

Overview**Useful For**

Monitoring tobacco use

Monitoring patients on nicotine-replacement therapy for concurrent use of tobacco products

Method Name

LiquidChromatography-TandemMassSpectrometry(LC-MS/MS)

NY State Available

Yes

Specimen**Specimen Type**

Urine

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Container/Tube: Plastic, 5 mL, aliquot tube

Specimen Volume: 3 mL

Collection Instructions:

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

Forms

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

Specimen Minimum Volume

2 mL

Reject Due To

Gross hemolysis	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Ambient (preferred)	28 days	
	Frozen	365 days	

Specimen Type	Temperature	Time	Special Container
	Refrigerated	28 days	

Clinical and Interpretive

Clinical Information

Tobacco use is the leading cause of death in the United States. Nicotine, coadministered in tobacco products such as cigarettes, pipe, cigar, or chew, is an addicting substance that causes individuals to continue use of tobacco despite concerted efforts to quit. Nicotine stimulates dopamine release and increases dopamine concentration in the nucleus accumbens, a mechanism that is thought to be the basis for addiction for drugs of abuse.

Nicotine is rapidly metabolized in the liver to cotinine, exhibiting an elimination half-life of 2 hours. Cotinine exhibits an apparent elimination half-life of 15 hours. Patients using tobacco products excrete nicotine in urine in the concentration range of 1,000 to 5,000 ng/mL. Cotinine accumulates in urine in proportion to dose and hepatic metabolism (which is genetically determined); most tobacco users excrete cotinine in the range of 1,000 to 8,000 ng/mL. Urine concentrations of nicotine and metabolites in these ranges indicate the subject is using tobacco or is receiving high-dose nicotine patch therapy.

In addition to nicotine and metabolites, tobacco products also contain other alkaloids that can serve as unique markers of tobacco use. Two such markers are anabasine and nornicotine. Anabasine is present in tobacco products, but not nicotine replacement therapies. Nornicotine is present as an alkaloid in tobacco products and as a metabolite of nicotine. The presence of anabasine greater than 10 ng/mL or nornicotine greater than 30 ng/mL in urine indicates current tobacco use, irrespective of whether the subject is on nicotine replacement therapy. The presence of nornicotine without anabasine is consistent with use of nicotine replacement products. Heavy tobacco users who abstain from tobacco for 2 weeks exhibit urine nicotine values below 30 ng/mL, cotinine values below 50 ng/mL, anabasine levels below 2 ng/mL, and nornicotine levels below 2 ng/mL.

Passive exposure to tobacco smoke can cause accumulation of nicotine metabolites in nontobacco users. Urine cotinine has been observed to accumulate up to 20 ng/mL from passive exposure. Neither anabasine nor nornicotine accumulates from passive exposure.

Tobacco users engaged in programs to abstain from tobacco require support in the form of counseling, pharmacotherapy, and continuous encouragement. Occasionally, counselors may elect to monitor abstinence by biochemical measurement of nicotine and metabolites in a random urine specimen to verify abstinence. If results of biologic testing indicate the patient is actively using a tobacco product during therapy, additional counseling or intervention may be appropriate.

Quantification of urine nicotine and metabolites while a patient is actively using a tobacco product is useful to define the concentrations that a patient achieves through self-administration of tobacco. Nicotine replacement dose can then be tailored to achieve the same concentrations early in treatment to assure adequate nicotine replacement so the patient may avoid the strong craving they may experience early in the withdrawal phase. This can be confirmed by measurement of urine nicotine and metabolite concentrations at steady-state (2-3 days after replacement therapy is started). Once the patient is stabilized on the dose necessary to achieve complete replacement and responding well to therapy, the replacement dose can be slowly tapered to achieve complete withdrawal.

Reference Values

Non-tobacco user with no passive exposure:

NICOTINE

<5.0 ng/mL

COTININE

<5.0 ng/mL

ANABASINE

<2.0 ng/mL

NORNICOTINE

<2.0 ng/mL

Interpretation

Urine nicotine in the range of 1,000 to 5,000 ng/mL with cotinine in the range of 1,000 to 8,000 ng/mL indicates the subject is either actively using a tobacco product or on high-dose nicotine patch therapy.

The presence of anabasine and nornicotine indicates a subject on patch therapy who is actively using a tobacco product.

Typical findings are as follows:

While using a tobacco product:

- Peak nicotine concentration: 1,000 to 5,000 ng/mL
- Peak cotinine concentration: 1,000 to 8,000 ng/mL
- Anabasine concentration: 10 to 500 ng/mL
- Nornicotine concentration: 30 to 900 ng/mL

Tobacco user after 2 weeks complete abstinence:

- Nicotine concentration: <30 ng/mL
- Cotinine concentration: <50 ng/mL
- Anabasine concentration: <2.0 ng/mL
- Nornicotine concentration: <2.0 ng/mL

Nontobacco user with passive exposure:

- Nicotine concentration: <20 ng/mL
- Cotinine concentration: <20 ng/mL
- Anabasine concentration: <2.0 ng/mL
- Nornicotine concentration: <2.0 ng/mL

Nontobacco user with no passive exposure:

-Nicotine concentration: <5.0 ng/mL

-Cotinine concentration: <5.0 ng/mL

-Anabasine concentration: <2.0 ng/mL

-Nornicotine concentration: <2.0 ng/mL

Cautions

Knowledge of time elapsed between last dose and specimen collection is important for interpretation of test results.

Clinical Reference

1. Dale LC, Hurt RD, Hays JT: Drug therapy to aid in smoking cessation. Tips on maximizing patients' chances for success. *Postgrad Med* 1998;104:75-78, 83-84

2. Moyer TP, Charlson JR, Enger RJ, et al: Simultaneous analysis of nicotine, nicotine metabolites, and tobacco alkaloids in serum or urine by tandem mass spectrometry, with clinically relevant metabolic profiles. *Clin Chem* 2002;48:1460-1471

Performance

Method Description

Nicotine and metabolites are extracted from urine by solid-phase extraction techniques. The extract eluate is quantified by high-performance liquid chromatography-tandem mass spectrometry. (Moyer TP, Charlson JR, Enger RJ, et al: Simultaneous analysis of nicotine, nicotine metabolites, and tobacco alkaloids in serum or urine by tandem mass spectrometry, with clinically relevant metabolic profiles. *Clin Chem* 2002;48:1460-1471)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

2 to 5 days

Specimen Retention Time

2 weeks

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 U.S. Food and Drug Administration.

CPT Code Information

80323

G0480 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
NICOU	Nicotine and Metabolites, U	43125-4

Result ID	Test Result Name	Result LOINC Value
82510	Nicotine	3854-7
21321	Cotinine	10366-3
21324	Nornicotine	33917-6
21323	Anabasine	33915-0