

STEPS

New Drug Reviews

Reverfenacin (Yupelri) for the Treatment of Chronic Obstructive Pulmonary Disease

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Reverfenacin (Yupelri) is a once-daily, nebulized, long-acting muscarinic antagonist labeled for the treatment of moderate to severe chronic obstructive pulmonary disease (COPD).

Safety

Reverfenacin is generally safe with minimal systemic adverse effects.¹ As with other long-acting treatments, reverfenacin should not be used to treat acute symptoms. Similar to other inhaled therapies, it has a theoretic risk of immediate hypersensitivity reaction and acute bronchospasm. Reverfenacin is anticholinergic and may induce narrow-angle glaucoma or worsen urinary retention. Reverfenacin has not been studied in pregnant women or breastfed infants. The manufacturer recommends against its use in patients with hepatic impairment or those taking rifampin or cyclosporine (Sandimmune).

Tolerability

Reverfenacin was shown to be well tolerated in clinical trials. In two 12-week placebo-controlled trials of 1,225 patients with moderate to severe COPD, adverse effects leading to discontinuation were more common in patients receiving placebo (19%) than reverfenacin (13%).²

STEPS new drug reviews cover Safety, Tolerance, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

This series is coordinated by Allen F. Shaughnessy, PharmD, MMedEd, assistant medical editor.

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Author disclosure: No relevant financial affiliations.

Drug	Dosage	Dose form	Cost*
Reverfenacin (Yupelri)	88 mcg once daily (up to 175 mcg once daily)	175 mcg per 3 mL aqueous solution via nebulizer	\$360

*—Estimated retail price for one month of treatment based on information obtained at <https://www.goodrx.com> (accessed November 22, 2019).

Effectiveness

Reverfenacin is superior to placebo in improving forced expiratory volume in one second (FEV₁) for patients with moderate to severe COPD. A 28-day randomized, double-blind study compared placebo and reverfenacin in 355 patients with COPD, a mean age of 62 years, and a mean FEV₁ of 44% of predicted. Patients were allowed to use inhaled corticosteroids and short-acting bronchodilators.³ Reverfenacin improved FEV₁ by at least 100 mL from baseline with effects lasting four hours or more; participants' mean number of albuterol puffs also decreased from three to two per day when using reverfenacin. These results were replicated in an 85-day randomized, double-blind study (619 patients older than 40 years) in which participants were also allowed to use long-acting muscarinic antagonists and inhaled steroid therapy.⁴ This study demonstrated improvements in FEV₁ that were sustained over the entire study period, but reverfenacin has not been evaluated for its effect in decreasing exacerbations, hospitalization rates, mortality, functional status, and quality of life.

Price

Reverfenacin costs approximately \$360 per month, compared with about \$415 per month for common inhaled long-acting muscarinic antagonists such as tiotropium (Spiriva). This cost is more than that of most commonly used COPD

medications. Revenefenacin may require prior authorization or formulary exemption to obtain insurance coverage.

Simplicity

Revenefenacin is administered as a nebulized solution once daily over eight minutes. The initial daily dosage is 88 mcg and can be increased to 175 mcg daily if needed. Patients should be instructed on how to use the accompanying nebulizer. The sterile solution is provided in individual vials.

Bottom Line

Revenefenacin is a once-daily nebulized alternative to metered dose long-acting muscarinic antagonists for patients with moderate to severe COPD. Given its expense, complicated administration process, and lack of evidence that it improves key patient-oriented outcomes, its use should be limited to patients who are unable to use a metered dose inhaler.

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References

1. DailyMed. Drug label information. Yupelri—revenefenacin solution. Accessed May 16, 2019. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6dfeb04-7c90-436a-9b16-750d3c1ee0a6>
2. Ferguson G, Pudi KK, Feldmann G, et al. Efficacy and safety of revenefenacin (REV), a long-acting muscarinic antagonist for nebulization: results of replicate randomized, double-blind, placebo-controlled, parallel-group phase 3 trials in participants with moderate to very severe COPD. *Eur Respir J*. 2017;50(suppl 61):1812.
3. Pudi KK, Barnes CN, Moran EJ, et al. A 28-day, randomized, double-blind, placebo-controlled, parallel group study of nebulized revenefenacin in patients with chronic obstructive pulmonary disease. *Respir Res*. 2017;18(1):182.
4. Ferguson GT, Feldman G, Pudi KK, et al. Improvements in lung function with nebulized revenefenacin in the treatment of patients with moderate to very severe COPD: results from two replicate phase III clinical trials. *Chronic Obstr Pulm Dis*. 2019;6(2):154-165. ■

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