SOCIÉTÉ CANADIENNE DE THORACOLOGIE | CANADIAN THORACIC SOCIETY

Asthma

Inhaled Salbutamol Shortage – Mitigation Strategy for Asthma

April 13, 2020

Background

1) Health Canada and the pharmaceutical industry have identified that there was a three-fold increase in the demand for salbutamol inhalers in the first 3 weeks of March 2020.
2) This has resulted in a Tier 3 shortage, which by definition is "a situation when a manufacturer/importer is unable to meet demand for the drug. A tier 3 shortage is a shortage with the greatest potential impact on the Canadian drug supply and healthcare systems by virtue of availability of alternate supplies, ingredients, or therapies."
3) Restrictions have been put in place by wholesalers and distributors to limit the supply of salbutamol which means that most patients will receive only one salbutamol inhaler or a one-month supply at a time.
4) It is possible that the surge in demand relates to individuals and organizations projecting future need and purchasing product in advance of actual need [Stockpiling].

Mitigation Strategy Step 1

Provider communication to patients regarding asthma medication:
If you have well controlled asthma, you should not need reliever medication. If you need reliever medication more than three times a week you should speak to your practitioner about ways to improve your asthma control.
It is important that you are taking your regular maintenance controller medication as prescribed. This will keep your asthma under control and reduce your need for reliever medication.
Short acting beta-agonists should only be used as reliever medication and should not be used on a regular basis prior to controller medication.
Oral steroids should be used for serious asthma exacerbations or as part of your asthma action plan even if you have COVID. Do not use reliever medications alone to treat serious exacerbations.
Ensure that you have a one month supply of asthma medication at home. Keep track of your medication supply and leave additional time to obtain your refills from the pharmacy.
There is a shortage of salbutamol inhalers in Canada, if you do not need it, do not attempt to refill your prescription.
You should expect that when you go to refill your inhaler prescriptions that you will receive a 1 month supply in response to inventory control measures put in place.
You should carefully track doses of salbutamol by dose counting.
You should use all salbutamol inhalers that you may have in various locations before refilling medication. If you have multiple salbutamol inhalers use the one with the earliest expiry date first.
If patients need a reliever medication and are unable to get a replacement, they should be advised to:
Not discard recently expired inhalers (e.g., expired in the last 6 months) until they have obtained a replacement. If they need to use their reliever inhaler and only have an expired inhaler, be aware that it may be less potent. They should use the expired inhaler and if not getting relief, seek medical attention.
Use the diskus inhaler even if it was removed from the wrapper more than 60 days ago.

Mitigation strategy Step 2: Recommended options for Salbutamol MDI substitutions in the event of a shortage

The CTS Asthma Assembly Steering Committee developed this rapid guidance for Canadian physicians treating patients with asthma for an emerging salbutamol inhaler shortage during to the COVID-19 pandemic. The recommendations are evidence-based and expert-opinion, and we recommend that treatment decisions be individualized.

Salbutamol Substitutions by Current Asthma Regimen

		Current Asthma Regimen				
		Short acting beta-agonist PRN	**Daily ICS, LTRA**	**Daily Fluticasone/Salmeterol, Fluticasone/Vilanterol**	**Daily Budesonide/Formoterol**	**Daily Mometasone/Formoterol**
Reliever Substitute (in order of preference[+])	**Preferred**	Budesonide/Formoterol Turbuhaler* ^ Terbutaline Turbuhaler* Salbutamol Diskus* Salbutamol Nebulized*#	Terbutaline Turbuhaler* Salbutamol Diskus* Salbutamol Nebulized*#	Terbutaline Turbuhaler* Salbutamol Diskus* Salbutamol Nebulized*	Budesonide/Formoterol Turbuhaler* Terbutaline Turbuhaler* Salbutamol Diskus* Salbutamol Nebulized*#	Terbutaline Turbuhaler* Salbutamol Diskus* Salbutamol Nebulized*#
	Alternative	Ipratropium/Salbutamol Respimat Ipratropium pMDI Mometasone/Formoterol pMDI Ipratropium/Salbutamol Nebulized # Ipratropium Nebulized #	Ipratropium/Salbutamol Respimat Ipratropium pMDI Formoterol Turbuhaler Ipratropium/Salbutamol Nebulized # Ipratropium Nebulized #	Ipratropium/Salbutamol Respimat Ipratropium pMDI Ipratropium/Salbutamol Nebulized # Ipratropium Nebulized #	Ipratropium/Salbutamol Respimat Ipratropium pMDI Formoterol Turbuhaler Ipratropium/Salbutamol Nebulized # Ipratropium Nebulized #	Ipratropium/Salbutamol Respimat Ipratropium pMDI Mometasone/Formoterol pMDI Formoterol Turbuhaler Ipratropium/Salbutamol Nebulized # Ipratropium Nebulized #
	If no other alternative	Levalbuterol pMDI (not currently available in Canada) Epinephrine pMDI (not currently available in Canada) Levalbuterol Nebulized# (not currently available in Canada) Orciprenaline PO*				

*Approved by Health Canada for use as a reliever in asthma, see Medications Substitutions Table for approved age of use and dosing suggestions

^ The use of budesonide/formoterol for use as reliever monotherapy has not been studied in children <12yo, in this age group short acting beta-agonist alternatives would be preferred

#Nebulizing medication is an aerosol generating procedure, it is not recommended to use nebulized medication in suspected or confirmed COVID cases in the healthcare settings unless there are no alternatives

+Order of preference centered on evidence base, device type, license in Canada

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Medication Substitutions for Salbutamol

List of Medication Substitutions for Salbutamol (Alphabetic order)	Approved age of use	Substitution Comment
Preferred Substitution (Health Canada approved for use as a reliever in asthma)		
Budesonide/Formoterol 200mcg/6mcg Turbuhaler (Symbicort)	≥12 years	**Patient Population**: Patients on salbutamol as needed as their only therapy who are able to use a dry powder inhaler Budesonide/Formoterol is a combination inhaled steroid and fast-acting-long acting bronchodilator. Budesonide/Formoterol 100mcg/6mcg is not Health Canada approved for this indication but could be considered if no other preferred reliever alternatives. **Dosing considerations**: 1 inhalation of 200/6 provides approximately equivalent effect to 1 to 2 inhalations of 100 mcg salbutamol. Maximum 6 inhalations on a single occasion, maximum of 8 inhalations per day.
Budesonide/Formoterol 100mcg/6mcg or 200mcg/6mcg Turbuhaler (Symbicort)	≥12 years	**Patient Population:** Patients on Budesonide/Formoterol as daily maintenance therapy Budesonide/Formoterol is a combination inhaled steroid and fast-acting-long acting bronchodilator There is no evidence of efficacy or safety to use Budesonide/Formoterol as reliever when other combination inhalers are used as daily maintenance. **Dosing considerations:** 1 inhalation of 200/6 provides approximately equivalent effect to 1 to 2 inhalations of 100ug salbutamol. Maximum 6 inhalations on a single occasion, maximum of 8 inhalations total (maintenance + reliever) per day. Patients should be encouraged to use the same inhaler for both daily maintenance controller and reliever and dispensing should be limited to one inhaler or a one month supply.
Salbutamol 200ug Diskus (Ventolin)	≥4 years	**Patient Population:** Any patient able to use a dry powder inhaler A direct substitution for salbutamol pMDI. **Dosing considerations:** The diskus form of Ventolin is 200ug compared to 100ug for pMDI.
Salbutamol 2.5, 5mg nebules or 5mg/ml solution (Ventolin)	≥5 years	**Patient population:** Any patient that has a nebulizer and compressor* A direct substitution for salbutamol pMDI **Dosing considerations:** >12yo 2.5-5mg q4h PRN, 5-12yo 1.25-5mg q4h PRN, <5yo (off label use) same dosing as 5-12yo *Note: do not use nebulizer if infected or under investigation for COVID in healthcare setting
Terbutaline 0.5 mg Turbuhaler (Bricanyl)	≥6 years	**Patient Population:** Any patient able to use a dry powder inhaler A direct substitution for salbutamol. **Dosing considerations:** 1 inhalation of terbutaline provides approximately equivalent effect to 2 inhalations of 100 mcg salbutamol

Alternative Substitution (Not approved by Health Canada as a reliever medication in asthma)		
Formoterol 6 mcg or 12mcg Turbuhaler (Oxeze) (6ug inhaler preferred, 12ug only if 6ug not available)	≥6 years	**Patient Population:** Patients on any daily inhaled corticosteroid or leukotriene receptor antagonist, or daily budesonide/formoterol, mometasone/formoterol that can use a dry powder inhaler* Formoterol is a fast-acting long-acting beta-agonist. It is Health Canada approved as add-on to an inhaled corticosteroid but not as a reliever medication. **Dosing considerations:** 6 mcg of formoterol provides approximately equivalent effect to 200ug of salbutamol. Maximum daily dose >16yo: 48ug, 6-16yo:24ug ***Note: There is a risk of death if formoterol is used as monotherapy, therefore this should ONLY be prescribed in patients adherent to daily maintenance controller medication***
Ipratropium Bromide 20ug pMDI (Atrovent)	≥18 years	**Patient population:** Any patient This bronchodilator is an anti-cholinergic medication. It is slower in onset (onset 15 min, peak 1-2h) and a less potent bronchodilator compared to salbutamol in patients with asthma. It is most effective when used in combination with salbutamol in acute asthma exacerbations. There is no Health Canada indication for its use as a reliever medication in asthma. **Dosing considerations:** 2 inhalations of 20 mcg provides approximately equivalent effect to 2 inhalations of 100 mcg salbutamol and should not be given closer than 4 hours part. Maximum daily dose of ipratropium: 240 mcg.
Ipratropium Bromide 250mcg in 1ml or 2ml, 500ug in 2ml nebules (Atrovent)	≥6 years	**Patient population:** Any patient with a nebulizer and compressor * This bronchodilator is an anti-cholinergic medication. It is slower in onset (onset 15 min, peak 1-2h) and a less potent bronchodilator compared to salbutamol in patients with asthma. It is most effective when used in combination with salbutamol in acute asthma exacerbations. There is no Health Canada indication for its use as a reliever medication in asthma. Dosing considerations: >12yo: 250ug-500ug q4h PRN, 6-12yo: 125-250ug q4h PRN, <6yo (off label): same dose as 6-12yo **Note: do not use nebulizer if infected or under investigation for COVID in healthcare setting*
Ipratropium Bromide 20mcg and Salbutamol 100mcg Respimat (Combivent)	≥18 years	**Patient population:** Any patient This bronchodilator is a combination of an anti-cholinergic and short acting beta-agonist. There is no Health Canada indication for its use as a reliever medication in asthma. **Dosing considerations:** 1 inhalation q4h PRN to a maximum of 6 inhalations/day.
Ipratropium Bromide 0.5mg and Salbutamol 2.5mg in 2.5ml nebules (Combivent)	≥18 years	**Patient population: Any patient with a nebulizer and compressor *** This bronchodilator is a combination of an anti-cholinergic and short acting beta-agonist. There is no Health Canada indication for its use as a reliever medication in asthma. **Dosing considerations:** 1 nebule q4h PRN up to 4 nebules/day. **Note: do not use nebulizer if infected or under investigation for COVID in healthcare setting*

Mometasone/Formoterol 100mcg/5mcg pMDI (Zenhale)	≥12 years	**Patient population:** **Patients on salbutamol as needed as their only therapy** Mometasone/Formoterol is a combination inhaled steroid and fast-acting-long acting bronchodilator. It is approved as a daily maintenance medication and **not** as a reliever. There are no studies that support the use of this medication as a reliever in place of salbutamol however given the similarity to Budesonide/Formoterol it would be expected to act similarly as a reliever. **Dosing considerations:** Extrapolating from data for Budesonide/Formoterol, we would recommend a maximum dose of 6 inhalations in one occasion and 8 inhalations/day. We would preferentially recommend mometasone/formoterol 100mcg/5mcg instead of 200mcg/5mcg given the potential for very high doses of inhaled steroids to be used with 200mcg/5mcg PRN and would suggest a maximum of 4 inhalations/day if the 200mcg/5mcg inhaler is used.
Mometasone/Formoterol 100mcg/5mcg or 200mcg/5mcg pMDI (Zenhale)	≥12 years	**Patient Population:** **Patients on Mometasone/Formoterol as daily maintenance therapy** Mometasone/Formoterol is a combination inhaled steroid and fast-acting-long acting bronchodilator There is no evidence of efficacy or safety to use mometasone/formoterol as a reliever in patients on maintenance with any type of ICS-LABA combination. **Dosing considerations:** Extrapolating from data for Budesonide/Formoterol, we would recommend a maximum dose of 6 inhalations in one occasion and 8 inhalations/day. We would preferentially recommend mometasone/formoterol 100mcg/5mcg instead of 200mcg/5mcg given the potential for very high doses of inhaled steroids to be used with 200mcg/5mcg PRN and would suggest a maximum of 4 inhalations/day if the 200mcg/5mcg inhaler is used. Patients should be encouraged to use the same inhaler for both daily maintenance controller and reliever and dispensing should be limited to one inhaler or a one month supply.
Substitution if no other option is available		
Epinephrine 0.125mg MDI (Primatene Mist)	≥12 years (FDA)	**Patient population:** Any patient This bronchodilator is a non-selective adrenergic agonist that is available in the United States as an over the counter medication. It is not available in Canada but may be made available in a shortage situation. **Dosing considerations:** 1 inhalation q4h PRN, maximum 8 inhalations/day
Levalbuterol 45ug pMDI (Xoponex)	≥4 years (FDA)	**Patient population**: Any patient This bronchodilator is a the (R)-enantiomer of racemic salbutamol. It is not currently available in Canada **Dosing considerations:** 45ug of levalbuterol provides approximately equivalent effect to 100ug of salbutamol. Standard dose 1-2 inhalations q4h PRN
Levalbuterol 0.31, 0.63, 1.25mg in 3ml nebules (Xoponex)	≥6 years (FDA)	**Patient population**: Any patient that has a nebulizer and compressor* This bronchodilator is a the (R)-enantiomer of racemic salbutamol. It is not currently available in Canada **Dosing considerations:** 0.63mg of levalbuterol provides approximately equivalent effect to 2.5mg of salbutamol. ≥12yo 0.63-1.25mg q6-8h PRN (max 1.25 mg tid), 6-12yo 0.31-0.63mg q6-8h PRN (max 0.63mg tid) **Note: do not use nebulizer if infected or under investigation for COVID in healthcare setting*
Orciprenaline oral solution (2 mg/mL)	≥4 years	**Patient population:** Any patient except in women of childbearing age or pregnant women, caution in patients with cardiac arrhythmias This oral solution is a systemic beta-agonist which is less selective for bronchial beta-adrenoreceptors compared to salbutamol and has a slower onset of action (60-90 minutes, lasts 3-6 hours) **Dosing considerations:** ≥12yo: 20mg per dose, maximum 3 doses per day, 4-12yo: 10mg per dose, maximum of 3 doses per day

Inhaler Devices

Many of the alternative options to salbutamol do not come in an MDI. If an alternative is required it is likely that the patient will be using a different type of inhaler device and it is imperative that proper instructions are given to ensure adequate deposition and efficacy(https://cts-sct.ca/covid-19/how-to-properly-use-an-inhaler/). Dry powder inhalers (turbuhaler, diskus) require a sufficient inspiratory force. Although children as young as 4 years old can be taught to use them, typically children need to be 6-8 years old to consistently use the proper technique particularly if they are having an exacerbation.

Nebulizers are not the preferred method of asthma medication delivery at any time due to decreased deposition and effectiveness, and the need for less portable and more expensive equipment. However, they are an alternative in a shortage situation particularly in children under the age of 6 or elderly patients who are unable to use dry powder inhalers. Nebulizing medication is an aerosol generating procedure and risks disseminating viruses such as COVID. Therefore, it is not recommended that nebulized medications are used in suspected or confirmed COVID cases in healthcare settings unless there are no other alternatives. In situations where nebulized medications are the best available option for a particular patient, they should be given using airborne precautions.

Considerations for dispensing

There are few inhaler devices that can be used in children under age 6 (Salbutamol nebules, Atrovent MDI/nebules, Atrovent+Salbutamol Respimat/nebules) and almost no Health Canada approved alternatives. Therefore, consideration should be given to preferentially prescribing/dispensing salbutamol MDIs to this age group.