Drug Monograph

Drug/Drug Class:	**Seebri® Neohaler™ (glycopyrrolate) capsule for inhalation / COPD**
Prepared for:	MO HealthNet
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☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Seebri® is available in a capsule that contains 15.6 mcg of glycopyrrolate for oral inhalation with the Neohaler™ inhalation device. Manufacturer: Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936
Summary of Findings:	The effect of Seebri® Neohaler™ twice daily inhalation on lung function was studied in two randomized, double-blind, placebo-controlled clinical trials in patients with COPD (N=867). Seebri® Neohaler™ improved lung function and health-related quality of life over 12 weeks compared with placebo.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [5]

Chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, is a chronic lung disease that makes it hard to breathe. The disease is increasingly common, affecting millions of Americans, and is the third leading cause of death in the U.S. COPD is often preventable and treatable.

Dosage Form(s) [1]

Seebri® is available in a capsule that contains 15.6 mcg of glycopyrrolate for oral inhalation with the Neohaler™ inhalation device.

Manufacturer [1]

Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936

Indication(s) [1]

Seebri® Neohaler™ is indicated for long term, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

Clinical Efficacy [1, 2,3,4] (mechanism of action/pharmacology, comparative efficacy)

Seebri® Neohaler™ is a long-acting anticholinergic agent that reversibly inhibits the M3 receptor at the smooth muscle, leading to bronchodilation.

Pharmacokinetics:

	Seebri® Neohaler™
Metabolism	Liver, 30% to 40% of total elimination via multiple CYP enzymes
Half-life	33 to 53 hours
Protein binding	38 to 41%
Volume of distribution	83 L, steady state
Excretion	Urine, 60% to 70%

COPD

Seebri® Neohaler™ given twice daily significantly improved the mean change in FEV1 and health-related quality of life compared with placebo over 12 weeks in patients with COPD.

STUDY DESIGN	Two randomized, double-blind, placebo-controlled, 12-week clinical trials (N=867)
INCLUSION CRITERIA	Patients 40 years or older with COPD, a smoking history of greater than 10 pack-years, and a post-bronchodilator FEV1 of 30% to 80% of predicted values
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized to receive Seebri® Neohaler™ 15.6 mcg or placebo twice daily.
RESULTS	Seebri® Neohaler™ significantly increased the mean change in FEV1 measurements by 0.115 L to 0.125 L from baseline compared with a 0.008 L to 0.014 L decrease observed with placebo. The mean peak FEV1 improvement from baseline for glycopyrrolate inhalation compared with placebo at day 1 and at day 85 was 0.142 L and 0.163 L in trial 1, and 0.137 L and 0.148 L in trial 2, respectively. Glycopyrrolate treatment was also associated with less daily rescue albuterol use and an increased responder rate on the St. George's Respiratory Questionnaire (49% to 55% vs 41% to 42%). The mean patient age was 63 years and the mean baseline post-bronchodilator percent predicted FEV1 was 55%.
SAFETY	Not specified.

Contraindications [(1)]

- Hypersensitivity to glycopyrrolate or any product component

Warnings and Precautions [(1)]

- Acute symptom relief use not recommended.
- Use not recommended for deteriorating COPD, acute, or potentially life-threatening.
- Paradoxical bronchospasm, potentially life-threatening, may occur; discontinue use immediately if occurs.
- Hypersensitivity reactions, including immediate reactions, may occur; discontinue immediately.
- Use with caution in patients with severe hypersensitivity to milk proteins.
- Avoid use with concomitant anticholinergic-containing drugs
- Use with caution in preexisting or new onset, narrow-angle glaucoma; worsening may occur; monitoring recommended.

- Worsening urinary retention may occur, especially in patients with prostatic hyperplasia or bladder neck obstruction.
- Severe renal impairment (GFR less than 30 ml/min/1.73m^2), including ESRD requiring dialysis; monitoring required and use only if benefit outweighs risk.

Adverse Effects [(1)]

Most common, ≥ 1%	Seebri® Neohaler™ (n=951)	Placebo (n=938)
Upper respiratory tract infection	3.4%	2.3%
Nasopharyngitis	2.1%	1.9%
Oropharyngeal pain	1.8%	1.2%
Urinary tract infection	1.4%	1.3%
Sinusitis	1.4%	0.7%

Drug Interactions [(1)]

- Anticholinergic agents

Dosage and Administration [(1)]

One oral inhalation (15.6 mcg/capsule) twice daily at the same time each day in the morning and evening.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	Dose	COST*/ Month
Glycopyrrolate	Seebri Neohaler	Novartis	15.6 mcg inhalation capsules	15.6 mcg twice daily	$297.60
Umeclidinium	Incruse Ellipta	GlaxoSmithKline	62.5 mcg/blister inhalation powder	62.5 mcg once daily	$224.70
Tiotropium bromide	Spiriva	Boehringer Ingelheim	18 mcg inhalation capsules	18 mcg once daily	$315.60

* Wholesale Acquisition Cost

Conclusion

Seebri® Neohaler™ is a twice-daily anticholinergic bronchodilator administered with a dry powder inhaler and approved for the long-term maintenance treatment of COPD. Seebri® Neohaler™ has demonstrated efficacy in improving lung function and health-related quality of life when compared

with placebo over 12 weeks in two randomized, double-blind clinical trials. However, its efficacy has not been evaluated in comparison with other FDA approved long acting anticholinergic agents. The most common adverse events with glycopyrrolate inhalation include upper respiratory tract infections and nasopharyngitis.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL).

References

1. Product Information: Seebri® Neohaler™, glycopyrrolate inhalation powder. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 10/2015.
2. D'Urzo A, Ferguson GT, van Noord JA et al: Efficacy and safety of once-daily NVA237 in patients with moderate-to-severe COPD: the GLOW1 trial. Respir Res 2011; 12:156.
3. Kerwin E, Hebert J, Gallagher N et al: Efficacy and safety of NVA237 versus placebo and tiotropium in patients with COPD: the GLOW2 study. Eur Respir J 2012; 40(5):1106-1114.
4. Frith PA, Thompson PJ, Ratnavadivel R et al: Glycopyrronium once-daily significantly improves lung function and health status when combined with salmeterol/fluticasone in patients with COPD: the GLISTEN study, a randomised controlled trial. Thorax 2015; 70(6):519-527.
5. COPD. Retrieved 3/4/16 from www.lung.org/lung-health-diseases

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