Effective Date **11/1/2023**
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Coverage Policy Number **IP0089**

Long-Acting Muscarinic Antagonists (Nebulized)

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Related Coverage Resources

Step Therapy - Legacy Prescription Drug Lists (Employer Group Plans) - (1803)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for formulary exceptions to the following non-covered nebulized Long-Acting Muscarinic Antagonist Products:

- **Lonhala™ Magnair™** (glycopyrrolate inhalation solution)
- **Yupelri™** (revefenacin inhalation solution)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Non-Covered Product	Criteria
Lonhala™ Magnair™ (glycopyrrolate inhalation solution)	**Standard/Performance/ Value / Advantage/ Cigna Total Savings** **Lonhala Magnair** is considered medically necessary when for the treatment of chronic obstructive pulmonary disease (COPD) when **ALL** of the following are met: 1. 18 years of age or older 2. **ONE** of the following: a. Documented failure, contraindication, or intolerance to **ONE** of the following Long-Acting Muscarinic Antagonist (LAMA) products: i. Incruse Ellipta ii. Spiriva Respimat iii. Spiriva HandiHaler b. Documented inability to use a dry-powder inhaler (DPI) or a soft-mist inhaler (for example, low inspiratory flow, unable to coordinate breath and actuation of device) **Legacy** **Lonhala Magnair** is considered medically necessary for the treatment of chronic obstructive pulmonary disease (COPD) when **ALL** of the following are met: 1. 18 years of age or older 2. **ONE** of the following: a. Documented failure, contraindication, or intolerance to **ONE** of the following Long-Acting Muscarinic Antagonist (LAMA) products: i. Incruse Ellipta ii. Spiriva Respimat iii. Spiriva HandiHaler iii. Tudorza Pressair b. Documented inability to use a dry-powder inhaler (DPI) or a soft-mist inhaler (for example, low inspiratory flow, unable to coordinate breath and actuation of device)
Yupelri™ (revefenacin inhalation solution)	**Standard/Performance/ Value /Advantage/ Cigna Total Savings** **Yupelri** is considered medically necessary for the treatment of chronic obstructive pulmonary disease (COPD) when **ALL** of the following are met: 1. 18 years of age or older 2. **ONE** of the following: a. Documented failure, contraindication, or intolerance to **ONE** of the following Long-Acting Muscarinic Antagonist (LAMA) products: i. Incruse Ellipta ii. Spiriva Respimat iii. Spiriva HandiHaler b. Documented inability to use a dry-powder inhaler (DPI) or a soft-mist inhaler (for example, low inspiratory flow, unable to coordinate breath and actuation of device) **Legacy** **Yupelri** is considered medically necessary for the treatment of chronic obstructive pulmonary disease (COPD) when **ALL** of the following are met: 1. 18 years of age or older 2. **ONE** of the following:

Non-Covered Product	Criteria
	a. Documented failure, contraindication, or intolerance to **ONE** of the following Long-Acting Muscarinic Antagonist (LAMA) products: i. Incruse Ellipta ii. Spiriva Respimat iii. Spiriva HandiHaler iii. Tudorza Pressair b. Documented inability to use a dry-powder inhaler (DPI) or a soft-mist inhaler (for example, low inspiratory flow, unable to coordinate breath and actuation of device)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of Nebulized long-acting muscarinic antagonist products (Lonhala™ Magnair™ or Yupelri™) are considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months.
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
COPD is a common preventable and manageable lung disease that affects nearly 16 million people in the US.[1,2] Exposure to tobacco smoke is considered to be the primary cause of COPD, but there are other risk factors as well.[1] Occupational exposures to chemical agents and fumes, indoor and outdoor air pollution, genetics, age, and socioeconomic status are some of the other factors that may also have a role in the development of COPD. This disease is generally characterized by persistent airflow limitation that is progressive and related to chronic inflammation in the airways in response to noxious particles or gasses. Two main components contribute to this chronic airflow limitation: small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). None of the existing medication therapies have been found to definitively modify the long-term lung function decline observed in COPD. However, pharmacologic therapy, including inhaled bronchodilators such as the long-acting muscarinic antagonists (LAMAs), has demonstrated symptom and exacerbation reduction, as well as improved exercise tolerance and health status.

It is well- established that proper training on device technique is critically important when considering inhaled therapy for COPD.[1] It is estimated that on average, more than two-thirds of patients make at least one error using an inhalation device. In an observational study of the use of inhaled therapy for the continuous treatment of COPD (n = 2,935), providers observed errors in more than 50% of COPD device handlings, regardless of the

device used.[3] This study also reported an association between critical handling errors and COPD exacerbation rates, with exacerbations reported more frequently in the presence of a critical error.

FDA Indications
The nebulized long-acting muscarinic antagonists (LAMAs) are similarly indicated for the treatment of chronic obstructive pulmonary disease (COPD).[4,5]

- Lonhala Magnair is indicated for the long-term maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.
- Yupelri is indicated for the maintenance treatment of patients with COPD.

Lonhala Magnair and Yupelri are not indicated for use in children. The safety and efficacy in pediatric patients have not been established.[4,5]

Availability/Dosing
There are differences in the dosing frequency and nebulizer devices used to administer Lonhala Magnair and Yupelri.[4,5]

- The recommended dose of Lonhala is one unit-dose vial (25 mcg/1 mL glycopyrrolate) twice daily (BID) using the Magnair nebulizer device. The Magnair nebulizer system is an eFlow® Closed System vibrating membrane nebulizer that uses tidal breathing to deliver glycopyrrolate aerosol droplets into the lung within 3 minutes. The Magnair device is intended only for use with Lonhala vials.
- The recommended dose of Yupelri is one single-dose vial (175 mcg/3 mL revefenacin) once daily (QD) administered via any standard jet nebulizer. The dose is delivered over approximately 8 minutes. Standard jet nebulizers may be used to administer other inhaled medications as well.

Clinical Efficacy
There are no studies comparing Lonhala Magnair and Yupelri. In their respective pivotal trials, both produced statistically significant improvements in the trough forced expiratory volume in 1 second (FEV1) compared with placebo.[9-14]

Other LAMA Therapies
In addition to Lonhala Magnair and Yupelri, there are five other single-entity inhaled LAMAs. These products are also indicated for the long-term maintenance treatment of COPD. These are available as dry-powder inhalers (DPIs) or a soft-mist inhaler.

- Each type of inhaled drug delivery has advantages and disadvantages, making it more or less suitable for certain patients. The nebulized LAMAs do not require hand-breath coordination or extra effort during inhalation, which may make them an attractive option for patients who have impaired dexterity or muscle weakness.

Guidelines
The Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of COPD (2022) lists Lonhala Magnair and Yupelri as available LAMA therapies, but does not make any specific recommendations.

- LAMA therapy is a recommended initial treatment option in patients for the management of stable COPD. It is the preferred initial option in the vast majority of patients who are experiencing more frequent exacerbations and may be used with or without a long-acting beta$_2$-agonist (LABA) depending on the patient's symptom severity.
- The choice of inhaler device should be tailored to the individual patient. Randomized controlled trials have not determined superiority of any one type of device over another.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J7677	Revefenacin inhalation solution, FDA-approved final product, noncompounded, administered through DME, 1 mcg

References

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