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Drug Shortage Alert
Dobutamine
December 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

- Dobutamine shortage affects both diagnostics and therapeutics of cardiology medicine.
- Dobutamine is used in the treatment of acute decompensated heart failure as well as cardiogenic shock. Dobutamine is also indicated in stress echocardiography for assessment of myocardial ischemia.
- This summary provides information in the event of a shortage and its impact on adult patients, by providing potential management strategies, pharmacotherapeutic considerations, and safety implications.
- 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

- Consider alternative inotropes or vasopressors when appropriate.
    - For postoperative management of reduced cardiac output after open heart surgery or heart transplant surgery, consider using milrinone or epinephrine.
    - For cardiogenic shock, consider using milrinone or epinephrine or mechanical circulatory support.
    - For chronic or advanced heart failure, consider using milrinone.
- For dobutamine stress echocardiography (DSE), consider alternative diagnostic modalities.
    - Adenosine nuclear stress test or stress cardiac magnetic resonance (CMR) for evaluation of ischemia, magnetic resonance imaging (MRI), positron emission tomography (PET), or single-photon emission computerized tomography (SPECT) with thallium or technetium
- Dobutamine should be reserved for evaluation of low-flow aortic stenosis because low-dose dobutamine is the only viable option.
- Multidisciplinary discussions are recommended to determine appropriate inotrope or vasopressor therapy based on patient-specific characteristics.

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

Table 1. Potential Management Strategies for Dobutamine Shortage in Adults

Indication in critically ill patients	Suggested strategies	Key points
Therapeutic uses of dobutamine		
Cardiogenic shock[1-5]	• Use the minimum necessary dose of alternative vasoactive medications to maintain adequate perfusion goals (e.g., MAP > 65 mm Hg). • Consider norepinephrine as the first-line vasopressor. • Milrinone can be used as an alternative inotropic agent to dobutamine. • Consider early use of MCS.	• Limited data support the use of norepinephrine as the preferred agent in cardiogenic shock. • In a retrospective study of patients with cardiogenic shock due to acute decompensated heart failure, milrinone use was associated with a lower risk of 30-day mortality and improved hemodynamics compared to dobutamine. • Common MCS devices include intra-aortic balloon pump, percutaneous left ventricular assist device, and extracorporeal membrane oxygenation, although data supporting MCS in cardiogenic shock is limited.
Chronic systolic heart failure[6-8]	Consider continuous intravenous milrinone as a bridge to MCS or heart transplantation, or for advanced heart failure patients requiring palliative treatment to improve symptoms.	• In retrospective studies comparing long-term effects of milrinone and dobutamine, mortality rate was significantly higher with dobutamine. • Milrinone dose should be adjusted in patients with renal impairment.
Perioperative management after open heart surgery or heart transplant surgery[9-11]	• In patients with normal ejection fraction, consider an inotrope-sparing strategy. • In patients with low cardiac output and inadequate tissue perfusion, consider milrinone or epinephrine.	Some institutions may adopt a practice in which inotropes are administered to all patients undergoing cardiac surgery. However, an inotrope-sparing strategy with judicious use of inotropes did not result in an increased mortality or worse outcomes in patients with normal ejection fraction.
Diagnostic uses of dobutamine		
Stress echocardiography for evaluation of ischemia[12]	• Exercise stress testing is preferred for patients who can attain an adequate level of exercise. • In patients who cannot exercise, DSE can be performed.	For pharmacologic stress testing, dobutamine is delivered in graded doses. • For detection of ischemia, dobutamine echocardiography has comparable sensitivity to SPECT but higher specificity. Alternative vasodilators such as dipyridamole or adenosine can be considered. However,

	Alternatives to DSE include adenosine nuclear stress test, MRI, PET, or SPECT with thallium or technetium.	they are contraindicated in reactive airway disease or severe hypotension. • Adenosine: infuse at 140 mcg/kg/min over 4-6 minutes to a maximum of 60 mg. • Dipyridamole: infuse up to 0.84 mg/kg over 6-10 minutes. Nonpharmacologic stress tests are also used to evaluate ischemia.
Stress echocardiography for myocardial viability[12-14]	• DSE is most commonly used for myocardial viability assessment. In many countries, no suitable pharmacologic alternative exists. • Alternative methods such SPECT with thallium or technetium, PET, or CMR with late gadolinium can be used	Limited pharmacologic alternatives are available for this indication. • Enoximone is an alternative inotrope to dobutamine that can potentially be used for stress echocardiography in countries where it is available. • Data is sparse regarding the use of milrinone in myocardial viability testing and it cannot be recommended at this time. Alternative nonpharmacologic diagnostic modalities can be used in place of DSE.
Echocardiography for evaluation of low-flow aortic stenosis[15]	DSE is the preferred method for grading the severity of aortic stenosis and detecting LV contractile reserve.	Consider reserving dobutamine for this indication because no suitable alternative modality exists.

CMR, cardiac magnetic resonance; DSE, dobutamine stress echocardiography; MAP, mean arterial pressure; MCS, mechanical circulatory support; MRI, magnetic resonance imaging; PET, positron emission tomography; SPECT, single-photon emission computerized tomography.

PHARMACOTHERAPEUTIC CONSIDERATIONS

- The use of dobutamine in the setting of drug shortages is indication dependent. See **Table 1** for more indication-specific dosing.
- Other vasoactive medications may be used in place of dobutamine. See **Table 2** for alternative vasoactive medications including vasopressors and inotropes.
- Monitoring daily use and assessment of appropriate indication and dosing may reduce usage in times of shortage.
- Clinician education on indications and alternate strategies is warranted.

SAFETY IMPLICATIONS

- Dobutamine is an inotropic agent with beta-1, beta-2, and alpha-1 agonist activity. When choosing an alternative, the selectivity for the different adrenergic receptors of the alternative agent should be considered.
- Multiple premix solutions of dobutamine are available in different concentrations (e.g., 500 mcg/ml, 2,000 mcg/ml, or 4,000 mcg/ml). Institutions may opt to acquire new concentrations due to shortage of the existing formulary concentrations. Care must be taken not to confuse the different bag sizes and concentrations, which may lead to dosing errors.

    - If able, consider limiting dobutamine to one concentration for each patient care area.
    - Update smart pump drug infusion libraries and electronic medical records (EMRs) to match the available dobutamine concentrations and bag sizes.
- Dobutamine and dopamine are look-alike-sound-alike (LASA) medications. Institutions must be cautious when removing or restricting dobutamine from the EMR to prevent prescribers from erroneously selecting dopamine from the available orders.
- Consider including a LASA alert for dobutamine and dopamine in the automatic dispensing cabinets (ADC) to minimize errors on drug withdrawal from the ADC.
- Milrinone is most commonly used as an alternative to dobutamine for numerous indications discussed. Clinicians who are not familiar with milrinone should be informed of its pharmacokinetics, dosing, renal adjustment, and warnings/precautions before prescribing and administering. Particularly, IV bolus loading doses of milrinone are not recommended due to risk of hypotension.

IMPACT ON ICU CARE

- The dobutamine shortage may necessitate careful resource allocation decisions with clinicians evaluating the most critical cases for dobutamine administration.
- Consider centralizing dobutamine stock to the pharmacy department so supply and usage can be closely monitored.
- Multidisciplinary teams should evaluate current available alternatives by indication and obtain increased stock of alternatives such as milrinone, dopamine, and other vasoactive agents.
- Education of staff is necessary to limit potential risks to patients. Clear and constant communication (e.g., clinical decision support, email) is recommended to provide clinicians necessary information on how to appropriately prescribe alternative medications.

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Table 2. Characteristics of Pertinent Vasoactive Medications[16,17]

Agent/characteristics	Dobutamine	Milrinone	Phenylephrine	Norepinephrine	Epinephrine	Vasopressin	Dopamine		
							Low dose	Moderate dose	High dose
Doses (in mcg/kg/min unless specified)	2.5-20	0.125-0.75	0.5-2	0.05-3.3	0.01-0.5	0.03-0.04 units/min	1-5	5-10	10-20
Half-life (in minutes unless specified)	2	1-3 hours; prolonged hours if CrCl < 50 mL/min	5	1-2	2-3	10-35	1-2		
Onset (minutes)	2-10	5 -15	10-15	3	< 5	1-2	5		
Metabolism	Liver	Liver	Liver	Liver	Mainly liver	Liver and kidney	COMT enzyme		
Excretion	Renal (66%)	Renal (80%-85%)	Renal	Renal	Renal	Renal	Renal		
Adverse effects	Tachyarrhythmias, cardiac ischemia	Ventricular and supraventricular	Reflex bradycardia, hypertension,	Tachyarrhythmias, hypertension, cardiac and	Tachyarrhythmias, hypertension, cardiac and	Hypertension, decreased CO, peripheral and	Tachyarrhythmias, hypertension,		

		arrythmias, hypotension	peripheral, and visceral ischemia	peripheral ischemia	peripheral ischemia	splanchnic vasoconstriction, cardiac ischemia	cardiac and peripheral ischemia		
Receptor Activity									
α-1	+	0	+++	+++	+++	0	0	+	++
β-1	++++	0	0	++	+++	0	+	++	++
β-2	++	0	0	0	++	0	0	0	0
DA	0	0	0	0	0	0	++	++	++
Other		PDE3 Inhibition				V1R and V2R agonism			
Hemodynamic Effects									
CO/CI	↑	↑	↔↓	↑	↑	↔↓	↑		
HR	↑	↔	↔↓	↑	↑	↔↓	↑		
SVR	↔	↓	↑	↑	↑	↑	↔		
PCWP	↔↓	↓	↑	↑	↑	↔	↔ ↑		

CO, cardiac output; COMT, catechol-O-methyltransferase; CrCl, creatinine clearance; HR, heart rate; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; PDE3, phosphodiesterase type 3; SVR, systemic vascular resistance; V1, vasopressin receptor type 1; V2, vasopressin receptor type 2.

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