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Drug Shortage Alert
Parenteral Corticosteroids
Date of last update: October 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

- Both hydrocortisone and methylprednisolone are used ubiquitously in the acute care setting. The magnitude and urgency of endocrine, immunology, oncology, pulmonary, and rheumatology emergencies significantly impact critical care. Managing these shortages requires a multiprofessional team of stakeholders to work together to mitigate its impact.
- This summary provides potential management strategies, pharmacotherapeutic considerations, and safety implications for adult patients in the event of an intravenous (IV) hydrocortisone or methylprednisolone 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
- This drug shortage alert is focused on the adult population; however, strategies listed here can be extrapolated for use in the pediatric population.

MANAGEMENT STRATEGIES

- Depending on your institution's supply, consider reserving IV hydrocortisone for adrenal crises or patients with adrenal insufficiency who cannot take hydrocortisone enterally.
- For relative adrenal insufficiency in patients with sepsis/septic shock, dexamethasone or methylprednisolone plus fludrocortisone 50 mcg daily can be used (hydrocortisone 200 mg = dexamethasone 7.5 mg = methylprednisolone 40 mg) depending on available supply. Use enteral formulations of steroids preferentially when clinically allowable, due to high bioavailability of enteral formulations.
    - Doses >500 mg of IV methylprednisolone should be reserved for immunologic, oncologic, or rheumatologic indications; use equivalent doses (e.g., IV methylprednisolone doses <125 mg) of alternative oral steroids whenever possible to preserve supplies of IV formulations.
- Daily IV steroid inventory should be performed to ensure enough supply is on hand for appropriate indications.
- The electronic medical record (EMR) should have an alternative use alert or an equivalent alert to guide prescribers on mitigation strategies, including indications and alternative medication options with dosages.

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

Table 1. Potential Management Strategies for Drug Shortage in Adult Patients

Indication in critically ill patients	Suggested strategies	Key points
Acute bacterial meningitis[1]	• Dexamethasone 0.15 mg/kg every 6 hours for 4 days	• Dexamethasone should be initiated shortly before or at the same time as the first dose of antibiotics.
ARDS[2-5]	• Dexamethasone 20 mg IV daily for 5 days followed by 10 mg IV daily for 5 days for early moderate-to-severe ARDS • Early moderate-to-severe ARDS: methylprednisolone 1 mg/kg/day on days 1-14, followed by slow taper for a total of 28 days	• Corticosteroids improved survival outcomes in moderate-to-severe ARDS when initiated within 72 hours based on a meta-analysis.
Anaphylaxis/ hypersensitivity reactions[6-7]	• Oral prednisone 1 mg/kg/day in 1-2 divided doses for 2-5 days • Methylprednisolone IV 1-2 mg/kg/day for 1-2 days • Hydrocortisone 200 mg IV × 1 • Dexamethasone 10 mg IV × 1	• IV formulations are preferred in emergent situations, including those affecting the airway.
Asthma exacerbation[8-13]	• Oral prednisone 40 to 80 mg/day divided in 1 or 2 daily doses • Dexamethasone oral, IM, or IV 12 to 16 mg as a single dose for 2 days (limited/no data for IV administration)	• Several studies and a meta-analysis found that dexamethasone IM or oral is as effective as prednisone. • IV corticosteroids should be reserved for patients who cannot tolerate oral intake, poor response to oral corticosteroids, or in cases of impending respiratory failure. • If IV corticosteroids are used, switch to oral corticosteroid formulation as soon as possible.
COPD exacerbation[14-17]	• Oral prednisone 40 mg daily for 5 days • Dexamethasone IV may be considered as an alternative to methylprednisolone in patients requiring IV therapy (limited/no data for oral dexamethasone) • IV corticosteroids should be reserved for patients who cannot tolerate oral intake, or in cases of impending respiratory failure.	• GOLD 2023 guidelines recommend 40 mg prednisone-equivalent daily for 5 days. • A recent RCT observed less treatment failure with personalized corticosteroids doses compared to the fixed dose in COPD exacerbation. • A small RCT found similar efficacy between dexamethasone and

		methylprednisolone in the management of COPD exacerbation. The dexamethasone dose was 0.375 mg/kg daily. • Another small RCT compared dexamethasone to hydrocortisone. There was significant improvement of peak expiratory flow and dyspnea symptoms in the dexamethasone group.
CAP, severe[18-24]	Corticosteroids are not routinely recommended for all CAP. When corticosteroids are indicated, consider using: • Hydrocortisone IV/oral 200 mg/day (in divided doses) for 4 or 7 days, followed by an 8- or 14-day taper significantly reduced mortality in ICU patients with severe pneumonia without septic shock. • In case hydrocortisone is unavailable, consider: ▪ Dexamethasone IV 5 mg daily for at least 4 days in non-immunocompromised patients with severe CAP ▪ Oral prednisone 40-50 mg daily for 5-7 days • Methylprednisolone has not shown benefit in the treatment of CAP COVID-19 pneumonia • Dexamethasone 6 mg IV/oral daily for 10 days in COVID-19 patients receiving supplemental oxygen	• The 2019 American Thoracic Society/Infectious Diseases Society of America guidelines for CAP do not routinely recommend corticosteroids for severe pneumonia, but they may reduce morbidity and mortality in patients with severe pneumonia when receiving 40-50 mg of oral prednisone equivalents for 5-7 days. • The Surviving Sepsis Campaign guidelines recommend corticosteroids in patients with severe pneumonia as the source of refractory septic shock. • Corticosteroids were associated with decreased mortality in patients with severe CAP in a Cochrane review. • Several studies found improved outcomes with the use of dexamethasone in patients with pneumonia.
Contrast allergy prevention in high-risk patients[25,26]	Elective premedication (12-13 hours prior to contrast) • Prednisone 50 mg oral administered at hours 13, 7, and 1 before contrast administration with diphenhydramine for non-urgent regimen • Hydrocortisone 200 mg IV administered at hours 13, 7, and 1 before contrast administration with diphenhydramine for non-urgent regimen	• Frequency of administration is based on the duration of the different steroids. • IV steroids should be given to patients who cannot take oral medications, as well as in emergencies. • Hydrocortisone, prednisolone, prednisone, and methylprednisolone all can be used.

	Accelerated premedication (4-5 hours before contrast) • Hydrocortisone 200 mg IV immediately, then 200 mg every 4 hours until contrast administration in combination with diphenhydramine • Methylprednisolone 40 mg IV immediately, then 40 mg every 4 hours until contrast administration in combination with diphenhydramine • Dexamethasone 7.5 mg IV immediately, then 7.5 mg every 4 hours until contrast administration in combination with diphenhydramine Emergent premedication (less than 4-5 hours before contrast) • Methylprednisolone 40 mg IV and diphenhydramine 1 hour before contrast • Hydrocortisone 200 mg IV and diphenhydramine 1 hour before contrast	
Post-extubation laryngeal edema[27]	• Dexamethasone IV 8 mg given 4 hours before planned extubation, at extubation, and 6 and 12 hours after extubation • Methylprednisolone 20 mg IV every 4 hours for 4 doses • Methylprednisolone 40 mg IV single dose at the time of extubation	• The use of steroids in planned extubation is beneficial in preventing laryngeal edema and reintubations.
Primary adrenal insufficiency, adrenal crisis[28,29]	• Hydrocortisone is the preferred agent • If hydrocortisone IV is unavailable, consider: ▪ Methylprednisolone IV 40 mg every 24 hours OR ▪ Oral prednisolone 50 mg every 24 hours OR ▪ Dexamethasone IV/oral (least preferred alternative) 4 mg every 12 hours (based on dosing equivalency; limited/no data) ▪ When using a steroid with minimal mineralocorticoid activity, consider the addition of fludrocortisone	• Hydrocortisone has mineralocorticoid activity, with 20 mg hydrocortisone equivalent to 100 mcg fludrocortisone; doses of hydrocortisone > 20 mg daily do not require additional mineralocorticoid activity with fludrocortisone. • Dexamethasone and prednisolone have mostly glucocorticoid effects with minimal mineralocorticoid activity and are less ideal replacements and therefore not recommended as first-line. • Dexamethasone is not recommended as a replacement regimen and is the least-

		preferred alternative for the management of adrenal crisis. • The usual starting dose of fludrocortisone to replace mineralocorticoid (i.e., aldosterone) deficiency is 50-100 mcg daily in adults. • Higher doses of fludrocortisone may be required with methylprednisolone, prednisone and dexamethasone. • Using dexamethasone without concurrent fludrocortisone may trigger an adrenal crisis.
Septic shock with escalating vasopressor requirement suspecting relative adrenal insufficiency[30-33]	• Dexamethasone 0.2 mg/kg every 36 hours × 3 doses plus oral fludrocortisone 50-100 mcg daily • Hydrocortisone IV 50 mg every 6 hours • If supply allows, consider a continuous infusion of hydrocortisone 200 mg/day • When conserving hydrocortisone supply, consider the use of 100 mg every 8 hours regimen to optimize package size Other suggested regimens (recommendations based on dosing equivalency; limited/no data): • Dexamethasone 7.5mg IV every 24 hours plus oral fludrocortisone 50-100 mcg daily • Methylprednisolone IV 40 mg/day divided into 1-4 doses	• The current Surviving Sepsis Campaign guidelines suggest IV hydrocortisone 200 mg/day for patients who cannot achieve hemodynamic stability with fluid resuscitation and vasopressor therapy. However, doses <400 mg/day have been described in the literature. Since hydrocortisone is available in 100 mg vials, the use of 100 mg every 8 hours regimen may be a suitable alternative during a shortage. • Very limited data exist for using prednisone in patients with septic shock, which is only available enterally. Enteral absorption during shock is unreliable. Dexamethasone does not have any mineralocorticoid activity. There are limited data on using dexamethasone for septic shock. • Treatment duration: 5-7 days • Therapy needs to be evaluated based on vasopressor trends at set time point (e.g., 24 hours) to ensure that only patients with benefit will continue therapy. Consider stopping or tapering steroids in patients requiring minimal vasopressor doses.

		• Consider tapering steroids to prevent rebound hypotension upon abrupt discontinuation of steroids if concerns for HPA axis suppression.
Thyroid storm[34]	• IV hydrocortisone 100 mg every 6-8 hours or dexamethasone 2 mg IV every 6 hours continued until resolution of the thyroid storm	• Glucocorticoids have been used as one of the treatment options for thyroid storm as they reduce the conversion of thyroxine (T4) to active triiodothyronine (T3).

ARDS, acute respiratory distress syndrome; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HPA, hypothalamic-pituitary-adrenal; IM, intramuscular; IV, intravenous; RCT: randomized controlled trial.

PHARMACOTHERAPEUTIC CONSIDERATIONS

- The use of corticosteroids and management strategies in the setting of drug shortages is indication dependent. Please refer to the above review for more information.
- Dexamethasone is the preferred agent for the following indications[28,29]:
    - COVID-19 pneumonia
    - Bacterial meningitis
    - Laryngeal edema
- Continue patient's home oral corticosteroid regimen whenever possible.
- When transitioning from one steroid to another due to a drug shortage, consideration should be given to its equipotent dose and drug pharmacokinetics, including duration of activity.
    - Dexamethasone has a prolonged duration of activity and can be given at a less frequent interval compared to other corticosteroids.
- Route of administration
    - Corticosteroids have high oral bioavailability; consider the use of oral therapy for non-emergent indications in patients with enteral access who do not have any concerns of malabsorption.
    - Methylprednisolone injectable solutions are available in two different salt forms (acetate, succinate); methylprednisolone acetate suspension is intended only for intramuscular or intra-articular administration and should not be used for IV injection.

Table 2. Comparison of Selected Glucocorticoid Agents[35-37]

Glucocorticoids	Route	Equivalent dose (mg)	Anti-inflammatory (glucocorticoid) potency	Mineralocorticoid Potency	Duration of activity (hours)	Half-life (hours)	Approximate bioavailability of oral form
Hydrocortisone	IV, PO	20	1	1	8-12	IV: 2 PO: 1.8	96%
Intermediate acting							
Prednisone	PO	5	4	0.8	12-36	2-3	70%
Prednisolone	PO	5	4	0.8	12-36	2-3	70%
Methylprednisolone	IV, PO	4	5	0.25	12-36	IV: 0.25 PO: 2.5	88%
Long acting							
Dexamethasone	IV, PO	0.75	30	No effect	36-72	IV: 1-5 PO: 4	75%
Betamethasone*	IM	0.6	30	No effect	36-72	6.5	NA
Mineralocorticoids							
Fludrocortisone	PO	0.1	No effect	125	12-36	≥3.5	100%

IV, intravenous; NA, not applicable; PO, oral.

*Betamethasone may be preferred in pregnant patients for cervical ripening.

SAFETY IMPLICATIONS

- Medication dosing errors may occur during the conversion from one corticosteroid to another.
- Healthcare team members may be unfamiliar with differences between corticosteroids agents (e.g., lack of mineralocorticoid activity with dexamethasone). This can lead to an increase in the incidence of adverse drug events due to the differences in potency and characteristics between different corticosteroid agents.
- Additionally, delay of emergency care (anaphylactoid reaction or adrenal crisis) may occur if the supply is exhausted.
- Hospitals and health systems should consider implementing education plans and institution-specific guidelines to avoid dosing errors or delays in care.

IMPACT ON ICU CARE

- Clear and constant communication (e.g., clinical decision support, email) is recommended to provide clinicians necessary information on how to appropriately prescribe these medications. The use of Best Practice Advisory notifications in the EMR can effectively communicate shortage issues and recommend alternatives that have been agreed upon by the institution.
- Multiprofessional groups should be created to develop appropriate drug shortage mitigation strategies, including available drugs on formulary and appropriate education.
- Dosing recommendations when transitioning from one steroid to another are generated using equipotent doses; high-quality data may not exist for the use of particular steroids in certain indications.
- Because of the numerous uses of steroids in critically ill patients, conservation strategies should focus on high-volume indications (e.g., septic shock, COPD exacerbation, ARDS) to reserve the supply for unique or rare indications and emergent therapies.
- When choosing an alternative steroid due to drug shortages, consider optimizing the dose to match commercially available product vial sizes to preserve alternative agent supply (e.g., dexamethasone injection is commonly available as 4 mg, 10 mg, or 20 mg vials; hydrocortisone as 100 mg vials).
- If smaller vial sizes for injection are not available, consider compounding commonly used doses (e.g., methylprednisolone 40 mg) in batches from a larger vial (e.g., methylprednisolone 125 mg) in a sterile preparation area.

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Commented [EE1]: References edited without tracking changes

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