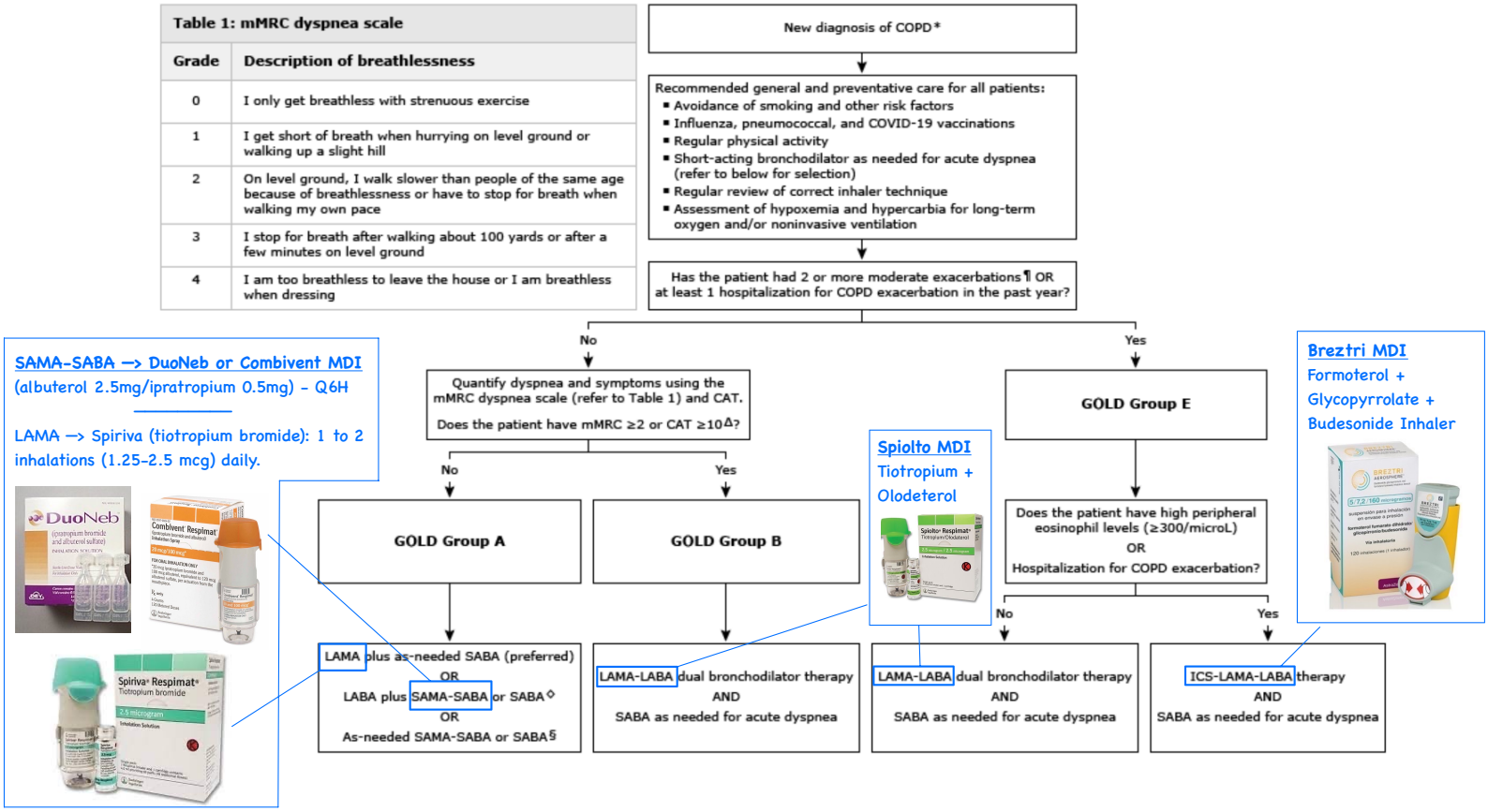
Treatment Algorithm for Newly Diagnosed COPD Patients (UpToDate)

(GOLD: Global Initiative for Chronic Obstructive Lung Disease)

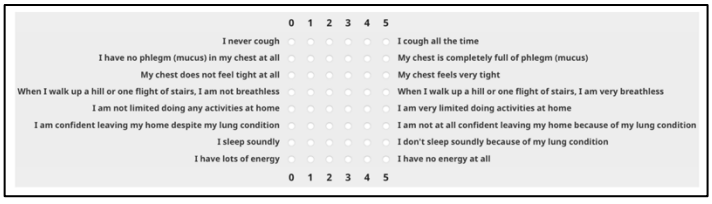
Table 1: mMRC dyspnea scale	
Grade	**Description of breathlessness**
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing



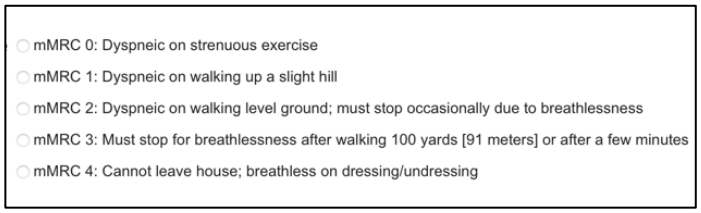
Summary Statements

- COPD is diagnosed based on the presence of chronic resp symptoms (dyspnea, cough, sputum production) accompanied by airflow limitation → severity of symptoms quantified with mMRC dyspnea scale and CAT (COPD Assessment Test) → graded scores determine the most effective treatment approaches for COPD (GOLD Tx Approach).
- The mainstay of drug treatment for stable COPD are inhaled bronchodilators: beta-2 agonists and muscarinic antagonists → commonly given in combination +/- inhaled corticosteroids (ICS).
- GOLD approach focuses on targeting therapies based on symptoms and exacerbation risk (A, B, E groups).

Modified Medical Research Council (mMRC) Scale for Dyspnea



COPD Assessment Test (CAT)



- All COPD patients should be prescribed a SABA for relief of dyspnea and treatment of exacerbations, instead of SAMA → SAMA is not recommended in patients using a LAMA.
- In patients who are taking LABAs without LAMA coadministration, we prefer using SABA-SAMA (e.g., DuoNeb) → dual therapy offers greater bronchodilator response than either agent alone.
- For patients prescribed a LAMA, a SAMA should not be prescribed concomitantly due to cumulative anticholinergic side effects and theoretical blockage of LAMA effects by the SAMA. Patients taking a LAMA should use a SABA alone for relief of dyspnea.

Follow-Up Management of COPD (UpToDate)

No exacerbations and no dypnea / low COPD impact (i.e., mMRC 0-1 or CAT < 10)

Current therapy	Actions
SABA or SABA-SAMA as needed	Continue current therapy
LAMA, LABA, or LAMA-LABA	Continue current therapy
LABA-ICS or LABA-LAMA-ICS	Taper or discontinue ICS dose to reduce adverse effects of ICS[Δ]

Persistent dyspnea or high COPD impact (i.e., mMRC > 2 or CAT > 10) with no exacerbations

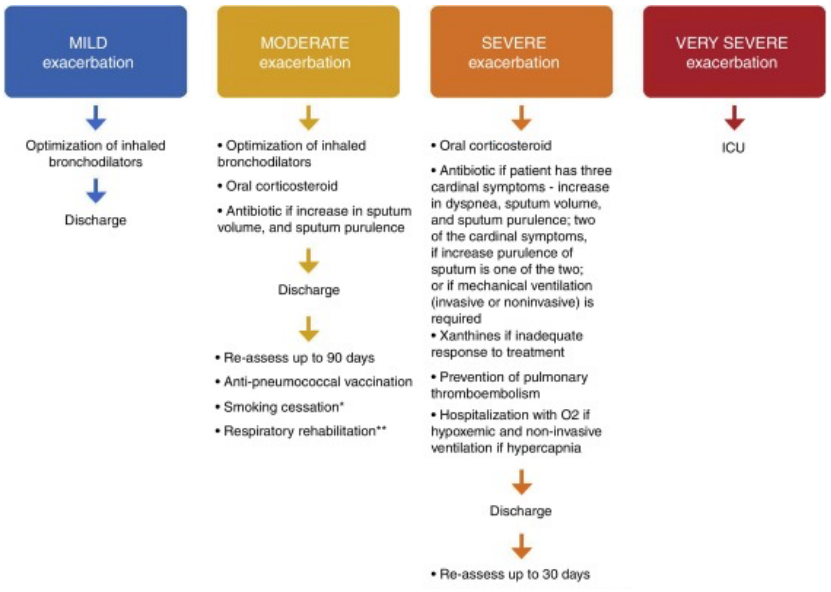
Current therapy	Actions
SABA or SABA-SAMA as needed	Add LAMA or LABA
LAMA or LABA monotherapy	Change to LAMA-LABA
LABA-ICS	▪ LAMA-LABA-ICS ▪ LAMA-LABA if lack of response to ICS or adverse effects from ICS
LAMA-LABA	▪ Substitute alternate delivery system or different LAMA-LABA agents ▪ Trial of LAMA-LABA-ICS, in patients with blood eosinophils ≥100 cells/microL[◇] ▪ Additional interventions may include low-dose theophylline, repeat pulmonary rehabilitation, and nonpharmacologic therapies[§]
LAMA-LABA-ICS	▪ Continue LAMA-LABA-ICS ▪ Additional interventions may include low-dose theophylline, repeat pulmonary rehabilitation, and nonpharmacologic therapies for COPD[§] ▪ Stop ICS, if initial indication unclear, lack of response, or adverse effect to ICS[Δ]

Persistent dyspnea or high COPD impact +/- 1 or more exacerbations in the past year

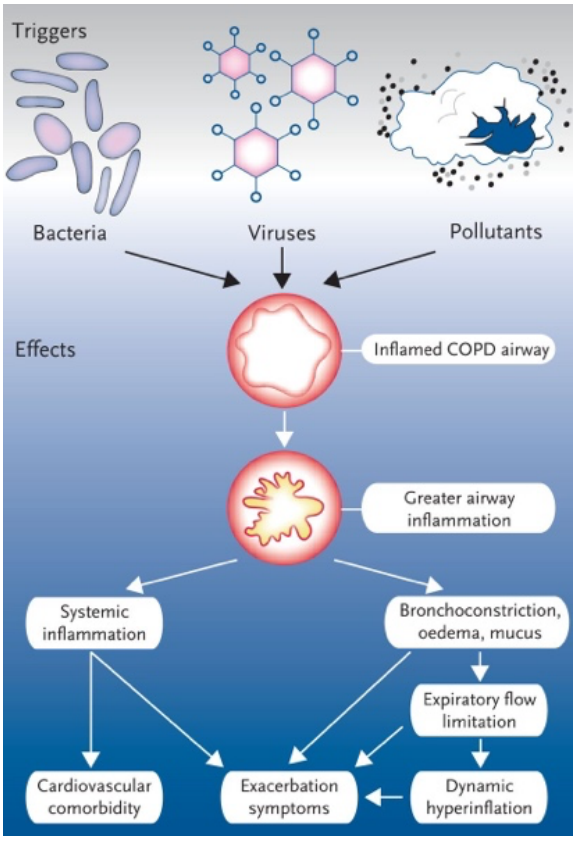
Current therapy[§]	Actions
SABA or SABA-SAMA as needed	Add LAMA
LAMA or LABA monotherapy	▪ LAMA-LABA, if blood eosinophil count <300/microL[◇] **or** ▪ LAMA-LABA-ICS, if blood eosinophil count ≥300/microL[◇] **or** hospitalization for COPD exacerbation **or** ▪ LABA-ICS, if blood eosinophil count ≥100/microL[◇] **and** LAMA contraindicated
LAMA-LABA	▪ LAMA-LABA-ICS, if blood eosinophil count ≥100/microL[◇] **or** ▪ Continue LAMA-LABA, if blood eosinophil count <100/microL[¥] Add roflumilast[‡] **or** Add azithromycin[†]
LABA-ICS	▪ LAMA-LABA-ICS **or** ▪ LAMA-LABA if lack of response to ICS or adverse effects from ICS[Δ]
LAMA-LABA-ICS	▪ Continue LAMA-LABA-ICS Add roflumilast[‡] **or** Add azithromycin[†] ▪ Stop ICS if initial indication unclear, lack of response, or adverse effects of ICS[Δ]

COPD Exacerbation

- The "Global Initiative for Chronic Obstructive Lung Disease (GOLD)" defines COPD exacerbation as "an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication."



- Antiviral Agents: The majority of COPD exacerbations are triggered by respiratory viral infections. Bacterial pathogens are secondary invaders after a viral trigger.
  - If COPD exacerbation is triggered by an influenza virus, oseltamivir (Tamiflu) is recommended.
    - Oseltamivir 75 mg PO BID x 5 days (CrCl ≥ 60 ml/min)
    - Oseltamivir 30 mg PO BID x 5 days (CrCl: 31-59 ml/min)
    - Oseltamivir 30 mg PO daily x 5 days (CrCl: 10-30 ml/min)
  - If COPD exacerbation is triggered by Covid-19, Paxlovid (nirmatrelvir 300 mg / ritonavir 100 mg) PO BID x 5 days is recommended over Lagevrio (molnupiravir) 800 mg PO BID x 5 days.
    - Nirmatrelvir 300 mg / Ritonavir 100 mg PO BID x 5 days (eGFR ≥ 60 ml/min)
    - Nirmatrelvir 150 mg / Ritonavir 100 mg PO BID x 5 days (eGFR 30-59 ml/min)
    - If eGFR < 30 ml/min, consider molnupiravir 800 mg PO BID x 5 days, since molnupiravir is eliminated by the liver.



- Moderate-severe COPD exacerbation is identified in patients who present with 2 of the 3 following symptoms OR in patients who require hospitalization.

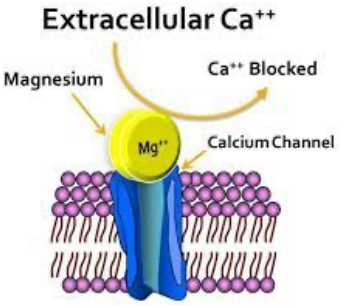
  (1) increased dyspnea (2) increased sputum volume (3) increased sputum purulence

- Antibiotics are prescribed in COPD exacerbation if increased dyspnea is accompanied with increased sputum volume or increased sputum purulence. Antibiotics are also prescribed in patients who require hospitalization.

- Bronchodilators: All patients with COPD exacerbation should receive treatment with a SABA since albuterol and levalbuterol (Xopenex) have a rapid onset of action and high efficacy.

  - SABA-SAMA (albuterol 2.5 mg / ipratropium 0.5 mg) combination therapy is superior to albuterol alone in stable COPD, but studies in acute exacerbations are limited; however most clinicians prefer using SABA-SAMA combination therapy rather than SABA alone in patients with COPD exacerbation.
  - Levalbuterol (Xopenex) dosing for nebulization is 0.63 - 1.25 mg and is administered at the same interval as albuterol.
  - Side effects of SABA include hypokalemia, tachycardia, cardiac arrythmias. Levalbuterol minimizes cardiac adverse effects.

- Magnesium sulfate 2 gm IVPB over 20 minutes in severe exacerbation that is not responding to short-acting bronchodilators.
  - MOA: Magnesium inhibits calcium influx into airway smooth muscle cells.
  - Magnesium sulfate is contraindicated in renal failure; hypermagnesemia may result in muscle weakness.



- Glucocorticoids: Short courses of oral or intravenous glucocorticoids are recommended in moderate to severe COPD exacerbation for inpatient and outpatient use.
  - Prednisone 40-60 mg PO daily x 5-14 days
  - Methylprednisolone (Solu-Medrol) 60 mg IV daily to Q6H, depending on severity.

Comparison of Systemic Glucocorticoid Preparations (UpToDate)

	Equivalent doses (mg)	Antiinflammatory activity relative to hydrocortisone*	Duration of action (hours)
Glucocorticoids			
Short acting			
Hydrocortisone (cortisol)	20	1	8 to 12
Cortisone acetate	25	0.8	8 to 12
Intermediate acting			
Prednisone	5	4	12 to 36
Prednisolone	5	4	12 to 36
Methylprednisolone	4	5	12 to 36
Triamcinolone	4	5	12 to 36
Long acting			
Dexamethasone	0.75	30	36 to 72
Betamethasone	0.6	30	36 to 72

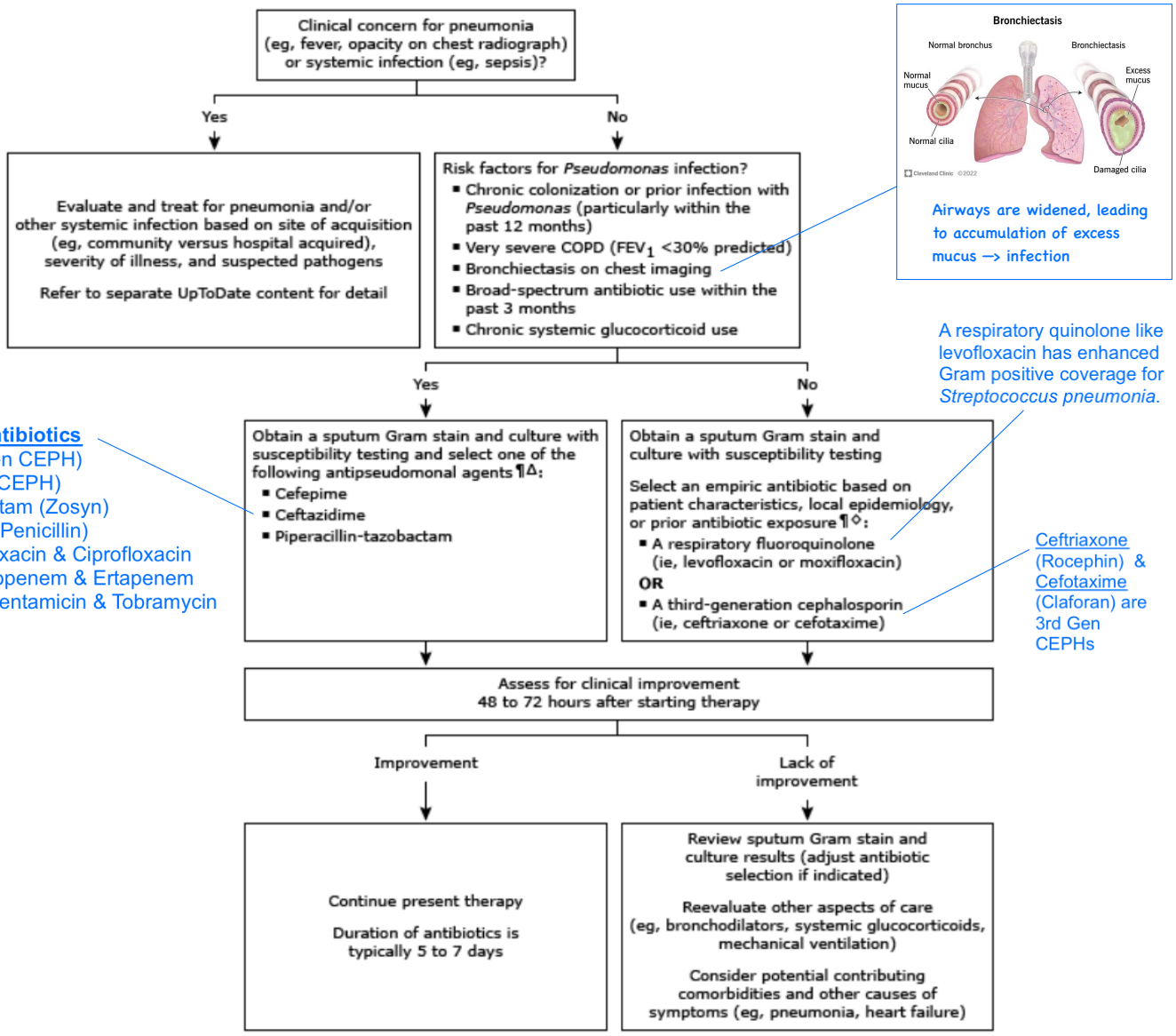
Antibiotic Treatment Options in COPD Exacerbation

- Empiric antibiotic regimens should target the most common bacterial pathogens in COPD:

  (1) *Haemophilus influenza* (2) *Streptococcus pneumoniae* (3) *Moraxella catarrhalis*

- Antibiotic coverage for *Pseudomonas aeruginosa* is indicated in patients with risk factors and patients who don't respond to empiric treatment.
  - Risk factors for *Pseudomonas* include: history of *Pseudomonas* infections, FEV_1 < 30% of predicted (i.e., very severe COPD), bronchiectasis on chest imaging, broad-spectrum antibiotics use within the past 3 months, and chronic use of systemic glucocorticoids.

Empiric Antibiotic Treatment of COPD Exacerbation in Hospitalized Patients (UpToDate)



Airways are widened, leading to accumulation of excess mucus → infection

A respiratory quinolone like levofloxacin has enhanced Gram positive coverage for *Streptococcus pneumonia*.

Antipseudomonal Antibiotics
- Ceftazidime (3rd Gen CEPH)
- Cefepime (4th Gen CEPH)
- Piperacillin/Tazobactam (Zosyn) (Anti-Pseudomonal Penicillin)
- Quinolones: Levofloxacin & Ciprofloxacin
- Carbapenems: Meropenem & Ertapenem
- Aminoglycosides: Gentamicin & Tobramycin
- Aztreonam

Ceftriaxone (Rocephin) & Cefotaxime (Claforan) are 3rd Gen CEPHs

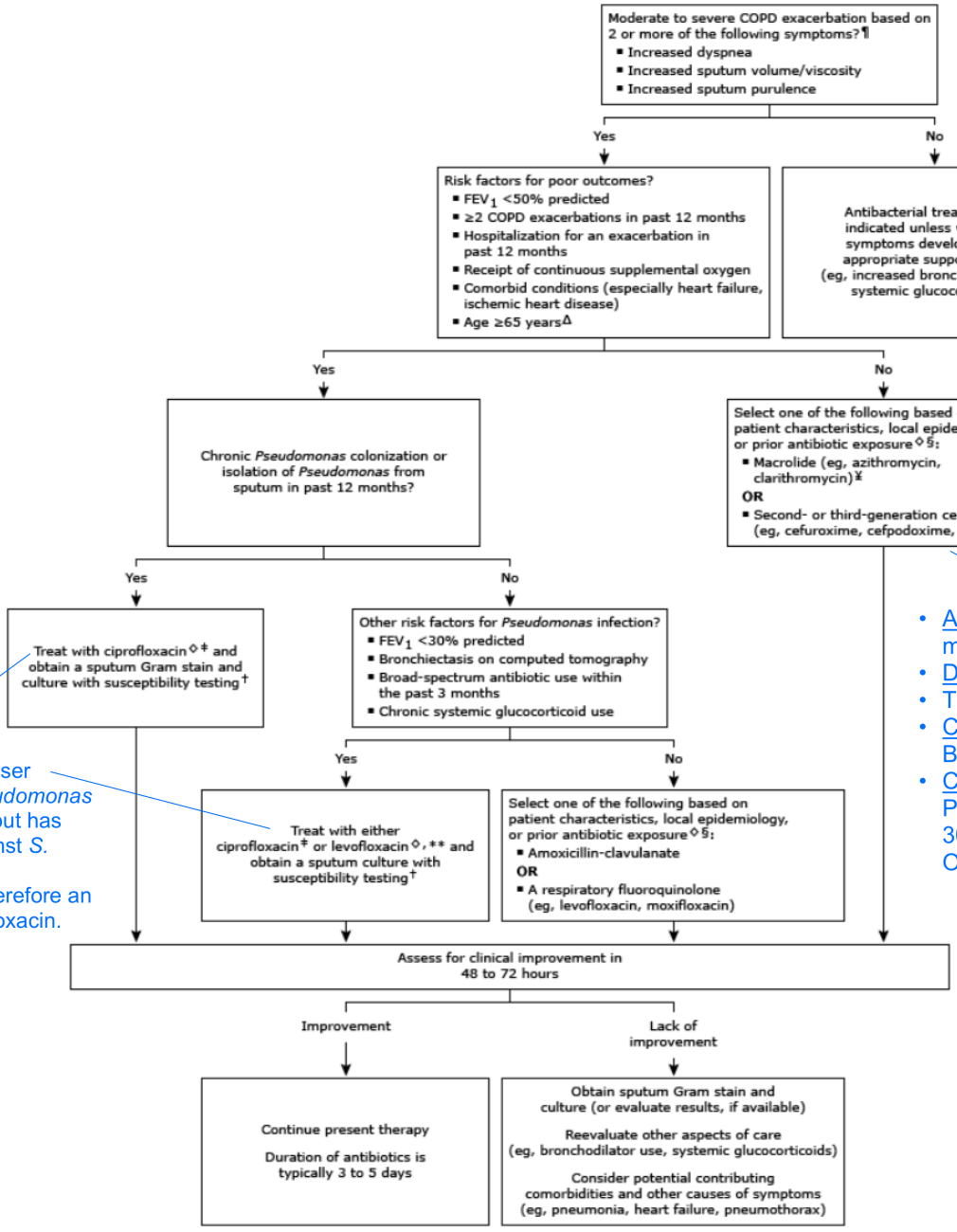
Note: The FEV_1 is used to classify the severity of obstructive lung diseases traditionally based on % predicted values into five levels: FEV_1 >70% of predicted is mild. FEV_1 60-69% of predicted is moderate. FEV_1 50-59% of predicted is moderate-severe. FEV_1 35-49% of predicted is severe.

Empiric Oral Antibiotic Treatment Regimens COPD Exacerbation in Outpatients

- The choice of antibiotics depends on community bacterial resistance patterns and individual risk of *Pseudomonas aeruginosa*, such as FEV_1 < 50% of predicted, recent hospitalization, more than 3 courses of antibiotics within the past year, use of systemic corticosteroids.

- Empiric antibiotic regimens (3-5 days) should target the most likely bacterial pathogens in COPD: *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*.

Empiric Antibiotic Treatment Algorithm of COPD Exacerbation in Outpatients (UptoDate)



- Azithromycin 500 mg then 250 mg PO daily
- Doxycycline 100 mg PO BID
- TMP/SMX (Bactrim DS) PO BID
- Cefuroxime (Ceftin) 500 mg PO BID is 2nd Gen CEPH
- Cefpodoxime (Vantin) 200 mg PO BID and Cefdinir (Omnicef) 300 mg PO BID are 3rd Gen Oral CEPHs

Levofloxacin has lesser activity against *Pseudomonas* than Ciprofloxacin, but has greater activity against *S. pneumonias* and *M. catarrhalis* and is therefore an alternative to ciprofloxacin.

Long-Term Antibiotic Prophylaxis in Severe COPD

- Patients with severe COPD with ≥ 2 exacerbations/year despite optimal medical management may benefit from prophylactic macrolide therapy:
    - Azithromycin 250-500 mg PO three times weekly
- Patients on long-term prophylactic macrolide therapy should be monitored closely for development of antimicrobial resistance, QT-interval prolongation, and *Clostridium difficile* infection.

Long-Acting Muscarinic Antagonists (LAMA) Inhalers for COPD (UpToDate 2023)

Agent	Brand name	Dosing
Aclidinium	Tudorza Pressair (United States)	DPI:* 1 inhalation (400 mcg/actuation) twice daily
	Tudorza Genuair (Canada)	
Glycopyrrolate (known as glycopyrronium in Canada and Europe)¶	Seebri Breezhaler (Canada, UK, EU, other areas)	DPI:* Inhale contents of 1 capsule (50 mcg/capsuleΔ) once daily
Tiotropium¶	Spiriva HandiHaler (United States), Spiriva (Canada)	DPI:* Inhale contents of 1 capsule (18 mcg/capsule) once daily
	Spiriva Respimat (United States, Canada)	SMI:◇ 2 inhalations (2.5 mcg/actuation) once daily
Umeclidinium	Incruse Ellipta (United States, Canada)	DPI:* 1 inhalation (62.5 mcg/actuation) once daily
Revefenacin§	Yupelri (United States)	Solution for nebulization: Inhale contents of 1 vial (175 mcg/3 mL) once daily via standard jet nebulizer¥

Combination LAMA, LABA, and ICS Products (UpToDate 2023)

Availability	Brand (trade) name	Dose	Content per inhalation capsule or MDI puff: Glycopyrrolate (glycopyrronium) base	Content per inhalation capsule or MDI puff: Glycopyrrolate (glycopyrronium) bromide salt	Drug delivered from mouthpiece: Glycopyrrolate (glycopyrronium) base	Drug delivered from mouthpiece: Glycopyrrolate (glycopyrronium) bromide salt
Combination LAMA, LABA, and inhaled corticosteroid (ICS) DPI						
Canada and Europe	Enerzair Breezhaler	1 inhalation once daily	50 mcg glycopyrronium base, 150 mcg indacaterol, and 160 mcg mometasone **(labeling within Canada)**	63 mcg glycopyrronium bromide, 150 mcg indacaterol, and 160 mcg mometasone	46 mcg glycopyrronium base, 114 mcg indacaterol, and 136 mcg mometasone **(labeling within Europe)**	58 mcg glycopyrronium bromide, 114 mcg indacaterol, and 136 mcg mometasone
Combination LAMA, LABA, and ICS MDI						
United States, Canada, and Europe	Breztri Aerosphere (United States and Canada), Trixeo Aerosphere (Europe)	2 puffs twice daily	8.2 mcg glycopyrrolate base, 4.7 mcg formoterol fumarate dihydrate, and 182 mcg budesonide per puff released from valve **(labeling within Canada)**	10.4 mcg glycopyrrolate bromide, 5.5 mcg formoterol fumarate, and 182 mcg of budesonide per puff released from valve	7.2 mcg glycopyrrolate base, 5 mcg formoterol fumarate dihydrate, and 160 mcg budesonide per puff delivered from mouthpiece **(labeling within Europe)**	9 mcg glycopyrrolate bromide, 4.8 mcg formoterol fumarate, and 160 mcg budesonide per puff delivered from mouthpiece **(labeling within United States)**

Combination ICS-SABA and ICS-Formoterol Inhalers

Drug name(s)	Preparation(s)	Dose
Inhaled corticosteroid and short-acting beta-agonist (ICS-SABA)		
Albuterol-budesonide MDI [*] (Brand name [United States]: Airsupra)	MDI: Albuterol 90 mcg and budesonide 80 mcg/actuation	▪ Usual dose: 2 inhalations as needed up to a maximum of 12 inhalations per day ▪ Acute exacerbation at home: 2 inhalations; may repeat every 20 minutes for a total of 6 inhalations, then as directed [¶]
ICS and formoterol combinations [Δ◇]		

Budesonide-formoterol MDI
(Brand names [United States]: Symbicort, Breyna)
	MDI: Budesonide 80 mcg and formoterol 4.5 mcg/actuation
	MDI: Budesonide 160 mcg and formoterol 4.5 mcg/actuation
		▪ Usual dose:
		  ▪ 80 mcg/4.5 mcg: 1 to 2 inhalations as needed; some experts use 2 inhalations unless infrequent rescue inhaler use; maximum dose: 12 inhalations per day
		  ▪ 160 mcg/4.5 mcg: 1 inhalation as needed; if symptoms persist after a few minutes, may repeat; maximum dose: 12 inhalations per day
		▪ Acute exacerbation at home: 1 to 2 inhalations as needed; wait for a few minutes between doses and use second dose if symptoms persist; may repeat 1 to 2 inhalations every 20 minutes for up to 6 inhalations in 1 hour, then as directed [¶]

Budesonide-formoterol DPI [§]
(Brand name [Canada]: Symbicort Forte)
	DPI: Budesonide 100 mcg and formoterol 6 mcg/actuation
	DPI: Budesonide 200 mcg and formoterol 6 mcg/actuation
		▪ Usual dose:
		  ▪ 100 mcg/6 mcg: 1 to 2 inhalations as needed; some experts use 2 inhalations unless infrequent rescue inhaler use; maximum dose: 12 inhalations per day
		  ▪ 200 mcg/6 mcg: 1 inhalation as needed; if symptoms persist after a few minutes, may repeat; maximum dose: 12 inhalations per day
		▪ Acute exacerbation at home: 1 to 2 inhalations as needed; wait for a few minutes between doses and use second dose if symptoms persist; may repeat 1 to 2 inhalations every 20 minutes for up to 6 inhalations in 1 hour, then as directed [¶]

Mometasone-formoterol MDI (Brand names: Dulera [United States], Zenhale [Canada])	MDI: Mometasone 100 mcg and formoterol 5 mcg/actuation MDI: Mometasone 200 mcg and formoterol 5 mcg/actuation	▪ Usual dose: 1 inhalation as needed; if insufficient relief, may administer a second dose a few minutes later; maximum dose: 12 inhalations per day ▪ Acute exacerbation at home: 1 to 2 inhalations as needed; wait for a few minutes between doses and use second dose if symptoms persist; may repeat 1 to 2 inhalations every 20 minutes for up to 6 inhalations in 1 hour, then as directed [¶]
Beclomethasone [beclometasone]-formoterol DPI [§] **or MDI** (Not available in United States or Canada, but available elsewhere [sample brand names: Formodual, Fostair, Foster])	DPI or MDI: Beclomethasone 100 mcg and formoterol 6 mcg/actuation DPI or MDI: Beclomethasone 200 mcg and formoterol 6 mcg/actuation	▪ Usual dose: 1 inhalation as needed; if insufficient relief, may administer a second dose a few minutes later; maximum dose: 12 inhalations per day ▪ Acute exacerbation at home: 1 to 2 inhalations as needed; wait for a few minutes between doses and use second dose if symptoms persist; may repeat 1 to 2 inhalations every 20 minutes for up to 6 inhalations in 1 hour, then as directed [¶]

Fluticasone propionate-formoterol MDI
(Not available in United States or Canada, but available elsewhere [sample brand name: Flutiform])
	MDI: Fluticasone 50 mcg and formoterol 5 mcg/actuation
	MDI: Fluticasone 125 mcg and formoterol 5 mcg/actuation
	MDI: Fluticasone 250 mcg and formoterol 5 mcg/actuation
		▪ Usual dose:
		  ▪ 50 mcg/5 mcg: 1 to 2 inhalations as needed; some experts use 2 inhalations unless infrequent rescue inhaler use; maximum dose: 12 inhalations per day
		  ▪ 125 mcg/5 mcg or 250 mcg/5 mcg: 1 inhalation as needed; if symptoms persist after a few minutes, may repeat; maximum dose: 12 inhalations per day
		▪ Acute exacerbation at home: 1 to 2 inhalations as needed; wait for a few minutes between doses and use second dose if symptoms persist; may repeat 1 to 2 inhalations every 20 minutes for up to 6 inhalations in 1 hour, then as directed [¶]

Combination ICS-LABA Inhalers

Medication	Low dose	Medium dose	High dose
ICS-LABA combinations			
Beclomethasone [beclometasone]-formoterol DPI or HFA (Not available in United States or Canada, but available elsewhere [sample brand names: Formodual, Fostair, Foster]) [¶ Δ]			
100 mcg/6 mcg	1 inhalation twice a day	2 inhalations twice a day	
200 mcg/6 mcg			2 inhalations twice a day
Budesonide-formoterol HFA (Brand names: Symbicort, Breyna) [¶]			
80 mcg/4.5 mcg	2 inhalations twice a day		
160 mcg/4.5 mcg		2 inhalations twice a day	
Fluticasone furoate-vilanterol DPI (Brand name: Breo Ellipta) [Δ]			
NOTE: Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only **once** daily.			
50 mcg/25 mcg [◇]	1 inhalation once daily		
100 mcg/25 mcg		1 inhalation once daily	
200 mcg/25 mcg			1 inhalation once daily
Fluticasone propionate-formoterol MDI (Not available in United States or Canada, but available elsewhere [sample brand name: Flutiform])			
50 mcg/5 mcg	2 inhalations twice daily		
125 mcg/5 mcg		2 inhalations twice daily	
250 mcg/10 mcg			2 inhalations twice daily
Fluticasone propionate-salmeterol DPI (Brand names: Advair Diskus, Wixela Inhub) [Δ]			
100 mcg/50 mcg	1 inhalation twice a day		
250 mcg/50 mcg		1 inhalation twice a day	
500 mcg/50 mcg			1 inhalation twice a day
Fluticasone propionate-salmeterol HFA (Brand name: Advair HFA)			
45 mcg/21 mcg	2 inhalations twice a day		
115 mcg/21 mcg		2 inhalations twice a day	
230 mcg/21 mcg			2 inhalations twice a day
Fluticasone propionate-salmeterol DPI (Brand names: AirDuo RespiClick, AirDuo Digihaler) [Δ §]			
55 mcg/14 mcg	1 inhalation twice a day		
113 mcg/14 mcg	1 inhalation twice a day	1 inhalation twice a day	
232 mcg/14 mcg			1 inhalation twice a day
Mometasone-formoterol HFA (Brand name: Dulera)			
100 mcg/5 mcg		2 inhalations twice a day	
200 mcg/5 mcg			2 inhalations twice a day
Mometasone-indacaterol DPI (Brand name: Atectura Breezhaler; available in Canada) [Δ]			
80 mcg/150 mcg	1 inhalation (capsule) once a day		
160 mcg/150 mcg		1 inhalation (capsule) once a day	
320 mcg/150 mcg			1 inhalation (capsule) once a day

SABA Inhalers

Drug name(s)	Preparation(s)[¶]	Dose
Albuterol MDI[Δ]	MDI: 90 mcg/inhalation (United States) MDI: 100 mcg/inhalation (Canada)	▪ Usual dose: 2 inhalations every 4 to 6 hours as needed ▪ Acute exacerbation at home: 2 to 4 inhalations, can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses[§], then taper depending on response to therapy
Albuterol DPI	DPI[Δ]: 90 mcg/actuation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours, as needed ▪ Acute exacerbation at home: 2 to 4 inhalations, can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses[§], then taper depending on response to therapy
Albuterol DPI (Canada)	DPI: 200 mcg/actuation (Canada)	▪ Usual dose: 1 inhalation every 4 to 6 hours, as needed ▪ Exercise-induced bronchoconstriction: 1 inhalation 15 minutes prior to exercise
Albuterol solution for nebulization	Nebulizer solutions: ▪ 0.083% (2.5 mg/3 mL) ▪ 0.5% (2.5 mg/0.5 mL) concentrate; must be diluted in 2.5 mL saline	▪ Usual dose: 2.5 mg every 4 to 6 hours, as needed ▪ Acute exacerbation at home: Administer 2.5 mg, can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated[¥] ▪ Acute care setting: Administer 2.5 to 5 mg, can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated ▪ Acute care setting (critically ill): Continuous nebulizer treatment: Use a large volume nebulizer, 10 to 15 mg/hour in monitored setting
Albuterol-budesonide MDI	MDI: Albuterol 90 mcg and budesonide 80 mcg/actuation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours as needed ▪ Acute exacerbation at home: 2 inhalations, can be repeated every 20 minutes for a total of 3 doses, then as directed[¥]
Levalbuterol MDI[Δ]	45 mcg/inhalation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours, as needed ▪ Acute exacerbation at home: 2 to 4 inhalations; can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses, then taper depending on response to therapy[§]
Levalbuterol solution for nebulization	Nebulizer solution: ▪ 0.63 mg/3 mL ▪ 1.25 mg/3 mL ▪ 1.25 mg/0.5 mL concentrate; must be diluted in 2.5 mL saline	▪ Usual dose: Administer 0.63 to 1.25 mg (equivalent to 1.25 to 2.5 mg albuterol) every 6 to 8 hours, as needed (up to 3 doses per 24 hours) ▪ Acute exacerbation at home: Administer 1.25 mg; can be repeated every 20 minutes for a total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated[¥] ▪ Acute care setting: Administer 1.25 mg to 2.5 mg (equivalent to 2.5 to 5 mg of albuterol); can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated
Terbutaline DPI	DPI: 0.5 mg/actuation (Canada)	▪ Usual dose: 1 inhalation every 4 hours, as needed ▪ If no effect after 5 minutes, can repeat dose
Ipratropium-albuterol SMI	SMI: Ipratropium 20 mcg and albuterol 100 mcg/inhalation (United States)	▪ Usual dose (off-label): 2 inhalations every 6 hours, as needed ▪ Acute exacerbation (off-label): 4 to 8 inhalations every 20 minutes for 3 doses, and then as needed for up to 3 hours
Ipratropium-albuterol solution for nebulization	Nebulizer solution: Ipratropium 0.5 mg and albuterol 2.5 mg per 3 mL/vial[‡]	▪ Usual dose (off-label): Administer 1 vial (3 mL) every 4 to 6 hours, as needed ▪ Acute exacerbation (off-label): Administer 1 vial (3 mL), every 20 minutes for 3 doses, and then as needed for up to 3 hours[¥]

Inhaled Corticosteroids (ICS)

Drug	Low dose (total daily dose)	Medium dose (total daily dose)	High dose (total daily dose)*
Beclomethasone HFA (Qvar RediHaler product available in United States) Administer as 2 divided doses	80 to 160 mcg	>160 to 320 mcg	>320 to 640 mcg
40 mcg per actuation	2 or 4 inhalations	¶	¶
80 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Beclomethasone HFA[Δ] (Qvar product available in Canada, Europe, and elsewhere) Administer as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPI (Pulmicort Flexhaler product available in United States) Administer as 2 divided doses	180 to 360 mcg	>360 to 720 mcg	>720 to 1440 mcg
90 mcg per actuation	2 or 4 inhalations	¶	¶
180 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPI[Δ] (Pulmicort Turbuhaler or Turbohaler product available in Canada, Europe, and elsewhere) Administer low doses (ie, ≤400 mcg/day) once daily; administer higher doses (ie, >400 mcg/day) as 2 to 4 divided doses	200 to 400 mcg	>400 to 800 mcg	>800 to 2400 mcg
100 mcg per actuation	2 to 4 inhalations	¶	¶
200 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
400 mcg per actuation	1 inhalation	2 inhalations	3 to 6 inhalations
Ciclesonide HFA (Alvesco product available in United States, Europe, and elsewhere) United States: Administer as 2 divided doses Australia, Europe, and elsewhere: Administer lower doses (ie, 160 to 320 mcg/day) once daily; administer 640 mcg dose as 2 divided doses	160 mcg	320 mcg	640 mcg
80 mcg per actuation	2 inhalations	4 inhalations	¶
160 mcg per actuation	◇	2 inhalations	4 inhalations
Ciclesonide HFA[Δ] (Alvesco product available in Canada) Administer lower doses (eg, 100 to 400 mcg) once daily; administer 800 mcg dose as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
100 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
200 mcg per actuation	1 inhalation	2 inhalations	3 to 4 inhalations
Fluticasone propionate HFA (Flovent HFA product available in United States) Administer as 2 divided doses	176 to 220 mcg	>220 to 440 mcg	>440 to 1760 mcg
44 mcg per actuation	4 inhalations	¶	¶
110 mcg per actuation	2 inhalations	4 inhalations	¶
220 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate HFA[Δ] (Flovent HFA product available in Canada; Flixotide Evohaler product available in Europe and elsewhere) Administer as 2 divided doses	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
125 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate DPI (Flovent Diskus product available in United States and Canada; Flixotide Accuhaler product available in Europe and elsewhere) Administer as 2 divided doses	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
500 mcg per actuation (strength not available in United States)	◇	◇	2 or 4 inhalations
Fluticasone propionate DPI (Armonair Digihaler product available in United States; Aermony Respiclick product available in Canada) Administer as 2 divided doses	110 mcg	226 mcg	464 mcg
55 mcg per actuation	2 inhalations	¶	¶
113 mcg per actuation	◇	2 inhalations	¶
232 mcg per actuation	◇	◇	2 inhalations
Fluticasone furoate DPI (Arnuity Ellipta product available in United States, Canada, Australia, and elsewhere, but not available in Europe or UK) Administer once daily **NOTE:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.	50 mcg (by use of pediatric DPI, which is off-label in adolescents and adults)	100 mcg	200 mcg
50 mcg per actuation	1 inhalation	¶	¶
100 mcg per actuation	◇	1 inhalation	2 inhalations
200 mcg per actuation	◇	◇	1 inhalation