Public Testimony for WV Medicaid CINQAIR® (reslizumab) Injection Upon Request to Present

Introduction & Purpose	• Good day, my name is Fawad Malik and I am a Sr. Medical Outcomes Liaison at Teva Pharmaceuticals. I'm here to provide information about CINQAIR® (reslizumab) Injection.[i]
Disease Burden of Illness	• Asthma is characterized by chronic airway inflammation and effects more than 26 million people in the US. Each year, asthma is responsible for 11 million office visits, 3 million emergency room & outpatient hospital visits, over 439,000 hospital stays, & 3518 deaths.[v]
No conclusions of safety and efficacy can be made based on this type of data.	
Indication	CINQAIR® (reslizumab) Injection is an interleukin-5 antagonist monoclonal antibody (IgG4 kappa) indicated for: • add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype.[i] • Limitations of Use: CINQAIR® is not indicated for treatment of other eosinophilic conditions or relief of acute bronchospasm or status asthmaticus.
Dosage & Administration	For intravenous use only[i] • Do not administer as an intravenous push or bolus. • CINQAIR® should be administered by a healthcare professional prepared to manage anaphylaxis. • Recommended dosage regimen is 3 mg/kg once every 4 weeks by intravenous infusion over 20-50 minutes.
Dosage Form and Strength	• Injection: 100 mg/10 mL (10 mg/mL) solution in single-use vials[i]
Contraindications Warnings and Precautions	• CINQAIR® is contraindicated in patients with a hypersensitivity to reslizumab or any of its excipients.[i] • Boxed Warning: Anaphylaxis occurred with CINQAIR® infusion in 0.3% of patients in placebo-controlled studies. Patients should be observed for an appropriate period of time after CINQAIR® infusion; healthcare professionals should be prepared to manage anaphylaxis that can be life-threatening. • Malignancy were noted in the clinical studies.[i] • Parasitic (Helminth) infections should be treated prior to starting CINQAIR®.[i] • Do not abruptly discontinue the use of systemic or inhaled corticosteroids.[i] • Additional risk information can be found in the full prescribing information.
Common Adverse Reactions	• The most common adverse reaction (incidence greater than or equal to 2%) includes oropharyngeal pain.[i]

Primary Studies	The asthma development program for CINQAIR® 3 mg/kg (administered once every 4 weeks) included 4 randomized, double-blind, placebo-controlled studies (Studies I-IV) 16 to 52 weeks in duration involving 981 patients 12 years of age and older.[i]
	• Studies I and II
	  ○ Studies I and II were 52-week studies in 953 patients with asthma who were required to have a blood eosinophil count of at least 400/mcL and at least 1 asthma exacerbation requiring systemic corticosteroid use over the past 12 months.
	  ○ The primary endpoint was the frequency of asthma exacerbations for each patient during the 52-week treatment period. Patients receiving CINQAIR® 3 mg/kg administered once every 4 weeks had significant reductions in the rate of all asthma exacerbations compared to placebo (Study 1: 0.90 vs 1.80; Study 2: 0.86 vs 2.11).
	• Study III
	  ○ Study III was a 16-week study in 315 patients who were required to have a blood eosinophil count of at least 400/mcL at screening (within 3 to 4 weeks of dosing). Maintenance OCS were not allowed.
	  ○ The primary endpoint was the effect of CINQAIR® 3 mg/kg administered once every 4 weeks on FEV_1 over time relative to placebo. Patients on CINQAIR® had an increase in FEV_1 from baseline of 160mL when compared to placebo.
	• Study IV
	  ○ Study IV was a 16-week study in 496 patients unselected for baseline blood eosinophil levels (approximately 80% of patients had a screening [within 3 to 4 weeks of dosing] blood eosinophil count of less than 400/mcL). The effect of CINQAIR® 3 mg/kg administered once every 4 weeks on FEV_1 over time relative to placebo. Patients on CINQAIR® had an increase in FEV_1 from baseline of 76mL when compared to placebo.

Post Hoc Analysis	In a subanalysis of Phase III pooled data of 953 patients, 69% (n=657) and 11% (n=106) were receiving Step 4 and Step 5 therapy.[ii] • Compared with placebo, reslizumab reduced exacerbation rates by 53% (95% CI 0.36–0.62) and 72% (95% CI 0.15–0.52), in Step 4 and Step 5 groups. By study end, reslizumab increased FEV_1 in Step 4 and Step 5 groups by 103 mL (95% CI 52–154 mL) and 237 mL (95% CI 68–407 mL). In patients with inadequately controlled late-onset asthma and elevated blood eosinophils[iii] • In a second post hoc analysis of pooled Phase 3 data evaluated patients with late onset eosinophilic asthma(n=273) and (n=658) with early onset asthma • Compared with placebo, reslizumab produced a 75% relative reduction in asthma exacerbations in patients with late-onset asthma. The adverse event profile of reslizumab was similar in patients with early- or late-onset asthma. • Reslizumab produced larger reductions in asthma exacerbations and larger improvements in lung function in patients with late versus early-onset asthma.

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Long Term Safety	In patients with inadequately controlled asthma who were oral corticosteroid (OCS) dependent.[v] • In a third post hoc analysis of pooled Phase 3 data, patients were randomized to reslizumab (n=477) or placebo (n=476). • A subset of OCS-dependent patients were evaluated at baseline (n=73 reslizumab; n=73 placebo). Reslizumab-treated patients had a lower mean cumulative systemic corticosteroid dose per patient (mg) compared to those on placebo (mean SCS dose (mg) = 245mg vs. 611mg) and fewer new systemic corticosteroid prescriptions issued per patient (0.5 ± 1.07 vs. 1.0 ± 1.52). In a post hoc analysis of Phase 3 data analyzing the changes in exacerbation rates and lung function with weight-based IV reslizumab dosing in patients with Baseline High Body Weight[vi]: • The overall population included 928 adults (465 on placebo, 463 on reslizumab) with a mean, median, and range of body weight of 75.7 kg, 74.0 kg, and 33.9-142.3 kg, respectively. The high body-weight tertile (≥81 kg) included 162 placebo patients and 157 reslizumab patients. Mean, median, and range of body weight in this tertile were 94.8 kg, 91.2 kg, and 81-142.3 kg, respectively. • Clinical exacerbation rate among adult patients in the subgroup with the highest baseline body weight, resulted in a 50% reduction over the 52 week treatment period as compared to the overall population of 44%. The overall population experienced a similar result in the mean number of CAE with reslizumab (n=1.83) compared to placebo (n=2.06). A long-term safety and efficacy study of reslizumab in patients with eosinophilic asthma[iv] • This open-label extension study evaluated safety and efficacy of reslizumab for up to 24 months in 1051 patients. Continuous exposure was 12 months for 740 patients and 24 months for 249 patients. • The most common AEs were worsening of asthma and nasopharyngitis. Serious AEs affected (7%) of patients; (2%) discontinued treatment because of AEs; and there were 3 deaths (all nontreatment-related). 1% had malignancies of diverse tissue types. • An improvement in mean FEV_1 was noted in the reslizumab-naïve group week 4 (0.082 L) and sustained over 96 weeks with a similar improvement noted in the reslizumab-experienced patients.

i. CINQAIR® [package insert]. Frazer, PA: Teva Respiratory, LLC; 2016.

ii. Brusselle G, Canvin J, Weiss S, et al. Stratification of eosinophilic asthma patients treated with reslizumab and GINA Step 4 or 5 therapy. ERJ Open Res 2017; 3: 00004-2017 [https://doi.org/10.1183/23120541.00004-2017]

iii. Brusselle G, Germinaro M, Weiss S, et al. Reslizumab in patients with inadequately controlled late-onset asthma and elevated blood eosinophils. Pulm Pharmacol Ther. 2017;43:39–45.

iv. Murphy K, Jacobs J, Bjermer L, et al. Long-term safety and efficacy of reslizumab in patients with eosinophilic asthma. J Allergy Clin Immunol Pract. 2017;5:1572–81.e3.

v. Parameswaran Nair 1, Philip Bardin et al Efficacy of Intravenous Reslizumab in Oral Corticosteroid-Dependent Asthma
J Allergy Clin Immunol Pract . 2020 Feb;8(2):555-564.

vi. Murphy K et al. Improvements in Exacerbation Rate and Lung Function with Weight-Based Intravenous Reslizumab Dosing in Patients with Baseline High Body Weight. Am J Respir Crit Care Med, 2018; 197:A1356.

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