



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 2023¹:
 - 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

Indication in critically ill patients	Suggested strategies	Key points
---------------------------------------	----------------------	------------

<p>Asthma exacerbation²</p>	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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 β_2-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 arrhythmias, 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
--	---	--

		refractory status asthmaticus administered as a continuous infusion. ¹² Use in adults has not been associated with improved outcomes. ^{13,14}
COPD exacerbation	<ul style="list-style-type: none"> • Reserve albuterol nebulizer supply for critically ill patients who cannot effectively utilize MDI, or use levalbuterol if available. • Deliver via MDI with or without a spacer device for all other patients. • Follow treatment recommendations for oral corticosteroids, antibiotics, and noninvasive mechanical ventilation concurrent with bronchodilator administration. 	<ul style="list-style-type: none"> • Short acting β_2-agonists with or without short-acting anticholinergics are recommended as initial bronchodilators to treat COPD exacerbations.¹⁵ • Oral corticosteroids and antibiotic therapy have conditional recommendations for the treatment of outpatient COPD exacerbations.¹⁶ • IV corticosteroids are recommended for patients hospitalized with COPD exacerbations only in cases where oral therapy is not tolerated.¹⁶ • Noninvasive mechanical ventilation is recommended for patients hospitalized with a COPD exacerbation associated with acute or acute-on-chronic hypercapnic respiratory failure.¹⁶
Acute hyperkalemia ^{17,18}	<ul style="list-style-type: none"> • Prioritize use in other disease states due to existing alternatives for hyperkalemia. • Consider use for patients in whom other modalities for intracellular potassium shift (e.g., insulin) are inappropriate or ineffective. • Recommend delivery via MDI, if albuterol is used.¹⁹ • Use levalbuterol 2.5 mg (equivalent to 10 mg albuterol) if available.²⁰ • Consider subcutaneous terbutaline 7 mcg/kg (actual body weight) if available.²¹ • For patients with hyperkalemic emergencies, other treatment modalities such as dialysis, loop diuretics, or gastrointestinal cation exchangers should be used to remove excess potassium. 	<ul style="list-style-type: none"> • 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. • If available, nebulized levalbuterol product may be used instead of albuterol.²⁰ • Subcutaneous terbutaline provides an option in patients without IV access.

COPD, chronic obstructive pulmonary disease; FEV₁, 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.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.

Original date: November 2023

Originally developed by:

Michelle Rausen, MS, RRT, RRT-NPS
Nicole T. Reardon, PharmD, BCPS, FCCM
Christina Smith, PharmD, BCPPS, BCCCP

Reviewed by:

Kristi S. Kim, PharmD, BCCCP
Mona K. Patel, PharmD, BCCCP, FCCM
Adrian Wong, PharmD, MPH, FCCP, BCCCP, FCCM

REFERENCES

1. American Society of Health-System Pharmacists. Current drug shortages. Albuterol inhalation solution. October 21, 2023. Accessed November 3, 2023. <https://www.ashp.org/drug-shortages/current-shortages/drug-shortage-detail.aspx?id=820&loginreturnUrl=SSOCheckOnly>
2. Handley DA, Tinkelman D, Noonan M, Rollins TE, Snider ME, Caron J. Dose-response evaluation of levalbuterol versus racemic albuterol in patients with asthma. *J Asthma*. 2000 Jun;37(4):319-327.
3. Reddel HK, Bacharier LB, Bateman ED, et al. Global initiative for asthma strategy 2021: executive summary and rationale for key changes. *Am J Respir Crit Care Med*. 2022 Jan;205(1):17-35.
4. Kirkland SW, Vandenberghe C, Voaklander B, Nickel T, Campbell S, Rowe BH. Combined inhaled beta-agonist and anticholinergic agents for emergency management in adults with asthma. *Cochrane Database Syst Rev*. 2017 Jan 11;11(1):CD001284.
5. Craven D, Kercksmar CM, Myers TR, O’Riordan MA, Golonka G, Moore S. Ipratropium bromide plus nebulized albuterol for the treatment of hospitalized children with acute asthma. *J Pediatr*. 2001 Jan;138(1):51-58.
6. Goggin N, MacArthur C, Parkin PC. Randomized trial of the addition of ipratropium bromide to albuterol and corticosteroid therapy in children hospitalized because of an acute asthma exacerbation. *Arch Pediatr Adolesc Med*. 2001 Dec;155(12):1329-1334.
7. Junior MG, Lago PM, Santana JCB, et al. Use of magnesium sulfate in continuous infusion in patients with severe acute asthma, in a pediatric emergency room. *Pediatr Pulmonol*. 2021 Jul;56(7):1924-1930.
8. Irazuzta JE, Paredes F, Pavlicich V, Dominguez S. High-dose magnesium sulfate infusion for severe asthma in the emergency department. *Pediatr Crit Care Med*. 2016 Feb;17(2):e29-e33.
9. Stephanopoulos DE, Monge R, Schell KH, Wyckoff P, Peterson BM. Continuous intravenous terbutaline for pediatric status asthmaticus. *Pediatr Crit Care Med*. 1998 Oct;26(10):1744-1748.
10. Wheeler DS, Jacobs BR, Kenreigh CA, Bean JA, Hutson TK, Brilli RJ. Theophylline versus terbutaline in treating critically ill children with status asthmaticus: a prospective, randomized, controlled trial. *Pediatr Crit Care Med*. 2005 Mar;6(2):142-147.
11. Mitra A, Bassler D, Goodman K, Lasserson TJ, Ducharme FM. Intravenous aminophylline for acute severe asthma in children over two years receiving inhaled bronchodilation. *Cochrane Database Syst Rev*. 2005 Apr 18;2:CD001276.

12. Allen JY, Macias CG. The efficacy of ketamine in pediatric emergency department patients who present with acute severe asthma. *Ann Emerg Med.* 2005 Jul;46(1):43-50.
13. Nedel W, Costa R, Mendez G, Marin L, Vargas T, Marques L. Negative results for ketamine use in severe acute bronchospasm: a randomized controlled trial. *Anaesthesiol Intensive Ther.* 2020;52(3):215-218.
14. La Va L, Sanfilippo F, Cuttone G, et al. Use of ketamine in patients with refractory severe asthma exacerbations: a systematic review of prospective studies. *Eur J Clin Pharmacol.* 2022 Oct;78(10):1613-1622.
15. Agustí A, Celli BR, Criner GJ, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD executive summary. *Am J Respir Crit Care Med.* 2023 Apr;207(7):819-837.
16. Wedzicha JA, Miravittles M, Hurst JR, et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J.* 2017 Mar 15;49(3):1600791.
17. Elliott MJ, Ronksley PE, Clase CM, Ahmed SB, Hemmelgarn BR. Management of patients with acute hyperkalemia. *CMAJ.* 2010 Oct 19;182(15):1631-1635.
18. Shingarev R, Allon M. A physiologic-based approach to the treatment of acute hyperkalemia. *Am J Kidney Dis.* 2010 Sep;56(3):578-584.
19. Mandelberg A, Krupnik Z, Houry S, et al. Salbutamol metered-dose inhaler with spacer for hyperkalemia: How fast? How safe? *Chest.* 1999 Mar;115(3):617-622.
20. Pancu D, LaFlamme M, Evans E, Reed J. Levalbuterol is as effective as racemic albuterol in lowering serum potassium. *J Emerg Med.* 2003 Jul;25(1):13-16.
21. Sowinski KM, Cronin D, Mueller BA, Kraus MA. Subcutaneous terbutaline use in CKD to reduce potassium concentrations. *Am J Kidney Dis.* 2005 Jun;45(6):1040-1045.
22. Kacmarek RM, Stoller JA, Heuer AJ, eds. *Egan's Fundamentals of Respiratory Care.* 12th ed. Mosby; 2020:847.

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