

# Ipratropium Bromide Shortage

### TABLE 1: SUPPLIERS OF INHALED IPRATROPIUM BROMIDE1

Product	Strength	DIN	Manufacturer	
Pressurized Metered Dose Inhalers (pMDIs)				
Atrovent HFA	20 mcg/actuation	02247686	Boehringer Ingelheim (Canada) Ltd.	
JAMP Ipratropium HFA		02542587	Jamp Pharma Corporation	
Nebules*				
PMS-Ipratropium	125 mcg/mL x 2 mL	02231135	Pharmascience Inc.	
	250 mcg/mL x 1 mL	02231244		
	250 mcg/mL x 2 mL	02231245		
Teva-Ipratropium Sterinebs	250 mcg/mL x 1 mL, 2 mL	02216221	Teva Canada Limited	
Respirator Solution for Nebulization*				
AA-Ipravent	250 mcg/mL x 20 mL	02126222	AA Pharma Inc.	

<sup>\*</sup> Preferably use pMDI if available. See note about nebulization in text. HFA = hydrofluoroalkane

Health Canada-approved indications for ipratropium pressurized metered dose inhalers (pMDIs) include:2

 as a bronchodilator for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Health Canada-approved indications for ipratropium solutions for nebulization include: 3,4

- the treatment of bronchospasm associated with acute exacerbations of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema, and
- the treatment of bronchospasm associated with acute severe exacerbations of bronchial asthma when used in conjunction with a beta2-adrenergic agonist such as salbutamol in patients 5 years and older.

## Considerations and Non-Pharmacological Management: 5-9

- Ensure proper inhaler technique and adherence.
- Have written action plans. Example plans for chronic obstructive pulmonary disease (COPD) and asthma are available from the <u>Canadian Lung Association</u><sup>10</sup> or the <u>Canadian Thoracic Society</u>.
- Recommend smoking cessation when applicable.
- Identify and avoid triggers, when possible, such as environmental allergens, pollution, and occupational irritants.
- Manage conditions that may exacerbate asthma: obesity, anxiety, depression, rhinitis, sinusitis, gastroesophageal reflux disease and seasonal allergies.

- Assess potential for medication-induced asthma.
  - 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.
  - o Oral and ophthalmic beta-blockers may cause bronchospasm. Continuation or initiation of these agents should be under close supervision when benefits outweigh risks.
- Recommend strategies to prevent respiratory infections, including up-to-date vaccination for influenza, COVID-19, pneumococcal, pertussis and respiratory syncytial virus.<sup>9,12</sup>
- Encourage physical activity.
- For patients with COPD, refer to pulmonary rehabilitation if appropriate and available.
  - <u>Living Well with COPD</u><sup>13</sup> is a resource accessible to patients and healthcare professionals (requires free registration) that offers print and video resources, including at-home pulmonary rehabilitation exercises.

### Therapeutic Alternatives/Considerations:

- Refer to Tables 2 and 3 for alternatives to ipratropium for use in COPD and acute severe exacerbations of asthma.
  - Availability of ipratropium and alternatives may fluctuate. Inventory management, especially prevention of stockpiling, is key to maintaining adequate supply for patients.
- Ensure optimal treatment of COPD and asthma.
  - Note: In general, nebulization is not preferred because of cost and lack of benefit compared to pMDI with spacer.
     Nebulization generates aerosols, meaning potentially greater transmission of respiratory pathogens.
     However, in some cases, nebulization may be the only option. This is most likely to be the case in the very young, very old, and/or for severe exacerbations.
  - See <u>CPS</u><sup>6</sup>, <u>RxFiles</u><sup>8</sup>, and <u>Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines</u><sup>12</sup> for stepped-care COPD treatment.
  - See <u>CPS</u> (Asthma in Adolescents/Adults<sup>5</sup>, Asthma Infants and Children<sup>15</sup>) and <u>Global Initiative for Asthma (GINA)</u>
     <u>Management and Prevention 2025 Update</u><sup>9</sup> for management of **severe acute asthma exacerbation**.
    - Ipratropium is considered for exacerbations requiring emergency medical care in which it is added to other therapies including short-acting beta<sub>2</sub>-agonists, oxygen, and corticosteroids.<sup>7,9,15</sup>
    - Prevention of exacerbations is of most importance. See Considerations and Non-Pharmacological Management.
- 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, those with dementia and those concerned about environmental impacts. RxFiles has resources to help select the best device: <u>pros and cons of devices</u><sup>14</sup>; <u>COPD inhalers</u>: hand vs. lung approach<sup>16</sup>; and information on <u>inhaler</u> technique. To Device selection may not be possible based on product availability.





### TABLE 2: PHARMACOLOGIC AGENTS FOR RELIEF OF COPD SYMPTOMS

Medication Dosage Form Strength <sup>6</sup>	Dosage			
Short-Acting Beta <sub>2</sub> -Agonists (SABA)				
Salbutamol (Ventolin, g)	1–2 INH TID-QID PRN <sup>6</sup>			
pMDI	Max: 800 mcg/day <sup>6</sup>			
100 mcg/ACT	Onset: 5–8 min <sup>18</sup>			
Salbutamol (Ventolin)	1 INH TID-QID PRN6			
Diskus (DPI)	Max: 800 mcg/day <sup>6</sup>			
200 mcg/ACT	Onset: ~5 min <sup>18</sup>			
Salbutamol (Ventolin, g)	2.5-5 mg QID PRN <sup>6</sup>			
Nebules*	Max: 15 mg/day <sup>8</sup>			
2.5 mg/2.5 mL; 5 mg/2.5 mL	Onset: ~5 min <sup>18</sup>			
Terbutaline (Bricanyl)	1 INH Q4-6H PRN <sup>6</sup>			
Turbuhaler (DPI)	Max: 3 mg/day <sup>6</sup>			
0.5 mg/ACT	Onset: ~5 min <sup>18</sup>			
Short-Acting Muscarinic Antagonist (SAMA)				
Ipratropium (Atrovent, g)	2–4 INH TID–QID <sup>2</sup>			
pMDI	Max: 12 INH/day <sup>2</sup>			
20 mcg/ACT	Onset: within 15 min <sup>19</sup>			
Ipratropium (g)	500 mcg TID–QID <sup>8</sup>			
Nebules*	Max: 2000 mcg/day <sup>8</sup>			
250 mcg/1 mL; 500 mcg/2 mL	Onset: within 15 min <sup>19</sup>			
Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta <sub>2</sub> -Agonist Combination (SABA)				
Ipratropium/Salbutamol (Combivent)	1 INH QID; additional doses PRN <sup>6</sup>			
Respimat	Max: 6 INH/day <sup>6</sup>			
20 mcg/100 mcg per ACT	Onset: 5–8 min <sup>18</sup> (based on salbutamol)			
Ipratropium/Salbutamol (g)	1 NEB Q6H PRN <sup>6</sup>			
Nebules*	Max: 4 NEB/day <sup>8</sup>			
0.5 mg/2.5 mg per 2.5 mL	Onset: 5–8 min <sup>18</sup> (based on salbutamol)			

<sup>\*</sup>Devices (e.g., pMDI, DPI) are preferred over nebules. See note about nebulization in text.

ACT = actuation; COPD = chronic obstructive pulmonary disease; DPI = dry powder inhaler; H = hours; g = generics;

INH = inhalation; Max = maximum; min = minutes; NEB = nebule(s); pMDI = pressurized metered dose inhaler;

PRN = as needed; Q = every; QID = four times daily; TID = three times daily





### TABLE 3: BRONCHODILATOR AGENTS FOR MANAGEMENT OF SEVERE ACUTE ASTHMA EXACERBATIONS

Medication Dosage Form Strength <sup>6</sup>	Dosage	Comments		
Short-Acting Beta <sub>2</sub> -Agonists (SAB				
Salbutamol (Ventolin, g) pMDI 100 mcg/ACT	6 y and older (including adults): 4 to 10 INH every 20 min x 3 doses If not controlled: 4 to 10 INH Q3-4H up to 6 to 10 INH Q1-2H, or more often <sup>9</sup> ≤ 5y: 4 to 6 INH every 20 min x 3 doses PRN If not controlled: 4 INH or more per hour PRN <sup>9</sup>			
Salbutamol (Ventolin, g) Nebules 2.5 mg/2.5 mL; 5 mg/2.5 mL	6 y and older (including adults): 2.5 to 5 mg every 20 min x 3 doses If not controlled: 2.5 to 5 mg Q1-4H PRN¹8 ≤ 5y: 2.5 mg every 20 min x up to 3 doses If not controlled: 2.5 mg or more per hour PRN⁰	pMDI + spacer preferred over nebulization. See text.		
Salbutamol (Ventolin) Diskus (DPI) 200 mcg/ACT	Off-label 6 y and older (including adults): 4 to 10 INH every 20 min x 3 doses If not controlled: 4 to 10 INH Q3-4H up to 6 to 10 INH Q1-2H, or more often <sup>9</sup>	DPI requires forceful inhalation to get full dose <sup>14</sup> so may not be appropriate during exacerbation.		
Short-Acting Muscarinic Antagonist (SAMA)				
Ipratropium (Atrovent, g) Respimat 20 mcg/ACT	Off-label In conjunction with SABA 6 y and older (including adults): 4 to 8 INH every 20 min x 3 doses, then Q1H PRN for up to 3 hours <sup>19</sup>	pMDI + spacer preferred over nebulization. See text. Initiated for severe exacerbation or for mild to moderate exacerbation that is unresponsive to salbutamol		
Ipratropium (g) Nebules 250 mcg/1 mL; 500 mcg/ 2 mL	≤ 5y: 4 INH every 20 min x 3 doses <sup>9</sup> In conjunction with SABA 6 y and older (including adults): 500 mcg every 20 min x 3 doses, then 500 mcg every 1 hour PRN for up to 3 hours <sup>19</sup> ≤ 5y (off-label): 250 mcg every 20 min x 3 doses <sup>9</sup>	monotherapy.		
Short-Acting Muscarinic Antagonist (SAMA)/Short-Acting Beta₂-Agonist Combination (SABA)				
Ipratropium/ Salbutamol (Combivent) Respimat 20 mcg/100 mcg per ACT	Off-label 6 y and older (including adults): 4 to 8 INH every 20 min x 3 doses then PRN <sup>20</sup>	Respimat preferred over nebulization. See text.  Respimat is designed so spacers should not be required; however, if needed, a spacer specifically for Respimat devices, Odapt™, is available. There is also limited data in COPD patients using Respimat with AeroChambers. Initiated for severe exacerbation or for mild to moderate exacerbation that is unresponsive to salbutamol.  Additional salbutamol may be required.		
Ipratropium/ Salbutamol (g) Nebules 500 mcg/2.5 mg per 2.5 mL	Off-label 6 y and older (including adults): 1 NEB every 20 min x 3 doses then 1 NEB PRN <sup>20</sup>			

ACT = actuation; g = generics; H = hour(s); INH = inhalation(s); min = minutes; pMDI = pressurized metered dose inhaler; PRN = as needed; Q = every; y = year(s)





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