



Clinical Update: June 2019

What Did My Patient Actually Take? An Overview of Amphetamine Results

When reviewing unexpected drug testing results, many providers question, “**What did my patient actually take?**” In this month’s clinical update, we examine the interpretation of amphetamine results from Aegis Sciences Corporation. Please note that the interpretation of amphetamine assays differs when using presumptive vs. definitive testing methods, and may differ among laboratories. The information provided here is intended to assist providers with deciphering amphetamine results from Aegis, which have undergone definitive testing by liquid chromatography / tandem mass spectrometry prior to reporting.

Results of drug testing may be **unexpectedly negative or positive**. In the case of **unexpected positive** amphetamine results, consider the following drug exposures:

- **Pharmaceutical amphetamine products** such as Adderall®, Adderall XR®, Vyvanse®, Dexedrine®, Evekeo®, Adzenys XR®, Dynavel XR®, Mydayis®, or the generic equivalents of these products.
- Amphetamine is also a **metabolite of methamphetamine**, but in the case of methamphetamine exposure, methamphetamine is typically also present.¹

Example of Expected Positive Amphetamine Result:

Medication Compliance

Drug and/or Metabolites	Result Interpretation	Result	Comment
Amphetamine	COMPLIANT	3,400 ng/mL	Test result is consistent and expected with prescribed drug.

Example of Unexpected Positive Amphetamine Result:

Medication Compliance

Drug and/or Metabolites	Result Interpretation	Result	Comment
Buprenorphine	COMPLIANT	954 ng/mL	Test result is consistent and expected with prescribed drug.
Amphetamine	PRESENT	4,230 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.

In the case of **unexpected negative** amphetamine results, there are several points to consider:

Medication Compliance

Drug and/or Metabolites	Result Interpretation	Result	Comment
Amphetamine	Inconsistent	<250 ng/mL	Test result indicates patient may not be taking drug prescribed.

Example of Unexpected Negative Amphetamine Result:

What medication is the patient prescribed?

The pharmaceutical amphetamine products mentioned above are detected as amphetamines on Aegis testing. However, a common misconception is that methylphenidate products are also included in this

testing. Methylphenidate is structurally distinct from amphetamine, and undergoes a separate testing process at Aegis. Providers wishing to assess compliance of methylphenidate medications (i.e., Daytrana®, Ritalin®, Quillivant XR®, Metadate ER®, Aptensio XR®, Cotempla XR-ODT®, QuilliChew ER®, Concerta®, Methylin®, Ritalin LA®, Focalin®, Focalin XR®) may consider adding this test which is currently only available in urine.

Example of unexpected negative amphetamine result in patient actually prescribed methylphenidate
(Methylphenidate testing was added for the sample after consultation with Aegis Clinical Team):

Medication Compliance

Drug and/or Metabolites	Result Interpretation	Result	Comment
Amphetamine	NON-COMPLIANT	<250 ng/mL	Test result indicates patient may not be taking drug prescribed.
Methylphenidate	PRESENT	8,420 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.

When was the patient’s last dose? Was the sample collected after a “drug holiday”?

Many patients taking amphetamines for attention or hyperactivity disorders take a break from their medication on weekends, holidays, or other times when their symptoms are not as disruptive (time away from school or work). This type of dosing schedule is typically discussed between provider and patient so the provider is aware of how often the patient may need a new prescription. If a patient provides a urine sample on a Monday, for example, and they have been without their amphetamine since the previous Friday, a negative result may be consistent with this dosing. In a study by Cody, *et al.*, where subjects ingested Adderall 20 mg daily for five days, urine drug concentrations declined following drug discontinuation to below the Aegis threshold of 250 ng/mL after 27 to 45 hours, depending on the patient.²

Has the patient recently experienced vomiting or diarrhea?

Vomiting and diarrhea can disrupt normal absorption and metabolism of medications and reduce excreted amounts to undetectable levels. Consider recent gastrointestinal illness in the interpretation of unexpected negative results.

If evaluating urine results, is the sample dilute? Is the urine pH elevated?

Aegis provides special report comments to alert providers when the urine creatinine falls below 20 mg/dL. Urine samples with such a low creatinine level are less concentrated, and urine drug concentrations may fall below the reporting threshold in such samples. Patients who drink a lot of water, consume caffeine, take diuretic medications, have disorders of antidiuretic hormone, or other physiologic disturbances affecting urinary concentration may produce less concentrated urine. Intentional dilution may occur either with intentional ingestion of copious amounts of water or by adding water to the urine sample from the restroom sink or toilet. Such aberrant behavior should be considered in the context of the entire patient presentation with a provider using his or her clinical judgment to assess this possibility. Coloring the toilet water blue prior to sample collection and assessing the urine temperature within 4 minutes of collection (should be between 90°F and 100°F) are additional measures to check for sample tampering.³⁻⁴ Although the impact of urine pH would not likely be so significant to cause unexpected negative results, providers may consider that an elevated urine pH may cause reduced excretion of unchanged amphetamine. Urine pH may be elevated as a natural physiologic response to regulate the body’s acid-base balance, or it may also be elevated if the urine was not stored properly prior to shipment.

Further information regarding specimen tampering is available in the Aegis Clinical Reference Guide at <https://www.aegislabs.com/resources/clinical-reference-guide/>. Click on the title “Specimen Validity Testing and Specimen Tampering” and download a copy of this chapter.

A discussion of unexpected amphetamine results must also include a quick review of some common **misconceptions**:

Prescription and Over-the-Counter Medications

Some point-of-care testing (POCT) devices may result in a false positive for amphetamines in patients who are taking certain prescription, over-the-counter, or illicit medications. Cross reactivity can occur with this type of testing among drugs with similar chemical structures.⁵⁻⁷ Non-amphetamine prescription, illicit, or over-the-counter drugs would **not** cause a false positive for amphetamine on Aegis definitive testing. Please see below for a list of drugs which may cause a false positive for amphetamine on POCT.^{4,8-17} Drugs marked with an asterisk (*) either contain or metabolize to amphetamine, and are therefore a true positive result. Because some of these are over-the-counter, the interpretation may not be easily obtained from the medical record. Please refer to the package insert that came with the POCT device being used or contact the manufacturer for more information regarding which drugs may cause false positive results as this information may differ among devices and manufacturers.

IMMUNOASSAY TEST	POTENTIAL DRUGS CAUSING A FALSE POSITIVE OR UNEXPECTED POSITIVE RESULT		
Amphetamines	Amantadine	Ginkgo	Phenylephrine
	Aripiprazole	Isometheptene	Phenylethylamine
	Benzphetamine*	Isoxsuprine	Phenylpropanolamine
	Brompheniramine	Labetalol	Promethazine
	Bupropion	l-Methamphetamine (OTC vapoinhaler)*	Propranolol
	Cathine	m-Chlorophenylpiperazine (mCPP)	Propylhexedrine
	Chloroquine	MDA	Pseudoephedrine
	Chlorpromazine	MDMA	Pyrovalerone
	Ciprofloxacin	MDPV	Ranitidine
	Clobenzorex	Mefanamic acid	Ritodrine
	Desipramine	Mephentermine	Selegiline
	Dimethylamylamine	Metformin	SodiumCyclamate
	Doxepin	Methamphetamine*	Thioridazine
	Ephedra	Methylphenidate	Trancyclopromine
	Ephedrine	Metronidazole	Trazodone
	Fenfluramine	Ofloxacin	Trimethobenzamide
	Fenproporex	Phenmetrazine	Trimipramine
	Fluorescein	Phenothiazines	Tyramine
	Fluoxetine	Phentermine	

Workout Enhancements / Dietary Supplements

Amphetamines are controlled substances and would not be expected to be found in over-the-counter supplements. While supplements are not developed or regulated with the same level of oversight as FDA-approved drugs, the presence of controlled substances such as amphetamines in over-the-counter supplements is not likely.

At Aegis, we understand your concerns as you evaluate definitive drug testing results. Unexpected amphetamine results may be indicative of noncompliance, drug misuse, or diversion, and we welcome your calls and e-mails for assistance in interpreting these results.

Please call our clinical team at 1-877-552-3232 if you require additional information.

NOTICE: The information above is intended as a resource for health care providers. Providers should use their independent medical judgment based on the clinical needs of the patient when making determinations of who to test, what medications to test, testing frequency, and the type of testing to conduct.

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