

## Inhaled Salbutamol Shortage

TABLE 1: SUPPLIERS OF INHALED SALBUTAMOL<sup>1</sup>

Product	Strength	DIN	Manufacturer
Airomir <sup>®</sup>	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)<sup>2</sup> and salbutamol dry powder inhaler (DPI)<sup>3</sup> 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:<sup>4-7</sup>

- Ensure proper inhaler technique and adherence.
- Post-use oral care is strongly suggested after inhaled corticosteroid (ICS) (+/- long-acting beta<sub>2</sub>-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.<sup>8</sup>
- 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;<sup>8</sup> 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.<sup>9</sup> Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens such as SARS-CoV-2.<sup>10,11</sup> 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.<sup>8</sup>

Medication Dosage Form Strength <sup>1</sup>	Dosage <sup>4</sup>	Pharmacokinetics <sup>12</sup>	Comments
<b>Short-Acting Beta<sub>2</sub>-Agonists (SABA)</b>			
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 <sup>2</sup>	Preferably use pMDI or Diskus if available. See note about nebulization in text.  Adverse effects: <sup>4</sup> 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 <sup>3</sup>	
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: <sup>4</sup> nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.
<b>Corticosteroid/Long-Acting Beta<sub>2</sub>-Agonist (LABA) Combination</b>			
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. <sup>4</sup> Adverse effects: <sup>4</sup> sore mouth, sore throat, dysphonia, oral thrush (can be reduced by rinsing mouth or using spacer). Nervousness, tremor, tachycardia, palpitations.

Medication Dosage Form Strength <sup>1</sup>	Dosage <sup>4</sup>	Pharmacokinetics <sup>12</sup>	Comments
Mometasone/ Formoterol (Zenhale®) pMDI 100 mcg/5 mcg per ACT; 200 mcg/5 mcg per ACT	Off-label as <b>reliever</b> 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 <b>See comments</b>	(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 <b>for use in shortage situations only.</b> <b>Use only the 100 mcg/5 mcg strength</b> if being used as reliever; the maximum daily dose is 800 mcg/20 mcg, <sup>13</sup> 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. <sup>6,8</sup> 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 <sub>2</sub> -agonists. <sup>4</sup>
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. <sup>4,6</sup> Adverse effects: <sup>4</sup> dry mouth, metallic taste; mydriasis and glaucoma if released into eye.

#### Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta<sub>2</sub>-Agonist Combination (SABA)

Ipratropium/ Salbutamol (Combivent®) Respimat 20 mcg/100 mcg per ACT	Off-label 2-3 INH Q6H PRN <sup>12</sup> Max: N/A	Based on individual ingredients (pMDI, not Respimat): Onset: 5-8 min (median) Duration: 2-4 h	Adverse effects: <sup>4</sup> 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 Beta<sub>2</sub>-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 <b>See Comments</b>	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. <b>Formoterol alone is not an appropriate reliever as it relies on the patient to add ICS;</b> fixed-dose combination products (e.g., Symbicort®) are preferred, if available. <sup>8</sup> <b>Reserve as last resort and ensure patient takes with ICS.</b>
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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 beta<sub>2</sub>-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 <sup>1</sup>	Dosage	Pharmacokinetics <sup>12</sup>	Comments
<b>Short-Acting Beta<sub>2</sub>-Agonists (SABA)</b>			
Salbutamol (Airmir®, Ventolin, g) pMDI 100 mcg/ACT	<4 y: 2 INH Q4-6H PRN <sup>11</sup> Max: N/A 4-11 y: 2 INH TID-QID PRN <sup>14</sup> Max: 600 mcg/day <sup>14</sup>	Onset: 5-8 min (median) Duration: 3-6 h <sup>2</sup>	Preferred agent when available. Adverse effects: <sup>14</sup> nervousness, tremor, tachycardia, palpitations.
Salbutamol (Ventolin) Diskus 200 mcg/ACT	≥4 y: 1 INH TID-QID PRN <sup>14</sup> Max: 800 mcg/day <sup>14</sup>  Adult doses may be required due to poor deposition <sup>14</sup>	Onset: ~5 min Duration: 3-6 h <sup>3</sup>	pMDI plus spacer may be used in children <4 y, though no trials have been done to assess optimal dose. <sup>14</sup>
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 <sup>11</sup> Max: N/A  5-12 y: 1.25-2.5 mg as a single dose QID PRN <sup>14</sup>  Max: 5 mg/dose <sup>14</sup>	Onset: ≤5 min Duration: 3-6 h	
Terbutaline (Bricanyl®) Turbuhaler 0.5 mg/ACT	≥6 y: 1 INH PRN <sup>15</sup> Max: 6 INH/day <sup>15</sup>	Onset: 5 min Peak: 15-60 min Duration: 3-6 h	Adverse effects: <sup>14</sup> nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.
<b>Short-Acting Antimuscarinic Antagonist (SAMA)</b>			
Ipratropium (Atrovent®) pMDI 20 mcg/ACT	Off-label <12 y: 1-2 INH Q6H <sup>12</sup> Max: 12 INH/day <sup>12</sup>	Onset: within 15 min Peak: 1-2 h Duration: 2-4 h	Less effective and slower acting than salbutamol <sup>6,8</sup> and generally used only as an adjunct to SABAs for exacerbations in children. <sup>11,14</sup>  Adverse effects: <sup>4</sup> 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 <sup>12</sup> Max: N/A	Onset: within 15 min Peak: 1-2 h Duration: 4-5 h, up to 7-8 h in some	
<b>Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta<sub>2</sub>-Agonist Combination (SABA)</b>			
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. <sup>9</sup>  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: <sup>5</sup> 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 = nebul(e)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<sup>6,8</sup>; optimize treatment with ICS<sup>8</sup>. Avoiding exercise in extreme cold/pollution (or covering mouth if unavoidable)<sup>16</sup> and warming up before exercise<sup>8,16</sup> may help.

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

TABLE 5: PHARMACOLOGIC AGENTS FOR RELIEF OF COPD SYMPTOMS<sup>5</sup>

Medication Dosage Form Strength	Dosage
<b>Short-Acting Beta<sub>2</sub>-Agonists (SABA)</b>	
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
<b>Short-Acting Muscarinic Antagonist (SAMA)</b>	
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
<b>Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta<sub>2</sub>-Agonist Combination (SABA)</b>	
Ipratropium/Salbutamol (Combivent®) Respimat 20 mcg/100 mcg per ACT	1 INH QID PRN Max: 6 INH/day Onset: 5-8 min <sup>12</sup> (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 <sup>12</sup> (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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