Drug Shortage Alert
Albuterol Sulfate Nebulized Solution
Date of last update: November 2023

Recommendations and information provided in this Drug Shortage Alert are compiled by experts in the field. Practitioners are advised to consult with their institution’s staff to ensure that response to any drug shortage is in line with internal policies and procedures.

INTRODUCTION

- Nebulized albuterol is utilized in a number of respiratory disease states to provide bronchodilation and relief of bronchospasm. It may also be used as an adjunct therapy for non-respiratory disease states including management of hyperkalemia.
- Albuterol nebulized solution has intermittently been on shortage due to increased demand, manufacturer discontinuation, and temporary supply issues, with the following formulations affected as of July 2023:
  - Albuterol inhalation solution 0.5% 5 mg/mL, 20 mL bottle
  - Albuterol inhalation solution 0.5% 2.5 mg/0.5 mL unit dose vial
  - Albuterol inhalation solution 0.083% 2.5 mg/3 mL unit dose vial
- This alert provides potential management strategies, pharmacotherapeutic considerations, and safety implications in relation to this ongoing shortage.
- The recommendations provided in this document are based on both current evidence, including a review of available literature by the SCCM Drug Shortages and Medication Safety Committee, and the need for conservation during this shortage.

MANAGEMENT STRATEGIES

- Depending on your institution’s supply, considerations for reserving albuterol for the following scenarios is prudent:
  - Status asthmaticus
- Albuterol metered-dose inhalers (MDIs) or levalbuterol can be considered as alternatives in certain situations (if also not on shortage).

Table 1 describes selected indications for the above-mentioned drug shortage, specifically in critically ill patients.

Table 1: Potential Management Strategies for Drug Shortage

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<tr>
<th>Indication in critically ill patients</th>
<th>Suggested strategies</th>
<th>Key points</th>
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Asthma exacerbation

- Use albuterol via MDI and spacer, or levalbuterol if available (0.63 mg levalbuterol is equivalent to 2.5 mg albuterol).²
- Administer IM epinephrine with concomitant anaphylaxis and angioedema.³
- Consider initiation or continuation of scheduled ipratropium; use albuterol/ipratropium combination product if not on shortage.
- Optimize/maximize IV steroids.
- While not first-line therapies, the addition of intermittent or continuous IV magnesium, terbutaline via continuous infusion, ketamine, or aminophylline/theophylline may be considered in selected scenarios.
- Consider reserving concentrated 0.5% albuterol for pediatric patients and/or those requiring high rates of continuous albuterol.

While use of an inhaled short-acting anticholinergic has shown to decrease hospitalization in patients with severe asthma exacerbation when administered in the emergency department, improved FEV₁ and PEF were also seen.⁴
- Although the use of inhaled anticholinergics in hospitalized patients has not shown benefit when added to standard of care in children, those with severe symptoms were excluded from one of these studies.⁵ ⁶ With potential benefit, it is reasonable to consider continuation in patients with severe exacerbation admitted to the ICU.

- The use of magnesium as a prolonged or continuous infusion may be beneficial in the management of severe acute asthma, with some studies showing improved outcomes with its use, including improvement in severity scores and decreased length of stay.⁷ ⁸ Use is cautioned in renal injury, and magnesium levels should be monitored while on therapy.
- While not a first-line therapy, replacement of inhaled with IV β₂-agonist therapy, most commonly terbutaline, has been described in children when bronchospasm limits the ability of albuterol to reach the lungs.⁹ ¹⁰ Concurrent drug shortages and adverse events such as tachycardia and hypertension may limit its use.
- Smooth muscle relaxation with a PDE3-inhibitor such as aminophylline or theophylline is occasionally used, but is not recommended due to significant drug interactions as well as adverse effects, including arrythmias, hypertension, headache, and seizures. If used, monitoring is recommended, with a goal level of 5-15 mcg/mL.¹⁰ ¹¹
- Ketamine provides some bronchodilatory effects and has been described for use in children with...
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<th>COPD exacerbation</th>
<th>Refractory status asthmaticus administered as a continuous infusion. Use in adults has not been associated with improved outcomes.</th>
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<tr>
<td>• Reserve albuterol nebulizer supply for critically ill patients who cannot effectively utilize MDI, or use levalbuterol if available.</td>
<td>• Short acting β₂-agonists with or without short-acting anticholinergics are recommended as initial bronchodilators to treat COPD exacerbations.</td>
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<td>• Deliver via MDI with or without a spacer device for all other patients.</td>
<td>• Oral corticosteroids and antibiotic therapy have conditional recommendations for the treatment of outpatient COPD exacerbations.</td>
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<td>• Follow treatment recommendations for oral corticosteroids, antibiotics, and noninvasive mechanical ventilation concurrent with bronchodilator administration.</td>
<td>• IV corticosteroids are recommended for patients hospitalized with COPD exacerbations only in cases where oral therapy is not tolerated.</td>
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<td>• Short acting β₂-agonists with or without short-acting anticholinergics are recommended as initial bronchodilators to treat COPD exacerbations.</td>
<td>• Noninvasive mechanical ventilation is recommended for patients hospitalized with a COPD exacerbation associated with acute or acute-on-chronic hypercapnic respiratory failure.</td>
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<td>• Prioritize use in other disease states due to existing alternatives for hyperkalemia.</td>
<td>• If additional therapy beyond insulin and dextrose is necessary, alternative delivery systems for albuterol such as the MDI may be most feasible during a shortage of nebulized products.</td>
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<tr>
<td>• Consider use for patients in whom other modalities for intracellular potassium shift (e.g., insulin) are inappropriate or ineffective.</td>
<td>• If available, nebulized levalbuterol product may be used instead of albuterol.</td>
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<td>• Recommend delivery via MDI, if albuterol is used.</td>
<td>• Subcutaneous terbutaline provides an option in patients without IV access.</td>
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<td>• Use levalbuterol 2.5 mg (equivalent to 10 mg albuterol) if available.</td>
<td>• For patients with hyperkalemic emergencies, other treatment modalities such as dialysis, loop diuretics, or gastrointestinal cation exchangers should be used to remove excess potassium.</td>
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<td>• Consider subcutaneous terbutaline 7 mcg/kg (actual body weight) if available.</td>
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COPD, chronic obstructive pulmonary disease; FEV\textsubscript{1}, forced expiratory volume in one second; ICU, intensive care unit; IM, intramuscular; IV, intravenous; MDI, metered-dose inhaler; PEF, peak expiratory flow.

PHARMACOTHERAPEUTIC CONSIDERATIONS

- The use of albuterol and management strategies in the setting of drug shortages is indication dependent. Please refer to the above review for more information.
  - Consider consolidating available albuterol sulfate solution to the pharmacy to allow for potential decrease in waste preparing continuous doses for status asthmaticus.
- When properly used, MDIs are at least as effective as nebulizers for drug delivery for intermittent dosing of albuterol.\textsuperscript{22}
  - Proper education, optimal technique, and appropriate accessories (spacers with or without masks) are essential to help reduce oropharyngeal deposition and the need for hand-breath coordination.
  - Respiratory therapist/nurse staffing availability should be considered prior to determination of frequency of intermittent dosing of albuterol.
- Concentrations of albuterol vary and, based on availability, may limit the rate at which continuous nebulization can occur based on nebulizer device volume limits.
- A routine evaluation of continuous albuterol therapy should be instituted to determine whether a patient has exhibited benefit to preserve supply.

SAFETY IMPLICATIONS

- If a common canister MDI process is used, infection prevention processes must be clearly outlined for device cleaning, control, and maintenance. Processes for disposal in the event of patient contamination are also needed.
- Medication safety issues may arise with changes in compounding of preparations of albuterol. Appropriate institutional guidance and safeguards (e.g., double-checks) should be instituted to minimize these events.
- Access to drug references or drug information alerts for clinicians is needed when using less familiar medications. Information should include dosing, route of administration, adverse effects, and monitoring of substitute agents.
- Specific alternatives (e.g., ketamine infusion) may require higher-level monitoring than albuterol or admission to a higher level of care.

IMPACT ON ICU CARE

- Challenges exist for the management of the current albuterol shortage due to existing manufacturer backorders for alternative agents, including terbutaline. Terbutaline is used for other indications including inhibition of uterine contraction in premature labor, which may be prioritized over hyperkalemia.
- Institution-specific formularies must be considered when determining alternative medication availability.
- Delays in care may occur depending on compounding requirements based on product availability.
- Education of staff is necessary when transitioning to MDI use to ensure proper technique, cleaning of devices, and disposal of aerosol containers.
REFERENCES


Please contact support@sccm.org if you have any suggestions or feedback on this alert.