

**Category**

Best Biotechnology Product

**Drug / Device Name**

TEZSPIRE®

**Compound/ Tech Name**

Tezepelumab

**Trade Name**

TEZSPIRE®

**Date of Approval**

2021-12-17

**Indications**

TEZSPIRE® is a first-in-class human monoclonal antibody (IgG2λ) that targets and blocks thymic stromal lymphopoietin (TSLP), a key epithelial cytokine located at the top of the inflammatory cascade. Due to this novel mechanism of action, TEZSPIRE is the first and only asthma biologic to reduce all key inflammatory biomarkers (e.g. eosinophils, FeNO and IgE) and airway hyperresponsiveness.

TEZSPIRE is indicated in the U.S. for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. TEZSPIRE is not a rescue medication.

TEZSPIRE consistently and significantly reduces asthma exacerbations across a broad population of people with severe asthma without phenotype – eosinophilic or allergic – or biomarker limitations. The priority approval and breakthrough designation marked a historic milestone for Amgen, AstraZeneca and patients living with severe asthma who previously did not have an effective biologic treatment option or were not eligible for any previously approved biologic.

**Therapeutic Categories**

Severe Uncontrolled Asthma

**Attached Files:**

- NEJMTezepelumabinAdultsandADolescents.pdf
- TEZE Digital Prescribing Information.pdf
- NEJMTezeinAdults.pdf

**Background information and need for drug/device**

Asthma is a heterogenous disease with multiple inflammatory pathways and factors that can trigger debilitating exacerbations and reduce quality of life. Approximately 1.3 million people in the U.S. live with severe asthma (SA) who are uncontrolled or biologic eligible.

Biologic therapies targeting drivers of airway inflammation have demonstrated efficacy in reducing the rate of exacerbations and improving asthma symptoms. However, despite their availability, in 2020 only about 20% of eligible patients were prescribed a biologic. Of those eligible patients, available biologics only targeted one or two inflammatory pathways and were solely approved for people with specific phenotype or biomarker levels. Data from 2020 showed nearly all biologic therapies had insufficient effectiveness in a subset of patients with SA, and all five biologics available in the U.S. in 2020 demonstrated sub-optimal or no efficacy in patients with SA with a non-eosinophilic phenotype (blood eosinophil count <300 cells/mL).

By inhibiting TSLP, which had never been targeted before in severe asthma, TEZSPIRE was able to regulate a key epithelial cytokine that initiates and perpetuates an immune response to asthma triggers (e.g., inhaled allergens, smoke).

TEZSPIRE is the only biologic to have broad and consistent effects on both airway inflammation and airway hyperresponsiveness. In fact, it is the first treatment not limited to a specific type of SA to consistently and significantly reduce exacerbations in a broad population of patients irrespective of phenotypes or biomarker levels. Results from pivotal clinical trial studies demonstrated that monthly doses of TEZSPIRE resulted in significantly fewer asthma attacks and hospitalizations among patients and better lung function than those receiving placebo.

TEZSPIRE has been achieving strong adoption in the U.S by allergists and pulmonologists. Most recently, it received FDA approval in a pre-filled pen giving patients the option for self-administration.

Attached Files:

- Unmet need in severe uncontrolled asthma.pdf
- Thymic stromal lymphopoietin its role and potential as a therapeutic target in asthma 2.pdf

### **History of the development of the drug/device**

In April 2012, Amgen and AstraZeneca entered into an agreement for the development and commercialization of five monoclonal antibodies that included AMG 157 (now known as tezepelumab/TEZSPIRE).

In a Phase 1b, proof-of-concept study in patients with mild allergic asthma, tezepelumab attenuated asthmatic responses to an allergen challenge and reduced biomarkers of inflammation when compared to placebo. In the tezepelumab group, blood eosinophil counts began to decline at 2 weeks post-dosing and reached normal levels by 4 weeks, while sputum eosinophils reached normal levels by 6 weeks (the first time point measured).

In the Phase 2b PATHWAY study, tezepelumab treatment was associated with significant reductions in annualized exacerbation rates of up to 71% versus placebo. Subgroup analyses showed that these reductions were significant irrespective of patient phenotype. The observed efficacy of tezepelumab in a broad range of patients with severe asthma in PATHWAY led to it being designated a 'breakthrough therapy' by the U.S. Food and Drug Administration (FDA) in 2019 for patients with severe asthma without an eosinophilic phenotype.

In the Phase 3 NAVIGATOR study, tezepelumab demonstrated significant and clinically meaningful

reductions in annualized asthma exacerbation rates (AAER) in patients irrespective of their eosinophil levels. Tezepelumab also reduced the rate of exacerbations that required hospitalization or an emergency room visit by 79%, compared with placebo.

Results from all three phases of the tezepelumab trials were featured in the New England Journal of Medicine and led to U.S. FDA approval in 2021.

In addition to severe asthma, tezepelumab is being developed by Amgen and AstraZeneca for the treatment of chronic obstructive pulmonary disease (COPD), chronic rhinosinusitis with nasal polyps (CRSwNP), chronic spontaneous urticaria (CSU) and eosinophilic esophagitis (EoE).

Attached Files:

- NEJMTezepelumabinAdultsandADolescents.pdf
- NEJMTezeinAdults.pdf
- NEJMEffectsofAntiTSLPAntibody.pdf

**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition**

Thymic stromal lymphopoietin (TSLP) was first discovered as having a connection to inflammation in the late 1990s. In 2002, scientists at Amgen discovered that TSLP is induced in epithelial cells in response to pro-inflammatory stimuli and drives inflammatory responses through activating the TSLPR/IL7Ra heterodimeric receptor expressed on immune cells, such as dendritic and mast cells. TSLP was found to polarize human and mouse T cells to a Th2 phenotype through its effects on dendritic cells. As such, it was postulated that inhibition of TSLP would have a role in asthma.

It was subsequently discovered that mice over-expressing TSLP in the lung developed asthma-like airway inflammation, whereas the TSLP blockade either through genetic knockout or antagonist antibody treatment ameliorated disease in the mouse asthma model. TSLP expression is increased in asthmatic airways correlating with disease severity.

In 2006, a lead anti-TSLP antibody, AMG 157 (tezepelumab), was advanced to development.

Tezepelumab is a human monoclonal antibody (IgG2 $\lambda$ ) that binds selectively to TSLP and blocks it from interacting with its heterodimeric receptor. Tezepelumab is innovative because its effects on multiple cell types and as a consequence the reduction in inflammatory cytokines results in improvement in asthma outcomes across a broad spectrum of phenotypes rather than being limited, for example, to only eosinophilic or allergic asthma. Both the biology and the genetic linkage of TSLP to other diseases, such as eosinophilic esophagitis and chronic rhinosinusitis with nasal polyps, provides the basis for ongoing and future research to expand the impact of tezepelumab on patients. Similarly, research is ongoing into the potential impact of TSLP inhibition by tezepelumab on CSU and COPD, diseases where there remains great unmet medical needs.

Attached Files:

- 2202202full.pdf

**Please provide appropriate references (ie Pubmed links)**

TSLP biology

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Supplementary assets:

Discovery video: <https://wwwext.amgen.com/stories/2021/12/behind-the-discovery-of-a-new-homegrown-molecule-for-severe-asthma>