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THREE NEW QUANTITATIVE URINE DRUG TESTS AVAILABLE THIS MONTH: 6-MONOACETYLMORPHINE, METHYLPHENIDATE, AND BUPRENORPHINE

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6-MONOACETYLMORPHINE (HEROIN METABOLITE), URINE

Effective October 8, 2012, a quantitative urine test for the heroin metabolite 6-monoacetylmorphine (6-MAM) will be available. This test should be ordered when heroin use is suspected. The test can be ordered on its own or in conjunction with other toxicology tests. Specimens are kept in the laboratory for six business days after the initial results are reported, therefore, 6-MAM testing can be ordered and/or added within this time frame if reported toxicology test results show the presence of unexpected morphine (i.e. codeine or morphine is not prescribed). The test is performed by a GC/MS method and the lowest reportable level is 2 ng/mL.

6-Monoacetylmorphine (6-MAM) is a metabolite of heroin (3,6-diacetylmorphine). After heroin exposure, either by inhalation, injection, or ingestion, the drug is rapidly deacetylated (half-life 2-6 minutes) at position 3 to form 6-MAM. 6-MAM is then deacetylated at position 6 at a slower rate (half-life 6-25 minutes) to morphine. Morphine is conjugated to glucuronic acid and excreted in urine. In one study, about 45% of the heroin was recovered as urinary metabolites over a 40 hour period: 4.2% free morphine, 38.3% conjugated morphine, 1.3% 6-MAM and 0.1% unchanged heroin (1).

6-MAM arises only from metabolism of heroin. It is not found in poppy seeds and is not a metabolic product of morphine, codeine, or any other opiate. Therefore, the presence of 6-MAM in urine is firm evidence of heroin use. Although 6-MAM can be present in urine of a majority of chronic

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heroin users, failure to detect 6-MAM does not rule out heroin use because 6-MAM is only present at low concentrations and for a relatively short time after use of the drug.

METHYLPHENIDATE AND METABOLITE (RITALINIC ACID), URINE

Effective October 15, 2012, a quantitative urine methylphenidate test will be performed by Marshfield Labs Toxicology Services.

Methylphenidate (Ritalin, Concerta, Methylin) is a psychostimulant drug approved by the FDA in 1955 for treatment of attention deficit hyperactivity disorder (ADHD) in adults and children. It has been heavily prescribed since the 1990s, when ADHD became more widely accepted. Methylphenidate is also prescribed for treatment of postural orthostatic tachycardia syndrome and narcolepsy.

Once ingested, methylphenidate is rapidly biotransformed to ritalinic acid, an inactive metabolite. About 80% of a dose is eliminated in the urine in a 24-hour period, primarily as ritalinic acid (60-81%) and 6-oxo-ritalinic acid (5-12%). Less than 1% of a dose is excreted unchanged in urine (2). The elimination half-life of methylphenidate is 1.4-4.2 hours. Methylphenidate is habit-forming, thus the potential for abuse and diversion is high with its high prescription rate.

The quantitative methylphenidate test by GC/MS will replace the current qualitative test, which can only detect the unchanged parent drug (methylphenidate) at levels above 200 ng/mL. The new test detects the parent drug (methylphenidate) and its major metabolite (ritalinic acid) at the sensitivity of 25 and 75 ng/mL, respectively. Normally, ritalinic acid is present in urine at concentrations 10 to 100 times more than methylphenidate, which makes the new test much more sensitive and accurate to monitor the use of methylphenidate.

BUPRENORPHINE AND METABOLITE (NORBUPRENORPHINE), URINE

Effective October 24, 2012, quantitative urine buprenorphine testing will be performed by Marshfield Labs Toxicology Services.

Buprenorphine (Buprenex, Buprex, Subutex, Transtec, Suboxone) is a synthetic thebaine derivative that has both analgesic and opioid antagonist properties. In October 2002, the FDA approved Subutex and Suboxone for detoxification and long-term replacement therapy as an alternative for methadone therapy

How to order: 6-Monoacetylemorphine (Heroin Metabolite), Urine:

Lab Test Code:
HEROIN

Clinic (Clinical Order Manager): 6-MAM (Heroin Metabolite), Urine

Hospital (Centricity): 6-MAM (Heroin Metabolite), Urine
Downtime: Write-In (Form I)

Specimen Requirements:
Urine, Minimum 5 mL

Storage:
Room temperature up to 48 hours; Refrigerate after 2 days.

How to order: Methylphenidate and Metabolite, Urine

Lab Test Code:
MPHEND

Clinic (Clinical Order Manager): Methylphenidate, Urine

Hospital (Centricity):
Methylphenidate, Urine
Downtime: Write-In (Form I)

Specimen Requirements:
Urine, Minimum 10 mL

Storage:
Refrigerate

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in opioid dependency, and it is used predominantly for this purpose. More recently, buprenorphine has been prescribed for managing moderate to severe chronic pain patients who are opioid intolerant. The rising use of buprenorphine has resulted in increased demand for testing to monitor patient compliance.

Buprenorphine (Bup) is metabolized in humans to norbuprenorphine (NorBup), which is pharmacologically active. Both forms are glucuronide conjugated prior to elimination (elimination half-lives averaged 28 and 83 hours for Bup and NorBup, respectively). Approximately 68% of a dose is eliminated in feces and 27% in urine (3). Free and conjugated Bup and NorBup are present in urine. A study of 2,477 urine samples submitted for Bup/NorBup analysis reported that over 99.32% of positive samples contained either one or both of the conjugated NorBup and free NorBup. Typically, the NorBup concentration is about 10 fold higher than that of the parent drug, Bup (4).

Our test uses an enzymatic digestion first to liberate the bound (conjugated) Bup and NorBup followed by a Liquid Chromatography/Quadrapole Time of Flight Mass Spectrometry (LCQToF) analysis to quantify the total (bound and free) Bup and NorBup. The sensitivity of the test is 2 ng/mL for Bup and 5 ng/mL for NorBup. Urinary Bup and NorBup concentrations and the ratio of these two forms vary significantly depending on the time since last exposure and other factors that can influence the metabolic rate of the drug. The range of the metabolic ratio of NorBup/Bup was reported between 0.5 to 316, with the mean around 20-32. However, when the ratio of NorBup/Bup is below 0.002, high Bup but little or no NorBup detected, adulteration is suspected (4).

For questions regarding these new tests, please call Marshfield Labs Toxicology Services directly at 800-331-3734 or 715-389-3734.

REFERENCES

1. Heroin. In *Disposition of Toxic Drugs and Chemicals in Man*, 8th edition, (R.C. Baselt) Biomedical Publications, 2008, pp. 730-735.
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3. Buprenorphine. In *Disposition of Toxic Drugs and Chemicals in Man*, 8th edition, (R.C. Baselt) Biomedical Publications, 2008, pp. 190-192.
4. G.A. McMillin, R Davis et al., Patterns of free (unconjugated) buprenorphine, norbuprenorphine, and their glucouronides in urine using liquid chromatography-tedem mass spectrometry. JAT 2012; 36:3681-87.

How to order:
Buprenorphine, Urine

Lab Test Code:
BUP

Clinic (Clinical Order Manager): Buprenorphine, Urine

Hospital (Centricity):
Buprenorphine, Urine
Downtime: Write-In (Form I)

Specimen Requirements:
Urine, Minimum 10 mL

Storage:
Room temperature up to 48 hours; Refrigerate after 2 days.