
Overview**Useful For**

Detection and quantification of codeine, hydrocodone, oxycodone, morphine, hydromorphone, oxymorphone, noroxycodone, noroxymorphone, norhydrocodone, dihydrocodeine, and naloxone in urine

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen**Specimen Type**

Urine

Ordering Guidance

For situations where chain of custody is required, a Chain-of-Custody Kit (T282) is available. For chain-of-custody testing, order OPATX / Opiates Confirmation, Chain of Custody, Random, Urine.

Additional drug panels and specific requests are available; call 800-533-1710 or 507-266-5700.

Additional Testing Requirements

If urine creatinine is required or adulteration of the sample is suspected, the following test should also be ordered, ADULT / Adulterants Survey, Random, Urine.

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Collection Container/Tube: Plastic urine container

Submission Container/Tube: Plastic, 5-mL tube

Specimen Volume: 3 mL

Collection Instructions:

1. Collect a random urine specimen.
2. No preservative.

Additional Information:

1. No specimen substitutions.
2. STAT requests are **not accepted** for this test.
3. Submitting <1 mL will compromise our ability to perform all necessary testing.

Forms

If not ordering electronically, complete, print, and send a [Therapeutics Test Request](#) (T831) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Refrigerated (preferred)	28 days	
	Frozen	28 days	
	Ambient	14 days	

Clinical and Interpretive
Clinical Information

Codeine is converted by hepatic metabolism to morphine and norcodeine with a half-life of 2 to 4 hours. If codeine is ingested, the ratio of codeine to morphine generally exceeds 1.0 in urine during the first 24 hours. The ratio may fall below 1.0 after 24 hours, and after 30 hours, only morphine may be detected.

Morphine is a naturally occurring narcotic analgesic obtained from the poppy plant, *Papaver somniferum*. Morphine is converted by hepatic metabolism to normorphine with a half-life of 2 to 4 hours. The presence of morphine in urine can indicate exposure to morphine, heroin, or codeine within 2 to 3 days. Ingestion of bakery products containing poppy seeds can also cause morphine to be excreted in urine. If excessively large amounts are consumed, this can result in urine morphine concentrations up to 2000 ng/mL for a period of 6 to 12 hours after ingestion.

Hydrocodone exhibits a complex pattern of metabolism including O-demethylation, N-demethylation, and 6-keto reduction to the 6-beta hydroxymetabolites. Hydromorphone and norhydrocodone are both metabolites of hydrocodone. Dihydrocodeine is also a minor metabolite. Trace amounts of hydrocodone can also be found in the presence of approximately 100-fold higher concentrations of oxycodone or hydromorphone since it can be a pharmaceutical impurity in these medications. The presence of hydrocodone greater than 100 ng/mL indicates exposure within 2 to 3 days prior to specimen collection.

Hydromorphone is metabolized primarily in the liver and is excreted primarily as the glucuronidated conjugate, with small amounts of parent drug and minor amounts of 6-hydroxy reduction metabolites. The presence of hydromorphone greater than 100 ng/mL indicates exposure within 2 to 3 days prior to specimen collection. Hydromorphone is also a metabolite of hydrocodone; therefore, the presence of hydromorphone could also indicate exposure to hydrocodone.

Dihydrocodeine is a semisynthetic narcotic analgesic prepared by the hydrogenation of codeine. It is also a minor metabolite of hydrocodone. It is metabolized to dihydromorphone and has a half-life of 3.4 to 4.5 hours.

Oxycodone is metabolized to noroxycodone, oxymorphone, and their glucuronides, and is excreted primarily via the kidney. The presence of oxycodone greater than 100 ng/mL indicates exposure to oxycodone within 2 to 3 days prior to specimen collection.

Oxymorphone is metabolized in the liver to noroxymorphone and excreted via the kidney primarily as the glucuronide conjugates. Oxymorphone is also a metabolite of oxycodone and, therefore, the presence of oxymorphone could also indicate exposure to oxycodone.

Naloxone is a synthetic narcotic antagonist and used for partial or complete reversal of opioid depression induced by natural or synthetic opioids. It has also been incorporated into oral tablets of opioids to discourage abuse. The duration of action is dependent on the dose and route of administration. The half-life in adults is approximately 30 to 81 minutes.

The detection interval for opiates is generally 2 to 3 days after last ingestion.

Reference Values

Negative

Cutoff concentrations by liquid chromatography-tandem mass spectroscopy:

Codeine: 25 ng/mL

Dihydrocodeine: 25 ng/mL

Hydrocodone: 25 ng/mL

Norhydrocodone: 25 ng/mL

Hydromorphone: 25 ng/mL

Oxycodone: 25 ng/mL

Noroxycodone: 25 ng/mL

Oxymorphone: 25 ng/mL

Noroxymorphone: 25 ng/mL

Naloxone: 25 ng/mL

Morphine: 25 ng/mL

Interpretation

This test reports the total urine concentration; this is the sum of the unconjugated and conjugated forms of the parent drug.

Cautions

This test detects drugs structurally similar to morphine. Other drugs in the opioid class, such as fentanyl, meperidine, and methadone are not detected.

Clinical Reference

1. Gutstein HB, Akil H: Opioid analgesics. In: Brunton LL, Lazo JS, Parker KL, eds. Goodman and Gilman's The

Pharmacological Basis of Therapeutics. 11th ed. McGraw-Hill; 2006:chap 21

2. Baselt RC: Disposition of Toxic Drugs and Chemical in Man. 9th ed. Biomedical Publication; 2011

3. Hackett LP, Dusci LJ, Ilett KF, Chiswell GM: Optimizing the hydrolysis of codeine and morphine glucuronides in urine. Ther Drug Monit. 2002;24(5):652-657

4. Langman LJ, Bechtel LK, Meier BM, Holstege C: Clinical toxicology. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:832-887

Performance

Method Description

Opiates exist in patient urine as both free and either sulfate or glucuronide conjugates. Enzyme hydrolysis is used to liberate the conjugated drug. Specimens are then centrifuged, diluted, and filtered and the analytes are separated by liquid chromatography tandem mass spectroscopy and analyzed by multiple reaction monitoring. (Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 5 days

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

80361

80365

80362

G0480 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
OPATU	Opiate Confirmation, U	In Process

Result ID	Test Result Name	Result LOINC Value
6543	Codeine-by LC-MS/MS	16250-3
42000	Dihydrocodeine-by LC-MS/MS	19448-0
21177	Hydrocodone-by LC-MS/MS	16252-9
42001	Norhydrocodone-by LC-MS/MS	61422-2
21179	Hydromorphone-by LC-MS/MS	16998-7
21178	Oxycodone-by LC-MS/MS	16249-5
42002	Noroxycodone-by LC-MS/MS	61425-5
35023	Oxymorphone-by LC-MS/MS	17395-5
42003	Noroxymorphone-by LC-MS/MS	90894-7
42004	Naloxone-by LC-MS/MS	77207-9
6542	Morphine-by LC-MS/MS	16251-1
21180	Opiates Interpretation	18390-5