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False-positive urine drug screens: What clinicians should know and when the laboratory should be consulted

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Urine drug screens (UDS) are frequently ordered on patients who exhibit symptoms of intoxication, experience trauma or offer a history of drug ingestion.[1] Rapid and accurate results are critical to manage patients effectively; however, inconsistencies between the laboratory results and the clinical picture may be present.

Consider the following scenarios: (1) A 60-year-old male tests positive for urine amphetamine, but adamantly denies amphetamine use and (2) an 80-year-old woman from a nursing home tests positive for urine opiates, but her list of medications does not include opioids. How should these scenarios be handled? Clinicians should understand what urine drug screens are designed to detect, which compounds can cross-react and when to refer to the laboratory for further testing or clarification.

Immunoassays for UDS are automated and offer rapid turnaround times.[1,2] The common drugs or classes of drugs in the UDS include amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine metabolite, methadone, opiates, phencyclidine and tricyclic antidepressants. Several different immunoassay techniques and platforms are available.[3] Depending on the assay, an antibody is designed to detect a specific class of compounds (i.e. barbiturates), a parent drug (i.e. methadone) or a metabolite (i.e. benzoylecgonine, a metabolite of cocaine).

Qualitative results are based on a specific calibrator concentration. Positive results reflect a concentration above the calibrator cutoff, while negative results reflect concentrations below the cutoff and do not exclude the presence of drug or metabolite. The antibody specificity varies within the drug class and each individual drug, within the class, requires a different urine concentration to trigger a positive result. Certain antibodies may also cross-react with medications outside the target drug class, thus leading to false-positive results.

The extent of cross-reactivity depends on the manufacturer's platform and the assay cutoff. The EMIT II and Triage meters are two common platforms.[4,5] The table contains a list of potential interferents in each assay. In the EMIT II

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platform, medications—such as ranitidine and drug metabolites of compounds, such as chlorpromazine and bupropion—can cross-react in the amphetamine assay.[6,7] Therapeutic concentrations of the fluoroquinolone antibiotics, ofloxacin and levofloxacin, can interfere in the EMIT II opioid assay.[4]

Over-the-counter remedies can produce false-positive results in the EMIT II phencyclidine and benzodiazepine assays and the Triage cannabinoid assay.[4,5] The muscle relaxant cyclobenzaprine can cross-react in the Triage tricyclic assay.[5] Neither the EMIT II nor the Triage has reported false positives in the barbiturate, methadone or cocaine assay.

Clinicians should appreciate the limitations of UDS in the medical setting, and consider potential interferences. If a physician suspects a false positive, the laboratory should be notified and the specimen should be sent for confirmatory testing. In the scenarios above, the laboratory, which performed the UDS using the EMIT II platform, was consulted. Confirmatory testing revealed that both urine drug screens were falsely positive.

Analytes	**Cutoff (EMIT II)**	**EMIT II (Syva)**	**Cutoff (Triage)**	**Triage (Biosite)**
Amphetamine and/or Methamphetamine	1000 ng/mL	**Ranitidine** **Chlorpromazine*** **Bupropion***	1000 ng/mL	
Barbiturates	200 ng/mL 300 ng/mL		300 ng/mL	
Benzodiazepins	200 ng/mL 300 ng/mL	**Oxaprozin**	300 ng/mL	
Cannabinoids	20 ng/mL 50 ng/mL 100 ng/mL		50 ng/mL	**Pantoprazole**
Cocaine	150 ng/mL 300 ng/mL		300 ng/mL	
Methadone	150 ng/mL 300 ng/mL		N/A	
Opiates	300 ng/mL 2000 ng/mL	**Ofloxacin** **Levofloxacin**	300 ng/mL	
PCP	25 ng/mL	**Dextromethorphan** **Dextrophan** **Mesoridazine**	25 ng/mL	
Tricyclics	N/A		300 ng/mL 1000 ng/mL	**Cyclobenzaprine**

Table: Possible Interferents in Two Common Urine Drug of Abuse Assays. The calibrator cutoff options for both the EMIT II plus and the Triage are listed. Note that the medications listed above are potential interferents and will not cross-react in all patients. Results must be interpreted in conjunction with the clinical impression result and confirmatory testing results.

- *In some instances, a metabolite, not the parent compound, is causing interference.

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Scenario 1 (Answer): The 60-year-old male was taking ranitidine for his gastroesophageal reflux disease, which cross-reacts in the EMIT amphetamine assay.

Scenario 2 (Answer): The 80-year-old woman was prescribed levofloxacin for pneumonia, which interferes with the EMIT opiate assay.

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