

Inhaled Salbutamol Shortage

TABLE 1: SUPPLIERS OF INHALED SALBUTAMOL¹

Product	Strength	DIN	Manufacturer
Airomir [®]	100 mcg/actuation	02232570	VAE
Apo-Salbutamol HFA		02245669	APX
Salbutamol HFA		02419858	SAN
Teva-Salbutamol HFA		02326450	TEV
Ventolin HFA		02241497	GSK
Ventolin Diskus	200 mcg/actuation	02243115	GSK
HFA = hydrofluoroalkane			

Health Canada-approved indications of salbutamol pressurized metered dose inhaler (pMDI)² and salbutamol dry powder inhaler (DPI)³ include:

- the symptomatic relief and prevention of bronchospasm due to bronchial asthma, chronic bronchitis and other chronic bronchopulmonary disorders in which bronchospasm is a complicating factor; and
- the prevention of exercise-induced bronchospasm.

Considerations and Non-Pharmacological Management:⁴⁻⁷

- Ensure proper inhaler technique and adherence.
- Post-use oral care is strongly suggested after inhaled corticosteroid (ICS) (+/- long-acting beta₂-agonist [LABA]) use including when used as reliever medication.
- Recommend smoking cessation when applicable.
- Identify and avoid triggers such as environmental allergens, pollution and occupational irritants.
- Treat conditions that may exacerbate asthma: obesity, anxiety, depression, rhinitis, sinusitis, gastroesophageal reflux disease, seasonal allergies.
- Acetylsalicylic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs) may cause asthma exacerbations in some patients; they are generally not contraindicated in patients with asthma unless they have caused previous exacerbations.⁸
- Encourage physical activity.
- Have written action plans. Examples are available from [The Lung Association](#) for asthma or the [Canadian Thoracic Society](#) for chronic obstructive pulmonary disease (COPD) and asthma.
- For patients with COPD, refer to pulmonary rehabilitation if appropriate and available.
 - **NOTE:** in a patient with an emerging pathogen or airborne infection such as COVID-19, pulmonary rehabilitation is not appropriate. [Living Well with COPD](#) is accessible to patients and health-care professionals (requires free registration) and offers print and video resources for at-home pulmonary rehabilitation exercises.

Pharmaceutical Alternatives/Considerations:

- It is possible some acute-care institutions are considering **common canister protocols** to conserve pMDIs. Refer to the [article](#) published by the Institute for Safe Medication Practices (ISMP), which explains the premise as well as provides merits and potential risks of the policy.

Therapeutic Alternatives/Considerations:

- Refer to Tables 2-5 for alternatives to salbutamol for use in asthma, exercise-induced bronchoconstriction (EIB) and COPD.
 - Availability of salbutamol and alternatives will be fluctuating. **Inventory management, especially prevention of stockpiling, will be key.**
- Ensure optimal treatment of asthma and COPD.

- See [RxTx](#), [RxFiles](#) and [Global Initiative for Asthma \(GINA\) 2019 guidelines](#) for stepped-care **asthma** treatment.
 - Note the 2019 GINA guidelines included fundamental changes, most notably recommending against SABA-only treatment of asthma of *any* severity in adolescents and adults;⁸ these may not be reflected in all references.
 - RxTx and RxFiles are available through [SHIRP](#).
- See [RxTx](#), [RxFiles](#) and [Global Initiative for Chronic Obstructive Lung Disease \(GOLD\) guidelines](#) for stepped-care COPD treatment.
 - RxTx and RxFiles are available through [SHIRP](#).
- ICS therapy is the cornerstone of treatment of moderate to severe asthma; these products may also be in short supply. [See fluticasone document](#).
- **Note:** In general, nebulization is not preferred because of cost and there being no added benefit compared to pMDI with spacer.⁹ Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens such as SARS-CoV-2.^{10,11} However, if no pMDI or DPI products are available, nebulization may be the only option. This is most likely to be the case in infants where few other relievers are appropriate.
- There are advantages and disadvantages to the various devices making some less appropriate for some patients. Patients for whom **device selection** may be important include children and those with reduced dexterity, those unable to achieve forceful inspiration, and those with dementia, for example. RxFiles has excellent resources to help [select the best device](#) and information on [inhaler technique](#). (Subscription to RxFiles or [SHIRP](#) is required.)
Device selection may be a luxury.

TABLE 2: PHARMACOLOGIC AGENTS FOR RELIEF OF ASTHMA SYMPTOMS IN ADULTS AND ADOLESCENTS ≥12 YEARS OF AGE

Note: GINA no longer recommends treatment of asthma in adults and adolescents with SABA alone. ICS-containing controller treatment, either as-needed or daily is preferred.⁸

Medication Dosage Form Strength ¹	Dosage ⁴	Pharmacokinetics ¹²	Comments
Short-Acting Beta₂-Agonists (SABA)			
Salbutamol (Airomir®, Ventolin, g) pMDI 100 mcg/ACT	1–2 INH TID to QID PRN; Max: 8 INH (800 mcg)/ day	Onset: 5–8 min (median) Duration: 3–6 h ²	Preferably use pMDI or Diskus if available. See note about nebulization in text. Adverse effects: ⁴ nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.
Salbutamol (Ventolin) Diskus 200 mcg/ACT	1 INH QID PRN; Max: 4 INH (800 mcg) / day	Onset: ~5 min Duration: 3–6 h ³	
Salbutamol (Ventolin, g) Nebules* 2.5 mg/2.5 mL; 5 mg/2.5 mL	2.5 to 5 mg QID PRN Max: N/A	Onset: ≤5 min Duration: 3–6 h	
Terbutaline (Bricanyl®) Turbuhaler 0.5 mg/ACT	1 INH Q4–6H PRN Max: 6 INH/day	Onset: 5 min Peak: 15–60 min Duration: 3–6 h	Adverse effects: ⁴ nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.
Corticosteroid/Long-Acting Beta₂-Agonist (LABA) Combination			
Budesonide/ Formoterol (Symbicort®) Turbuhaler 100 mcg/6 mcg per ACT; 200 mcg/6 mcg per ACT	Controller and reliever therapy: 1–2 INH BID or 2 INH once daily. Take 1 additional INH PRN in response to symptoms; if symptoms persist after a few min, an additional dose should be taken Max: 6 INH on any single occasion; 8 INH/day	(Formoterol) Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients	LABA <u>monotherapy</u> should be avoided in asthma as it is associated with higher rates of death. Formoterol alone (Foradil, Oxeze®) is not an appropriate reliever as it relies on the patient to add ICS; fixed-dose combination products are preferred, if available. ⁴ Adverse effects: ⁴ sore mouth, sore throat, dysphonia, oral thrush (can be reduced by rinsing mouth or using spacer). Nervousness, tremor, tachycardia, palpitations.

Medication Dosage Form Strength ¹	Dosage ⁴	Pharmacokinetics ¹²	Comments
Mometasone/ Formoterol (Zenhale®) pMDI 100 mcg/5 mcg per ACT; 200 mcg/5 mcg per ACT	Off-label as reliever controller dose: 2 INH BID Extrapolating from Symbicort®, for reliever, take 1 additional INH PRN in response to symptoms; if symptoms persist after a few min, an additional dose should be taken Max: 6 INH on any single occasion; 8 INH/day See comments	(Formoterol) Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients	See comments for Symbicort®. In addition: Evidence of reliever therapy with ICS/formoterol combination is available only for budesonide/formoterol and not mometasone/formoterol. However, it is reasonable to extrapolate for use in shortage situations only. Use only the 100 mcg/5 mcg strength if being used as reliever; the maximum daily dose is 800 mcg/20 mcg, ¹³ which is reached with controller dose when using the 200 mcg/5 mcg strength. Extrapolating from Symbicort®, up to 48 mcg formoterol/day is acceptable.

Short-Acting Antimuscarinic Antagonist (SAMA)

Ipratropium (Atrovent®, g) pMDI 20 mcg/ACT	Off-label 2 INH Q6-8H PRN Max: 12 INH/day	Onset: within 15 min Peak: 1-2 h Duration: 2-4 h	Less effective & slower acting than salbutamol. ^{6,8} Preferably use pMDI, if available. See note about nebulization in text. Useful alternative for patients who are unusually susceptible to tremor or tachycardia from beta ₂ -agonists. ⁴
Ipratropium (g) Nebules* 250 mcg/1 mL; 500 mcg/2 mL	Off-label 250-500 mcg Q6-8H PRN Max: N/A	Onset: within 15 min Peak: 1-2 h Duration: 4-5 h, up to 7-8 h in some	May also be useful in beta-blocker-induced bronchospasm. ^{4,6} Adverse effects: ⁴ dry mouth, metallic taste; mydriasis and glaucoma if released into eye.

Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)

Ipratropium/ Salbutamol (Combivent®) Respimat 20 mcg/100 mcg per ACT	Off-label 2-3 INH Q6H PRN ¹² Max: N/A	Based on individual ingredients (pMDI, not Respimat): Onset: 5-8 min (median) Duration: 2-4 h	Adverse effects: ⁴ dry mouth, metallic taste; mydriasis and glaucoma if released into eye. Nervousness, tremor, tachycardia, palpitations.
Ipratropium/ Salbutamol (g) Nebules* 0.5 mg/2.5 mg per 2.5 mL	Off-label 1 NEB Q4-6H PRN Max: N/A	Based on individual ingredients: Onset: ≤5 min Duration: 4-5 h, up to 7-8 h in some	

Long-Acting Beta₂-Agonist (LABA)

Formoterol (Oxeze®) Turbuhaler 6 mcg/ACT; 12 mcg/ACT	Off-label Extrapolated from Symbicort® (available only as 6 mcg so only use 6 mcg Oxeze®) 1 INH PRN Max: 6 INH on any single occasion; 8 INH/day See Comments	Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients	LABA <u>monotherapy</u> should be avoided in asthma as it is associated with higher rates of death. Formoterol alone is not an appropriate reliever as it relies on the patient to add ICS; fixed-dose combination products (e.g., Symbicort®) are preferred, if available. ⁸ Reserve as last resort and ensure patient takes with ICS.
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* Preferably use pMDI or DPI, if available. See note about nebulization in text.

ACT = actuation; BID = twice daily; g = generics; H or h = hour(s); ICS = inhaled corticosteroid; INH = inhalation(s); LABA = long-acting beta₂-agonist; max = maximum; min = minute(s); N/A = not available; NEB = nebule(s); pMDI = pressurized metered dose inhaler; PRN = as needed; Q = every; QID = four times daily; TID = three times daily

TABLE 3: PHARMACOLOGIC AGENTS FOR RELIEF OF ASTHMA SYMPTOMS IN CHILDREN < 12 YEARS OF AGE

Medication Dosage Form Strength ¹	Dosage	Pharmacokinetics ¹²	Comments
Short-Acting Beta₂-Agonists (SABA)			
Salbutamol (Airmir®, Ventolin, g) pMDI 100 mcg/ACT	<4 y: 2 INH Q4-6H PRN ¹¹ Max: N/A 4-11 y: 2 INH TID-QID PRN ¹⁴ Max: 600 mcg/day ¹⁴	Onset: 5-8 min (median) Duration: 3-6 h ²	Preferred agent when available. Adverse effects: ¹⁴ nervousness, tremor, tachycardia, palpitations.
Salbutamol (Ventolin) Diskus 200 mcg/ACT	≥4 y: 1 INH TID-QID PRN ¹⁴ Max: 800 mcg/day ¹⁴ Adult doses may be required due to poor deposition ¹⁴	Onset: ~5 min Duration: 3-6 h ³	pMDI plus spacer may be used in children <4 y, though no trials have been done to assess optimal dose. ¹⁴
Salbutamol (Ventolin, g) Nebules* 2.5 mg/2.5 mL; 5 mg/2.5 mL	<5 y: 0.63-2.5 mg Q4-6H PRN ¹¹ Max: N/A 5-12 y: 1.25-2.5 mg as a single dose QID PRN ¹⁴ Max: 5 mg/dose ¹⁴	Onset: ≤5 min Duration: 3-6 h	
Terbutaline (Bricanyl®) Turbuhaler 0.5 mg/ACT	≥6 y: 1 INH PRN ¹⁵ Max: 6 INH/day ¹⁵	Onset: 5 min Peak: 15-60 min Duration: 3-6 h	Adverse effects: ¹⁴ nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.
Short-Acting Antimuscarinic Antagonist (SAMA)			
Ipratropium (Atrovent®) pMDI 20 mcg/ACT	Off-label <12 y: 1-2 INH Q6H ¹² Max: 12 INH/day ¹²	Onset: within 15 min Peak: 1-2 h Duration: 2-4 h	Less effective and slower acting than salbutamol ^{6,8} and generally used only as an adjunct to SABAs for exacerbations in children. ^{11,14} Adverse effects: ⁴ dry mouth, metallic taste; mydriasis and glaucoma if released into eye.
Ipratropium (g) Nebules* 250 mcg/1 mL; 500 mcg/2 mL	Off-label <12 y: 250-500 mcg Q6-8H ¹² Max: N/A	Onset: within 15 min Peak: 1-2 h Duration: 4-5 h, up to 7-8 h in some	
Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)			
Ipratropium/ Salbutamol (Combivent®) Respimat 20 mcg/100 mcg per ACT	Off-label Children able to use device: If extrapolated from individual dosing for acute symptom relief: 4-11 y: 1-2 INH TID-QID PRN Max: 6 INH/day	Based on individual ingredients (pMDI, not Respimat): Onset: 5-8 min (median) Duration: 2-4 h	Respimat not approved for children or for use with a spacer. ⁹ Use for acute symptom relief is off-label. Doses provided have been extrapolated from individual ingredient information and are not supported by any data.
Ipratropium/ Salbutamol (g) Nebules* 0.5 mg/2.5 mg per 2.5 mL	Off-label If extrapolated from individual dosing for acute symptom relief: <12 y: 0.5-1 NEB Q6-8H PRN Max: N/A	Based on individual ingredients: Onset: ≤5 min Duration: 4-5 h, up to 7-8 h in some	Adverse effects: ⁵ dry mouth, metallic taste; mydriasis and glaucoma if released into eye. Nervousness, tremor, tachycardia, palpitations.
* Preferably use pMDI or DPI if, available. See note about nebulization in text.			
ACT = actuation; g = generics; h or H = hour(s); INH = inhalation(s); max = maximum; min = minute(s); N/A = not available; NEB = nebule(s); pMDI = pressurized metered dose inhaler; PRN = as needed; Q = every; QID = four times daily; TID = three times daily; y = year(s)			

TABLE 4: PHARMACOLOGIC AGENTS FOR PREVENTION OF EXERCISE-INDUCED BRONCHOSPASM (EIB)

EIB is often an indication of poorly controlled asthma^{6,8}; optimize treatment with ICS⁸. Avoiding exercise in extreme cold/pollution (or covering mouth if unavoidable)¹⁶ and warming up before exercise^{8,16} may help.

Medication Dosage Form Strength	Dosage (to be provided 15 min prior to exercises unless otherwise noted)	Comments
Short-Acting Beta₂-Agonists (SABA)		
Salbutamol (Airomir [®] , Ventolin, g) pMDI 100 mcg/ACT	4 to <12 y: 1-2 INH ² ≥12 y: 2 INH ²	Tachyphylaxis likely to develop if used >once/day. ^{16,17}
Salbutamol (Ventolin) Diskus 200 mcg/ACT	≥4 y (incl adults): 1 INH ⁵	
Terbutaline (Bricanyl [®]) Turbuhaler 0.5 mg/ACT	Off-label ≥6 (incl adults): 1-2 INH ⁶	
Long-Acting Beta₂-Agonists (LABA)		
Formoterol (Oxeze [®]) Turbuhaler 6 mcg/ACT; 12 mcg/ACT	≥6 y (incl adults): 6-12 mcg ¹⁸ Max - children and adolescents: 24 mcg/24 h ¹⁸ Max - adults: 48 mcg/24 h ¹⁸	In patients with asthma, formoterol should not be used as monotherapy and needs to be used with ICS.^{16,17} Fixed-dose combination product (e.g., Symbicort[®]) preferred. Not to be used for prevention of EIB in patients using regularly for asthma maintenance. ¹² Tachyphylaxis likely to develop if used >once/day. ^{16,17}
Formoterol (Foradil) Dry powder capsule 12 mcg/CAP	Off-label Canada ≥6 y (incl adults): inhale contents of 1 CAP ¹² Max: 24 mcg/24 h ¹²	
Salmeterol (Serevent [®]) Diskhaler Disk, Diskus 50 mcg/ACT	Off-label Canada ≥4 y (incl adults): 1 INH 30 min before exercise; no more additional doses for next 12 h ¹²	
Leukotriene Receptor Antagonist (LTRA)		
Montelukast (Singulair [®] , g) Oral tablet 10 mg Oral chewable tablet 4 mg, 5 mg Oral granules 4 mg	6-12 y: 5 mg PO once daily ¹⁶ >12 y: 10 mg PO once daily ¹⁶ taken ≥ 2 h prior to exercise ¹⁶ Duration of action: 24 h ¹⁷	Intended as prophylactic for EIB; ensure rescue treatment available. ¹⁹ Useful for those exercising for prolonged durations (e.g., >3 h) or more than once daily. ¹⁷ Be aware that neuropsychiatric events, including suicidal ideation, associated with montelukast have been reported in pediatric, adolescent and adult patients. ¹⁹
Corticosteroid(CS)/Long-Acting Beta₂-Agonist (LABA) Combinations		
Budesonide/ Formoterol (Symbicort [®]) Turbuhaler 100 mcg/6 mcg per ACT; 200 mcg/6 mcg per ACT	Off-label ≥12 y: 1 INH ¹⁷	Good option for those already using (as controller or reliever). ¹⁶ This is the only ICS/LABA combination with evidence in EIB. ⁸ A different device formulation was used in studies, which is why it is off-label.
Short-Acting Antimuscarinic Antagonist (SAMA)		
Ipratropium (Atrovent [®] , g) pMDI (20 mcg/ACT)	Off-label ≥12 y: 2-4 INH ¹⁶ 15-30 min prior to exercise	Time before use estimated based on time to onset of 15 min. ¹² Less effective than SABAs but likely provides partial protection. ¹⁷
Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)		
Ipratropium/ Salbutamol (Combivent [®]) Respimat 20 mcg/100 mcg per ACT	Off-label ≥12 y: 2 INH See comments	No dosing information available regarding use of this product for EIB and is based on composite ingredients. Dose extrapolated from single-ingredient product information.
ACT = actuation; CAP= capsule; EIB = exercise-induced bronchoconstriction; g = generics; h = hour(s); incl = including; INH = inhalation(s); max = maximum; min = minute(s); pMDI = pressurized metered dose; PO = by mouth; inhaler; SABA = short-acting beta ₂ -agonists; y = year(s)		

TABLE 5: PHARMACOLOGIC AGENTS FOR RELIEF OF COPD SYMPTOMS⁵

Medication Dosage Form Strength	Dosage
Short-Acting Beta₂-Agonists (SABA)	
Salbutamol (Airomir®, Ventolin, g) pMDI 100 mcg/ACT	1-2 INH QID PRN Max: 800 mcg/day Onset: 5-8 min
Salbutamol (Ventolin) Diskus 200 mcg/ACT	1 INH QID PRN Max: 800 mcg/day Onset: ~5 min
Salbutamol (Ventolin, g) Nebules* 2.5 mg/2.5 mL; 5 mg/2.5 mL	2.5 mg QID PRN Max: 15 mg/day Onset: ≤5 min
Terbutaline (Bricanyl®) Turbuhaler 0.5 mg/ACT	1 INH QID PRN Max: 3 mg Onset: 5 min
Short-Acting Muscarinic Antagonist (SAMA)	
Ipratropium (Atrovent®, g) pMDI 20 mcg/ACT	2 INH TID-QID Max: 12 INH/day Onset: 15-20 min
Ipratropium (g) Nebules* 250 mcg/1 mL; 500 mcg/2 mL	500 mcg TID-QID Max: 2000 mcg/day Onset: 15-20 min
Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)	
Ipratropium/Salbutamol (Combivent®) Respimat 20 mcg/100 mcg per ACT	1 INH QID PRN Max: 6 INH/day Onset: 5-8 min ¹² (based on salbutamol)
Ipratropium/Salbutamol (g) Nebules* 0.5 mg/2.5 mg per 2.5 mL	1 NEB QID PRN Max: 4 NEB/day Onset: 5-8 min ¹² (based on salbutamol)
* Preferably use pMDI or DPI, if available. See note about nebulization in text. ACT = actuation; g = generics; INH = inhalation; Max = maximum; MDI = pressurized metered dose inhaler; min = minutes; NEB = nebule(s); PRN = as needed; QID = four times daily; TID = three times daily	

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