

November 2022 ~ Resource #381116

Inhaled Medications for COPD

The goals of COPD treatment are to reduce symptoms and to decrease the risk and severity of future exacerbations.¹ The choice of inhalation device depends on availability, cost, and the patient (e.g., preference, 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 chart below includes inhalation therapy indicated for the treatment of COPD and their role in therapy of **stable** disease.^c

Medication ^c	Dosing Frequency ^a	Approximate 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 beta-2 agonists are also available as nebulizer solutions which may be less expensive but less convenient to use.		
Beta-2 Agonist Inhalers		
Albuterol (also called salbutamol) (US: <i>ProAir HFA</i> , <i>ProAir RespiClick</i> , <i>ProAir Digihaler</i> , <i>Proventil HFA</i> , <i>Ventolin HFA</i> , generics; Canada: <i>Airomir</i> , <i>Ventolin Diskus</i> , <i>Ventolin HFA</i> , generics)	Every four to six hours as needed. ^{2,a}	US: \$36/200 doses Canada: \$6/200 doses
Levalbuterol (US only) (<i>Xopenex HFA</i> , generics)		US: \$59/200 doses
Terbutaline (Canada only) (<i>Bricanyl Turbuhaler</i>)	As required, up to six doses/24 hours.	Canada: \$11/120 doses
Anticholinergic (Maintenance)		
Ipratropium (<i>Atrovent HFA</i> , <i>Ipravent</i> [Canada], generics)	US MDI: four times daily. Canada MDI: three to four times daily. Nebulizer: every six to eight hours. ²	US: MDI \$445/200 doses; neb \$9/120 doses Canada: MDI \$22/200 doses; neb \$160/120 doses
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} US neb: same as MDI above. ² Canada neb: three to four times daily.	US: MDI \$460/120 doses; neb \$55/120 doses Canada: MDI \$33/120 doses; neb \$105/120 doses

Medication ^c	Dosing Frequency ^a	Approximate 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 (US only) (<i>Brovana</i> nebulizer solution, generics)	Twice daily.	US: \$385
Formoterol (US: <i>Perforomist</i> nebulizer solution, generics; Canada: <i>Foradil</i>)	Twice daily.	US: \$960 Canada: \$60
Indacaterol (Canada only) (<i>Onbrez Breezhaler</i>)	Once daily.	Canada: \$50
Olodaterol (US only) (<i>Striverdi Respimat</i>)	Once daily.	US: \$245
Salmeterol (<i>Serevent Diskus</i>)	Twice daily.	US: \$425 Canada: \$72
Long-Acting Muscarinic Antagonists (LAMAs)		
Aclidinium (<i>Tudorza Pressair</i> [US], <i>Tudorza Genuair</i> [Canada])	Twice daily.	US: \$625 Canada: \$57
Glycopyrrolate (also called Glycopyrronium) (US: <i>Lonhala Magnair</i> nebulizer solution; Canada: <i>Seebri Breezhaler</i>)	US: twice daily. Canada: once daily.	US: \$1,133 Canada: \$57
Revefenacin (US only) (<i>Yupelri</i> nebulizer solution)	Once daily.	US: \$1,260
Tiotropium (<i>Spiriva HandiHaler</i> , <i>Spiriva Respimat</i>)	Once daily.	US: \$495 (<i>Handihaler/Respimat</i>) Canada: \$59 (<i>Handihaler/Respimat</i>)
Umeclidinium (<i>Incruse Ellipta</i>)	Once daily.	US: \$355 Canada: \$54

Medication ^c	Dosing Frequency ^a	Approximate Cost ^b
Long-Acting Bronchodilators, continued		
Combination LABA/LAMA		
Formoterol/Aclidinium (<i>Duaklir Pressair</i> [US], <i>Duaklir Genuair</i> [Canada])	Twice daily.	US: \$625 Canada: \$65
Formoterol/Glycopyrrolate (US only) (<i>Bevespi Aerosphere</i>)	Twice daily.	US: \$405
Indacaterol/Glycopyrrolate (Canada only) (<i>Ultibro Breezhaler</i>)	Once daily.	Canada: \$85
Olodaterol/Tiotropium (<i>Stiolto Respimat</i> [US], <i>Inspiolto Respimat</i> [Canada])	Once daily.	US: \$455 Canada: \$67
Vilanterol/Umeclidinium (<i>Anoro Ellipta</i>)	Once daily.	US: \$450 Canada: \$95
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> , generics [US]; <i>Symbicort Turbuhaler</i> [Canada])	Twice daily.	US: \$250 Canada: \$95
Salmeterol/Fluticasone propionate (<i>Advair Diskus</i> , <i>Wixela Inhub</i> , generics)	Twice daily.	US: \$115 Canada: \$80
Vilanterol/Fluticasone furoate (<i>Breo Ellipta</i> , generic [US only])	Once daily.	US: \$250 Canada: \$100

Medication ^c	Dosing Frequency ^a	Approximate Cost ^b
Long-Acting Bronchodilators, continued		
Combination ICS/LAMA/LABA: Consider for patients with severe or very severe COPD with continued frequent and/or serious exacerbations despite optimized use of LABA and LAMA or LABA/ICS. ¹		
Budesonide/Glycopyrrolate/Formoterol (<i>Breztri Aerosphere</i>)	Twice daily.	US: \$610 Canada: \$135
Fluticasone furoate/Umeclidinium/Vilanterol (<i>Trelegy Ellipta</i>)	Once daily.	US: \$620 Canada: \$150

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

- a. **US product labeling used within this resource:** *Advair Diskus* (August 2020), *Anoro Ellipta* (August 2020), *Atrovent HFA* (February 2020), *Bevespi Aerosphere* (May 2019), *Breo Ellipta* (January 2019), *Breztri Aerosphere* (July 2020), *Brovana* (May 2019), *Combivent Respimat* (December 2021), *Duaklir Pressair* (March 2019), *Incruse Ellipta* (June 2019), *Lonhala Magnair* (August 2020), *Perforomist* (May 2019), *Serevent Diskus* (December 2018), *Spiriva Handihaler* (November 2021), *Spiriva Respimat* (November 2021), *Stiolto Respimat* (November 2021), *Striverdi Respimat* (November 2021), *Symbicort* (December 2017), *Trelegy Ellipta* (May 2022), *Tudorza Pressair* (April 2019), *Yupelri* (November 2021).
Canadian product labeling used within this resource: *Advair Diskus* (June 2020), *Airomir* (December 2020), *Anoro Ellipta* (August 2017), *Atrovent HFA* (November 2019), *Breztri Aerosphere* (July 2021), *Breo Ellipta* (January 2019), *Bricanyl Turbuhaler* (June 2021), *Combivent Respimat* (November 2019), *Duaklir Genuair* (September 2022), *Foradil* (July 2021), *Incruse Ellipta* (September 2020), *Inspiolto Respimat* (November 2019), ipratropium nebulizer solution (Teva, February 2022), *Onbrez Breezhaler* (March 2021), *Seebri Breezhaler* (September 2016), *Serevent Diskus* (March 2021), *Spiriva Handihaler* (April 2022), *Spiriva Respimat* (May 2019), *Striverdi Respimat* (May 2019), *Symbicort Turbuhaler* (February 2021), *Trelegy Ellipta* (January 2022), *Tudorza Genuair* (September 2022), *Ultibro Breezhaler* (January 2020).
- b. Pricing based on wholesale acquisition cost (WAC) for an MDI or 30-day supply of highest strength of generic if available. US medication pricing by Elsevier, accessed October 2022.
- c. The only long-acting inhalation therapies included are FDA- or Health Canada-approved for treatment of COPD. Not all available strengths are approved for treatment of COPD; check product labeling for approved strengths/dosing.

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.

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.*	<ol style="list-style-type: none"> High-quality randomized controlled trial (RCT) Systematic review (SR)/Meta-analysis of RCTs with consistent findings All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> Lower-quality RCT SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings Cohort study 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).

[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.

<https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html#>.]

References

- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the prevention, diagnosis, and management, of chronic obstructive pulmonary disease (2022 report). https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf. (Accessed October 6, 2022).
- Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2022. <http://www.clinicalkey.com>. (Accessed October 6, 2022).
- Criner GJ, Bourbeau J, Diekemper RL, et al. Prevention of acute exacerbations of COPD: American College of Chest Physicians and Canadian Thoracic Society Guideline. *Chest*. 2015 Apr;147(4):894-942.
- Bafadhel M, Peterson S, De Blas MA, et al. Predictors of exacerbation risk and response to budesonide in patients with chronic obstructive pulmonary disease: a post-hoc analysis of three randomised trials. *Lancet Respir Med*. 2018 Feb;6(2):117-126.

Cite this document as follows: Clinical Resource, *Inhaled Medications for COPD. Pharmacist's Letter/Prescriber's Letter*. November 2022. [381116]

—To access hundreds more clinical resources like this one, visit trchealthcare.com to log in or subscribe—