



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.

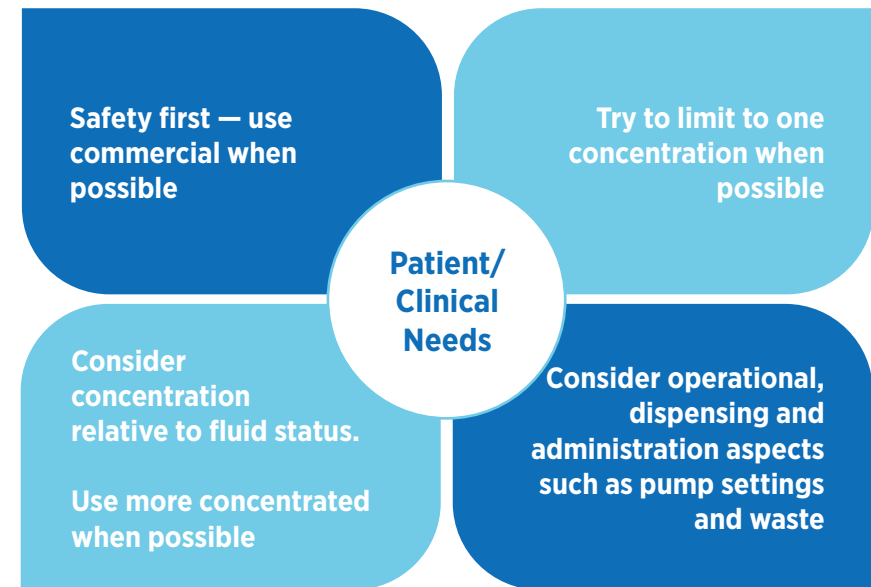
³ Joint Commission. Preventing Pediatric Medication Errors. <https://www.jointcommission.org/-/media/tjc/documents/resources/patient-safety-topics/sentinel-event/sea-39-ped-med-errors-rev-final-4-14-21.pdf>. (accessed March 15, 2024)

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. 290-2007-10062-1.) 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 PCA AND EPIDURAL STANDARD CONCENTRATIONS



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.

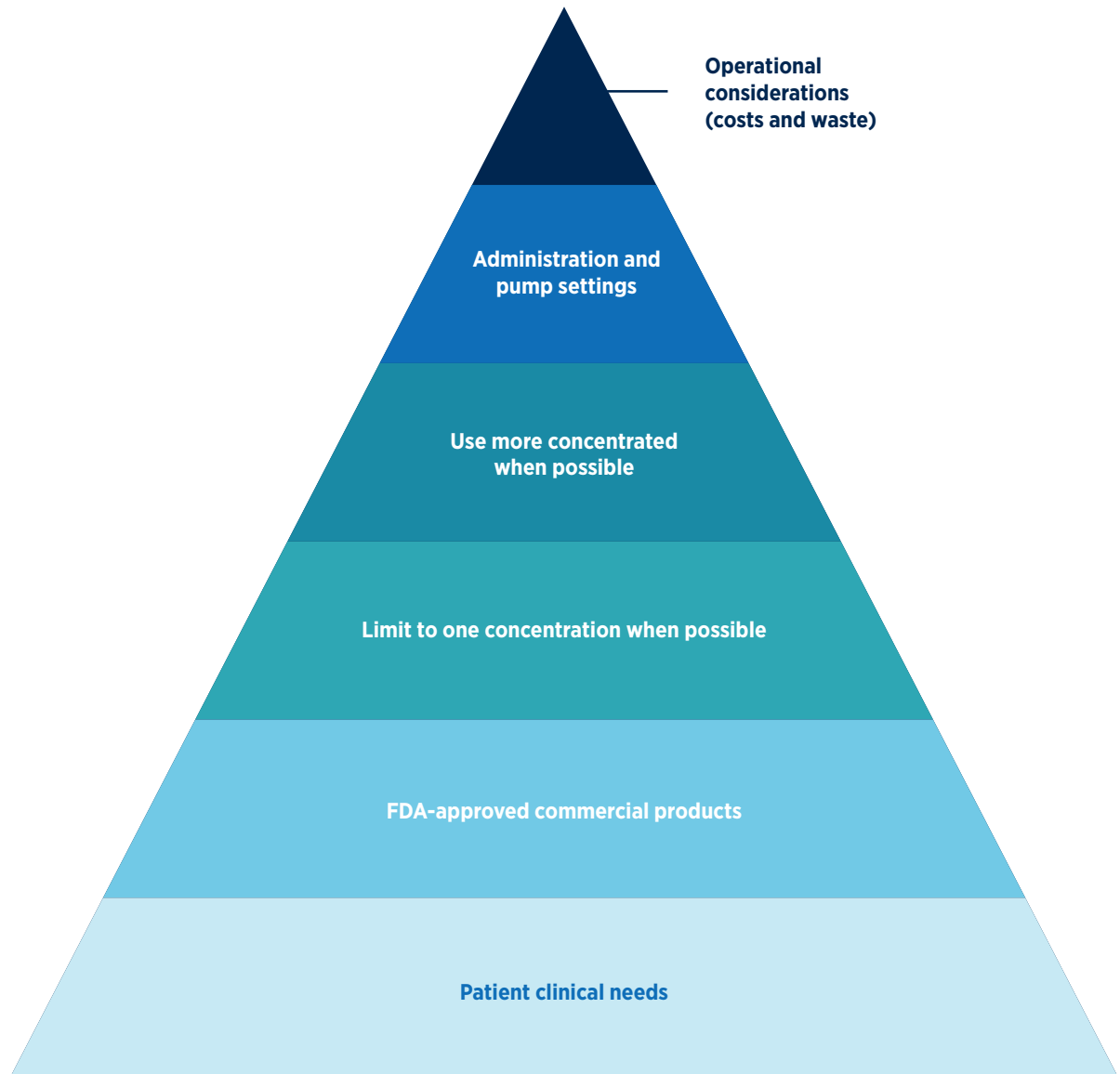
8 Sutherland A, Canobbio M, Clarke J, et.al. Incidence and prevalence of intravenous medication errors in the UK: a systematic review. *Eur J Hosp Pharm*. 2020 Jan; 27(1): 3–8.

9 Lloyd R. Does Standardization Mean the End of Autonomy? Institute for Healthcare Improvement. <https://www.ihl.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.

PRINCIPLES FOR EXPERT PANEL DELIBERATIONS



EXPERT PANEL

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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.
- 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 PCA AND EPIDURAL 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 extremely small neonates, 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).

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>.

The pediatric PCA and epidural standards are intended for the smallest newborns to children less than 50 kg.

PEDIATRIC PCA STANDARD CONCENTRATIONS

Drug	Concentration Standards	Dosing Units	Stability References
Fentanyl	10 mcg/mL 50 mcg/mL	mcg/kg/hr	- Anderson C, MacKay M. Stability of Fentanyl Citrate, Hydromorphone Hydrochloride, Ketamine Hydrochloride, Midazolam, Morphine Sulfate, and Pentobarbital Sodium in Polypropylene syringes. <i>Pharmacy</i>. 2015;3:379-385. - Anderson C, MacKay M. Stability of Fentanyl Citrate, Hydromorphone Hydrochloride, Ketamine Hydrochloride, Midazolam, Morphine Sulfate, and Pentobarbital Sodium in Polypropylene syringes. <i>Pharmacy</i>. 2015;3:379-385. - Donnelly RF. Chemical stability of fentanyl in polypropylene syringes and polyvinyl chloride bags. <i>Int J Pharmaceut Compound</i>. 2005; 9:482-3.
Hydromorphone	0.05 mg/mL 0.2 mg/mL 1 mg/mL*	mg/kg/hr	- Ping L et.al. Stability of hydromorphone hydrochloride and morphine under different clinical infusion conditions. <i>Indian J of Pharm Sci</i>. 2019;p1140-1146. - Khondkar D, et al. Chemical stability of hydromorphone hydrochloride in patient-controlled analgesia injector. <i>Int J Pharmaceut Compound</i>. 2010; 14:160-4. - Walker SE, et al. Hydromorphone and morphine stability in portable infusion pump cassettes and minibags. <i>Can J Hosp Pharm</i>. 1988; 41:177-82.
Ketamine	2 mg/mL 10 mg/mL	mg/kg/hr	- Hospira, Inc. Ketamine hydrochloride injection prescribing information. Lake Forest, IL; 2020 Apr. - Gupta VD. Stability of Ketamine hydrochloride injection after reconstitution in water for injection and storage in 1 mL tuberculin polypropylene syringes for pediatric use. <i>Int J Pharmaceut Compound</i>. 2002;6:316-7.

PEDIATRIC PCA STANDARD CONCENTRATIONS cont.

Drug	Concentration Standards	Dosing Units	Stability References
Midazolam	0.1 mg/mL 2 mg/mL 5 mg/mL	mg/kg/hr	- Good PD. The compatibility and stability of midazolam and dexamethasone in infusion solutions. J Pain Symptom Manage. 2004;27:471-475. - Stiles ML, Allen LV Jr. Stability of deferoxamine mesylate, floxuridine, fluorouracil, hydromorphone hydrochloride, lorazepam and midazolam hydrochloride in polypropylene infusion-pump syringes. Am J Health-Syst Pharm. 1996;53:1583-8. - Hospira, Inc. Midazolam hydrochloride (preservative-free) injection prescribing information. Lake Forest, IL; 2019 May.
Morphine	0.25 mg/mL 1 mg/mL* 5 mg/mL	mg/kg/hr	- Veechio M, et.al. the stability of morphine intravenous infusion solutions. Can J Josp Pharm. 1988;41:5-9. a. Nguyen-Xuan T, et al. Stability of morphine sulfate in polypropylene infusion bags for use in patient-controlled analgesia pumps for postoperative pain management. Int J Pharmaceut Compound. 2006; 10:69-73. b. 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. a. Strong ML, et al. Shelf-lives and factors affecting the stability of morphine sulphate and meperidine (pethidine) hydrochloride in plastic syringes for use in patient-controlled analgesic devices. J Clin Pharm Ther. 1994; 19:361-9. b. Stiles ML, Tu YH. Stability of morphine sulfate in portable pump reservoirs during storage and simulated administration. Am J Hosp Pharm. 1989; 46:1404-7.

* Caution if both medications are used to avoid confusion in selection as both have the same concentraion.

ADULT PCA STANDARD CONCENTRATIONS



Drug	Concentration Standards	Dosing Units	Stability References
Fentanyl	10 mcg/mL 50 mcg/mL	mcg/kg/hr	- Anderson C, MacKay M. Stability of Fentanyl Citrate, Hydromorphone Hydrochloride, Ketamine Hydrochloride, Midazolam, Morphine Sulfate, and Pentobarbital Sodium in Polypropylene syringes. Pharmacy. 2015;3:379-385. - Anderson C, MacKay M. Stability of Fentanyl Citrate, Hydromorphone Hydrochloride, Ketamine Hydrochloride, Midazolam, Morphine Sulfate, and Pentobarbital Sodium in Polypropylene syringes. Pharmacy. 2015;3:379-385. - Donnelly RF. Chemical stability of fentanyl in polypropylene syringes and polyvinyl chloride bags. Int J Pharmaceut Compound. 2005; 9:482-3.
Hydromorphone	0.2 mg/mL 1 mg/mL* 5 mg/mL	mg	- Khondkar D, et al. Chemical stability of hydromorphone hydrochloride in patient-controlled analgesia injector. Int J Pharmaceut Compound. 2010; 14:160-4. - Walker SE, et al. Hydromorphone and morphine stability in portable infusion pump cassettes and minibags. Can J Hosp Pharm. 1988; 41:177-82. - Walker SE, et.al. Hydromorphone and morphine stability in portable infusion pump cassettes and minibags. Can J Hosp Pharm. 1988;41:177-82.
Ketamine	5 mg/mL 10 mg/mL	mg/kg/hr	- Hospira. Ketamine hydrochloride injection, solution, concentrate. 2020 Dec. note for 2 mg/mL conc. - Gupta VD. Stability of Ketamine hydrochloride injection after reconstitution in water for injection and storage in 1 mL tuberculin polypropylene syringes for pediatric use. int J Pharmaceut Compound. 2002;6:316-7.
Midazolam	1 mg/mL 5 mg/mL	mg/kg/hr	- Good PD. The compatibility and stability of midazolam and dexamethasone in infusion solutions. J Pain Symptom Manage. 2004;27:471-475. - Hospira, Inc. Midazolam hydrochloride (preservative-free) injection prescribing information. Lake Forest, IL; 2019 May.

ADULT PCA STANDARD CONCENTRATIONS cont.

Drug	Concentration Standards	Dosing Units	Stability References
Morphine	1. 1 mg/mL* 2. 5 mg/mL 3. 10 mg/mL	mg	1. Duafala, ME et al. Stability of morphine sulfate in infusion devices and containers for intravenous administration. Am J Hosp Pharm. 1990; 47:143-6. 2a. Strong ML, et al. Shelf-lives and factors affecting the stability of morphine sulphate and meperidine (pethidine) hydrochloride in plastic syringes for use in patient-controlled analgesic devices. J Clin Pharm Ther. 1994; 19:361-9. 2b. Stiles ML, Tu YH. Stability of morphine sulfate in portable pump reservoirs during storage and simulated administration. Am J Hosp Pharm. 1989; 46:1404-7. 3. Walker et.al. Stability of sulfite free high potency morphine sulfate solutions in portable infusion pump cassettes. Can J Hosp Pharm. 1989;42:195-200.

* Caution if both medications are used to avoid confusion in selection as both have the same concentraion.

PEDIATRIC EPIDURAL SINGLE DRUG STANDARD CONCENTRATIONS

Drug	Concentration Standards	Stability References
Fentanyl	1. 0.3 mcg/mL 2. 2 mcg/mL 3. 5 mcg/mL	1. unavailable 2. Kowalski SR et.al. Stability of fentanyl citrate in glass and plastic containers. Am J Hosp Pharm.1990;47:1584-7 3a. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998. 3b. McCluskey et.al. Stability of fentanyl 5 mcg/mL diluted with 0.9% sodium chloride injection and stored in polypropylene syringes. Am J Health Syst Pharm. 2009;66:860-3
Hydromorphone plain	1. 5 mcg/mL 2. 10 mcg/mL	1. unavailable 2. Hildebrand KR et.al. Stability and compatibility of Hydromorphone Hydrochloride in an Implantable Infusion system. J Pain Symptom Mang. 2001; 22:P1042-47.
Morphine plain	1. 0.5 mg/mL 2. 1 mg/mL	1. Hospira. Morphine sulfate Preservative-Free Injection USP. Lake Forest, IL Oct. 2019. 2. Strong ML, et al. Shelf-lives and factors affecting the stability of morphine sulphate and meperidine (pethidine) hydrochloride in plastic syringes for use in patient-controlled analgesic devices. J Clin Pharm Ther. 1994; 19:361-9.
Clonidine	1. 0.3 mcg/mL 2. 0.5 mcg/mL	1. unavailable 2. Lu D, Harmanjeet H, Wanandy T et al. Physicochemical stability of extemporaneously prepared clonidine solutions for use in neonatal abstinence syndrome. J Clin Pharm Ther. 2019
Bupivacaine plain	1. 0.0625% 2. 0.125%	1. Christen C, Johnson CE. Stability of bupivacaine hydrochloride and hydromorphone hydrochloride during simulated epidural coadministration. Am J Health-Syst Pharm. 1996; 53:170-3 2a. Christen C, Johnson CE. Stability of bupivacaine hydrochloride and hydromorphone hydrochloride during simulated epidural coadministration. Am J Health-Syst Pharm. 1996; 53:170-3 2b. Jones JW, Davis AT. Stability of bupivacaine hydrochloride in polypropylene syringes. Am J Hosp Pharm. 1993; 50:2364-5.
Ropivacaine Plain	1. 0.1% 2. 0.2%	1. unavailable 2. Fresenius Kabi Inc. Naropin (ropivacaine HCl) Injection 11/2018.
Chloroprocaine	1%	B Braun Medical Inc. Clorotekal® (Chloroprocaine HCl Injection, USP) 2021

PEDIATRIC EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Bupivacaine with Morphine	Bupivacaine 1. 0.0625% 2. 0.125%	Morphine 1. 0.5 mg/mL 2. 0.5 mg/mL		1. Johnson CE, Christen C, Perez MM et al. Compatibility of bupivacaine hydrochloride and morphine sulfate. Am J Health-Syst Pharm. 1997; 54:61-4. 2. Johnson CE, Christen C, Perez MM et al. Compatibility of bupivacaine hydrochloride and morphine sulfate. Am J Health-Syst Pharm. 1997; 54:61-4.
Bupivacaine with Hydromorphone	Bupivacaine 1. 0.0625% 2. 0.0625% 3. 0.125% 4. 0.125%	Hydromorphone 1. 5 mcg/mL 2. 10 mcg/mL 3. 5 mcg/mL 4. 10 mcg/mL		1. unavailable 2. Goucke RC et.al. Stability and Tolerability of High Concentrations of Intrathecal Bupivacaine and Opioid Mixtures in Chronic Noncancer Pain: An Open-Label Pilot Study. Pain Medicine 2010; 11:1612-18. 3. unavailable 4. Goucke RC et.al. Stability and Tolerability of High Concentrations of Intrathecal Bupivacaine and Opioid Mixtures in Chronic Noncancer Pain: An Open-Label Pilot Study. Pain Medicine 2010; 11:1612-18.
Bupivacaine with Fentanyl	Bupivacaine 1. 0.0625% 2. 0.0625% 3. 0.125% 4. 0.125%	Fentanyl 1. 2 mcg/mL 2. 5 mcg/mL 3. 2 mcg/mL 4. 5 mcg/mL		1. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998; 53:386-91. 2. Tu YH, et.al. Stability of fentanyl citrate and bupivacaine hydrochloride in portable pump reservoirs. Am J of Hosp Pharm. 1990;47:2037-40. 3. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998; 53:386-91. 4. Tu YH, et.al. Stability of fentanyl citrate and bupivacaine hydrochloride in portable pump reservoirs. Am J of Hosp Pharm. 1990;47:2037-40.

PEDIATRIC EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Bupivacaine with Clonidine	Bupivacaine 1. 0.0625% 2. 0.125% 3. 0.125%		Clonidine 1. 0.3 mcg/mL 2. 0.5 mcg/mL 3. 1 mcg/mL	- Note not exact concentrations: Schobelock MJ (Medical Affairs Department, Roxane Laboratories, Inc.); Personal communication;1997 Nov 4. In ASHP Injectable Drug Information 2020 - Note not exact concentrations: Schobelock MJ (Medical Affairs Department, Roxane Laboratories, Inc.); Personal communication;1997 Nov 4. In ASHP Injectable Drug Information 2020 - Note not exact concentrations: Schobelock MJ (Medical Affairs Department, Roxane Laboratories, Inc.); Personal communication;1997 Nov 4. In ASHP Injectable Drug Information 2020
Bupivacaine with Fentanyl and Clonidine	Bupivacaine 1. 0.0625% 2. 0.0625% 3. 0.125% 4. 0.125%	Fentanyl 1. 2 mcg/mL 2. 2 mcg/mL 3. 2 mcg/mL 4. 2 mcg/mL	Clonidine 1. 0.3 mcg/mL 2. 0.5 mcg/mL 3. 0.3 mcg/mL 4. 0.5 mcg/mL	- Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanyl citrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanyl citrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanyl citrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanyl citrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21.

PEDIATRIC EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Ropivacaine with Morphine	Ropivacaine 0.1%	Morphine 0.5 mg/mL		Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45
Ropivacaine with Hydromorphone	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%	Hydromorphone 1. 5 mcg/mL 2. 10 mcg/mL 3. 5 mcg/mL 4. 10 mcg/mL		Unavailable
Ropivacaine with Fentanyl	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%	Fentanyl 1. 2 mcg/mL 2. 5 mcg/mL 3. 2 mcg/mL 4. 5 mcg/mL		1. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 2. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 3. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 4. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma.

PEDIATRIC EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Ropivacaine with Clonidine	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2%		Clonidine 1. 0.5 mcg/mL 2. 1 mcg/mL 3. 1 mcg/mL	- Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Svedberg KO et.al. Compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45
Ropivacaine with Fentanyl and Clonidine	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%	Fentanyl 1. 2 mcg/mL 2. 2 mcg/mL 3. 2 mcg/mL 4. 2 mcg/mL	Clonidine 1. 0.3 mcg/mL 2. 0.5 mcg/mL 3. 0.3mcg/mL 4. 0.5 mcg/mL	- Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45

ADULT EPIDURAL SINGLE DRUG STANDARD CONCENTRATIONS

Drug	Concentration Standards	Stability References
Fentanyl plain	2 mcg/mL 5 mcg/mL 10 mcg/mL	- Kowalski SR et.al. Stability of fentanyl citrate in glass and plastic containers. Am J Hosp Pharm.1990;47:1584-72 a. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998. b. McCluskey et.al. Stability of fentanyl 5 mcg/mL diluted with 0.9% sodium chloride injection and stored in polypropylene syringes. Am J Health Syst Pharm. 2009;66:860-3 - Anderson c, MacKay M. Stability of fentanyl citrate, hydromorphone hydrochloride, ketamine hydrochloride, midazolam, morphine sulfate and pentobarbital sodium in polypropylene syringes. Pharmacy. 2015;3:379-85.
Hydromorphone plain	10 mcg/mL	Hildebrand KR et.al. Stability and compatibility of Hydromorphone Hydrochloride in an Implantable Infusion system. J Pain Symptom Mang. 2001; 22:P1042-47.
Morphine plain	0.5 mg/mL 1 mg/mL	- Hospira. Morphine sulfate Preservative-Free Injection USP. Lake Forest, IL Oct. 2019. - Strong ML, et al. Shelf-lives and factors affecting the stability of morphine sulphate and meperidine (pethidine) hydrochloride in plastic syringes for use in patient-controlled analgesic devices. J Clin Pharm Ther. 1994; 19:361-9.
Clonidine	100 mcg/mL	Schobelock MJ (Medical Affairs Department, Roxane Laboratories, Inc.): Personal communication; 1997 Nov 4; ASHP® Injectable Drug Information 2021
Bupivacaine plain	0.0625% 0.125%	- Christen C, Johnson CE. Stability of bupivacaine hydrochloride and hydromorphone hydrochloride during simulated epidural coadministration. Am J Health-Syst Pharm. 1996; 53:170-3 a. Christen C, Johnson CE. Stability of bupivacaine hydrochloride and hydromorphone hydrochloride during simulated epidural coadministration. Am J Health-Syst Pharm. 1996; 53:170-3 b. Jones JW, Davis AT. Stability of bupivacaine hydrochloride in polypropylene syringes. Am J Hosp Pharm. 1993; 50:2364-5.
Ropivacaine Plain	0.1% 0.2%	- unavailable - Fresenius Kabi Inc. Naropin (ropivacaine HCl) Injection 11/2018.
Chloroprocaine	1%	B Braun Medical Inc. Clorotekal® (Chloroprocaine HCl Injection, USP) 2021
Methadone	1 mg/mL	Denson DD, Crews JC, Grummich KW et al. Stability of methadone hydrochloride in 0.9% sodium chloride injection in single-dose plastic containers. Am J Hosp Pharm. 1991; 48:515-7

ADULT EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Bupivacaine with Morphine	Bupivacaine 1. 0.0625% 2. 0.125%	Morphine 1. 0.5 mg/mL 2. 1 mg/mL		1a. Johnson CE, Christen C, Perez MM et al. Compatibility of bupivacaine hydrochloride and morphine sulfate. Am J Health-Syst Pharm. 1997; 54:61-4. 1b. Lohman JJ, et al, "Compatibility of morphine HCl and bupivacaine HCl in a portable pump reservoir", Pharm Weekbl Sci Ed, 1992; Volume 14: F27. 2a. Johnson CE, Christen C, Perez MM et al. Compatibility of bupivacaine hydrochloride and morphine sulfate. Am J Health-Syst Pharm. 1997; 54:61-4. 2b. Lohman JJ, et al, "Compatibility of morphine HCl and bupivacaine HCl in a portable pump reservoir", Pharm Weekbl Sci Ed, 1992; Volume 14: F27.
Bupivacaine with Hydromorphone	Bupivacaine 1. 0.0625% 2. 0.125%	Hydromorphone 1. 10 mcg/mL 2. 10 mcg/mL		1. Goucke RC et.al. Stability and Tolerability of High Concentrations of Intrathecal Bupivacaine and opioid Mixtures in Chronic Noncancer Pain: An Open-Label Pilot Study. Pain Medicine 2010; 11:1612-18. 2. Goucke RC et.al. Stability and Tolerability of High Concentrations of Intrathecal Bupivacaine and opioid Mixtures in Chronic Noncancer Pain: An Open-Label Pilot Study. Pain Medicine 2010; 11:1612-18.

ADULT EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Bupivacaine with Fentanyl	Bupivacaine 1. 0.0625% 2. 0.0625% 3. 0.125% 4. 0.125%	Fentanyl 1. 2 mcg/mL 2. 5 mcg/mL 3. 2 mcg/mL 4. 5 mcg/mL		1a. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998; 53:386–91. 1b. Priston MJ et. Al. Stability of an epidural analgesic admixture containing epineprine, fentanyl and bupivacaine. Anaesthesia. 2004;59:979-983. 2. Tu YH, et.al. Stability of fentanyl citrate and bupivacainehydrochloride in portable pump resevoirs. Am J Of Hosp Pharm. 1990;47:2037-40. 3a. Sattler A, Jage J. Physico-chemical stability of infusion solutions for epidural administration containing fentanyl and bupivacaine or lidocaine. Pharmazie. 1998; 53:386–91. 3b. Priston MJ et. Al. Staility of an eidural analgesic admixture containing epineprine, fentanyl and bupivacaine. Anaesthesia. 2004;59:979-983. 4. Tu YH, et.al. Stability of fentanyl citrate and bupivacainehydrochloride in portable pump resevoirs. Am J of Hosp Pharm. 1990;47:2037-40.
Bupivacaine with Clonidine	Bupivacaine 0.125%		Clonidine 1 mcg/mL	Note not exact concentrations: Schobelock MJ (Medical Affiars Department, Roxane Laboratories, Inc.); Personal communication;1997 Nov 4. In ASHP Injectable Drug Information 2020

ADULT EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Bupivacaine with Fentanyl and Clonidine	Bupivacaine 1. 0.0625% 2. 0.0625% 3. 0.125% 4. 0.125%	Fentanyl 1. 2 mcg/mL 2. 5 mcg/mL 3. 2 mcg/mL 4. 5 mcg/mL	Clonidine 1. 1 mcg/mL 2. 1 mcg/mL 3. 1 mcg/mL 4. 1 mcg/mL	- Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanylcitrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: Jappinen A et.al. chemical stability of a mixture of fentanylcitrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: JappinenA et.al. chemical stability of a mixture of fentanylcitrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21. - Note not exact concentrations: JappinenA et.al. chemical stability of a mixture of fentanylcitrate, bupivacaine hydrochloride and clonidine hydrochloride in 0.9% sodium chloride injection stored in syringes and medication cassettes. Pharm World Sci Suppl. 1996;A11:119-21.
Ropivacaine with Morphine	Ropivacaine 1. 0.1% 2. 0.2%	Morphine 1. 0.5 mg/mL 2. 1 mg/mL		- Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 - Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45

ADULT EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.



Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Ropivacaine with Hydromorphone	Ropivacaine 0.2%	Hydromorphone 10 mcg/mL		unavailable
Ropivacaine with Fentanyl	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%	Fentanyl 1. 2 mcg/mL 2. 5 mcg/mL 3. 2 mcg/mL 4. 5 mcg/mL		1. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 2. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 3. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma. 4. Trissel LA, Xu QA, "Stability of ropivacaine hydrochloride 1 and 2 mg/mL with fentanyl citrate 2, 5, and 10 mcg/mL in 0.9% sodium chloride injection at 4, 23, and 37 °C", Compatibility data, 2001; Volume 1: TriPharma.

ADULT EPIDURAL COMBINATION DRUG STANDARD CONCENTRATIONS cont.

Drug Combinations	Anesthetic concentration	Narcotic Concentration	Alpha Agonist Concentration	Stability References
Ropivacaine with Clonidine	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%		Clonidine 1. 1 mcg/mL 2. 2 mcg/mL 3. 1 mcg/mL 4. 2 mcg/mL	1. Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 2. Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 3. Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 4. Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45
Ropivacaine with Fentanyl and Clonidine	Ropivacaine 1. 0.1% 2. 0.1% 3. 0.2% 4. 0.2%	Fentanyl 1. 2 mcg/mL 2. 2 mcg/mL 3. 2 mcg/mL 4. 2 mcg/mL	Clonidine 1. 0.3 mcg/mL 2. 0.5 mcg/mL 3. 0.3 mcg/mL 4. 0.5 mcg/mL	1. Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 2. Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 3. Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45 4. Note not exact concentrations: Svedberg KO et.al. compatibility of ropivacaine with morphine, sufentanil, fentanyl and clonidine. J Clin Pharm Ther. 2002;27:39-45

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