COPD

NEW DRUGS, NEW DEVICES AND CONSIDERATIONS FOR BEST PRACTICE

September 2015

INSIDE

RESOURCES & LINKS

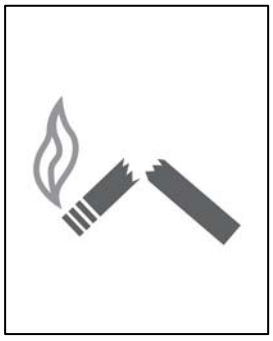
(may follow links via the PDF posted online at www.RxFiles.ca)

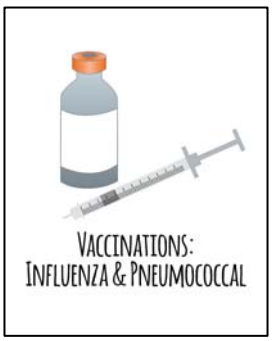
- Canadian 2007 guidelines
- Canadian 2008 guidelines for family physicians
- GOLD 2015 guidelines
- CHEST 2015 guidelines for prevention of AECOPD
- Pulmonary rehab programs in Saskatchewan
- COPD action plan templates
- Link to ***SK Lung Association*** for
  a) Inhaler Education Videos
  b) COPD Educator List

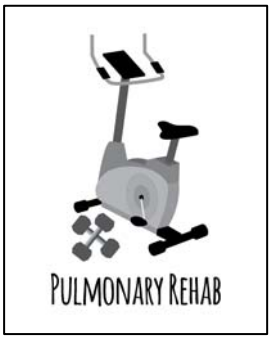
COMING THIS NOVEMBER

Geri-RxFiles
2nd Edition

There are lots of developments on the landscape of chronic obstructive pulmonary disease (COPD) management. This RxFiles release contains a variety of information that we hope will assist you in navigating new treatment options and looking for ways to optimize clinical endpoints.





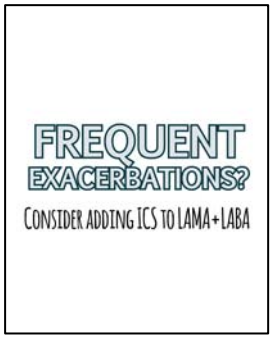


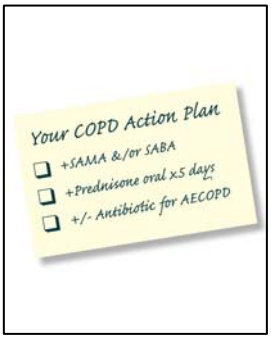
Highlights for COPD Management

1) Encourage ***smoking cessation***
2) Ensure patient has the recommended ***vaccinations*** (influenza & pneumococcal)
3) Refer for ***pulmonary rehabilitation*** whenever possible, especially after a recent exacerbation
4) Assess for proper ***inhaler technique*** and/or refer to a pharmacist or a respiratory educator
5) Choose a ***device*** that is best suited for the patient
6) Consider the role of an ***action plan***
7) Reserve ***inhaled corticosteroids*** for those who present with frequent exacerbations or poor control with LAMA + LABA

In one recent study, 59% of patients misused their inhaler devices![1]

Above: Zack is just being silly!





1. Batterink J, Dahri K, Aulakh A, Rempel C. Evaluation of the use of inhaled medications by hospital inpatients with chronic obstructive pulmonary disease. Can J Hosp Pharm. 2012 Mar;65(2):111-8.

What is it?
- Progressive, partially reversible airway limitation
- Damage to the walls of the lungs → reduced elasticity → reduced ability of patient to exhale
- 4th leading cause of death in Canada; prevalence ~5%
- Primary cause (85% of cases) is **smoking**
- An estimated 15-20% of smokers develop COPD

Symptoms: Cardinal triad: dyspnea, chronic cough, and sputum production. Dyspnea is typically progressive, worsens with exercise, persistent; described as gasping.
Definitions: Emphysema describes the damage to the lungs. Chronic bronchitis is defined as increased cough and sputum. Most COPD patients have features of both.
Diagnosis: Spirometry post-bronchodilator $FEV_1/FVC < 0.7$

Indicators: symptoms (dyspnea, cough, sputum), smoking history (10-20 pack-years or more), family history of COPD, environmental exposure to dust/chemicals. Screen for α_1-antitrypsin deficiency in select patients (e.g. if atypical features, disease onset <45 years).
Goals of therapy: ↓ dyspnea, ↑ exercise tolerance, ↑ quality of life, & ↓ complications such as exacerbations & cor pulmonale.
Comorbidities: common, especially depression and CV disease.

Therapeutic Pearls / Nonpharmacologic Approach FOR ALL PATIENTS
- An estimated 50% of patients are non-adherent to COPD therapy and 50% of patients cannot demonstrate **proper inhaler technique**! Reassess at every visit.
- Establish **individualized action plan** e.g. respiratoryguidelines.ca/updated-cts-copd-action-plan
- **Pulmonary rehab** has proven benefits in symptomatic and recently hospitalized patients (NNT = 4 to prevent one hospitalization in patients with recent exacerbation)
- Encourage **smoking cessation**. Benefits (40% ↓ in both death & rate of lung function decline) apparent even in severe COPD ("never too late to quit!")
- **Annual influenza vaccine** ↓ death by up to 50% and hospitalizations by up to 40%
- **Pneumococcal vaccine** recommended by guidelines (x1 dose, ?repeat in 5-10 years in severe COPD); however, only weak evidence of benefit available

An Approach to Treatment	Pharmacotherapy	General Agents
STEP 1: Start short-acting bronchodilators. **Start here if:** mild COPD, or $ barriers to LAMA or LABA	• **SAMA ± SABA** **Benefit:** ↓ symptoms, may not ↓ AECOPD/hospitalizations	• **SABA**: salbutamol VENTOLIN, terbutaline BRICANYL • **SAMA**: ipratropium ATROVENT • **Combo:** salbutamol/ipratropium COMBIVENT
STEP 2: Reassess inhaler technique.* Start long-acting agents. **Start here if:** moderate to severe COPD **Move here if:** treatment failure in Step 1	• **LAMA + SABA PRN** or **LABA + SABA PRN ± SAMA PRN** **Benefit:** ↓ symptoms, ↓ AECOPD/hospitalizations LAMA often preferred as it may have ↑ efficacy/tolerability vs LABA	• **LAMA:** tiotropium SPIRIVA, aclidinium TUDORZA, glycopyrronium SEEBRI, umeclidinium INCRUSE • **LABA**: formoterol OXEZE, salmeterol SEREVENT, indacaterol ONBREZ, olodaterol STRIVERDI
STEP 3: **Reassess inhaler technique* Optimize long-acting agents.** **Move here if:** treatment failure in Step 2	**Poor symptom control:** Maximize bronchodilator therapy first, since AE are associated with adding ICS • **LAMA & LABA + SABA PRN** **Benefit:** Limited evidence vs LAMA alone; may ↓ symptoms • **Poor symptom control despite LAMA + LABA:** **LAMA + (ICS+LABA) + SABA PRN** **Benefit:** Limited evidence vs LAMA+LABA; possibly ↓ symptoms **Frequent AECOPD (≥1 year):** • **LAMA + (ICS+LABA) + SABA PRN** **Benefit:** ICS+LABA ↓ AECOPD/hospitalizations vs LABA alone {If on LAMA+LABA+ICS⇒ option to stop ICS: similar exacerbation risk} WISDOM	• **LAMA + LABA:** single agent products as above, or • **LAMA + LABA combinations:** aclidinium + formoterol DUAKLIR; glycopyrronium + indacaterol ULTIBRO; tiotropium + olodaterol INSPIOLTO; umeclidinium + vilanterol ANORO • **LABA + ICS combinations:** formoterol + budesonide SYMBICORT; salmeterol + fluticasone ADVAIR; vilanterol + fluticasone BREO
STEP 4: Reassess inhaler technique.* Specialist Referral.	• oxygen therapy • theophylline low dose UNIPHYL or roflumilast DAXAS • prophylactic azithromycin ZITHROMAX • n-acetylcysteine	
Move here if: COPD severe or unresponsive to therapy; α_1 antitrypsin deficiency; exacerbations severe/recurrent; respiratory failure; ? in diagnosis/management; symptoms disproportionate to FEV_1		

*Refer to a pharmacist or COPD Educator to review inhaler technique with the patient. Teaching sheets available online at www.RxFiles.ca & patient handouts at sk.lung.ca/health-professionals/resources/resptrec-resources

FEV_1	MRC	Symptom/Disability	COPD Stage
≥ 80%	1	Not troubled by breathlessness except with strenuous exercise.	At Risk
	2	Short of breath when hurrying on the level or walking up a slight hill.	Mild
50-79%	3	Walks slower than most people of the same age on the level because of breathlessness, or has to stop for breath when walking at own pace on the level.	Moderate
	4	Stops for breath after walking about 100 meters (~ 1 block) or after a few minutes on the level.	
30-49%	5	Too breathless to leave the house, or breathless when dressing or undressing.	Severe
< 30%			Very Severe

Should I choose a LAMA or a LABA?

Both will improve symptoms; LAMAs (tiotropium) may be superior in ↓ exacerbations (but unclear if this applies to newer agents). LAMAs may also be better tolerated than LABAs (↓ withdrawal in RCTs). Often in clinical practice, LAMAs are the preferred starting point.

Which LAMA / which LABA should I choose?

Consider: evidence (tiotropium, salmeterol, & formoterol are the most studied), device-specific advantages (see **Asthma & COPD: Inhalation Devices**), adherence (once vs twice daily regimens), & onset (see **COPD: Drug Comparison Chart**). If a patient frequently makes mistakes using their device, re-educate or consider a switch to an alternate device.

Management of AECOPD (acute worsening of symptoms over >48 hours): ❶ Initiate scheduled **salbutamol and ipratropium**; long-acting inhalers can be continued but should not replace short-acting bronchodilators. ❷ Initiate **prednisone** 30-50mg po daily x **5** REDUCE - 10days. ❸ **Add antibiotic if both** change in sputum purulence (colour) AND at least one of increased sputum volume or increased dyspnea vs baseline. Antibiotics should also be strongly considered if patient requires hospitalization. Antibiotic choice: amoxicillin, doxycycline, TMP/SMX, clarithromycin, azithromycin, cefuroxime, or cefprozil for low risk patients; amoxi-clav, levofloxacin, or moxifloxacin for high risk patients (high risk: severe COPD, coronary artery disease, chronic steroids, ≥ 4 exacerbations/yr, home oxygen, or recent antibiotics).

Prevention of AECOPD: optimization and adherence to meds; vaccinations (influenza, pneumococcal); avoid environmental triggers; smoking cessation; pulmonary rehab.

AE=adverse events **AECOPD**=acute exacerbation of COPD **CV**=cardiovascular **DPI**=dry powder inhaler **FEV_1**=forced expiratory volume in 1 second **FVC**=forced expiratory vital capacity **ICS**=inhaled corticosteroid **LABA**=long-acting Beta2-Agonist **LAMA**=long-acting muscarinic antagonist **MRC**=Medical Research Council dyspnea scale **SABA**=short-acting Beta2-Agonist **SAMA**=short-acting muscarinic antagonist **TMP/SMX**=trimethoprim/sulfamethoxazole

	GENERIC/TRADE (Strength & formulations)	USUAL DOSE [MAX DAILY DOSE]	COMMENTS / ADVERSE EVENT AE / CONTRAINDICATIONS CI / DRUG INTERACTIONS DI / MONITORING M	$/30 day
Anticholinergics	**Short-Acting Muscarinic Antagonist (SAMA)**: binds unselectively to pulmonary muscarinic receptors, reducing smooth muscle contraction. Duration 4-6 hours. 1st line in mild COPD.			
	Ipratropium **ATROVENT** P L 20mcg MDI; 250, 500 mcg/2mL nebs; inhalation soln (for dilution)	**HFA**: 40mcg (**2 puffs**) inhaled TID-QID [16 puffs/day] **Neb**: 500mcg (1 neb) inhaled TID-QID [2000mcg]	• Improves COPD symptoms; does not reduce exacerbations. Onset <20 min. • AE similar to LAMA; ↓ incidence of dry mouth vs tiotropium (less potent). Avoid eye contact (can precipitate acute glaucoma) - especially with nebs.	$ 33 $ 195
	Long-Acting Muscarinic Antagonist (LAMA): slow to dissociate from pulmonary M_3 receptors = long-lasting ↓ in smooth muscle contraction. For mod-sev COPD, or after SABA +/- SAMA failure.			
	Tiotropium **SPIRIVA** P L 18mcg cap ☎ ✆ ; 2.5mcg soft mist ✗ ⊗	**HandiHaler**: 18mcg (1 cap) inhaled once daily ⊘ SWALLOW [UPLIFT] **Respimat**: 5mcg **(2 puffs)** inhaled once daily	• Tiotropium: may ↓COPD exacerbations by 20-30%/yr. Other LAMAs: limited data but appear similar. {Respimat: ↑ bioavailability, previous CV concerns} • AE: dry mouth, cough, constipation, urinary retention, headache. Avoid eye contact. Rinse mouth after inhalation to ↓ dry mouth AE. Glycopyrronium < dry mouth vs tiotropium, but URTI and UTI. [GLOW5] • Tiotropium, glycopyrronium: may accumulate in renal impairment; clinical significance unknown. Aclidinium, umeclidinium: not renally eliminated. • Fastest onset: glycopyrronium (<15 min).	$ 87 $ 87
	Aclidinium **TUDORZA** P L 400mcg DPI ☎ ✆	**Genuair**: 400mcg (1 puff) inhaled BID		$ 73
	Glycopyrronium **SEEBRI** P L 50mcg cap ☎ ✆	**Breezhaler**: 50mcg (1 cap) inhaled once daliy ⊘ SWALLOW [GLOW]		$ 73
	Umeclidinium **INCRUSE** P L 62.5mcg DPI ✗ ⊗	**Ellipta**: 62.5mcg (1 puff) inhaled once daily		$ 81
Sympathomimetics	**Short-Acting Beta$_2$-Agonist (SABA)**: binds to β_2 pulmonary receptors, which ↑ cAMP; cAMP responsible for the relaxation of bronchial smooth muscle. 1st line in mild COPD.			
	Salbutamol **VENTOLIN**, **g** P L 100mcg MDI; 200mcg DPI ✗ ⊗; 1.25, 2.5, & 5 mg/2.5mL nebs; inhal'n soln	**HFA**: 100-200mcg (1-2 puffs) inhaled QID prn [1200mcg] **Diskus**: 200mcg (1 puff) inhaled QID prn [1600mcg] **Neb**: 2.5mg inhaled QID prn [15mg]	• Improves COPD symptoms; does not reduce exacerbations. Useful as "rescue" therapy due to short onset (salbutamol <5 min; faster than SAMA). • AE: tremor, ↑ nervousness, ↑ HR (esp. neb), ↑QT, headache. At high doses: ↓ K^+, ↑ insulin secretion	$ 17 $ 38 $ 107
	Terbutaline **BRICANYL** 500mcg DPI P L	**Turbuhaler**: 500mcg (1 puff) inhaled QID prn [4000mcg]		$ 20
	Long-Acting Beta$_2$-Agonist (LABA): slow to dissociate from pulmonary β_2 receptors, resulting in long-lasting bronchodilation. For mod-severe COPD, or use after SABA +/- SAMA failure.			
	Formoterol **FORADIL**, **OXEZE** P L 12mcg caps ☎ ✆ ; 6mcg, 12mcg DPI ☎ ✆	**Aerolizer**: 12mcg (1 cap) inhaled BID ⊘ SWALLOW **Turbuhaler**: 6-12mcg inhaled BID [72mcg]	• LAMA vs LABA: both first line COPD therapy. Tiotropium shown to have greater reduction in exacerbations than salmeterol [POET]; unclear whether this is a class effect. LAMAs may ↑ tolerability vs LABAs (less discontinuation). • AE: tremor, ↑ HR. Similar AE to SABAs, but less substantial. Indacaterol: 18% incidence of cough following inhalation [INLIGHT]; may lessen after 1 week. • Fastest onset: indacaterol, formoterol, olodaterol, and vilanterol (<5 min). • Higher indacaterol doses (150, 300mcg) approved in Europe; not available in North America due to the potential for cardiovascular risk.	$ 69 $ 63
	Salmeterol **SEREVENT** P L 50mcg DPI ☎ ✆	**Diskus**: 50mcg (1 puff) inhaled BID		$ 77
	Indacaterol **ONBREZ** P L 75mcg cap ☎ ✆	**Breezhaler**: 75mcg (1 cap) inhaled once daily ⊘ SWALLOW		$ 65
	Olodaterol **STRIVERDI** P L 2.5mcg soft mist ✗ ⊗	**Respimat**: 5mcg **(2 puffs)** inhaled once daily		not set
Combinations	**SAMA + SABA combination**: useful as prn therapy in any stage of COPD, and as treatment for acute exacerbations of COPD.			
	Ipratropium + Salbutamol **COMBIVENT** P L 0.5+2.5mg/2mL nebs; 20+100mcg soft mist	**Respimat**: 20/100mcg (1 puff) inhaled QID prn [6 puffs] **Neb**: 0.5/2.5mg (1 neb) inhaled QID prn [4 nebs]	• In AECOPD: use high dose; may continue long-acting agents; limited evidence for combination over a single agent (but commonly used)	$ 44 $ 113
	LAMA + LABA combination: decreased cost and increased convenience vs using a LAMA + LABA in separate inhalers (but drug coverage for combo products varies)			
	Aclidinium + Formoterol **DUAKLIR** 400+12mcg DPI ✗ ⊗ P L	**Genuair**: 400/12mcg (1 puff) inhaled twice daily	• Data for dual therapy is limited, but evidence suggests a statistically significant, although not clinically significant, ↑ in quality of life & lung function. [SPARK] Dual therapy is reasonable in patients poorly controlled on monotherapy.	$ 98
	Glycopyrronium + Indacaterol **ULTIBRO** 50+110mcg DPI ☎ ⊗ P L	**Breezhaler**: 50/110mcg (1 cap) inhaled once daily ⊘ SWALLOW		$ 105
	Tiotropium + Olodaterol **INSPIOLTO** 2.5+2.5mcg soft mist ✗ ⊗ P L	**Respimat**: 5/5mcg **(2 puffs)** inhaled once daily		$ 85
	Umeclidinium + Vilanterol **ANORO** 62.5+25mcg DPI ☎ ⊗ P L	**Ellipta**: 62.5/25mcg (1 puff) inhaled once daily		$ 107
	LABA + Inhaled Corticosteroid (ICS) combination: addition of ICS further ↓ exacerbations vs LABA alone; useful in severe COPD if frequent exacerbations; withdrawal of ICS an option in some [WISDOM]			
	Formoterol + Budesonide **SYMBICORT** P L 6+100, 6+200 mcg DPI ☎ ✆	**Turbuhaler**: 12/400mcg (**2 puffs**) inhaled BID [24/800mcg]	• Choose LAMA over LABA+ICS: same ↓ in exacerbations, less AE & cost [INSPIRE] (Guideline-directed & evidence to support, but some ambiguity in the evidence). • Triple therapy (LAMA + LABA + ICS) is rational, but evidence is limited: may not ↓ exacerbations vs LAMA, but may ↑ quality of life & lung function • **Avoid** ICS monotherapy: increases mortality [TORCH] NNH = 87/yr vs LABA+ICS • AE: thrush 5% & hoarseness 5% (dose related: rinse mouth [swish & spit] after use; add a spacer when using an MDI), ↑ risk of pneumonia [NNH = 16 over 3 years vs LABA], may ↑ osteoporosis/fractures (conflicting evidence). • BREO: fluticasone furoate - more potent/longer lasting vs fluticasone propionate	$ 110
	Formoterol + Mometasone **ZENHALE** P L 5+100, 5+200 mcg DPI ✗ ⊗ (EDS asthma)	**HFA**: 10/200mcg (**2 puffs**) inhaled BID **Not officially approved for COPD**		$ 116
	Salmeterol + Fluticasone propionate **ADVAIR** P L 50+100, 50+250, 50+500 mcg DPI ☎ ✆	**Diskus**: 50/250mcg (1 puff) inhaled BID [100/1000mcg] (**ADVAIR HFA** 25+125, 25+250mcg **not officially COPD** approval)		$ 126 [$ 175]
	Vilanterol + Fluticasone furoate **BREO** P L 25+100mcg DPI ☎ ⊗	**Ellipta**: 25/100mcg (1 puff) inhaled once daily [SUMMIT]		$ 153
Other	Roflumilast **DAXAS** 500mcg tab ✗ ✆ P L	500mcg po once daily	AE: diarrhea, nausea, HA, abd pain, ↓wt. Rare: depression/suicide, ↑AST DI [3A4,1A2]: CBZ, phenobarb, phenytoin	$ 85
	Theophylline **LA**, **SR**, **UNIPHYL** P L 100, 200, 300, (400ˢ, 600ˢmg) [UNIPHYL] SR tabs	200-400mg SR po daily	Infrequently used due to AE/toxicity/DI. AE: ↑ HR, nausea, tremor M: HR, CNS effects (insomnia, irritability), serum levels (<83 µmol/L) DI CYP 3A4,1A2: ↓theo: CBZ, phenytoin, rifampin, smoking ↑theo: allopurinol, cimetidine, ciprofloxacin, erythromycin, febuxostat, fluvoxamine, norfloxacin, verapamil.	$ 15 - 24

⊘=Do not ☎=**EDS** ✗ =Non Forumulary Sask ✆=prior approval NIHB ⊗=not covered by NIHB **AECOPD**=acute exacerbation of COPD **CNS**=central nervous system **COPD**=chronic obstructive pulmonary disease **DPI**=dry powder inhaler **FEV_1**=forced expiratory volume in 1 second **HA**=headache **HR**=heart rate **HFA**=hydrofluoroalkane **inhal'n soln**=inhalation solution **MDI**=metered dose inhaler **URTI**=upper respiratory tract infection **UTI**=urinary tract infection **PDE**=phosphodiesterase

ASTHMA AND COPD: INHALATION DEVICES CHART

A Crawley BSP, L Regier BSP, B Jensen BSP © www.RxFiles.ca Sept 2015

There is no evidence to suggest one device works better than another. Poor inhaler technique: ↓ efficacy. Pt device dissatisfaction: ↓ adherence. Choose device based on pros/cons below & patient preference.

	beclomethasone QVAR ciclesonide ALVESCO fluticasone FLOVENT formoterol/mometasone ZENHALE salmeterol/fluticasone ADVAIR ipratropium ATROVENT salbutamol VENTOLIN 	olodaterol STRIVERDI salbutamol/ipratropium COMBIVENT tiotropium SPIRIVA tiotropium/olodaterol INSPIOLTO 	**HandiHaler:** tiotropium SPIRIVA   **Breezhaler:** glycopyrronium SEEBRI glycopyrronium/indacaterol ULTIBRO indacaterol ONBREZ	formoterol OXEZE formoterol/budesonide SYMBICORT terbutaline BRICANYL 	salbutamol VENTOLIN salmeterol SEREVENT salmeterol/fluticasone ADVAIR 	aclidinium TUDORZA aclidinium/formoterol DUAKLIR 	umeclidinium INCRUSE vilanterol/fluticasone BREO vilanterol/umeclidinium ANORO fluticasone furoate ARNUITY 
DEVICE	**MDI**	**Respimat**	**HandiHaler, Breezhaler**	**Turbuhaler**	**Diskus**	**Genuair**	**Ellipta**
Description	Delivers aerosolized stream of medication over ~0.2 seconds.	Uses a spring to deliver a "soft mist" of medication over ~1.5 seconds.	Capsules containing medication are pierced, then powder inside is inhaled.	Dry powder inhaler containing a reservoir of medication.	Dry powder inhaler containing single dose blisters of medication.		
Pros	Low inspiratory flow ≈ 20L/min required		Breath-actuated: reduces need for hand-breath coordination				
	• Suitable for **all ages.** Note: spacer strongly recommended regardless of age (see comments below). • Spacer with a mask available for cognitive impairment, frail, < 5 years old, etc. • Can be used with mechanical ventilation (e.g. in critical care units)	• Slower actuation may improve technique vs MDI • **DOSE COUNTER:** numbered by interval (frequency of interval varies by medication); loading base **locks** to signal empty • **COMBIVENT** Respimat has cost advantage over **COMBIVENT** nebules. **INSPIOLTO** Respimat has cost advantage over other LAMA/LABA combos. **Note:** Pharmacies should pre-load the Respimat canister before dispensing	• Rattling or whirring heard if capsule's contents inhaled correctly. Can look to view empty capsules (and Breezhaler has clear capsules). • Low inspiratory effort needed • **DOSE COUNTER:** each capsule equals 1 dose; thus no dose counter required	• Few steps, easy to use (compared to HandiHaler or Breezhaler). • Dose is not lost even if base is twisted multiple times; however dose counter will no longer be accurate • **DOSE COUNTER:** every 20th dose numbered to give approximation of doses remaining	• **DOSE COUNTER:** displays exact number of remaining doses	• Simple to use & less errors during dose preparation vs HandiHaler • Provides visual (window changes **green** → **red**) & audible ("**click**") feedback when dose taken correctly • In one study, majority of patients (80%) preferred Genuair over HandiHaler. • **DOSE COUNTER:** every 10th dose numbered; loading button **locks** to signal empty	• Simple to use; one step to open & load dose. Sub-analysis of RCT data: 95% of asthmatics able to use correctly after only one demonstration • In one study, majority of patients (>60%) preferred Ellipta over MDI, Diskus, or HandiHaler. • **DOSE COUNTER:** displays exact number of remaining doses with **large** numbers
Cons	• **DOSE COUNTER:** most devices lack dose counter (exceptions: **ADVAIR, ZENHALE**) • Spacer can be cumbersome; however, if using only at home in the morning/evening, additional burden is low. • Susceptible to freezing • Requires priming (x 4 sprays) if not used for ≥ **5 days**	• Requires reasonable strength to spring-load dose • Incorrect rate of inhalation results in cough • Not approved for kids or for use with a spacer • New device to the market - limited real-world experience • Requires priming (until mist is visible, then 3 more sprays) if **first time use** OR if not used for ≥ **21 days**. Requires priming (x 1 spray) if not used for ≥**3** (**COMBIVENT**) or ≥ **7 days** (**SPIRIVA**/**INSPIOLTO**).	• **Multi-step process:** may be difficult to use for patients with poor manual dexterity (eg: arthritic hands, Parkinson's disease) or cognitive impairment • Capsules are packaged in foil blisters; may be difficult to remove (for some) and are light and moisture sensitive • Patients have been known to swallow capsules instead of inhaling them. • Pieces of capsule may be inhaled if pierced more than once.	• Tipping device before inhalation (e.g. upside down) **can expel the dose** • When empty, remaining desiccant can still be heard - patients may think there are doses left • **DOSE COUNTER:** displays a "zero", but it can be difficult to tell when the indicator reaches this mark • Humidity/moisture (e.g. exhaling into device, storing in bathroom) can clump drug in reservoir	• Short expiry date after removal from protective packaging: **ADVAIR** = 1 month; **SEREVENT** = 6 weeks - Exception: **VENTOLIN** = 1 year • Medications for Diskus inhalers tend to be among the most expensive in their class	• Some patients may experience a bitter taste with aclidinium • New device to the market - limited real-world experience.	• No way to identify if proper inspiratory effort is being achieved • Short expiry date (6 weeks) after removal from protective packaging
				• Requires sharp, forceful inhalation of breath to get full dose - some patients (e.g. < 5 years old, some COPD patients with severe symptoms) will be unable to achieve adequate flow rate.			

COPD=chronic obstructive pulmonary disease **MDI**=metered dose inhaler **RCT**=randomized controlled trial

More inhalation devices listed & compared at www.rxfiles.ca

- **Use a spacer with an MDI:** ↑ drug delivery to lungs;↓ need for hand-breath coordination; ↓ systemic absorption; ↓ local adverse effects e.g. hoarseness & thrush with corticosteroids, dry mouth with anticholinergics.
- **If on more than one inhaler:** (1) consider using the same device for all medications; (2) use the bronchodilator first & the anti-inflammatory last; (3) wait ~5 minutes between puffs of different medications.
- **Nebulizer/compressor solution:** (available for budesonide, ipratropium, salbutamol, and salbutamol/ipratropium) expensive without added benefit versus spacer except possibly in very young & very old, drug entering room air may ↑ infection transmission, time consuming, & can affect eyes. Useful during exacerbations for patients in too much distress to use proper inhaler technique, but spacer preferred.
- **General inhaler technique:** (1) prepare dose, (2) breathe out, (3) inhale medication, (4) hold 10 seconds, (5) breathe out. (See RxFiles Inhaler Technique.) May take a **second breath** from dry powder devices to ensure the entire dose is inhaled. Rinsing mouth (and spitting) after anticholinergics and corticosteroids decreases side effects. Best to wait ~1 minute between puffs of the same medication.

	Inhaler Device	Step 1: PREPARE DOSE	Step 2: BREATHE OUT	Step 3: BREATHE MEDICATION IN	Step 4: HOLD BREATH x10 SECS Step 5: BREATHE OUT	Comments
AEROSOLIZED	**Metered Dose Inhaler (MDI)** Ipratropium ATROVENT Salbutamol VENTOLIN Formoterol/mometasone ✗ ⊗ ZENHALE Salmeterol/fluticasone ☎ ✆ ADVAIR	- Shake inhaler gently. - Remove cap (cap prevents foreign objects from entering device when not in use). • Prime inhaler (x 4 sprays) if not used for ≥ **5 days**.	For dry powder inhalers (HandiHaler; Breezhaler; Turbuhaler; Diskus; Genuair; Ellipta), breathe **AWAY** from the device to avoid disturbing the powder. Avoid tipping the device.	- Place lips over mouthpiece - Time the release of the dose **just after** the start of the inhalation - Take a slow, deep inhalation (5 seconds) Press top of **MDI** to release dose Press **Respimat** button to release dose	**Step 4** - Hold medication in the lungs for 10 seconds. If unable to achieve 10 seconds, hold breath for as long as comfortable **Step 5** Exhale. Do not exhale into the device. If using a corticosteroid inhaler, rinse mouth (gargle and spit) as final step to prevent thrush, dysphonia, etc. May also rinse mouth when using an anticholinergic (e.g. LAMA) inhaler - this can decrease the incidence of dry mouth. Ideal to wait ~1 minute between inhalations of the same medication and ~5 minutes between different medications.	• Visible mist from the top of inhaler or sides of mouth an indicator of mistimed breath. • **Adding spacer** reduces need for hand-breath coordination. • Common error: breathing too fast
SOFT MIST	**Respimat** Tiotropium ✗ ⊗ SPIRIVA Olodaterol ✗ ⊗ STRIVERDI Salbutamol/ipratropium COMBIVENT Tiotropium/olodaterol ✗ ⊗ INSPIOLTO	- Turn the clear base ½ turn (counter-clockwise). Remove cap. • Prime inhaler (until mist is visible, then 3 more sprays) if **first time use** OR if not used for ≥ **21 days**. Prime inhaler (x 1 spray) if not used for ≥ **3 days** (COMBIVENT) or ≥ **7 days** SPIRIVA/INSPIOLTO).				• Do not cover air vent with fingers or mouth during inhalation. • Requires prior setup to load canister into base. • After loading, canister expires in 3 months.
DRY POWDER INHALERS (breath actuated)	**HandiHaler** Tiotropium ☎ ✆ SPIRIVA	- Open device and insert one capsule. Close mouthpiece portion. - Pierce capsule by pressing the side button, pressing once only.		- Place lips over mouthpiece - Take a forceful, deep inhalation *"Inhale as hard as you can, for as long as you can."*		• After inhalation, open to see empty capsule; discard it. • Keep capsules in foil packaging until immediately before use. • **Rattling** capsule heard if dose inhaled correctly.
	Breezhaler Glycopyrronium ☎ ✆ SEEBRI Glycopyrronium/indacaterol ☎ ⊗ ULTIBRO Indacaterol ☎ ✆ ONBREZ	- Remove cap. - Open device and insert one capsule. Close mouthpiece. - Pierce capsule by pressing the side buttons, pressing once only.				• After inhalation, open to see empty capsule; discard it. • Keep capsules in foil packaging until immediately before use. • "**Whirring**" noise heard if dose inhaled correctly. • May leave sweet after-taste.
	Turbuhaler Formoterol ☎ ✆ OXEZE Formoterol/budesonide ☎ ✆ SYMBICORT Terbutaline BRICANYL	- Remove cap. - Keep device upright. - Twist base counter-clockwise as far as it will go. - Twist base clockwise until "**click**" is heard.				• Doses will not be lost even if base is twisted multiple times; however, dose counter will no longer be accurate. • "Red" dose indicator signals approximately 20 doses remaining.
	Diskus Salbutamol ✗ ⊗ VENTOLIN Salmeterol ☎ ✆ SEREVENT Salmeterol/fluticasone ☎ ✆ ADVAIR	- Slide cover open. - Push dose-release lever until "**click**" is heard.				• Hold Diskus level & horizontal to ensure dose is not lost.
	Genuair / USA: Pressair Aclidinium ☎ ✆ TUDORZA Aclidinium/formoterol ✗ ⊗ DUAKLIR	- Remove cap. - Press and release top button; control window changes from **red** to **green**.		May take second breath from dry powder devices to ensure entire dose inhaled. For HandiHaler and Breezhaler, take a second breath if capsule still contains powder.		• Control window changes from **green** to **red** if dose inhaled correctly. • "**Click**" heard if dose inhaled correctly. • When no doses remain, green button remains depressed ("locked").
	Ellipta Umeclidinium ✗ ⊗ INCRUSE Vilanterol/fluticasone ☎ ⊗ BREO Vilanterol/umeclidinium ☎ ⊗ ANORO Fluticasone furoate ✗ ⊗ ARNUITY (for asthma)	- Flip over cover until "**click**" is heard.				• Do not cover air vent with fingers during inhalation. • Dose is lost if Ellipta is opened and closed without inhaling the dose. • Expires 6 weeks after removal from protective packaging.

☎=**EDS** ✗ =Non Forumulary Sask ✆=prior approval NIHB ⊗=not covered by NIHB **MDI**=metered dose inhaler

Chronic obstructive pulmonary disease (COPD) is most commonly the result of **progressive exposure** to cigarette smoke and other lung irritants. Lung damage takes time to manifest; thus, the prevalence of disease increases with age. Symptoms include shortness of breath (dyspnea), chronic cough, and sputum (phlegm) production. People with COPD often have difficulty exhaling - their damaged lungs have lost elasticity, and no longer can contract properly. The result is airflow limitation.

Airflow limitation can be measured through spirometry, and this is how COPD is diagnosed. An individual has COPD if, after taking a bronchodilator, the volume of air exhaled in 1 second (FEV_1) is less than 70% of the total amount of air that leaves the lungs with full exhalation (FVC). (Another way of saying this is that $FEV_1/FVC < 0.7$). Unlike in asthma, the airflow limitation in COPD is "fixed" - using a bronchodilator results in only a minimal increase in FEV_1.

The goals of therapy in COPD are to reduce exacerbations, reduce symptoms, and improve ability to do physical exercise & activities of daily living.

Approach to COPD Management in Older Adults (see page 125 for AECOPD)

❑ Encourage smoking cessation

- Quitting smoking conveys a **mortality** benefit (decreasing the risk of death by ~40%) AND slows decline in lung function (decreasing the rate of decline by ~40%).[5, 6] See Figure 1.[7]

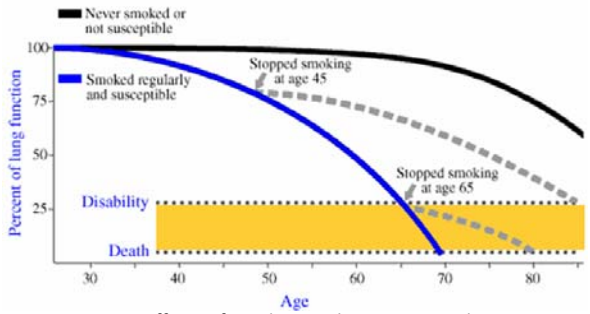


Figure 1. Effects of Smoking and Stopping Smoking on FEV_1.

- Refer to **RxFiles Tobacco / Smoking Cessation: Pharmacotherapy** for the therapeutic alternatives available to help people quit smoking (e.g. nicotine replacement therapy, bupropion, varenicline, nortriptyline).

❑ Ensure influenza vaccination is up to date

- A flu shot should be given each autumn. It decreases COPD mortality by 50% and respiratory disease hospitalizations by 40%.[8, 9]

❑ Ensure pneumococcal vaccination is up to date

- The pneumococcal vaccine Pneu-P-23 is covered x 1 dose in Saskatchewan for individuals with COPD or anyone > 65 years. (A repeat dose after 5 to 10 years in high risk individuals may be given; however, this second dose is not covered in SK, ~$65).
  - American Advisory Committee on Immunization Practices recommends administering both Pneu-C-13 PREVNAR 13 and Pneu-P-23 PNEUMOVAX 23 in series to all adults ≥ 65 years. Canadian National Advisory Committee on Immunization, however, only recommends administering both in series to adults with immunocompromising conditions (e.g. solid organ or stem cell transplant, congenital immunodeficiencies, asplenia).

❑ Select the inhaled pharmacotherapy best suited for the individual

The recent addition to the market of new inhalers and dosage forms has created a diversity of choices, allowing therapy to be selected based on individualized factors. Healthcare providers must have an understanding of the relative advantages and disadvantages of each agent.

Medications Approved for COPD

Table 1. Short-acting beta agonists (SABAs) and short-acting muscarinic antagonists (SAMAs)

Medication		Available In	Usual Dose
SABA	Salbutamol VENTOLIN	Metered dose inhaler 100mcg Diskus 200mcg Nebules 1.25, 2.5, 5mg/2.5mL	1-2 puffs inhaled QID prn 1 puff inhaled QID prn 2.5mg inhaled QID prn
	Terbutaline BRICANYL	Turbuhaler 500mcg	1 puff inhaled QID prn
SAMA	Ipratropium ATROVENT	Metered dose inhaler 20mcg Nebules 250, 500mcg/2mL	2 puffs inhaled QID prn 500mcg inhaled QID prn
SABA + SAMA	Salbutamol + Ipratropium COMBIVENT	Nebules 2.5/0.5mg per 2.5mL Respimat 20/100mcg	1 neb inhaled QID prn 1 puff inhaled QID prn

Table 2. Long-acting muscarinic antagonists (LAMAs)*

Medication	Available In	Dose
Tiotropium SPIRIVA UPLIFT Trial	HandiHaler 18mcg capsule Respimat 2.5mcg	1 cap inhaled once daily 2 puffs inhaled once daily
Aclidinium TUDORZA	Genuair 400mcg	1 puff inhaled BID
Glycopyrronium SEEBRI	Breezhaler 50mcg capsule	1 cap inhaled once daily
Umeclidinium INCRUSE	Ellipta 62.5mcg	1 puff inhaled once daily

*some references refer to LAMAs as LAACs (long-acting anticholinergics)

Table 3. Long-acting beta agonists (LABAs)

Medication	Available In	Dose
Salmeterol SEREVENT	Diskus 50mcg	1 puff inhaled BID
Formoterol FORADIL, OXEZE	Aerolizer 12mcg capsule Turbuhaler 6, 12mcg	1 cap inhaled BID 6 to 12mcg inhaled BID
Indacaterol ONBREZ	Breezhaler 75mcg capsule	1 cap inhaled once daily
Olodaterol STRIVERDI	Respimat 2.5mcg	2 puffs inhaled once daily

Table 4. Combination LAMA and LABA

Medication	Available In	Dose
Umeclidinium + Vilanterol ANORO	Ellipta 62.5/25mcg	1 puff inhaled once daily
Glycopyrronium + Indacaterol ULTIBRO	Breezhaler 50/110mcg	1 puff inhaled once daily
Tiotropium + Olodaterol INSPIOLTO	Respimat 2.5/2.5mcg	2 puffs inhaled once daily
Aclidinium + Formoterol DUAKLIR	Genuair 340/12mcg	1 puff inhaled BID

Table 5. Combination LABA and Inhaled corticosteroids (ICS)*

Medication	Available In	Dose
Formoterol + Budesonide SYMBICORT	Turbuhaler 6/100, 6/200mcg	12/400mcg inhaled BID
Salmeterol + Fluticasone ADVAIR TORCH Trial	Diskus 50/100, 50/250, 50/500mcg	50/250mcg inhaled BID
Vilanterol + Fluticasone BREO SUMMIT Trial	Ellipta 25/100mcg	1 puff inhaled once daily

*Also available: Formoterol + Mometasone ZENHALE, but not officially indicated for COPD & Salmeterol + Fluticasone ADVAIR HFA, not officially indicated for COPD ADVAIR DISKUS is indicated

Considerations for Selection of Pharmacotherapy

- **Relating therapy to stage of COPD.** Initial therapy may be based on severity of disease. Both symptoms and spirometry should be assessed to achieve the most accurate staging.[10]

Table 6. Staging of COPD based on symptoms and spirometry

COPD Stage	*MRC	mMRC	Symptom/Disability	FEV_1
At Risk	1	0	I only get breathless with strenuous exercise.	> 80%
Mild	2	1	I get short of breath when hurrying on the level or walking up a slight hill.	
Moderate	3	2	On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level.	50-80%
	4	3	I stop for breath after walking about 100 meters (~ 1 street block) or after a few minutes on level ground.	
Severe	5	4	I am too breathless to leave the house or I am breathless when dressing.	30-50%
Very Severe				< 30%

FEV_1=forced expiratory volume in 1 second; MRC=Medical Research Council dyspnea scale; mMRC=Modified Medical Research Council dyspnea scale.
*MRC used in Canadian guidelines and for EDS criteria in Saskatchewan; mMRC preferred by some physicians.

Once the stage of disease is determined, Figure 2 can be used to guide decision-making.

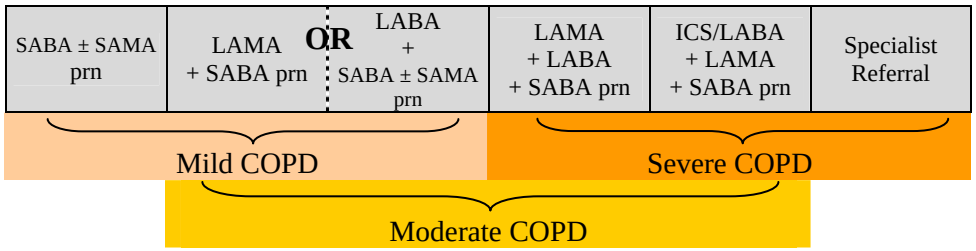


Figure 2. Management of COPD based on disease severity.

- **Relating therapy to therapeutic goals.** In mild COPD, symptoms may be successfully managed using a SAMA or SABA. As COPD progresses, symptoms increase in frequency and intensity. Here a LAMA or LABA (see Tables 2 & 3) should be added to reduce symptoms, which will also reduce the risk of exacerbations. If symptoms further worsen, combine a LAMA and a LABA for additional bronchodilation (see Table 4). In individuals with frequent exacerbations (≥ 1 per year), adding an ICS may be considered (see Table 5).

  Repeating spirometry is not required before changing therapy.

- **Deciding between SAMA and SABA therapy.** When choosing initial therapy, weak evidence suggests that prescribing a SAMA may lead to improved symptom outcomes and reduced adverse effects over a SABA.[11] When choosing PRN add-on therapy, preference may be given to combining medications from different classes to take advantage of different mechanisms of action (i.e. combine a LAMA with a SABA, and combine a LABA with a SAMA).

- **Deciding between LAMA and LABA therapy.** There are several points to consider.

  a) ***Exacerbation reduction*** - LAMAs (specifically, tiotropium in the major trials) appear to show a greater reduction in exacerbations than LABAs (relative risk reduction 11% tiotropium vs salmeterol; NNT = 24 to prevent one additional moderate to severe exacerbation per year).[12, 13]

  b) ***Improving symptoms and increasing activity*** - Both LAMAs and LABAs are effective; differences between the two drug classes do not appear to be clinically important.[14]

  c) ***Adverse effects*** - LAMAs and LABAs have different side effect profiles. LAMAs can cause anticholinergic effects such as dry mouth (5%) and constipation (5%).[15] LABAs can cause headache (5%) and dose-dependent cardiovascular effects (rare, < 1%) such as palpitations and increased heart rate.[16] The risks are low, but caution is required for individuals with severe cardiovascular disease.

  Of note, LAMAs may be better tolerated than LABAs, as evidenced by less people withdrawing from therapy when these agents were studied.[17] Further, dry mouth side effects can be decreased by rinsing (and spitting) after using a LAMA inhaler. Unlike other anticholinergics, LAMAs do not appear to be associated with cognitive impairment in older adults. This may be due to their low systemic absorption (e.g. inhaled tiotropium has 20% bioavailability).[18]

  d) ***Costs*** - Most LAMAs and LABAs are similarly priced between $60 to $90 per month. See RxFiles COPD Pharmacotherapy for a full comparison.

- **Deciding between medications in the same class.** Once the decision has been made to choose LAMA or LABA therapy, the next step is to pick *which* LAMA (or LABA). The following points can inform the decision.
  a) ***Evidence*** - The most studied (i.e., oldest) COPD agents are the LAMA tiotropium and the LABAs salmeterol and formoterol; these medications have the most evidence supporting their use.
  b) ***Available devices*** - Some people will have a preference for which inhalation device they use. This is because some devices are easier to use than others, especially for people with arthritic hands or cognitive impairment. See **RxFiles Asthma & COPD: Inhalation Devices** for a full comparison. Consider using the same type of device for each medication.
  c) ***Adherence*** - Once-daily regimens (for LAMAs: tiotropium, glycopyrronium, umeclidinium; for LABAs: indacaterol, olodaterol) may offer an adherence advantage over twice-daily regimens.
  d) ***Onset*** - Formoterol, indacaterol, olodaterol, and vilanterol (LABAs), and glycopyrronium (LAMA) work within minutes. The other agents take longer (an hour or more) to start having an effect. Fast-acting agents may give individuals more confidence in the medication's efficacy.
- **When to add an ICS?** Inhaled steroids should not be used as monotherapy in COPD - this is associated with **increased mortality** (NNH = 29 over three years vs combination therapy with LABA).[TORCH] ICSs have evidence for reducing exacerbations in COPD (a LABA/ICS combo reduces exacerbations by the same amount as a LAMA), but evidence is inconsistent regarding symptom improvement.[19] ICSs also have side effects (e.g. thrush 5%, hoarseness 5%, increased risk of pneumonia NNH = 16 over three years).[20, 21, 22, 23] Thus the best use of ICSs may be in individuals with frequent exacerbations (1 or more per year), or with severe symptoms unresponsive to other treatments.

	TORCH Trial
Medications (intervention)	Salmeterol + Fluticasone [ADVAIR] 50/500mcg **OR** fluticasone 500mcg **OR** salmeterol 50mcg **OR** placebo – all BID
Study Design	3 year multicentre, randomised, double-blind, parallel group, placebo-controlled
Trial Population	Moderate-to-severe COPD with at least a 10 pack-year smoking history
1° End-Point	All-cause mortality at 3 years
Results	Probability of death: salmeterol + fluticasone 12.6%, salmeterol 13.5%, fluticasone 16.0%, placebo 15.2%. These findings were non-significant. Exacerbation rate: Salmeterol + Fluticasone 0.85/year, Salmeterol 0.96/year, fluticasone 0.93/year, placebo 1.13/year. These findings were non-significant.

SUMMIT Trial: fluticasone furoate/vilanterol (100/25 µg) [BREO] **OR** fluticasone furoate (100 µg) **OR** vilanterol (25 µg) **OR** placebo with mortality as the primary end-point. Preliminary findings are also non-significant for the primary end-point.

❑ **Refer to pulmonary rehabilitation**

- Pulmonary rehab reduces dyspnea (shortness of breath), and improves exercise tolerance and quality of life. It may also reduce the anxiety and depression associated with COPD.[24]
- Pulmonary rehab is standard of care for individuals with uncontrolled symptoms despite optimized bronchodilators.[25] As well, in individuals with a recent (30 days ago or less) acute exacerbation of COPD, 25 weeks of pulmonary rehab resulted in a significant reduction in hospitalizations (NNT = 4 to prevent one hospitalization).[26]
- Visit www.lung.ca/lung-health/get-help for a list of pulmonary rehab programs across Canada.

Individuals with COPD Require Long-Term Follow-Up

❑ **Create an individualized COPD action plan with the individual**

- Visit www.respiratoryguidelines.ca/updated-cts-copd-action-plan for templates to create a COPD action plan.

❑ **Monitor adherence and ensure appropriate inhaler technique**

- About 50% of individuals with COPD are non-adherent, and about 50% cannot demonstrate appropriate inhaler technique.[27, 28, 29] Re-evaluate inhaler technique regularly.
- Consider referral for teaching by a pharmacist or certified COPD educator.
- See ***Geri-RxFiles: COPD Inhaler Technique*** on page 128

❑ **For individuals with severe COPD, supplemental oxygen may be considered**

- In hypoxic (low blood oxygen saturation) individuals, 15 hours per day or more of oxygen is associated with improved survival and quality of life.[30] Funding is available in Saskatchewan for home oxygen.[31] The target is an oximetry saturation of 90% to 92%.

❑ **For individuals with severe disease progression, refer to a respiratory specialist**

- Referral may be appropriate when:
  a) there is uncertainty in the management or diagnosis;
  b) symptoms are disproportionate to the level of air flow obstruction;
  c) the decline in pulmonary function is accelerated;
  d) exacerbations of COPD are severe or recurrent or cause hospitalization;
  e) there is an inadequate response to therapy; or
  f) the individual enters respiratory failure.[32]
- Specialists may consider starting oxygen therapy, theophylline, roflumilast, prophylactic azithromycin, or n-acetylcysteine.

Acute Exacerbations of COPD (AECOPD)

COPD exacerbations are a sustained worsening (> 48 hours) of respiratory symptoms. Exacerbations become more frequent as disease severity progresses.

Older adults are often slow to recover from COPD exacerbations. It may take weeks (or more) to return to baseline. Great efforts should be made to **prevent** exacerbations - because exacerbations can accelerate the decline in lung function and have significant mortality risk.

❑ Prevent acute exacerbations of COPD

There are several evidence-based interventions to prevent acute exacerbations of COPD:[33]

1. Optimization and **adherence** to prescribed pharmacotherapy
2. Vaccinations (i.e. influenza, pneumococcal)
3. Avoid environmental triggers (e.g. dust, pollutants)
4. Smoking cessation
5. Pulmonary rehabilitation

❑ Treat acute exacerbations of COPD

- Treatment consists of short-acting bronchodilators, oral corticosteroids, and antibiotics when indicated.

AECOPD Bronchodilator Therapy

Initiate inhaled SAMA and SABA therapy scheduled every 4 to 6 hours (e.g. salbutamol 100mcg MDI 1 to 2 puffs QID with ipratropium 20mcg MDI 1 to 2 puffs QID). Temporary use of higher doses of SAMA/SABA therapy is often used in severe cases / hospitalized individuals. There is clinical controversy on whether a SAMA/SABA combination is more effective than a single agent; the combination is often used despite a lack of evidence.[34]

- Bronchodilator therapy may be administered via MDI and spacer; nebulized therapy can be valuable if an individual is unable to use proper inhaler technique.
- Long-acting inhalers may be continued (if the individual is able to take), but should **not** be used as a substitute for short-acting bronchodilators.

AECOPD Corticosteroid Therapy

- Initiate oral prednisone 30 to 50mg for 5 to 14 days. **REDUCE Trial**: 5-day treatment of prednisone 40mg was non-inferior to 14-day treatment with regard to re-exacerbation within 6 months of follow-up, but significantly ↓ corticosteroid exposure. These findings support the use of a 5-day corticosteroid treatment in AECOPD.[35] Choose a lower dose in individuals who are frail or have a low body weight. Tapering is not usually required for these short courses of corticosteroids, unless the individual has received frequent courses (expert opinion: ≥ 4) over the past year.
- Consider matching the duration of steroid therapy with the duration of antibiotic therapy (if an antibiotic is indicated). Monitor for corticosteroid side effects, e.g. hyperglycemia, nausea, insomnia.

AECOPD Antibiotic Therapy

Approximately half of COPD exacerbations have an infectious cause. An assessment of symptoms (sputum purulence, sputum volume, and dyspnea) can predict the likelihood of a bacterial etiology.

❑ Evaluate probable etiology of COPD exacerbation

- Ideally, two criteria should be met before initiating antibiotics:[36]

1. Presence of sputum purulence (change in phlegm colour to yellow or green)

AND

2. At least one of:
a. increased sputum volume from baseline
b. increased dyspnea (shortness of breath) from baseline

Table 7. AECOPD antibiotic choice and oral dosing

Low risk individuals	amoxicillin 500mg TID for 7 to 10 days	CrCl 10-30mL/min → 500mg BID
	doxycycline 100mg BID for 7 to 10 days	
	TMP/SMX 800/160mg BID for 7 to 10 days	CrCl 15-30mL/min → 400/80mg BID
	clarithromycin 500mg BID for 5 to 10 days	CrCl <30mL/min → 250mg BID
	azithromycin 500mg load on day 1; 250mg daily on days 2 to 5	
	cefuroxime 500mg BID for 5 to 10 days	CrCl < 10mL/min → 500mg daily
	cefprozil 500mg BID for 5 to 10 days	CrCl <30mL/min → 250mg BID
High risk individuals*	Amoxi-clav 875/125mg BID for 5 to 10 days	CrCl 10-30mL/min → 500/125mg BID
	levofloxacin 750mg daily for 5 days	CrCl 10-50mL/min → 750mg load; 500mg daily
	moxifloxacin 400mg daily for 5 to 10 days	

BID=twice daily; CrCl=creatinine clearance; TID=three times daily; TMP/SMX=trimethoprim/sulfamethoxazole; Amoxi-clav=amoxicillin + clavulanic acid

***High risk individuals (↑ potential for treatment failure or drug-resistant bugs)**

- FEV_1 < 50% (i.e. severe COPD)
- Coronary artery disease
- Chronic oral corticosteroid use (e.g. RA)
- ≥ 4 exacerbations per year
- Use of home oxygen
- Antibiotics used in last 3 months

RA=rheumatoid arthritis

When selecting the antibiotic for an older adult, be sure to consider the following:

- Some antibiotics (e.g. azithromycin, moxifloxacin) prolong QT interval. Older adults are often more susceptible to this effect; evaluate whether the individual is on other QT-prolonging agents (see ***Geri-RxFiles: QT Prolongation & Torsades de Pointes***).
- Prevalence of renal dysfunction increases with advancing age; many antibiotics will require renal dose adjustment in this population.
- Older adults with COPD have a high prevalence (> 30%) of coronary artery disease; many will fall into the "high risk" category.[37]
- If an individual has had antibiotics in the last 3 months, choose an antibiotic from a different class.

Considerations for COPD End-of-Life Management

"Hope for the best. Prepare for the worst."

As COPD progresses, individuals typically experience a gradual decline in function & ability. Exacerbations may become more frequent, and after each exacerbation a full return to baseline function may not be possible.

An individual with severe COPD (FEV_1 less than 50%) has a 40% chance of mortality over 4 years, and as FEV_1 deteriorates the risk of death rises.[38] One validated way to predict the likelihood of mortality in someone with COPD is to use additional factors beyond FEV_1, such as exercise capacity, amount of dyspnea, and Body Mass Index. This is summarized in a tool called the Bode Index, and a calculator can be found here: http://www.qxmd.com/calculate-online/respirology/bode-index

❑ **For COPD patients with a high risk of death in the near future, initiate an end-of-life care discussion**

- Discussions about end-of-life care often occur too late. As a result, individuals may be too sick to properly make care decisions.
- The best time and place to plan for end-of-life care is with a scheduled appointment in a physician's office. Participants should include the individual, the physician, and the family member(s) who may be making future decisions for the individual.

Considerations for COPD End-of-Life Management continued

❑ **For COPD patients with a high risk of death in the near future, initiate an end-of-life care discussion *continued***

- In general, end-of-life care discussions should include the following:[39]
  a) A decision on the location and provider of terminal care.
  b) The role of family members in making future decisions.
  c) Documentation of the desire to use or withhold mechanical ventilation.
  d) Re-assurance that symptoms will be managed and dignity preserved.
- For pearls on how to initiate and frame an end-of-life discussion, refer to page 40 of the Alosa Foundation's COPD highlights at http://www.alosafoundation.org/wp-content/uploads/2013/12/COPD-Smoking-Cessation-Evidence-Document.pdf

❑ **Manage the symptoms of end-stage COPD**

- In people with end-stage COPD, two common symptoms to address are persistent dyspnea and its accompanying anxiety.[1] First ensure that bronchodilator therapy is optimized (see Figure 2). Next, opioids can be used to reduce the sensation of dyspnea (e.g. morphine 2.5 to 5 mg orally in older adults every 4 hours if needed).[40] Opioid tolerant individuals may require an increase in their current dose (e.g. increase by 25-50%). There is no evidence that nebulized opioids are better than oral or subcutaneous. Benzodiazepine can be added to opioid therapy for management of anxiety (e.g. lorazepam 1-2mg orally every hour until relaxed, then every 4 hours as needed). See **RxFiles Palliative Care**.
- Non-pharmacological approaches to manage dyspnea include sitting the individual upright, removing smoke and other irritants (e.g. perfume), ensuring fresh air with sufficient humidity is supplied, and minimizing other factors that can increase anxiety.[41]

REMEMBER TO ALWAYS RE-ASSESS INHALER TECHNIQUE, WHENEVER POSSIBLE.
It is not uncommon to find those who think they are using correctly…and everything is ok…till you ask them to demonstrate.
{Some of our team had a bit too much fun when asked to demonstrate an incorrect technique!}

COPD: STOPP & Beers Criteria

For more detailed medication information, see the RxFiles Drug Comparison Charts

Drug or Drug Class	STOPP / Beers / RxFiles	When a Medication Could be Problematic for Older Adults[1-4]	Clinical Concern[1-4]
		QE = Quality of Evidence *SR = Strength of Recommendation*	
Anti-Muscarinic Bronchodilators **Ipratropium** Atrovent **Tiopropium** Spiriva	S	With a history of **Narrow Angle Glaucoma**	• May exacerbate glaucoma
	S	With **Bladder Outflow Obstruction**	• May cause urinary retention
Benzodiazepines ↘ Short- & Intermediate-Acting: **Alprazolam** Xanax $t_{1/2}$ ~ 12 hours **Bromazepam** Lectopam $t_{1/2}$ ~ 20 hours **Lorazepam** Ativan $t_{1/2}$ ~ 15 hours **Oxazepam** Serax $t_{1/2}$ ~ 8 hours **Temazepam** Restoril $t_{1/2}$ ~ 11 hours **Triazolam** Halcion $t_{1/2}$ ~ 2 hours Long-Acting: **Chlordiazepoxide** Librium $t_{1/2}$ ~ 100 hours **Clonazepam** Rivotril $t_{1/2}$ ~ 34 hours **Clorazepate** Tranxene $t_{1/2}$ ~ 100 hours **Diazepam** Valium $t_{1/2}$ ~ 100+ hours **Flurazepam** Dalmane $t_{1/2}$ ~ 100+ hours **Nitrazepam** Mogadon $t_{1/2}$ ~ 30 hours	S	With **Acute or Chronic Respiratory Failure** (i.e. pO_2 <8.0 kPa ± pCO_2 >6.5 kPa)	• Risk of exacerbation of respiratory failure
Corticosteroids, Systemic ↘ **Budesonide** Entocort **Dexamethasone** Decadron **Hydrocortisone** Cortef **Methylprednisolone** Medrol **Prednisolone** **Prednisone**	S	For **Maintenance Therapy in Moderate to Severe COPD** (instead of inhaled corticosteroids) **Acute Exacerbations COPD (AECOPD) – oral or parenteral corticosteroids (dosages of 30 to 50 mg of prednisone equivalent per day for 5 days) are recommended and are appropriate in most patients with moderate to severe AECOPD [42].*	• Unnecessary exposure to long-term side effects of systemic corticosteroids (will be dependent upon dose & duration of treatment): Fluid/electrolyte imbalance, pituitary-adrenal suppression, hypertension, cutaneous effects (dermal thinning, easy bruising, & acne), hyperglycemia, glycosuria, peptic ulcer, behavioural disturbances (insomnia, euphoria), posterior subcapsular cataracts, glaucoma, ↓ bone mineral density, cushingoid syndrome, avascular necrosis of bone including hip (rare).
Xanthine, Oral Bronchodilator **Theophylline** Theolair, Uniphyl	S	Monotherapy for **COPD**	• Safer, more effective medications available • Risk of adverse effects due to narrow therapeutic index
	B	With **Insomnia** *QE = Moderate; SR = Strong*	• CNS stimulation

GERI-RXFILES COPD REFERENCES

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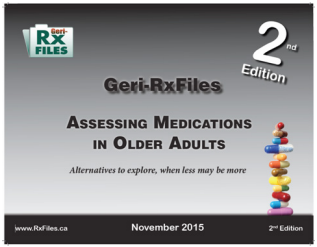

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