IOWA | Health and Human Services

Iowa PDL New Drug Review

Proprietary Name: Brinsupri®
Common Name: brensocatib
PDL Category: Dipeptidyl Peptidase 1 (DPP1) Inhibitors

Pharmacology/Usage: Brensocatib, the active ingredient of Brinsupri®, is a dipeptidyl peptidase 1 (DPP1) inhibitor. It is a competitive, reversible inhibitor of DPP1, which activates pro-inflammatory neutrophil serine proteases (NSPs) during neutrophil maturation in the bone marrow. Activated NSPs are implicated in the pathogenesis of neutrophil-mediated non-cystic fibrosis bronchiectasis inflammation. In cell-based assays, DPP1 inhibition by brensocatib reduces the activity of NSPs, including neutrophil elastase, cathepsin G, and proteinase 3.

Indication: For the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age and older.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. The safety and efficacy of use in the pediatric population younger than 12 years of age have not been established.

Dosage Form: Film-Coated Tablets: 10mg and 25mg.

Recommended Dosage: Take 10mg or 25mg PO QD, with or without food. Patients who miss a dose should take the next dose at their regular time the next day. Do not double the dose to make up for the missed dose.

Drug Interactions: The concomitant use of Brinsupri® and live attenuated vaccines has not been evaluated. It is not known whether administration of live attenuated vaccines during Brinsupri® treatment will affect the safety or effectiveness of these vaccines. The use of live attenuated vaccines should be avoided in patients receiving Brinsupri®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Brinsupri® 10mg/25mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included upper respiratory tract infection (2%/4%), headache (0%/2%), rash (0%/2%), dry skin (2%/3%), hyperkeratosis (0%/2%), and hypertension (2%/0%).

Treatment with Brinsupri® is associated with an increase in dermatologic adverse reactions, including rash, dry skin, and hyperkeratosis. Monitor patients for development of new rashes or skin conditions and refer patients to a dermatologist for evaluation of new dermatologic findings.

Treatment with Brinsupri® is associated with an increase in gingival and periodontal adverse reactions. Refer patients to dental care services for regular dental checkups while taking Brinsupri®. Advise patients to perform routine dental hygiene.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Insmed Incorporated

Analysis: The efficacy of Brinsupri® was assessed in two randomized, double-blind, placebo-controlled, parallel-group, multicenter, multinational clinical trials (ASPEN and WILLOW). In both studies, all adult patients had a history of confirmed NCFB by chest computed tomography with at least 2 documented pulmonary exacerbations (PEx) prior to screening in the past 12 months. In ASPEN, pediatric patients 12 years of age and older had at least one PEx in the prior 12 months.

ASPEN was a 52-week trial that included adult and pediatric patients 12 years of age and older (N=1721) with NCFB (N=1680 adults and N=41 pediatric patients 12 years of age to less than 18 years of age) who were randomized to Brinsupri® 10mg (N=583), Brinsupri® 25mg (N=575), or placebo (N=563) administered once daily. The mean age of included patients was 60 years, while 64% were female, 74% were White, 30% were former smokers, 29% had ≥3 pulmonary exacerbations in the prior 12 months, and 19% had chronic macrolide therapy. The ppFEV1 post-bronchodilator, mean was 74.

The primary efficacy endpoint in this study was the annualized rate of PEx over the 52-week treatment period. Pulmonary exacerbations were defined as worsening of 3 or more of the following major symptoms over 48 hours, including increased cough, increased sputum volume or change in sputum consistency, increased sputum purulence, increased breathlessness, decreased exercise tolerance, fatigue and/or malaise, and hemoptysis, resulting in a healthcare providers decision to prescribe systemic antibiotics. Pulmonary exacerbations were considered severe if requiring treatment with intravenous antibacterial drugs and/or resulted in hospitalization.

Treatment with Brinsupri® 10mg or 25mg in patients with NCFB demonstrated reductions in the mean rate of PEx over 52 weeks as compared with placebo. Results of the primary endpoint and key secondary endpoints are presented in the table below, which was adapted from the prescribing information.

	Placebo (N=563)	Brinsupri® 10mg (N=583)	Brinsupri® 25mg (N=575)
Annualized Rate of PEx	1.29	1.02	1.04
Rate Ratio		0.79	0.81
Median Time to first PEx (weeks)	36.71	49.00	50.71
Hazard Ratio (HR)		0.81	0.83
Proportion of patients that were PEx Free at week 52, %	40.3%	48.5%	48.5%
Odds Ratio		1.41	1.40
Annualized Rate of Severe PEx	0.19	0.14	0.14
Rate Ratio		0.74	0.74
Least Squares (LS) mean change from baseline in post-bronchodilator FEV1 (ml) at week 52	-62	-50	-24
Difference vs placebo		11	38

WILLOW was a 24-week trial that included adults patients (N=256) with NCFB who were randomized to Brinsupri® 10mg (N=82), Brinsupri® 25mg (N=87), or placebo (N=87) administered once daily. The mean age of included

patients was 64 years, while 68% were female, 88% were White, 34% were former smokers, 33% had ≥3 pulmonary exacerbations in the prior 12 months, and 16% had chronic macrolide therapy. The ppFEV1 post-bronchodilator, mean was 68.

The primary efficacy endpoint of this study was the time to first PEx over the 24-week treatment period. The time to first PEx was longer for patients receiving Brinsupri® 10mg and 25mg compared to placebo (HR Brinsupri® 10mg and 25mg vs placebo: 0.58 and 0.62, respectively).

Place in Therapy: Brinsupri® is a DPP1 inhibitor indicated for the treatment of non-cystic fibrosis bronchiectasis in adult and pediatric patients 12 years of age and older. Gingival and periodontal adverse reactions can occur with use; refer patients to dental care services for regular dental checkups and advise patients to perform routine dental hygiene. The efficacy of Brinsupri® was assessed in two randomized, double-blind, placebo-controlled studies. ASPEN included both adult and pediatric patients 12 years of age and older with NCFB while WILLOW included adults with NCFB. The primary endpoint in the ASPEN study was the annualized rate of PEx over the 52-week treatment period, and results suggested that Brinsupri® 10mg and 25mg treatment in patients with NCFB demonstrated reductions in the mean rate of PEx over 52 weeks as compared with placebo. The primary endpoint in the WILLOW study was the time to first PEx over the 24-week treatment period, and results suggested that the time to first PEx was longer for patients receiving Brinsupri® 10mg and 25mg as compared to placebo. Per the ASPEN full-text study by Chalmers et al[2], statistically significant better results were obtained with Brinsupri® 10mg (p=0.004) and Brinsupri® 25mg (p=0.005) as compared with placebo for the primary endpoint.

Summary

It is recommended that Brinsupri® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement:
- ☐ **Preferred**
- ☒ **Non-Preferred**

References

[1] Brinsupri [package insert]. Bridgewater, NJ: Insmed Incorporated; 2025.
[2] Chalmers JD, Burgel PR, Daley CL, et al. Phase 3 trial of the DPP-1 inhibitor brensocatib in bronchiectasis. *NEJM*. 2025; 392)16): 1569-1581.