ADULT CONTINUOUS INFUSION STANDARDS

Updated: September 2024

STANDARDIZE 4 SAFETY INITIATIVE

Standardize 4 Safety is the first national, interprofessional effort to standardize medication concentrations to reduce errors, especially during transitions of care.

These national standards will cover:

- Concentrations and dosing units for intravenous continuous medications for adult patients.
- Concentrations for compounded oral liquid medications.
- Concentrations and dosing units for intravenous continuous medications for pediatric patients.
- Doses for oral liquid medications.
- Concentrations for intravenous intermittent medications.
- Concentrations for PCA and epidural medications.

The Standardize 4 Safety initiative began in 2008 when a multi-stakeholder IV summit was held to address preventing patient harm and death from intravenous (IV) medication errors. Among the recommendations made by the participants was to establish national standards for IV medications in hospitals including standardized concentrations and dosing. In addition, it was recommended that the national standards be created in collaboration with the Food and Drug Administration (FDA), the pharmaceutical industry, and other stakeholders. Since the summit, establishing standardized concentrations has garnered strong support from ASHP members, the Joint Commission, the Institute for Safe Medication Practices (ISMP), and others.[1] [2] [3] [4]

In 2015 the FDA, through its Safe Use Initiative, awarded ASHP a grant to develop and implement national standardized concentrations for IV and oral liquid medications. The aims of the grant were to: (1) identify a nationwide expert interprofessional panel consisting of physicians, nurses, and pharmacists; (2) create standards for adult continuous IV infusions, compounded oral liquid medications, pediatric continuous IV infusions, doses for liquid medications, intravenous intermittent infusions, and PCA and epidural medications; (3) disseminate the standards and assess their adoption.

1 ASHP Best Practices: Position and guidance documents of ASHP. 2014. ASHP, Bethesda, Maryland.

2 Larsen GY, Parker HB, Cash J. et.al. Standard Drug Concentrations and Smart-Pump Technology Reduce Continuous-Medication-Infusion Errors in Pediatric Patients. Pediatrics 2005;116:e21–e25.

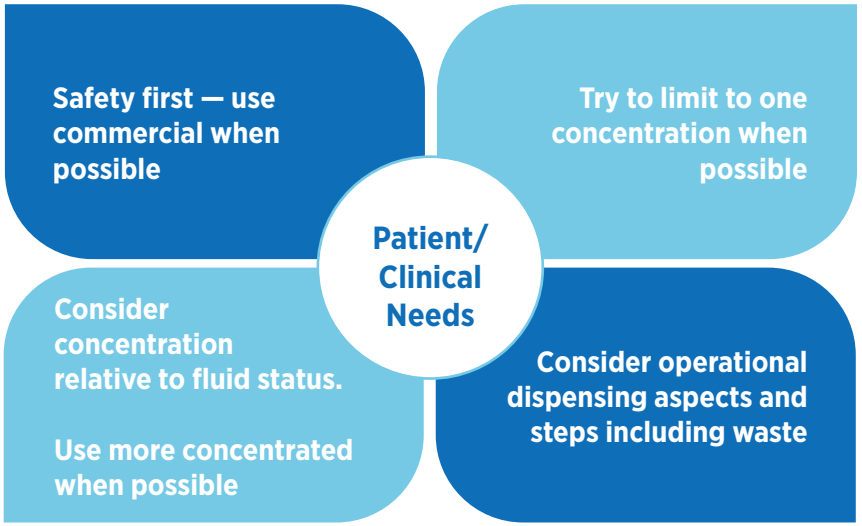
3 Joint Commission. Preventing Pediatric Medication Errors. https://www.jointcommission.org/-/media/tjc/documents/resources/patient-safety-topics/sentinel-event/sea-39-ped-med-errors-rev-final-4-14-21.pdf. (accessed March 15, 2024)

4 Shekelle PG, Wachter RM, Pronovost PJ, et.al. An Updated Critical Analysis of the Evidence for Patient Safety Practices. Comparative Effectiveness Review No. 211. (Prepared by the Southern California-RAND Evidence-based Practice Center under Contract No. 290-2007-10062-I.) AHRQ Publication No. 13-E001-EF. Rockville, MD: Agency for Healthcare Research and Quality. March 2013. www.ahrq.gov/research/findings/evidence-based-reports/ptsafetyuptp.html. (accessed September 20, 2020)

WHY STANDARDIZE

To Err is Human was published in 1999 and highlighted the harm to patients from healthcare error. In that report, medication errors were stated to be responsible for one of 131 outpatient and one of 854 inpatient deaths.[5] Healthcare continues to struggle to eliminate harm to patients. A systematic review and meta-analysis in 2019 estimated one in 20 patients are exposed to preventable medical harm with the highest incidence of events due to medications. Compounded medications,[6] especially those given intravenously, are known to be high risk for error due to added complexity and multiple steps required for determining dosing when ordering, concentrations for preparation and rates of infusion for administering.[7] [8] Using standardization as a quality improvement tool decreases variation, improves safety, and is the foundation for using clinical pathways and evidence-based guidelines. Standardization allows providers to manage excessive and unintended variation as they customize care for patients.[9]

PRINCIPLES FOR ADULT CONTINUOUS INFUSION STANDARDS



5 Kohn LT, Corrigan J, Donaldson Molla S, eds; Institute of Medicine Committee on Quality of Health Care in America. To Err is Human: Building a Safer Health System. Washington, DC: National Academy Press; 2000.

6 Panagioti, M, Khan K, Keers RN, et.al. Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. BMJ 2019;366:l4185 | doi: 10.1136/bmj.l4185.

7 Hedlund N, Beer I, Hoppe-Tichy T, Trbovich P. Systematic evidence review of rates and burden of harm of intravenous admixture drug preparation errors in healthcare settings. BMJ Open. 2017; 7(12): e015912.

8 Sutherland A, Canobbio M, Clarke J, et.al. Incidence and prevalence of intravenous medication errors in the UK: a systematic review. Eur J Hosp Pharm. 2020 Jan; 27(1): 3–8.

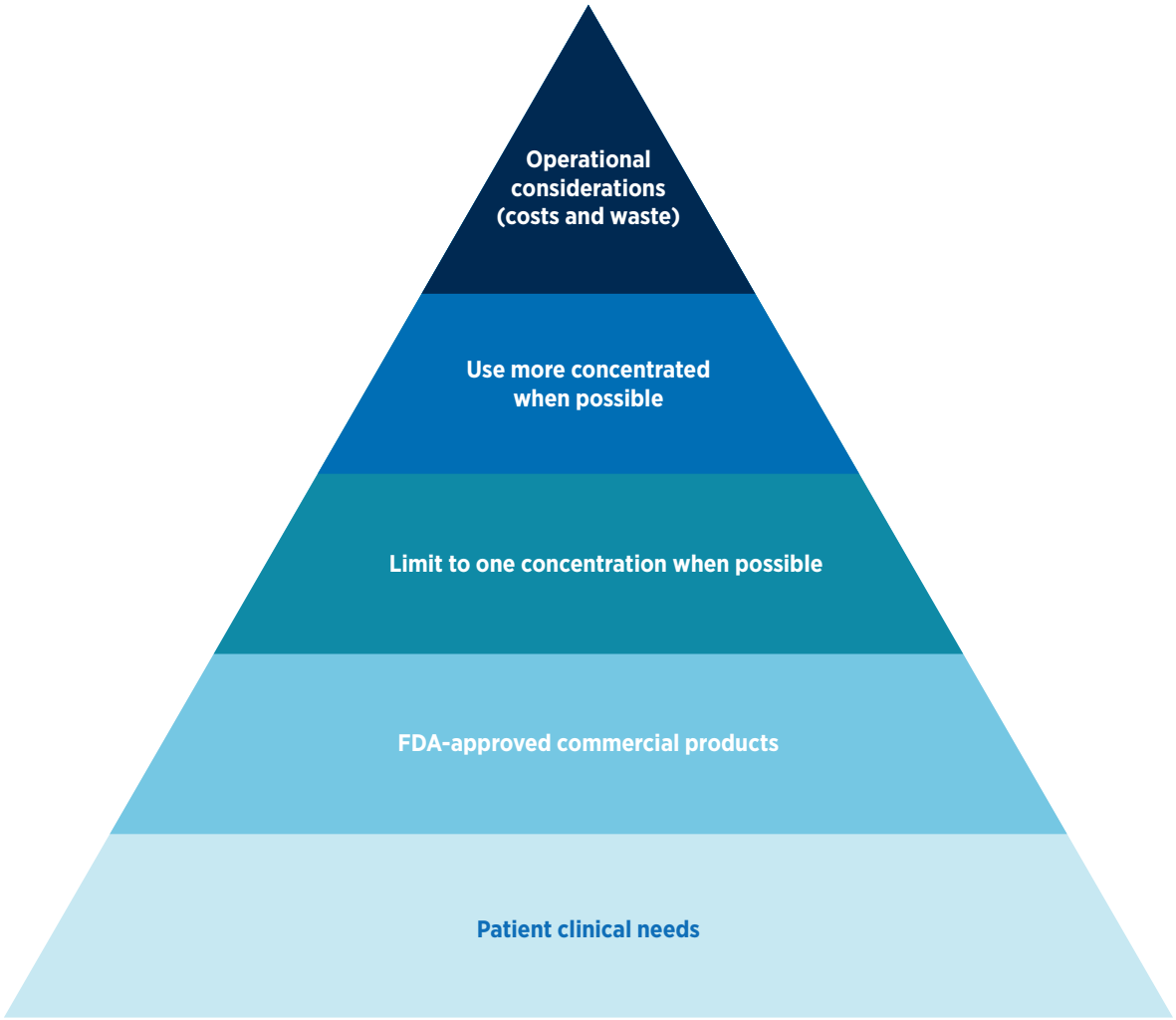
9 Lloyd R. Does Standardization Mean the End of Autonomy? Institute for Healthcare Improvement. https://www.ihi.org/insights/does-standardization-mean-end-autonomy. (accessed March 20, 2024)

HOW THE NATIONAL MEDICATION CONCENTRATION STANDARDS WERE DEVELOPED

A comprehensive environmental scan was conducted to identify the appropriate medications to be addressed in the respective standard concentrations. A multi-disciplinary expert panel was convened for each standard concentration category. Members were selected based on their expertise in the subject matter and identified with assistance from organizations such as The American Society of Anesthesiologists, Society of Critical Care Medicine, and American Association of Critical-Care Nurses. Each expert panel was charged to establish standard principles to guide their decisions in creating the respective standard concentration recommendations. Once a draft of standards was established, it was released for public comment and review by ASHP staff and ISMP. The expert panel subsequently met to address all comments and generate the National Medication Concentration Standards.

The concept of bracketing was employed for references for stability. For more information review: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q1d-bracketing-and-matrixing-designs-stability-testing-new-drug-substances-and-products.

PRINCIPLES FOR EXPERT PANEL DELIBERATIONS



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DISCLAIMERS

- Suggested concentrations may differ from the package insert (PI) information for a drug. This is due to clinical needs that may have transpired postmarket. When this is the case, studies are available to support the use of a concentration different than what the parent company originally pursued through the new drug application (NDA) process.
- Please use the utmost caution when using a concentration different than the PI, especially if rate information is used from the PI.
- Dosing units were derived from PI information, commonly used drug-reference guides, and clinical practice guidelines.
- Of special note, the expert panel is recommending that weight-based dosing be used for vasopressors (i.e., per kg, per minute), which may differ from institution specific guidelines. We strongly encourage that drug libraries and electronic health records (EHRs), including the electronic medication administration record, make distinct differences for weight-based vs. non-weight-based dosing so nurses can easily distinguish what pump programming is needed.
- These concentrations are guidelines only and are not mandatory. It is our hope that organizations will voluntarily adopt these concentrations and join a national movement to use standardization across the care continuum as an error-prevention strategy for patient safety.
- The information contained in this table is subject to the professional judgment and interpretation of the practitioner. ASHP has made reasonable efforts to ensure the accuracy and appropriateness of the information presented. However, any reader of this information is advised that ASHP is not responsible for the continued currency of the information, for any errors or omissions, and/or for any consequences arising from the use of the information in the self-assessment tool. Any user of the table is cautioned that ASHP makes no representation, guarantee, or warranty, express or implied, as to the accuracy and appropriateness of the information contained in it, and will bear no responsibility or liability for the results or consequences of its use.

CONSIDERATIONS IN USING THE ADULT CONTINUOUS INFUSION STANDARDS

The 80/20 rule was applied by the expert panel to determine recommended standard concentrations. The concentrations listed reflect those applicable to most patient care circumstances. The panel recognizes situations occur where the most appropriate concentration for a patient may not be the recommended standard.

Whenever possible one standard infusion concentration is the recommendation. When more than one standard concentration was recommended it was to accommodate patient care needs for fluid restrictions, differences required for peripheral versus central lines, to simplify calculations and accommodate limitations of pump infusion rates.

Medications with more than one recommended concentration are listed from lowest to highest concentration, with the numbering corresponding to the respective stability reference(s).

Drug	Concentration Standards	Dosing units	Commercially available	References
Alteplase	1 mg/mL	mg/hour	Yes, comes in a kit with diluent	1. Product Information: Activase(R) intravenous injection, alteplase intravenous injection. Genentech, Inc.(per Manufacturer), South San Francisco, CA, 2015
Amiodarone	1.8 mg/mL	mg/min	Yes	1. Product Information: amiodarone HCl intravenous injection, amiodarone HCl intravenous injection. Teva Canada Limited (per Health Canada), Toronto, ON, Canada, 2016.
Argatroban	1 mg/mL	**mcg/kg/min***	Yes	1. Product Information: argatroban injection, argatroban injection. GlaxoSmithKline, Research Triangle Park, NC, 2009. Product Information: argatroban IV injection aqueous solution, argatroban IV injection aqueous solution. The Medicines Company (per DailyMed), Parsippany, NJ, 2011.
Bumetanide	0.25 mg/mL	mg/hour	Administer undiluted	1. Hospira. Bumetanide Injection, USP. Lake Forest, IL. 2021 March.
Cisatracurium[1 2]	2 mg/mL	**mcg/kg/min***	Administer undiluted	1. Abbvie. Nimbex® (cisatracurium besylate) injection prescribing information. North Chicago, IL; 2016 Dec.
Dexmede**TOMID**ine	4 mcg/mL	mcg/kg/hour	Yes	1. Hospira. Precedex® (dexmedetomidine) injection prescribing information. Lake Forest, IL; 2016 Apr.
Dil**TIAZ**em	1 mg/mL	mg/hour	No	1. Diltiazem HCL 0.5% intravenous injection, Akor, Inc. (per DailyMed) Lke Forest, IL. 2012.
DOBUTamine	1. 2000 mcg/mL 2. 4000 mcg/mL	mcg/kg/min	Yes	1. Hospira. Dobutamine in 5% dextrose injection prescribing information. Lake Forest, IL; 2006 June. 2. Hospira. Dobutamine in 5% dextrose injection prescribing information. Lake Forest, IL; 2006 June.
DOPamine[3]	1. 1600 mcg/mL 2. 3200 mcg/mL	mcg/kg/min	Yes	1. Hospira. Dopamine hydrochloride and 5% dextrose injection prescribing information. Lake Forest, IL; 2014 May. 2. Hospira. Dopamine hydrochloride and 5% dextrose injection prescribing information. Lake Forest, IL; 2014 May.

Drug	Concentration Standards	Dosing units	Commercially available	References
EPINEPHrine[4]	1. 20 mcg/mL 2. 40 mcg/mL	mcg/kg/min	No	1a. Allwood MD. The stability of four catecholamines in 5% glucose infusions. J Clin Pharm Ther. 1991:16:337-40. 1b. VanMatre ET, Ho KC, Lyda C, et.al. Extended Stability of Epinephrine Hydrochloride Injection in Polyvinyl Chloride Bags Stared in Amber Ultraviolet Light-Blocking Bags. Hospital Pharmacy. 2017;52:570-573. 2a. Carr RR, Decarie D, EnsomMHH. Stability of Epinephrine at Standard Concentrations. Can J Hosp Pharm. 2014;67:197-202 2b. Peddicord TE, Olsen KM, ZumBrunnen TL, et.al. Stability of high-concentration dopamine hydrochloride, norepinephrine bitartrate, epinephrine hydrochloride and nitroglycerin 5% dextrose injetion. Am J Health-Syst Pharm. 1997;54:1417-19.
Esmolol	1. 10 mg/mL 2. 20 mg/mL	**mcg/kg/min***	Yes	1. Baxter. Brevibloc® injection (esmolol hydrochloride) prescribing information. (dated 2022, Feb.). In: Physicians' desk reference. 54th ed. Montvale NJ: Medical Economics Company Inc; 2000:655-7. 2. Baxter. Brevibloc® injection (esmolol hydrochloride) prescribing information. (dated 2022, Feb.). In: Physicians' desk reference. 54th ed. Montvale NJ: Medical Economics Company Inc; 2000:655-7.
Fenta**NYL**[5]	1. 10 mcg/mL 2. 50 mcg/mL	mcg/hour	No	1a. Allen LV Jr, Stiles ML. Stability of fentanyl citrate in 0.9% sodium chloride solution in portable infusion pumps. Am J Hosp Pharm. 1990:47;1572-4. 1b. Kowalski SR, Gourlay GK. Stability of fentanyl citrate in glass and plastic containers and in a patient-controlled delivery system. Am J Hop Pharm. 1990;47:1584-7. 2. Hospira, INC. Fentanyl Citrate injection, solution.prescribing information. Lake Forest, IL; 2019, December.
Furosemide	1. 2 mg/mL 2. 10 mg/mL	mg/hour	Yes	1. Donnelly RF. Chemical stability of furosemide in minibags and polypropylene syringes. Int J Pharmaceut Compound. 2002;6:468-70 2. American Pharmaceutical Partners, Inc. Furosemide Injection, USP prescribing information. Schaumburg, IL; 2002 Apr.
Heparin[6]	100 units/mL	units/hour or units/kg/hour	Yes	1. B.Braun Medical Inc. Heparin Sodium in Dextrose Injection prescribing information. Bethlehem, PA. 2018. April

Drug	Concentration Standards	Dosing units	Commercially available	References
HYDROmorphone[5]	1. 0.2 mg/mL 2. 1 mg/mL 3. 5 mg/mL (based upon high dose requirements	mg/hour	No	1. Khondkar D, et.al. Chemical stability of hydromorphone hydrochloride in patient controlled analgesia injector. In J Pharmaceut Compound. 2010;14:160-4. 2. Walker SE et. al. Hydromorphone and morphine stability in portable infusion pump cassettes and minibags. Can J Hosp Pharm. 1988;4:177-82. 3. Walker SE et. al. Hydromorphone and morphine stability in portable infusion pump cassettes and minibags. Can J Hosp Pharm. 1988;4:177-82.
Insulin (regular)	1 unit /mL	units/ hour, DKA protocols may require units/kg/ hour	Yes	1. Product Information: HUMULIN(R) R subcutaneous injection, intravenous injection, insulin human subcutaneous injection, intravenous injection. Lilly USA LLC (per FDA), Indianapolis, IN, 2018. Micromedex
Isoproterenol[6]	4 mcg/mL	mcg/min or mcg/kg/ min	No	1. ISUPREL (R) IV injection, isoproterenol hcl IV injection. Hospira, Inc, Lake Forest, IL, 2004.
Ketamine	1. 2 mg/mL 2. 10 mg/mL	***BASED ON INDICATION*** mg/kg/hr or mcg/kg/ min	Yes, undiluted drug from the vial of 10 mg/ mL	1. Product Information: KETALAR intravenous injection, intramuscular injection, ketamine HCl intravenous injection, intramuscular injection. Par Pharmaceutical (per FDA), Chestnut Ridge, NY, 2017. 2. Product Information: KETALAR intravenous injection, intramuscular injection, ketamine HCl intravenous injection, intramuscular injection. Par Pharmaceutical (per FDA), Chestnut Ridge, NY, 2017.
Labetalol	1. 1 mg/mL 2. 5 mg/mL	mg/min	Yes	1. Labetalol Hydrochloride in Sodium Chloride and Labetalol Hydrochloride in Dextrose Injection. Hikma Pharmaceuticals USA Inc. Eatontown, NJ. 2020 2. Product Information: labetalol HCl intravenous injection, labetalol HCl intravenous injection. Hospira, Inc. (per DailyMed), Lake Forest, IL, 2015.
Lidocaine	8 mg/mL	mg/min	Yes	1a. Stewart JT, Warren FW. Stability of ranitidine hydrochloride and seven medications. *Am J Hosp Pharm*. 1994; 51:1802–7. 1b. Product Information: Lidocaine HCl dextrose 5% intravenous injection, lidocaine HCl dextrose 5% intravenous injection. Baxter Healthcare Corporation (per FDA), Deerfield, IL, 2017.

Drug	Concentration Standards	Dosing units	Commercially available	References
LORazepam	1 mg/mL	mg/hour	No	1a. Share MJ, et.al. Stability of lorazepam 1 and 2 mg/ml in glass bottles and polypropylene syringes. Am J Health-Syst Pharm. 1998; 55:2013-5 1b. Norenburg JP, et.al. Stability of lorazepam in 0.9% sodium chloride in polyolefin bags. Am J Health Syst Pharm. 2004; 61:1039-41
Magnesium Sulfate[7]	1. 40 mg/mL	**gms***	Yes	1. Thompson D.E. Shimanek M. Stability and sterility study with magnesium sulfate admixtures. Infusion. 1983; 7: 83, 86.
Morphine[6]	1. 1 mg/mL 2. 5 mg/mL (based upon high dose requirements)	mg/hour	Yes	1. Stiles ML, Tu YH, & Allen LV Jr: Stability of morphine sulfate in portable pump reservoirs during storage and simulated administration. *Am J Hosp Pharm* 1989; 46:1404-1407. 2a. Stiles ML, Tu YH, & Allen LV Jr: Stability of morphine sulfate in portable pump reservoirs during storage and simulated administration. *Am J Hosp Pharm* 1989; 46:1404-1407. 2b. Altman L, Hopkins RJ, Ahmed S, et al: Stability of morphine sulfate in Cormed III (Kalex) intravenous bags. *Am J Hosp Pharm* 1990; 47:2040-2042.
Midazolam	1. 1 mg/mL 2. 5mg/mL	mg/hour	No	1a. Karlage K, Earhart Z, Green-Boesen K, Myrdal PB. Stability of midazolam hydrochloride injection 1-mg/mL solutions in polyvinyl chloride and polyolefin bags. *Am J Health Syst Pharm*. 2011;68(16):1537-1540.[PubMed 218 17086] 1b. McMullin ST, Schaiff RA, and Dietzen DJ, "Stability of Midazolam Hydrochloride in Polyvinyl Chloride Bags Under Fluorescent Light," *Am J Hosp Pharm*, 1995, 52(18), 2018-20. 2a. Pramar YV, Loucas VA, & El-Rachidi A: Stability of midazolam hydrochloride in syringes and IV fluids. Am J Health-Syst Pharm 1997; 54:913-915. 2b. Product Information: MIDAZOLAM HCl intravenous intramuscular injection, midazolam HCl intravenous intramuscular injection. Heritage Pharmaceuticals (per DailyMed), Eatontown, NJ, 2017.
Milrinone	200 mcg/mL	mcg/kg/min	Yes	1a. Wilson TD, Forde MD, Crain AVR, Dombrowski LJ, Joyce MA. Stability of milrinone in 0.45% sodium chloride, 0.9% sodium chloride, or 5% dextrose injections. *Am J Hosp Pharm*. 1986;43(9):2218-2220. 1b. Wong F, Gill MA. Stability of milrinone lactate 200 mcg/mL in 5% dextrose injection and 0.9% sodium chloride injection. *Int J Pharm Compound*. 1998; 2(2):168b

Drug	Concentration Standards	Dosing units	Commercially available	References
Naloxone	1. 16 mcg/mL 2. 40 mcg/mL	**mg/hr*** mcg/kg/hr - pruritus	No	1a. Product Information: Naloxone Hydrochloride Injection, solution. Hospira Inc. Lake Forest, IL. 9/2019. 4 mcg/ml. 1b. Lewis JM, Klein-Schwartz W, Benson BE, et al. Continuous naloxone infusion in pediatric narcotic overdose. *Am J Dis Child*. 1984;138(10):944–946. 8 mcg/ml 2. American Pain Society. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain. 6th ed. Glenview, IL: American Pain Society; 2008.
Ni**CAR**dipine	1. 0.1 mg/mL 2. 0.2 mg/mL	mg/hour	Yes	1. Product Information: CARDENE(R) IV solution for IV infusion, nicardipine HCL solution for IV infusion. EKR Therapeutics, Inc, Bedminster, NJ, 2014. 2. Product Information: CARDENE(R) IV solution for IV infusion, nicardipine HCL solution for IV infusion. EKR Therapeutics, Inc, Bedminster, NJ, 2014.
Nitroglycerin	200 mcg/mL	mcg/min	Yes	1. Product Information: Nitroglycerin Injection. Abbott Laboratories, North Chicago, IL, October 2014
Nitroprusside	1. 200 mcg/mL 2. 500 mcg/mL	mcg/kg/min	No	1. Product Information: NIPRIDE RTU intravenous injection, sodium nitroprusside intravenous injection. Exela Pharma Sciences, LLC (per FDA), Lenoir, NC, 2017. 2. Product Information: NIPRIDE RTU intravenous injection, sodium nitroprusside intravenous injection. Exela Pharma Sciences, LLC (per FDA), Lenoir, NC, 2017.
Norepinephrine[4]	1. 16 mcg/mL 2. 32 mcg/mL 3. 128 mcg/mL	mcg/kg/min	Yes - 16 mcg/mL and 32 mcg/mL	1. Allwood MC. The stability of four catecholamines in 5% Glucose Infusion. J Clin Pharm Ther. 1991; 16:337-40. 2a. Allwood MC. The stability of four catecholamines in 5% Glucose Infusion. J Clin Pharm Ther. 1991; 16:337-40. 2b. Walker SE et.al. Stability of norepinephrine solutions in normal saline and 5% destrose in water. Can J Hosp Pharm. 2010; 63:113-8. 3a. Gilliot S, et.al. Long-term stability of ready-to-use norepinephrine solution at 0.2 and 0.5 mg/ml. Eur J of Hosp Pharm. 2020; 27:e93-98. 3b. Walker SE et.al. Stability of norepinephrine solutions in normal saline and 5% destrose in water. Can J Hosp Pharm. 2010; 63:113-8.
Oxytocin[7]	1. 0.06 Units/mL	**milliunits/min***	Yes	1. Kumar V, et.al. Development and Validation of an HPLC Method for Oxytocin in Ringer's Lactate and its Application in Stability Analysis. J. Liq Chromatogr Relat. 2006; 29: 2353–2365.

Drug	Concentration Standards	Dosing units	Commercially available	References
Phenylephrine	1. 80 mcg/mL 2. 400 mcg/mL	mcg/kg/min	No	1a. West-Ward Pharmaceuticals. Phenylephrine hydrochloride injection prescribing information. Eatontown, NJ; 2012 Dec 1b. Éclat Pharmaceuticals. Vazculep® (phenylephrine hydrochloride) injection prescribing information. Chesterfield, MO; 2014 2. Jansen JJ, Oldland AR, Kiser TH. Evaluation of phenylephrine stability in polyvinyl chloride bags. *Hosp Pharm*. 2014; 49:455-7.
Propofol	10 mg/mL	mcg/kg/min	Yes	1. Fresenius Kabi USA, LLC. Diprivan® (propofol) injectable emulsion prescribing information. Lake Zurich, IL; 2017 Nov.
Rocuronium[1]	10 mg/mL	mcg/kg/min	Administer undiluted	1. Hospira. Rocuronium bromide injection prescribing information. Lake Forest, IL: 2014 Feb.
Vasopressin[6]	1. 0.2 unit/mL 2. 0.4 unit/mL 3. 1 unit/mL	units/min or units/kg/min	No	1. Par Pharmaceutical. Vasostrict® (vasopressin injection, USP) For Intravenous Infusion. 2021. Chestnut Ridge, NY. 2. Par Pharmaceutical Companies, Inc. Vasostrict® (vasopressin) injection prescribing information. Chestnut Ridge, NY; 2021. 3. Par Pharmaceutical Companies, Inc. Vasostrict® (vasopressin) injection prescribing information. Chestnut Ridge, NY; 2021.
Vecuronium[1]	1 mg/mL	**mcg/kg/min***	No	1. Product Information: Vecuronium bromide ntravenous injection lyophilized powder for solution. Fresenius Kabi USA, LLC (per DailyMed) Lake Zurich, IL. 2016

*** BOLD - dosing units differ from concentration units**

ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations
Use mcg for Microgram. https://www.ismp.org/tools/errorproneabbreviations.pdf

NOTES

1 Paralytics are recommended to be administered as straight drug. This provides consistency between operating room and the ICU, and eliminates potential compounding errors.

2 This is a concentration that differs from the package insert, therefore infusion related calculations will differ from the PI

3 Consider limiting to one bag size for each recommended concentration (250 vs 500 ml). This may reduce errors and also reduce inventory needs.

4 The expert panel and ISMP recommend different concentrations of epinephrine and norepinephrine.

5 These concentrations are for continuous infusions not delivered by a PCA device.

6 We recommend trying to standardize dosing units but understand some protocols may use "flat" dosing while others may require weight based dosing.

7 See ISMP for best practices. https://www.ismp.org/resources/taking-closer-look-medication-errors-involve-oxytocin; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3956395/