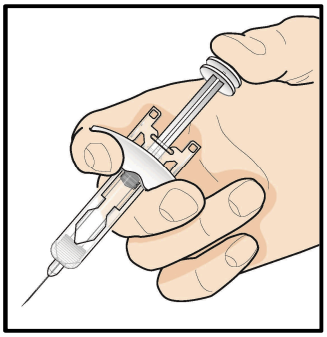
Step 7 – Pull off the needle cover

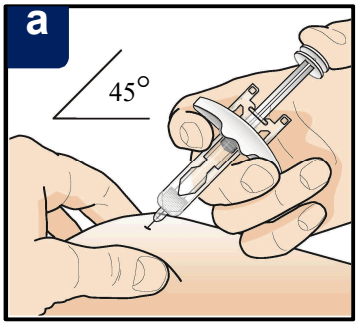
Do not remove the cap until you are ready to inject.
Hold the syringe body with 1 hand, and carefully pull the needle cover straight off with your other hand.
Do not hold the plunger or plunger head while removing the needle cover.
Put the needle cover to the side and throw it away later.
You may see 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.



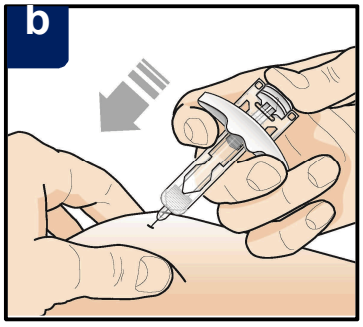
Step 8 – Inject Tezspire

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**.

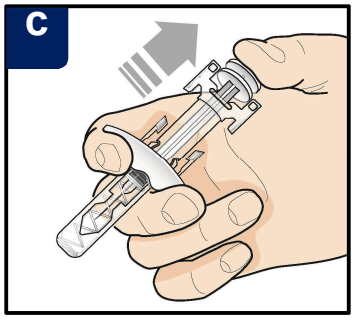




Using a 45 degree angle, fully insert the needle into the pinched skin.
Do not try to change the position of the pre-filled syringe after you insert it into the skin.



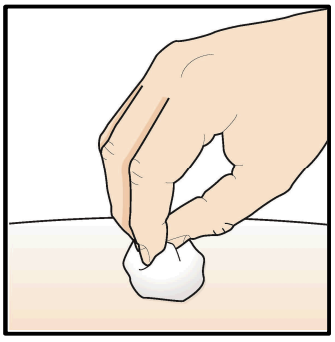
Use your thumb to push down on the plunger head.
Keep pushing until it is down as far as it will go to make sure you inject all of the medicine.



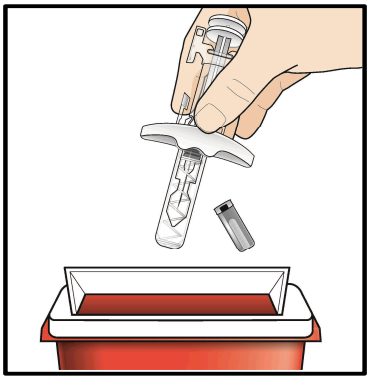
Keep your thumb pressed down on the plunger head as you take the needle out of the skin.
Slowly let go of the plunger until the needle guard covers the needle.

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 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.