Drug Monograph

Drug/Drug Class:	**Yupelri™ (revefenacin) solution for inhalation / COPD**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **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:	Yupelri™ is available in an inhalation solution containing 175 mcg revefenacin per 3 ml of aqueous solution administered via a standard jet nebulizer. Manufactured for: Mylan Specialty L.P. Morgantown, WV 26505
Summary of Findings:	The clinical development program for Yupelri included two 12-week, randomized, double blind, placebo-controlled, multiple dose, parallel-group confirmatory trials in subjects with moderate to very severe COPD designed to evaluate the efficacy of once daily Yupelri's effect on lung function. In both trials, at day 85, Yupelri 175 mcg demonstrated significant improvement in lung function (mean change from baseline in trough FEV1) compared to placebo.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Non-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 [2]

Almost 15.7 million Americans reported that they have been diagnosed with COPD, with 80-90% of COPD cases due to a history of smoking cigarettes. COPD accounts for the majority of deaths from chronic lower respiratory diseases, which was the third leading cause of death in the United States in 2015 and the fourth leading cause in 2016.

Dosage Form [1]

Yupelri™ is available in an inhalation solution containing 175 mcg revefenacin per 3 ml of aqueous solution administered via a standard jet nebulizer.

Manufacturer [1]

Manufactured for: Mylan Specialty L.P. Morgantown, WV 26505

Indication(s) [1]

Yupelri™ is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease.

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

Yupelri is a long-acting muscarinic antagonist (LAMA), which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5.

Pharmacokinetics:

	Yupelri
Metabolism	Via hydrolysis of the primary amide to a carboxylic acid forming its major active metabolite
Volume of Distribution	218 L – suggesting extensive distribution to tissues
Half-life	22-70 hours

Clinical Trial:

STUDY DESIGN	Two 12-week, randomized, double blind, placebo-controlled, multiple dose, parallel-group confirmatory trials in subjects with moderate to severe COPD designed to evaluate the efficacy of once daily Yupelri's effect on lung function.
INCLUSION CRITERIA	40 years of age or older, have a clinical diagnosis of COPD, a history of smoking greater than or equal to 10 pack-years, moderate to very severe COPD, and an FEV1/FVC ratio of 0.7 or less.
EXCLUSION CRITERIA	Not specified
TREATMENT REGIMEN	In both trials, patients were randomized to receive Yupelri 175 mcg once daily via a standard jet nebulizer or placebo.
RESULTS	The primary endpoint in both trials was change from baseline in trough (predose) FEV1 at Day 85. In trial 1, Yupelri had a Least Square (LS) mean difference from placebo of 146. In trial 2, Yupelri had a LS mean difference from placebo of 147. These numbers demonstrate a significant improvement in lung function compared to placebo.
SAFETY	Not specified.

Contraindications [(1)]

- Known hypersensitivity to revefenacin or any component of the product

Warnings and Precautions [(1)]

- Yupelri should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD.
- Yupelri can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs following dosing with Yupelri, it should be treated immediately with an inhaled, short-acting bronchodilator
- Yupelri should be used with caution in patients with narrow-angle glaucoma.
- Yupelri should be used with caution in patients with urinary retention.
- Immediate hypersensitivity reactions may occur after administration of Yupelri.

Adverse Effects [(1)]

Most common, ≥ 2%	Yupelri (n=395) **%**	Placebo (n=418) %
Cough	4	4
Nasopharyngitis	4	2
Upper respiratory tract	3	2

infection		
Headache	4	3
Back pain	2	1

Drug Interactions [(1)]

- Anticholinergics – there is potential for an additive interaction with concomitantly used anticholinergic medicines
- OATP1B1 and OATP1B3 inhibitors could lead to an increase in systemic exposure of the active metabolite

Dosage and Administration [(1)]

The recommended dosage regimen of Yupelri is one 175 mcg unit-dose vial administered once daily via a standard jet nebulizer using a mouthpiece.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost/month**
Revefenacin	Yupelri	Theravance/Mylan	175 mcg vial daily	$1,029.60
Glycopyrrolate	Lonhala Magnair	Sunovion	25 mcg vial twice daily	$1,132.80

** Wholesale Acquisition Cost

Conclusion

Yupelri is the first once-daily nebulized long-acting muscarinic antagonist to be approved for COPD. In clinical trials, Yupelri demonstrated significant improvement in lung function compared to placebo. Nebulized therapy can be helpful in maintenance therapy for COPD adults. Nebulizers are used with patients at any age, regardless of disease severity and acuity, and can be appropriate in all clinical settings. Compared with multi-dose inhalers and dry powder inhalers, nebulizers require little or no hand-breath coordination and effort during inhalation.

Recommendation

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

References

1) Yupelri™ (revefenacin). Retrieved 1/18/2019 from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6dfebf04-7c90-436a-9b16-750d3c1ee0a6&audience=consumer
2) Yupelri (revefenacin). IPD Analytics Rx Insights_New Drug Approval Review_Yupelri_11 2018.pdf

Prepared by: Luke Boehmer PharmD

Date: January 18, 2019