

April 2019 ~ Resource #350407

Inhaled Medications for COPD

The goals of COPD treatment are to reduce symptoms and to decrease the risk and severity of future exacerbations.¹ COPD risk factors (e.g., occupational exposures, air pollution, etc) should be reduced when possible, the most important being smoking cessation.¹ There are several different inhalation devices and nebulizers available for the treatment of COPD. Inhalation delivery appears to be equal between devices, so the choice will depend on availability, cost, as well as the patient's preference and ability to operate the devices properly.¹ Nebulizers may be easier to use in sicker patients. Note that some nebulizer solutions can be used with standard nebulizers (e.g., *Yupelri*) while others require a special nebulizer (e.g., *Lonhala Magnair*).² Appropriate instruction on inhalation technique is very important. Technique should always be assessed prior to determining efficacy of therapy.¹ The following table lists inhalation therapy indicated for the treatment of COPD and their role in therapy of **stable** disease.

Medication ^c	Dosing Frequency ^a	Cost ^b
Short-Acting Bronchodilators		
As-needed, for occasional symptoms. ¹ Can combine beta-2 agonists and ipratropium to improve efficacy and/or limit side effects. ^{1,3} A long-acting bronchodilator (LABA or LAMA) is preferred to regular use of short-acting bronchodilator [Evidence Level A-1]. ¹ However, regular use of short-acting bronchodilators does improve symptoms and FEV1 in patients with COPD. ¹ Note that these agents are also available as nebulizer solutions which may be less expensive but may be more inconvenient to use.		
Beta-2 Agonist Inhalers	Every four to six hours as needed. ^{2,a}	U.S.: \$36/200 doses Canada: \$6/200 doses
Albuterol (also called Salbutamol) (U.S.: <i>ProAir HFA</i> , <i>ProAir RespiClick</i> , <i>Proventil HFA</i> , <i>Ventolin HFA</i> , generics Canada: <i>Airomir</i> , <i>Ventolin Diskus</i> , <i>Ventolin HFA</i> , generics)		
Levalbuterol (U.S. only) (<i>Xopenex HFA</i> , generics)		U.S.: \$59/200 doses
Terbutaline (Canada only) (<i>Bricanyl Turbuhaler</i>)		Canada: \$9/100 doses
Anticholinergic (Maintenance)	U.S. MDI: Four times daily Canada MDI: Three to four times daily Nebulizer: Every six to eight hours	U.S.: MDI \$388/200 doses; Neb: \$22/120 doses Canada: MDI \$21/200 doses; Neb: \$171/120 doses
Ipratropium (<i>Atrovent HFA</i> ; nebulizer solution)		
Combination Beta-2 Agonist/ Anticholinergic: Can use this combination to improve efficacy and/or limit adverse effects. ¹		
Albuterol/Ipratropium (<i>Combivent Respimat</i> ; nebulizer solution)	MDI: Four times daily (in place of long-acting bronchodilator), and/or as needed. ^{2,a} U.S. Neb: Same as MDI above ² Canada Neb: Three to four times daily	U.S.: MDI \$402/120 doses; Neb: \$73/120 doses Canada: MDI \$32/120 doses; Neb: \$172/120 doses

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Medication ^c	Dosing Frequency ^a	Cost ^b
Long-Acting Bronchodilators		
Long-Acting Beta-2 Agonists (LABAs) and Long-Acting Muscarinic Antagonists (LAMAs): First-line option for patients with persistent symptoms despite use of a short-acting bronchodilator. ¹ Therapy can start with one or two long-acting bronchodilators (depending on severity of symptoms and exacerbations). ¹ Add a LAMA to a LABA (or vice versa) if one does not control symptoms. ¹ LAMAs are superior to LABAs in preventing exacerbations [Evidence Level A-1] and possibly hospitalizations [Evidence Level B-1], so may be preferred in patients with two or more exacerbations or at least one hospitalization in the last year. ^{1,3}		
Long-Acting Beta-2 Agonists (LABAs)		
Arformoterol (U.S. only) (<i>Brovana</i> nebulizer solution)	Twice daily	U.S.: \$1,030
Formoterol (<i>Perforomist</i> nebulizer solution [U.S.], <i>Foradil</i> [Canada])	Twice daily	U.S.: \$972 Canada: \$57
Indacaterol (<i>Arcapta Neohaler</i> [U.S.], <i>Onbrez Breezhaler</i> [Canada])	Once daily	U.S.: \$235 Canada: \$50
Olodaterol (<i>Striverdi Respimat</i>)	Once daily	U.S.: \$212 Canada: Approved but not marketed at time of publication.
Salmeterol (<i>Serevent Diskus</i>)	Twice daily	U.S.: \$388 Canada: \$63
Long-Acting Muscarinic Antagonists (LAMAs)		
Aclidinium (<i>Tudorza Pressair</i> [U.S.], <i>Tudorza Genuair</i> [Canada])	Twice daily	U.S.: \$352 Canada: \$57
Glycopyrrolate (also called Glycopyrronium) (<i>Seebri Neohaler</i> , <i>Lonhala Magnair</i> nebulizer solution [U.S.], <i>Seebri Breezhaler</i> [Canada])	U.S.: Twice daily Canada: Once daily	U.S.: <i>Seebri Neohaler</i> \$394; <i>Lonhala Magnair</i> \$1,133 Canada: <i>Seebri Breezhaler</i> \$57
Revefenacin (U.S. only) (<i>Yupelri</i> nebulizer solution)	Once daily	U.S.: \$1,030
Tiotropium (<i>Spiriva HandiHaler</i> , <i>Spiriva Respimat</i>)	Once daily	U.S.: \$429 (<i>HandiHaler/Respimat</i>) Canada: \$57 (<i>HandiHaler/Respimat</i>)
Umeclidinium (<i>Incruse Ellipta</i>)	Once daily	U.S.: \$334 Canada: \$54

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Medication ^c	Dosing Frequency ^a	Cost ^b
Long-Acting Bronchodilators, continued		
Combination LABA/LAMA		
Formoterol/Aclidinium (<i>Duaklir Pressair</i> [U.S.], <i>Duaklir Genuair</i> [Canada])	Twice daily	U.S.: \$995 Canada: \$65
Formoterol/Glycopyrrolate (<i>Bevespi Aerosphere</i>)	Twice daily	U.S.: \$365 Canada: Approved but not marketed at time of publication.
Indacaterol/Glycopyrrolate (<i>Utibron Neohaler</i> [U.S.], <i>Ultibro Breezhaler</i> [Canada])	U.S.: Twice daily Canada: Once daily	U.S.: \$367 Canada: \$85
Olodaterol/Tiotropium (<i>Stiolto Respimat</i> [U.S.], <i>Inspiroto Respimat</i> [Canada])	Once daily	U.S.: \$398 Canada: \$67
Vilanterol/Umeclidinium (<i>Anoro Ellipta</i>)	Once daily	U.S.: \$410 Canada: \$89
Combination LABA/ICS: Consider when exacerbations continue despite appropriate long-acting bronchodilator therapy. ¹ Patients with blood eosinophil counts of about 2% (100 cells/mcL [0.1 x 10 ⁹ cells/L]) or more have been shown to have benefit with the addition of an ICS [Evidence Level B-2]. ^{1,4} Patients with eosinophil counts of less than about 2% (100 cells/mcL [0.1 x 10 ⁹ cells/L]) may not benefit from ICS. May be used first-line in patients with blood eosinophil counts of about 4% (300 cells/mcL [0.3 x 10 ⁹ cells/L]) or more, or in patients who also have asthma. ¹ Can combine with LAMA. ¹ Chronic ICS use increases pneumonia risk in patients with severe COPD. ¹		
Formoterol/Budesonide (<i>Symbicort</i> [U.S.], <i>Symbicort Turbuhaler</i> [Canada])	Twice daily	U.S.: \$347 Canada: \$95
Salmeterol/Fluticasone propionate (<i>Advair Diskus</i> , <i>Wixela Inhub</i> [U.S. only], generic [U.S. only]) *Strengths approved for COPD: ^a U.S.: 250/50 Canada: 250/50 and 500/50	Twice daily	U.S.: <i>Advair Diskus</i> \$394; <i>Wixela Inhub</i> \$116; generic \$354 Canada: \$155
Vilanterol/Fluticasone furoate (<i>Breo Ellipta*</i>) *Only the 100/25 mcg strength is approved for COPD. ^a	Once daily	U.S.: \$351 Canada: \$91

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Medication ^c	Dosing Frequency ^a	Cost ^b
Long-Acting Bronchodilators, continued		
Combination ICS/LAMA/LABA: Consider for patients with severe or very severe COPD with continued exacerbations despite use of LABA and LAMA or LABA/ICS. ¹		
Fluticasone furoate/Umeclidinium/Vilanterol (<i>Trelegy Ellipta</i>)	Once daily	U.S.: \$546 Canada: \$143

Abbreviations: COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist (or anticholinergic); MDI = metered-dose inhaler; Neb = nebulizer solution.

- a. **Information from product labeling unless otherwise indicated:** *Airomir* Canada (October 2017); *Atrovent HFA* (August 2012); *Atrovent HFA* Canada (February 2016); Ipratropium nebulizer solution (Actavis; April 2017); Ipratropium nebulizer solution Canada (Pharmascience; May 2017); *Bricanyl Turbuhaler* Canada (January 2018); *Combivent Respimat* Canada (June 2016); *Combivent UDV* Canada (November 2015); *Brovana* (February 2014); *Perforomist* (October 2018); *Foradil* Canada (May 2013); *Arcapta Neohaler* (March 2017); *Onbrez Breezhaler* Canada (January 2015); *Striverdi Respimat* (April 2018); *Striverdi Respimat* Canada (July 2016); *Serevent Diskus* (December 2018); *Serevent Diskus* Canada (January 2017); *Tudorza Pressair* (November 2018); *Tudorza Genuair* Canada (June 2018); *Seebri Neohaler* (January 2017); *Lonhala Magnair* (January 2018); *Seebri Breezhaler* Canada (September 2016); *Yupelri* (November 2018); *Spiriva Handihaler* (February 2018); *Spiriva Respimat* (February 2019); *Spiriva Handihaler* Canada (November 2017); *Spiriva Respimat* Canada (June 2016); *Incruse Ellipta* (October 2017); *Incruse Ellipta* Canada (July 2017); *Duaklir Pressair* (March 2019); *Duaklir Genuair* Canada (June 2018); *Bevespi Aerosphere* (August 2017); *Utibron Neohaler* (January 2017); *Ultibro Breezhaler* Canada (January 2018); *Stiolto Respimat* (October 2018); *Inspiolto Respimat* Canada (June 2018); *Anoro Ellipta* (October 2017); *Anoro Ellipta* Canada (August 2017); *Symbicort* (December 2017); *Symbicort Turbuhaler* Canada (October 2016); *Advair Diskus* (January 2019); *Advair Diskus* Canada (October 2018); *Breo Ellipta* (January 2019); *Breo Ellipta* Canada (January 2019); *Trelegy Ellipta* (January 2019); *Trelegy Ellipta* Canada (October 2018).
- b. Pricing based on wholesale acquisition cost (WAC) for an MDI or 30-day supply of highest strength, of generic if available. U.S. medication pricing by Elsevier, accessed March 2019.
- c. The only long-acting inhalation therapies included are specifically approved for treatment of COPD.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality RCT 2. SR/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	



*Outcomes that matter to patients (e.g., morbidity, mortality, symptom improvement, quality of life).

RCT = randomized controlled trial; SR = systematic review [Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <http://www.aafp.org/afp/2004/0201/p548.pdf>.]



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