    - The proportion of subjects who discontinued treatment due to AEs was 2.4% for SEEBRI NEOHALER-treated patients and 3.8% for placebo-treated patients.
  - In the 52-week trial (GEM 3), 507 subjects were treated for up to 52 weeks with glycopyrrolate 15.6 mcg BID or indacaterol 75 mcg once-daily.
    - The AEs reported in the 52-week trial were consistent with those observed in the placebo-controlled trials of 12 weeks.
    - Additional AEs that occurred with a frequency of ≥2% in the group receiving glycopyrrolate 15.6 mcg BID that exceeded the frequency of indacaterol 75 mcg once-daily in this trial were: diarrhea, nausea, upper abdominal pain, fatigue, bronchitis, pneumonia, rhinitis, back pain, arthralgia, dyspnea, and wheezing.

IMPORTANT SAFETY INFORMATION[1]

- SEEBRI NEOHALER is contraindicated in patients who have demonstrated hypersensitivity to glycopyrrolate, or to any of the ingredients.
- SEEBRI NEOHALER should not be initiated in patients with acutely deteriorating or potentially life-threatening episodes of COPD, or used as rescue therapy for acute symptoms. Acute symptoms should be treated with an inhaled short-acting beta$_2$-agonist.
- SEEBRI NEOHALER can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs following dosing of SEEBRI NEOHALER, it should be treated immediately with an inhaled short-acting bronchodilator. SEEBRI NEOHALER should be discontinued immediately, and alternative therapy instituted.
- Immediate hypersensitivity reactions have been reported after administration of SEEBRI NEOHALER. If signs suggesting allergic reactions occur, in particular, angioedema (including difficulties in breathing or swallowing, or swelling of tongue, lips, and face), urticaria, or skin rash, SEEBRI NEOHALER should be discontinued immediately and alternative therapy instituted. SEEBRI NEOHALER should be used with caution in patients with severe hypersensitivity to milk proteins.
- Use with caution in patients with narrow-angle glaucoma. Instruct patients to consult a physician immediately if signs or symptoms of acute narrow-angle glaucoma develop (e.g., eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema).
- Use with caution in patients with urinary retention. Instruct patients to consult a physician immediately if signs or symptoms of urinary retention develop (e.g., difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or bladder-neck obstruction.
- Avoid co-administration of SEEBRI NEOHALER with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects.

Reference

1. SEEBRI NEOHALER [Prescribing Information]. Novartis Pharmaceuticals Corporation. October 2015.

SEEBRI™ NEOHALER® (glycopyrrolate) inhalation powder
Clinical Summary for Formulary Review
Please consult complete Prescribing Information

INDICATIONS AND USAGE[1]

SEEBRI NEOHALER is an anticholinergic indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

DOSAGE AND ADMINISTRATION[1]

- For oral inhalation only. Do not swallow SEEBRI capsules, as the intended effects on the lungs will not be obtained. SEEBRI capsules should only be used with the NEOHALER device
- The recommended dose of SEEBRI NEOHALER is the inhalation of the contents of one SEEBRI capsule twice-daily using the SEEBRI NEOHALER device.
- SEEBRI NEOHALER should be administered at the same time of the day, (1 capsule in the morning and 1 capsule in the evening), every day. More frequent administration or a greater number of inhalations (more than 1 capsule twice-daily) of SEEBRI NEOHALER is not recommended.
- Store SEEBRI capsules in the blister, and only remove IMMEDIATELY BEFORE USE with the NEOHALER device.
- No dosage adjustment is required for geriatric patients, patients with hepatic impairment, or patients with mild to moderate renal impairment.

EFFICACY[1]

- The clinical development program for SEEBRI NEOHALER included two (GEM 1 and GEM 2) similar 12-week, randomized, double-blinded, placebo-controlled, parallel-group trials in subjects with COPD designed to evaluate the efficacy and safety of SEEBRI NEOHALER on lung function.
- GEM 1 (N=438) and GEM 2 (N=428) evaluated SEEBRI NEOHALER (glycopyrrolate) 15.6 mcg twice-daily (BID) and placebo BID. The primary endpoint was the change from baseline in FEV_1 $AUC_{0\text{-}12h}$ following the morning dose at Day 85 (defined as the mean FEV_1 change from baseline over 0 to 12 hours divided by 12 hours) compared with placebo.
- In both trials, SEEBRI NEOHALER demonstrated a larger increase in mean change from baseline in FEV_1 $AUC_{0\text{-}12h}$ compared to placebo The least squares (LS) mean change from baseline (SE) and LS mean treatment difference (SE) (95% CI) in FEV_1 $AUC_{0\text{-}12h}$ at Day 85 were:
    - GEM 1: 0.125 L (0.0162) in the SEEBRI NEOHALER arm and -0.014 L (0.0165) in the placebo arm; treatment difference (SEEBRI NEOHALER vs placebo): 0.139 L (0.0225) (95% CI: 0.095, 0.184)
    - GEM 2: 0.115 L (0.0153) in the SEEBRI NEOHALER arm and -0.008 L (0.0153) in the placebo arm; treatment difference (SEEBRI NEOHALER vs placebo): 0.123 L (0.0213) (95% CI: 0.081, 0.165)
- The peak FEV_1 was defined as the maximum FEV_1 recorded within 4 hours after the morning dose on Days 1 and 85. The mean peak FEV1 improvement from baseline for SEEBRI NEOHALER compared with placebo at Day 1 and at Day 85 was 0.142 L and 0.163 L (GEM 1), and 0.137 L and 0.148 L (GEM 2), respectively.
- In GEM 1 and 2, patients treated with SEEBRI NEOHALER used less daily rescue albuterol during the trial compared to patients treated with placebo.
- In GEM 1, the St. George's Respiratory Questionnaire (SGRQ) responder rate (defined as an improvement in score of 4 or more as threshold) for the SEEBRI NEOHALER treatment arm was 49% compared to 41% for placebo (OR: 1.43; 95% CI: 0.95, 2.15). In GEM 2, the SGRQ responder rate for the SEEBRI NEOHALER treatment arm was 55% compared to 42% for placebo (OR: 1.78; 95% CI: 1.17, 2.71).

ADVERSE EVENT PROFILE[1]

- The SEEBRI NEOHALER safety database included 3415 subjects with COPD in four 12-week lung function trials and one 52-week long-term safety study. A total of 1202 subjects received treatment with SEEBRI NEOHALER 15.6 mcg BID.
    - In the four 12-week, placebo-controlled trials in 2908 subjects with COPD, 951 subjects received SEEBRI NEOHALER 15.6 mcg BID, 511 subjects received indacaterol 27.5 mcg BID, 508 subjects received a fixed-dose combination of indacaterol/glycopyrrolate 27.5 mcg/15.6 mcg BID, and 938 subjects received placebo.
        - Adverse events (AEs) reported with SEEBRI NEOHALER, with an incidence of ≥1% and higher than placebo, in COPD patients were upper respiratory tract infection, nasopharyngitis, urinary tract infection, sinusitis, and oropharyngeal pain.
        - Other AEs occurring more frequently with SEEBRI NEOHALER than with placebo, but with an incidence of <1% include rash, pruritus, gastroenteritis, hypersensitivity, atrial fibrillation, insomnia, pain in extremity, dysuria, vomiting, productive cough, and diabetes mellitus/hyperglycemia.