Inhaled Salbutamol Shortage

TABLE 1: SUPPLIERS OF INHALED SALBUTAMOL

<table>
<thead>
<tr>
<th>Product</th>
<th>Strength</th>
<th>DIN</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airomir®</td>
<td>100 mcg/actuation</td>
<td>02232570</td>
<td>VAE</td>
</tr>
<tr>
<td>Apo-Salbutamol HFA</td>
<td></td>
<td>02245669</td>
<td>APX</td>
</tr>
<tr>
<td>Salbutamol HFA</td>
<td></td>
<td>02419858</td>
<td>SAN</td>
</tr>
<tr>
<td>Teva-Salbutamol HFA</td>
<td></td>
<td>02326450</td>
<td>TEV</td>
</tr>
<tr>
<td>Ventolin HFA</td>
<td></td>
<td>02241497</td>
<td>GSK</td>
</tr>
<tr>
<td>Ventolin Diskus</td>
<td>200 mcg/actuation</td>
<td>02243115</td>
<td>GSK</td>
</tr>
</tbody>
</table>

HFA = hydrofluoroalkane

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

- 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.
- 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.
o 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; these may not be reflected in all references.
  - RxTx and RxFiles are available through SHIRP.

o 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.

o 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. Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens such as SARS-CoV-2. 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.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form Strength1</th>
<th>Dosage4</th>
<th>Pharmacokinetics12</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Beta2-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Airomir®, Ventolin, g)</td>
<td>pMDI 100 mcg/ACT</td>
<td>1-2 INH TID to QID PRN; Max: 8 INH (800 mcg)/day</td>
<td>Onset: 5–8 min (median) Duration: 3–6 h²</td>
<td>Preferably use pMDI or Diskus if available. See note about nebulization in text. Adverse effects: nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.</td>
</tr>
<tr>
<td>Salbutamol (Ventolin) Diskus</td>
<td>200 mcg/ACT</td>
<td>1 INH QID PRN; Max: 4 INH (800 mcg) /day</td>
<td>Onset: ~5 min Duration: 3–6 h³</td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Ventolin, g) Nebules*</td>
<td>2.5 mg/2.5 mL; 5 mg/2.5 mL</td>
<td>2.5 to 5 mg QID PRN Max: N/A</td>
<td>Onset: ≤5 min Duration: 3–6 h</td>
<td></td>
</tr>
<tr>
<td>Terbutaline (Bricanyl®) Turbuhaler</td>
<td>0.5 mg/ACT</td>
<td>1 INH Q4–6H PRN Max: 6 INH/day</td>
<td>Onset: 5 min Peak: 15–60 min Duration: 3–6 h</td>
<td>Adverse effects: nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Corticosteroid/Long-Acting Beta2-Agonist (LABA) Combination</strong></th>
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<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Budesonide/ Formoterol (Symbicort®) Turbuhaler</td>
<td>100 mcg/6 mcg per ACT; 200 mcg/6 mcg per ACT</td>
<td>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</td>
<td>(Formoterol) Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients</td>
<td>LABA monotherapy 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. Adverse effects: sore mouth, sore throat, dysphonia, oral thrush (can be reduced by rinsing mouth or using spacer). Nervousness, tremor, tachycardia, palpitations.</td>
</tr>
</tbody>
</table>

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**Inhaled Salbutamol Shortage | April 7, 2020**

[Subscription to RxFiles or SHIRP is required.]

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**RxTx** and **RxFiles** are available through SHIRP.

**Note:** In general, nebulization is not preferred because of cost and there being no added benefit compared to pMDI with spacer. Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens such as SARS-CoV-2. 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.

- **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.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form Strength¹</th>
<th>Dosage⁴</th>
<th>Pharmacokinetics¹²</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Beta2-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Airomir®, Ventolin, g)</td>
<td>pMDI 100 mcg/ACT</td>
<td>1-2 INH TID to QID PRN; Max: 8 INH (800 mcg)/day</td>
<td>Onset: 5–8 min (median) Duration: 3–6 h²</td>
<td>Preferably use pMDI or Diskus if available. See note about nebulization in text. Adverse effects: nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.</td>
</tr>
<tr>
<td>Salbutamol (Ventolin) Diskus</td>
<td>200 mcg/ACT</td>
<td>1 INH QID PRN; Max: 4 INH (800 mcg) /day</td>
<td>Onset: ~5 min Duration: 3–6 h³</td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Ventolin, g) Nebules*</td>
<td>2.5 mg/2.5 mL; 5 mg/2.5 mL</td>
<td>2.5 to 5 mg QID PRN Max: N/A</td>
<td>Onset: ≤5 min Duration: 3–6 h</td>
<td></td>
</tr>
<tr>
<td>Terbutaline (Bricanyl®) Turbuhaler</td>
<td>0.5 mg/ACT</td>
<td>1 INH Q4–6H PRN Max: 6 INH/day</td>
<td>Onset: 5 min Peak: 15–60 min Duration: 3–6 h</td>
<td>Adverse effects: nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Corticosteroid/Long-Acting Beta2-Agonist (LABA) Combination</strong></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide/ Formoterol (Symbicort®) Turbuhaler</td>
<td>100 mcg/6 mcg per ACT; 200 mcg/6 mcg per ACT</td>
<td>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</td>
<td>(Formoterol) Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients</td>
<td>LABA monotherapy 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. Adverse effects: sore mouth, sore throat, dysphonia, oral thrush (can be reduced by rinsing mouth or using spacer). Nervousness, tremor, tachycardia, palpitations.</td>
</tr>
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**Note:** In general, nebulization is not preferred because of cost and there being no added benefit compared to pMDI with spacer. Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens such as SARS-CoV-2. 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.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form Strength</th>
<th>Dosage</th>
<th>Pharmacokinetics</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone/Formoterol</td>
<td>pMDI 100 mcg/5 mcg per ACT; 200 mcg/5 mcg per ACT</td>
<td>Off-label as <strong>releiver</strong> controller dose: 2 INH BID</td>
<td>(Formoterol) Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients</td>
<td>See comments for <strong>Symbicort</strong>*. 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. <strong>Use only the 100 mcg/5 mcg strength</strong> if being used as reliever; the maximum daily dose is 800 mcg/20 mcg, 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.</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td><strong>Short-Acting Antimuscarinic Antagonist (SAMA)</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Ipratropium (Atrovent®, g)</td>
<td>pMDI 20 mcg/ACT</td>
<td>Off-label 2 INH Q6–8H PRN Max: 12 INH/day</td>
<td>Onset: within 15 min Peak: 1–2 h Duration: 2–4 h</td>
<td>Less effective &amp; slower acting than salbutamol. Preferably use pMDI, if available. See note about nebulization in text. Useful alternative for patients who are unusually susceptible to tremor or tachycardia from beta2-agonists. May also be useful in beta-blocker−induced bronchospasm. Adverse effects: dry mouth, metallic taste; mydriasis and glaucoma if released into eye.</td>
</tr>
<tr>
<td>Ipratropium (g) Nebules*</td>
<td>250 mcg/1 mL; 500 mcg/2 mL</td>
<td>Off-label 250–500 mcg Q6–8H PRN Max: N/A</td>
<td>Onset: within 15 min Peak: 1–2 h Duration: 4–5 h, up to 7–8 h in some</td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta2-Agonist Combination (SABA)</strong></td>
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</tr>
<tr>
<td>Ipratropium/Salbutamol</td>
<td>Respimat 20 mcg/100 mcg per ACT</td>
<td>Off-label 2–3 INH Q6H PRN Max: N/A</td>
<td>Based on individual ingredients (pMDI, not Respimat): Onset: 5–8 min (median) Duration: 2–4 h</td>
<td>Adverse effects: dry mouth, metallic taste; mydriasis and glaucoma if released into eye. Nervousness, tremor, tachycardia, palpitations.</td>
</tr>
<tr>
<td>Ipratropium/Salbutamol (g) Nebules*</td>
<td>0.5 mg/2.5 mg per 2.5 mL</td>
<td>Off-label 1 NEB Q4–6H PRN Max: N/A</td>
<td>Based on individual ingredients: Onset: ≤5 min Duration: 4–5 h, up to 7–8 h in some</td>
<td></td>
</tr>
<tr>
<td><strong>Long-Acting Beta2-Agonist (LABA)</strong></td>
<td></td>
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</tr>
<tr>
<td>Formoterol (Oxeze*)</td>
<td>Turbuhaler 6 mcg/ACT; 12 mcg/ACT</td>
<td>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</td>
<td>Onset: within 3 min Peak: within 15 min Duration: 12 h in most patients</td>
<td>LABA monotherapy should be avoided in asthma as it is associated with higher rates of death. <strong>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.</strong> Reserve as last resort and ensure patient takes with ICS.</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Dosage</th>
<th>Pharmacokinetics</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Beta₂-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Airomir®, Ventolin, g)</td>
<td>pMDI</td>
<td>100 mcg/ACT</td>
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<tr>
<td></td>
<td></td>
<td>&lt;4 y: 2 INH Q4–6H PRN¹³</td>
<td>Onset: 5–8 min (median) Duration: 3–6 h²</td>
<td>Preferred agent when available. Adverse effects:¹⁴ nervousness, tremor, tachycardia, palpitations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max: N/A</td>
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<tr>
<td></td>
<td></td>
<td>4–11 y: 2 INH TID–QID PRN¹⁴</td>
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<tr>
<td></td>
<td></td>
<td>Max: 600 mcg/day¹⁴</td>
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</tr>
<tr>
<td>Salbutamol (Ventolin) Diskus</td>
<td>200 mcg/ACT</td>
<td>≥4 y: 1 INH TID–QID PRN¹⁴</td>
<td>Onset: &lt;5 min Duration: 3–6 h³</td>
<td>pMDI plus spacer may be used in children &lt;4 y, though no trials have been done to assess optimal dose.¹⁴</td>
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<tr>
<td></td>
<td></td>
<td>Max: 800 mcg/day¹⁴</td>
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<td>Adult doses may be required due to poor deposition¹⁴</td>
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</tr>
<tr>
<td>Salbutamol (Ventolin, g) Nebules⁴</td>
<td>2.5 mg/2.5 mL; 5 mg/2.5 mL</td>
<td>&lt;5 y: 0.63–2.5 mg Q4–6H PRN¹⁳</td>
<td>Onset: ≤5 min Duration: 3–6 h</td>
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<tr>
<td></td>
<td></td>
<td>Max: N/A</td>
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<tr>
<td></td>
<td></td>
<td>5–12 y: 1.25–2.5 mg as a single dose QID PRN¹⁴</td>
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<tr>
<td></td>
<td></td>
<td>Max: 5 mg/dose¹⁴</td>
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<tr>
<td>Terbutaline (Bricanyl⁵) Turbuhaler</td>
<td>0.5 mg/ACT</td>
<td>≥6 y: 1 INH PRN¹⁵</td>
<td>Onset: 5 min Peak: 15–60 min Duration: 3–6 h</td>
<td>Adverse effects:¹⁴ nervousness, tremor, tachycardia, palpitations, hypokalemia (high dose), restlessness, dizziness, headache, nausea.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max: 6 INH/day¹⁵</td>
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<tr>
<td><strong>Short-Acting Antimuscarinic Antagonist (SAMA)</strong></td>
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<td></td>
</tr>
<tr>
<td>Ipratropium (Atrovent⁶*) pMDI</td>
<td>20 mcg/ACT</td>
<td>Off-label</td>
<td>Onset: within 15 min Peak: 1-2 h Duration: 2-4 h</td>
<td>Less effective and slower acting than salbutamol⁶,⁸ and generally used only as an adjunct to SABAs for exacerbations in children.¹¹⁴⁻¹⁵ Adverse effects:⁴ dry mouth, metallic taste; mydriasis and glaucoma if released into eye.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;12 y: 1-2 INH Q6H¹² Max: 12 INH/day¹²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium (g) Nebules⁴</td>
<td>250 mcg/1 mL; 500 mcg/2 mL</td>
<td>Off-label</td>
<td>Onset: within 15 min Peak: 1-2 h Duration: 4-5 h, up to 7-8 h in some</td>
<td>Adverse effects:⁴ dry mouth, metallic taste; mydriasis and glaucoma if released into eye.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;12 y: 250-500 mcg Q6–8H¹² Max: N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium/ Salbutamol (Combivent⁷*) Respimat</td>
<td>20 mcg/100 mcg per ACT</td>
<td>Off-label</td>
<td>Based on individual ingredients (pMDI, not Respimat): Onset: 5-8 min (median) Duration: 2-4 h</td>
<td>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. Adverse effects:⁵ dry mouth, metallic taste; mydriasis and glaucoma if released into eye. Nervousness, tremor, tachycardia, palpitations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>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</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium/ Salbutamol (g) Nebules⁴</td>
<td>0.5 mg/2.5 mg per 2.5 mL</td>
<td>Off-label</td>
<td>Based on individual ingredients: Onset: ≤5 min Duration: 4-5 h, up to 7-8 h in some</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>If extrapolated from individual dosing for acute symptom relief: &lt;12 y: 0.5–1 NEB Q6–8H PRN Max: N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Preferably use pMDI or DPI if, available. See note about nebulization in text.
² 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\(^8,^6\); optimize treatment with ICS\(^8\). Avoiding exercise in extreme cold/pollution (or covering mouth if unavoidable)\(^6,^16\) and warming up before exercise\(^8,^16\) may help.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form Strength</th>
<th>Dosage (to be provided 15 min prior to exercises unless otherwise noted)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Beta(_2)-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Airomir\textsuperscript{\textregistered}, Ventolin, g) pMDI 100 mcg/ACT</td>
<td>4 to &lt;12 y: 1–2 INH(^2) ≥12 y: 2 INH(^2)</td>
<td>Tachyphylaxis likely to develop if used &gt;once/day(^6,^17)</td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Ventolin) Diskus 200 mcg/ACT</td>
<td>≥4 y (incl adults): 1 INH(^3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terbutaline (Bricanyl\textsuperscript{\textregistered}) Turbuhaler 0.5 mg/ACT</td>
<td>Off-label ≥6 (incl adults): 1–2 INH(^6)</td>
<td></td>
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</tr>
<tr>
<td><strong>Long-Acting Beta(_2)-Agonists (LABA)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Formoterol (Oxeze\textsuperscript{\textregistered}) Turbuhaler 6 mcg/ACT; 12 mcg/ACT</td>
<td>≥6 y (incl adults): 6–12 mcg(^{18}) Max - children and adolescents: 24 mcg/24 h(^{18}) Max - adults: 48 mcg/24 h(^{18})</td>
<td>In patients with asthma, formoterol should not be used as monotherapy and needs to be used with ICS(^{16},^7) Fixed-dose combination product (e.g., Symbicort\textsuperscript{\textregistered}) preferred. Not to be used for prevention of EIB in patients using regularly for asthma maintenance.(^{12}) Tachyphylaxis likely to develop if used &gt;once/day(^6,^17)</td>
<td></td>
</tr>
<tr>
<td>Formoterol (Foradil) Dry powder capsule 12 mcg/CAP</td>
<td>Off-label Canada ≥6 y (incl adults): inhale contents of 1 CAP(^ {12}) Max: 24 mcg/24 h(^{12})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol (Serevent\textsuperscript{\textregistered}) Diskhaler Disk, Diskus 50 mcg/ACT</td>
<td>Off-label Canada ≥4 y (incl adults): 1 INH 30 min before exercise; no more additional doses for next 12 h(^{12})</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Leukotriene Receptor Antagonist (LTRA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast (Singulair\textsuperscript{\textregistered}, g) Oral tablet 10 mg Oral chewable tablet 4 mg, 5 mg Oral granules 4 mg</td>
<td>6–12 y: 5 mg PO once daily(^ {16}) &gt;12 y: 10 mg PO once daily(^ {16}) taken ≥2 h prior to exercise(^ {16}) Duration of action: 24 h(^ {17})</td>
<td>Intended as prophylactic for EIB; ensure rescue treatment available.(^ {19}) Useful for those exercising for prolonged durations (e.g., &gt;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})</td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroid (CS)/Long-Acting Beta(_2)-Agonist (LABA) Combinations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide/ Formoterol (Symbicort\textsuperscript{\textregistered}) Turbuhaler 100 mcg/6 mcg per ACT; 200 mcg/6 mcg per ACT</td>
<td>Off-label ≥12 y: 1 INH(^{17})</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting Antimuscarinic Antagonist (SAMA)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ipratropium (Atrovent\textsuperscript{\textregistered}, g) pMDI (20 mcg/ACT)</td>
<td>Off-label ≥12 y: 2–4 INH(^ {16}) 15–30 min prior to exercise</td>
<td>Time before use estimated based on time to onset of 15 min.(^ {15}) Less effective than SABAs but likely provides partial protection.(^ {17})</td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta(_2)-Agonist Combination (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium/ Salbutamol (Combivent\textsuperscript{\textregistered}) Respimat 20 mcg/100 mcg per ACT</td>
<td>Off-label ≥12 y: 2 INH See comments</td>
<td>No dosing information available regarding use of this product for EIB and is based on composite ingredients. Dose extrapolated from single-ingredient product information.</td>
<td></td>
</tr>
</tbody>
</table>

\(\text{ACT} = \text{actuation}; \text{CAP} = \text{capsule}; \text{EIB} = \text{exercise-induced bronchoconstriction}; \text{g} = \text{generics}; \text{h} = \text{hour(s)}; \text{incl} = \text{including}; \text{INH} = \text{inhalation(s)}; \text{max} = \text{maximum}; \text{min} = \text{minute(s)}; \text{pMDI} = \text{pressurized metered dose}; \text{PO} = \text{by mouth}; \text{inhaler}; \text{SABA} = \text{short-acting beta} _2\text{-agonists}; \text{y} = \text{year(s)}\)
### TABLE 5: PHARMACOLOGIC AGENTS FOR RELIEF OF COPD SYMPTOMS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage Form</th>
<th>Strength</th>
<th>Dosage</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting Beta$_2$-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (Airomir®, Ventolin, g)</td>
<td>pMDI</td>
<td>100 mcg/ACT</td>
<td>1–2 INH QID PRN</td>
<td>Max: 800 mcg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Onset: 5–8 min</td>
</tr>
<tr>
<td>Salbutamol (Ventolin) Diskus</td>
<td>Diskus</td>
<td>200 mcg/ACT</td>
<td>1 INH QID PRN</td>
<td>Max: 800 mcg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Onset: ≤5 min</td>
</tr>
<tr>
<td>Salbutamol (Ventolin, g) Nebules*</td>
<td>Nebules*</td>
<td>2.5 mg/2.5 mL; 5 mg/2.5 mL</td>
<td>2.5 mg QID PRN</td>
<td>Max: 15 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Onset: ≤5 min</td>
</tr>
<tr>
<td>Terbutaline (Bricanyl®)</td>
<td>Turbuhaler</td>
<td>0.5 mg/ACT</td>
<td>1 INH QID PRN</td>
<td>Max: 3 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Onset: 5 min</td>
</tr>
</tbody>
</table>

| **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*           | 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 Beta$_2$-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* | 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.

Prepared by Dorothy Sanderson BSP and Carmen Bell BSP
Reviewed by Kelly Kizlyk BSP; Kirsten Bazylak BSP; Neil Skjodt, MD, FRCPC, FCCP, DABSM, FAASM; Kristine Petrasko, BScPharm, CRE, CTE
References


