

Guidelines for Adequate Length of Observation After Opioid Overdose

This document describes our guidelines for the minimum suitable length of observation in an ED or other appropriate healthcare setting following opioid overdose for typical situations. However, extenuating circumstances may make a different approach preferable in some instances.

The Asymptomatic Patient

The onset of potentially life-threatening respiratory depression may be delayed following an opioid overdose, particularly following an oral overdose. The patient should be observed in an ED setting (or similar healthcare setting with the same capabilities) able to treat respiratory depression for sufficient time to exclude even delayed respiratory depression. The period recommended should be the longest one (from the table below) into which any of the involved agents falls. If the patient remains asymptomatic during this observation period, they may be discharged from further medical observation to a setting suitable given any psychiatric and drug-dependence considerations.

The Symptomatic Patient

This patient requires more prolonged observation due to the possibility of further drug absorption from the GI tract (following ingestion) and redistribution from tissue stores (particularly for specific agents like diphenoxylate). We recommend that they be observed in an appropriate medical setting for at least the period below *off of all narcotic antagonist agents (e.g., naloxone)*.

Drug group	Observation time - asymptomatic	Observation time - symptomatic
Very slow onset OR sustained-release preparation	12 hrs.	24 hrs.
Moderate onset, not SR	8 hrs.	12 hrs.
Rapid onset, not SR	4 hrs.	3-6 hrs. ^{1,2^}

[^] 3-6 hours is recommended based on variability in the literature regarding observation time following the administration of naloxone. Please note that all patients should be awake with a return to their mental status baseline and stable hemodynamics prior to discharge.

TYPICAL OPIOID CLINICAL PHARMACOKINETICS

Drug Name	Oral morphine equivalent (OME) conversion factor ^{3†}	Approx. Time to Peak Plasma Level (hr.) ^{4†}	Elimination Half-Life (hr.) ⁴
Very Slow Onset (2hr), Prolonged Resp. Effects (7-14 hr.)			
Diphenoxylate	-	2	2.5
Loperamide	-	5 (capsule) 2.5 (liquid) 4 (tablet)	9-10.8
Buprenorphine	38.8 (BUC/SL) 2.2 (TD)	2.5-3 (BUC) 2.5 (SL)	1.2-7.2 (IV) 31-35 (SL)

	75 (PAR)	60 (TD)	
Moderate onset (1hr), Mod. Prolonged Resp. Effects (4-8 hr.)			
Methadone	4.7	1-7.5	8-59
Rapid Onset (15min), Limited Resp. Effect Duration (1-2 hr.)			
Codeine	0.1	1	3
Dihydrocodeine	0.1	1.6-1.8	3.4-4.5
Fentanyl*	0.1 (BUC/SL) 2.7 (TD) 0.2 (PAR)	0.67-1.5 (SL) 20-40 min (oral transmucosal) 20-72 (TD patch) 15-20 min (intranasal)	3.3-4.1 ⁷
Heroin	3.3 (PAR)	3-5 min (intranasal/IM) 5-10 min (SC)	1-1.5
Hydrocodone	1.2	1.3 (IR) 14 (ER tablet) 5 (ER capsule)	3.8 – 4.5 (IR) 7-9 (ER tablet) 8 (ER capsule)
Hydromorphone	5 17.5 (PAR)	0.75 (IR) 12 (ER) 12-16.5 (SR)	1.8 – 3 ⁷ 8-15 (ER)
Levorphanol	13.8 20 (PAR)	1	11-16
Meperidine	0.1 0.4 (PAR)	25 min (IM)	3-8
Morphine	1.0 3.0 (PAR)	1 (IR) 8.6-10.3 (ER capsule) 2.5-4.4 (ER tablet) 8.4 (SR capsule) 3-3.8 (SR tablet)	1.4-2.4 ⁷ 11-13 (ER capsule) 15 (SR)
Oxycodone	1.5 3 (PAR) 1.5 (rectal)	4.5	5.6
Oxymorphone	3 30 (PAR) 3.5 (rectal)	30 min ⁶	7.3 - 9.4
Pentazocine (Mixed agonist- antagonist)	0.6 1.1 (PAR)	0.25-1 (IM) 0.5-1 (SC)	-
Propoxyphene	0.23 ⁵	1-4	6-12
Tapentadol	0.4	1.25 (IR)	4-5

		3-6 (ER)	
Tramadol	0.2	1-2.3 (IR) 4-12 (ER)	5.6-6.7 (IR) 6.5-10 (ER)

IR = immediate release; ER = extended-release; SR = sustained-release; IM = intramuscular; SC = subcutaneous; SL = sublingual; TD = transdermal; PAR = parenteral; IV = intravenous; BUC = buccal

†Routes are oral unless otherwise indicated

*All doses are in mg except for fentanyl (doses in mcg/hr for patch and mcg for other routes)

OME formula: strength per unit × (number of units/day (or total)) × OME conversion factor = OME units per day (or total)⁴

Example OME calculation:

An individual is prescribed oxycodone 10mg #30 tablets
10mg x 30 tablets x 1.5 = **450 OME (total)**

References

1. Heaton JD, Bhandari B, Faryar KA, Huecker MR. Retrospective Review of Need for Delayed Naloxone or Oxygen in Emergency Department Patients Receiving Naloxone for Heroin Reversal. *J Emerg Med.* 2019;56(6):642-651. doi:10.1016/j.jemermed.2019.02.015
2. Boyer EW. Management of opioid analgesic overdose. *N Engl J Med.* 2012;367(2):146-155. doi:10.1056/NEJMra1202561
3. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. *Pharmacoepidemiol Drug Saf.* 2016;25(6):733-737. doi:10.1002/pds.3945
4. Data obtained from aggregated sources via Micromedex; accessed 11/14/2022
5. Jeffery MM, Morden NE, Laroche M, Shah ND, Hooten WM, Meara E. Response to Propoxyphene Market Withdrawal: Analgesic Substitutes, Doses, and Adverse Events. *Med Care.* 2020;58(1):4-12. doi:10.1097/MLR.0000000000001221
6. Adams MP, Ahdieh H. Single- and multiple-dose pharmacokinetic and dose-proportionality study of oxymorphone immediate-release tablets. *Drugs R D.* 2005;6(2):91-99. doi:10.2165/00126839-200506020-00004
7. Thummel KE, Shen DD, Isoherranen N. Design and Optimization of Dosage Regimens: Pharmacokinetic Data. In: Brunton LL, Hilal-Dandan R, Knollmann BC. eds. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics*, 13e. McGraw Hill; 2017. Accessed August 17, 2022. <https://accessmedicine-mhmedical-com.proxy.library.emory.edu/content.aspx?bookid=2189§ionid=172472741>
8. Allen T. "Narcotics", in Rosen P et al (eds). *Emergency Medicine: Concepts and Clinical Practice*. Ed 3. St. Louis: Mosby, 1992: 2603-2617.

9. Baselt RC, Cravey RH. "Oxycodone", in Baselt RC, Cravey RH. Disposition of Toxic Drugs and Chemicals in Man. Ed 3. Chicago: Yearbook Medical, 1989.

10. Ellenhorn MJ, Barceloux DG. "Opiates, Opioids, and Designer Drugs", in Ellenhorn MJ, Barceloux DG. Medical Toxicology: Diagnosis and Treatment of Human Poisoning. NY: Elsevier, 1988: 689-751.

Last Revised: October 11, 2012

Reviewed April 22, 2015

Reviewed BWM 3/2022