PHARMACY COVERAGE GUIDELINE

YUPELRI™ (revefenacin) oral inhalation solution
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Yupelri (revefenacin) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is 18 years of age or older

2. Individual has a confirmed diagnosis of chronic obstructive pulmonary disease (COPD)

3. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **TWO** trials of the following inhaled anticholinergic/anti-muscarinic with an inhaled long-acting beta-agonist with or without an inhaled corticosteroid:
    a. Incruse ellipta (umeclidinium)
    b. Lonhala Magnair (glycopyrrolate)

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c. Spiriva (tiotropium)
d. Tudorza (aclidinium)

4. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for ipratropium bromide solution for nebulization or oral inhaler (e.g.., Atrovent HFA, Combivent Respimat)

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is a non-smoker or is quitting through use of behavior modification and/or medications aimed at smoking cessation

7. Individual does not have any degree of hepatic impairment

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as OATP1BI/1B3 inhibitors (e.g., rifampin, cyclosporine, etc.)

9. There are **NO** FDA-label contraindications, such as previous hypersensitivity to revefenacin or any component of this product

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Yupelri (revefenacin) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:
   a. Achieved and maintains an improved FEV1 over baseline
   b. Achieved and maintains a reduced number and frequency of exacerbations over baseline

2. Individual has been adherent with the medication

3. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. Individual is a non-smoker or is quitting through use of behavior modification and/or medications aimed at smoking cessation

5. Individual does not have any degree of hepatic impairment

6. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as: Paradoxical bronchospasm

7. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as OATP1BI/1B3 inhibitors (e.g., rifampin, cyclosporine, etc.)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Yupelri (revefenacin) inhalation solution is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Yupelri (revefenacin) is a long-acting muscarinic antagonist (LAMA). It has similar affinity to the subtypes of muscarinic receptors M1-M5. In the airways, it exhibits pharmacological effects through inhibition of M3 receptor at the smooth muscle leading to bronchodilation. The safety and efficacy of Yupelri (revefenacin) have been established in clinical trials when administered using the PARI LC® Sprint nebulizer with a mouthpiece and the PARI Trek® S compressor. The safety and efficacy delivered from non-compressor based nebulizer systems have not been established.

Characteristics COPD includes small airways disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). The presence of chronic inflammation causes structural changes and narrowing of the small airways.

No one COPD product adds superior clinical value over alternatives within any pharmacologic class. Guidelines recommend COPD medications by class, not by specific medication. A stepwise approach is used to minimize symptoms and reduce frequency and severity of exacerbations. COPD evidence-based clinical practice guidelines recommend combining medications from various pharmacologic classes for long-term management of COPD in a stepwise fashion as symptoms progress. As of yet, no medication modifies long-term decline in lung function.

Initial management of COPD patients includes either an inhaled long-acting beta agonist (LABA) or a LAMA, both agents relax bronchial smooth muscle. An inhaled corticosteroid (ICS) is used for those patients who are at high risk for exacerbations. Other COPD medications include inhaled short-acting bronchodilators (beta-agonists and antimuscarinic agents), methylxanthines, oral corticosteroids, and phosphodiesterase-4 (PDE-4) inhibitors.

Patients with COPD may be classified according to symptoms and exacerbation history into three groups (A, B, and E) using a validated instrument, such as the modified Medical Research Council (mMRC) dyspnea scale or the COPD assessment Test (CAT). For patients newly initiating therapy, exacerbation risk should be determined based on the patient's history of exacerbations and their severity in the past year; two or more exacerbations

requiring systemic glucocorticoids or one or more COPD hospitalizations indicate a greater risk of future exacerbations.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Modified Medical Research Council (mMRC) Dyspnea Scale:

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards of after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

COPD Assessment Test (CAT):

	Circle the number that best describes you	
I never cough	1 2 3 4 5	I cough all the time
I have no phlegm in my chest at all	1 2 3 4 5	My chest is completely full of phlegm
My chest does not feel tight at all	1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	1 2 3 4 5	I have no energy at all

Global Initiative for Chronic Obstructive Lung Disease (GOLD) assessment:

GOLD: severity of airflow limitation (based on postbronchodilator FEV1)		
Stage	**Severity**	**FEV1 (%predicted)**
In patients with FEV1 / FVC < 0.7		
GOLD 1	Mild	≥ 80
GOLD 2	Moderate	50-79
GOLD 3	Severe	30-49
GOLD 4	Very severe	< 30

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GOLD: Assessment of symptoms and risk for exacerbations		
Exacerbations/Hospitalizations	**Symptom assessment**	
	mMRC 0-1; CAT < 10	**mMRC ≥ 2; CAT ≥ 10**
0-1 exacerbations without hospitalization	A	B
≥ 2 exacerbations or ≥ 1 hospitalization	E	E
A: Low risk, less symptoms (mMRC 0-1 or CAT less than 10 & 0-1 exacerbation/year without hospitalization) B: Low risk, more symptoms (mMRC 2 or more or CAT 10 or more & 0-1 exacerbation/year without hospitalization) E: High risk (2 or more exacerbations/year or 1 or more hospitalizations for exacerbation) CAT: COPD Assessment Test mMRC: modified Medical Research Council dyspnea scale		

Management of Stable COPD based on GOLD ABE assessment of symptoms and risk of exacerbation:

Category	Symptoms	Risk	Suggested treatment
A	Less symptomatic: Mild or infrequent symptoms (breathless with strenuous exercise or when hurrying on level ground or walking up a slight hill) or CAT <10	Low: 0 or 1 exacerbations in the past year without associated hospitalization	Regular treatment with a long-acting bronchodilator, either LAMA or LABA, based on patient preference. Patients with very infrequent dyspnea may be appropriate for short-acting bronchodilators alone. Short-acting bronchodilator (SABA, SAMA, or combination of SABA-SAMA), as needed.
B	More symptomatic: Moderate to severe symptoms (patient has to walk more slowly than others of same age due to breathlessness, has to stop to catch breath when walking on level ground at own pace, or has more severe breathlessness) or CAT ≥10	Low: 0 or 1 exacerbations in the past year without associated hospitalization	Regular treatment with combination long-acting bronchodilator (LAMA-LABA) therapy. SABA available for symptom relief as needed.
E		High risk: ≥ 2 exacerbations per year or at least one exacerbation leading to hospitalization	Regular treatment with LABA plus LAMA. Combination glucocorticoid-LAMA-LABA inhaler may be appropriate in Group E patients presenting with hospitalization or elevated peripheral eosinophilia (≥300 cells/microL). SABA available for symptom relief as needed.

Resources:

Yupelri (revefenacin) oral solution for inhalation product information, revised by Mylan Specialty, L.P. 05-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 27, 2024.

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