



Tiotropium bromide and olodaterol (Stiolto™ Respimat®) Agents Abbreviated New Drug Update

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OVERVIEW¹

- Combination of the anticholinergic, tiotropium, and the long-acting beta2-adrenergic agonist (LABA), olodaterol.
- Approved for:
 - Maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD)
 - Limitations: Not indicated to treat acute deterioration of COPD or asthma
- Strengths: 2.5 mcg each of tiotropium and olodaterol per actuation; two actuations equal one dose.
- Dosage and Administration:
 - Two oral inhalations once daily
 - Cartridge is inserted into inhaler and primed
- Contraindications: hypersensitivity to any component; all LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication; Stiolto Respimat is not indicated for asthma.
- Warnings:
 - Boxed warning regarding LABA (olodaterol) use and increased risk of asthma-related death; excessive use of a LABA, or use in conjunction with other medications containing LABA, can lead to potentially fatal cardiovascular (CV) effects; should not be used as rescue therapy for acute episodes of bronchospasm
 - Immediate hypersensitivity reactions, life-threatening paradoxical bronchospasm; use with caution in patients with CV or convulsive disorders, thyrotoxicosis, or sensitivity to sympathomimetic drugs; may cause worsening of narrow-angle glaucoma and urinary retention; monitor for hypokalemia and hyperglycemia
- Adverse Reactions (≥ 3%): nasopharyngitis, cough, and back pain.
- Drug Interactions: Caution with other adrenergic drugs, beta blockers, monoamine oxidase (MAO) inhibitors, tricyclic antidepressants, and QTc-prolonging drugs, as well as drugs that may potentiate hypokalemia or electrocardiogram (ECG) changes (e.g., xanthine derivatives, steroids, diuretics); avoid use with anticholinergic-containing drugs.
- Renal impairment: Patients with moderate/severe impairment (creatinine clearance of ≤60ml/min) should be closely monitored for anticholinergic adverse effects.

- The efficacy of Stiolto Respimat is based on two four-week dose-ranging trials (n=592) and two 52-week confirmatory active-controlled trials (n=5,162) in patients with COPD. Dose selection was based on trials for the individual components of the drug, tiotropium and olodaterol.

CLINICAL CONSIDERATIONS²

- Tiotropium/olodaterol (Stiolto Respimat) is the second combination containing an anticholinergic and LABA to be approved for maintenance treatment of COPD, following the Food and Drug Administration (FDA) approval of umeclidinium/vilanterol (Anoro™ Ellipta™) in 2013. Stiolto Respimat is dosed as two inhalations once daily, while Anoro Ellipta is dosed as one inhalation once daily. The components of Stiolto Respimat are available as single agents.
- Additional combination products available for the maintenance treatment of COPD:
 - fluticasone furoate/vilanterol (Breo® Ellipta®): one inhalation once daily
 - fluticasone propionate/salmeterol (Advair® Diskus): one inhalation twice daily
 - budesonide/formoterol (Symbicort®): two inhalations twice daily
 - ipratropium/albuterol (Combivent® Respimat®): indicated for treatment of COPD in patients requiring a second bronchodilator; dosed four times daily
- Available inhaled anticholinergics: aclidinium bromide (Tudorza™ Pressair™), ipratropium (Atrovent® HFA), tiotropium (Spiriva HandiHaler®, Spiriva® Respimat®), umeclidinium (Incruse® Ellipta®).
- Available inhaled LABAs: arformoterol (Brovana®), formoterol (Foradil® Aerolizer®, Perforomist™), indacaterol (Arcapta™ Neohaler™), olodaterol (Striverdi® Respimat®), and salmeterol (Serevent® Diskus).
- Roflumilast (Daliresp™) is an oral phosphodiesterase-4 (PDE-4) inhibitor indicated for use in patients with severe COPD.
- The 2015 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of COPD guidelines continue to identify bronchodilator medication as being central to symptom management in COPD across all patient groups.
 - Group B: Regular use of one of more long-acting bronchodilators (LABA or anticholinergic) is recommended in patients with more significant symptoms but low risk of exacerbations. There is insufficient evidence to recommend one product over another. The choice between a LABA, anticholinergic, theophylline, or combination therapy depends on individual response.
 - Group C, D: Initial treatment for patients ranging from less to more symptoms with a high risk of exacerbations is a fixed combination of an inhaled corticosteroid (ICS)/bronchodilator (LABA or anticholinergic), PDE-4 inhibitor/bronchodilator, or a combination of a LABA and anticholinergic. There is some evidence for the use of triple therapy for Group D patients (ICS plus two bronchodilators).

REFERENCES

1 Stiolto Respimat [Package Insert]. Ridgefield, CT; Boehringer Ingelheim Pharmaceuticals; May 2015.

2 Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) Updated 2015. Available from: <http://www.goldcopd.org/>. Accessed June 15, 2015.