

Opioid Interpretation Aids

Opioid Cut-off and Approximate Urine Detection Times		
Drug/Metabolite	LC-MS/MS Cut-off (ng/mL)	Approximate Urine Drug Detection Window
Buprenorphine	10	1-7 days
Buprenorphine-glucuronide	50	1-14 days
Norbuprenorphine	10	1-14 days
Norbuprenorphine-glucuronide	10	1-14 days
Codeine	50	1-3 days
Codeine-glucuronide	50	
Heroin metabolite (6-MAM)	10	< 1 day
Hydrocodone	50	1-3 days
Norhydrocodone	50	
Dihydrocodeine	50	1-3 days
Hydromorphone	50	
Hydromorphone-glucuronide	50	
Morphine	50	1-3 days
Morphine-3-glucuronide	25	
Morphine-6-glucuronide	25	
Fentanyl	2	1-3 days
Norfentanyl	2	
Meperidine	50	1-2 days
Normeperidine	50	1-4 days
Oxycodone	50	1-3 days
Noroxycodone	50	
Oxymorphone	50	
Noroxymorphone	50	
Oxymorphone-glucuronide	50	
Tramadol	50	1-3 days
O-desmethyiltramadol	50	
Naloxone	25	1-3 days
Methadone	50	1-14 days
EDDP	50	

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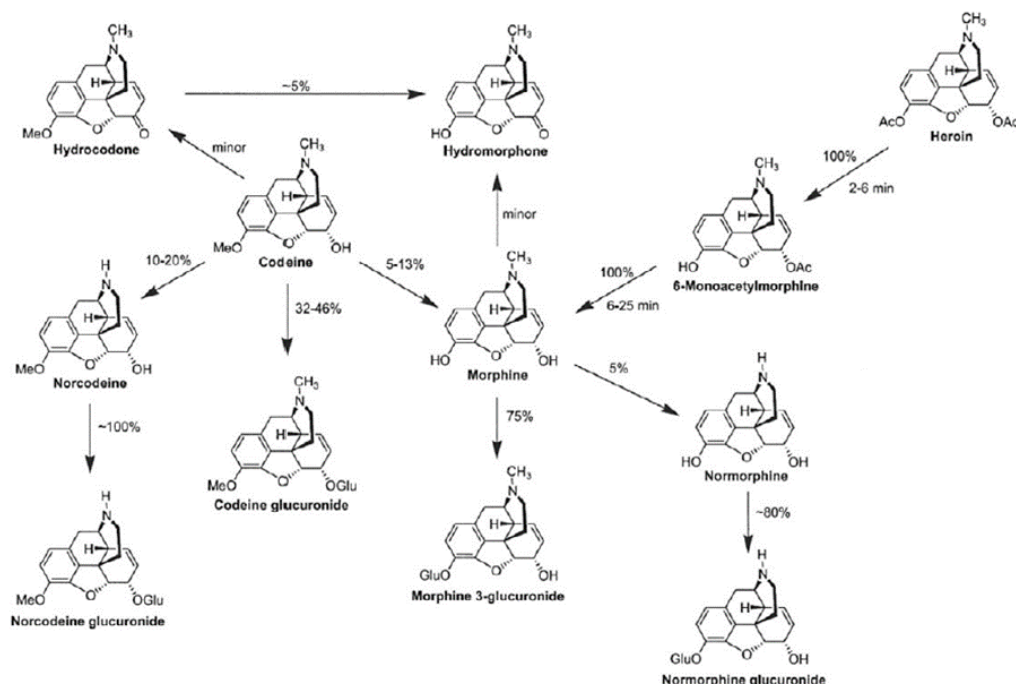


Image from Pesce, A., et al. Interpretation of Urine Drug Testing in Pain Patients. Pain Medicine 2012;13:868-885.

Opioid Expected Drug/Metabolite Patterns and Pharmaceutical Impurities		
Opioid parent	Urine drug/metabolites	Known Impurities/Contaminants ^{1,2}
Codeine	Codeine; Codeine-glucuronide; Morphine; hydrocodone;	Morphine Allowable limit 0.15% Typical 0.01 – 0.1%
Morphine	Morphine; Hydromorphone; Morphine-3-glucuronide; Morphine-6-glucuronide	Codeine Allowable limit 0.5% Typical 0.01 – 0.05%
Hydrocodone	Hydrocodone; Norhydrocodone; Hydromorphone; Hydromorphone-glucuronide; Dihydrocodeine	Codeine Allowable limit 0.15% Typical 0 – 0.1%
Hydromorphone	Hydromorphone; Hydromorphone-glucuronide	Morphine Allowable limit 0.15% Typical 0 – 0.025% Hydrocodone Allowable limit 0.1% Typical 0 – 0.025%
Oxycodone	Oxycodone; Noroxycodone; Oxymorphone; Oxymorphone-glucuronide	Hydrocodone Allowable limit 1% Typical 0.02 – 0.12%
Oxymorphone	Oxymorphone; Oxymorphone-glucuronide	Hydromorphone Allowable limit 0.15% Typical 0.03 – 0.1% Oxycodone Allowable limit 0.5% Typical 0.05 – 0.4%
Fentanyl	Fentanyl; Norfentanyl	None
Methadone	Methadone; EDDP	None
Buprenorphine	Buprenorphine; Buprenorphine-glucuronide; Norbuprenorphine; Norbuprenorphine-glucuronide	None
Tramadol	Tramadol; O-desmethyltramadol	None
Meperidine	Normeperidine	None

Heroin	6-MAM; Morphine	Acetylcodeine (which is further metabolized to codeine)
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1. Pesce, A., et al. Interpretation of Urine Drug Testing in Pain Patients. *Pain Medicine* 2012;13:868-885.

2. Nagpal, G., et al. Interpretation of Urine Drug Screens. *JAMA* 2017;318(17):1704-5.

Opioid Notes

Opioids undergo phase I metabolism by the CYP pathway, phase II metabolism by conjugation, or both. Phase I metabolism of opioids primarily involves CYP3A4 and CYP2D6 enzymes. Drug-drug interactions may occur when opioids are used concurrently with inducers or inhibitors of CYP enzymatic pathways. Morphine, oxycodone, and hydromorphone undergo phase II glucuronidation, and their glucuronide forms are directly detected by this assay.

Unlike immunoassays, the LC-MS/MS method can identify both parent compounds and their metabolites. Historically patient chronic opioid therapy (COT) non-adherence may have been presumed if both parent compound and metabolite were not present. However, more recently published evidence has demonstrated that in some cases only the metabolite may be present with no evidence of parent medication. In other cases, only high levels of the parent medication are present with little to no metabolite.

Approximately 7-10% of Caucasians lack an active CYP2D6 enzyme and are unable to metabolize codeine to morphine. Metabolism of codeine can also be impacted due to the influence of CYP2D6 inhibitors, including Paxil® or Wellbutrin®.

Hydromorphone is a minor metabolite of morphine, and its concentration rarely exceeds 2% of urine morphine concentration in patients taking morphine³.

For patients prescribed Suboxone® a metabolite-to-parent drug ratio of about 4.52 is expected³.

For patients prescribed methadone a ratio of methadone to EDDP (inactive metabolite) of about 1:1 is expected in urine³, although absolute concentrations found in a given urine sample may be highly variable. Urinary excretion of methadone decreases with increasing urine pH.

The presence of 6-acetylmorphine (6-MAM) is conclusive evidence of prior heroin use. Because half-life for 6-MAM is short, it may be detected in urine only up to 8 hours after administration. Morphine or its metabolites may be the only compound(s) detected following heroin use. Illicit heroin frequently contains small amounts of acetylcodeine, which is further metabolized to codeine. The presence of both codeine and morphine in urine does not rule out the use of heroin.

3. Sobolesky, P., et al. Interpretation of Pain Management Testing Results Using Case Examples. *JALM* 2018;2(4):610-621.