Anthem

Clinical UM Guideline

Subject: Drug Testing or Screening in the Context of Substance Use Disorder and Chronic Pain
Guideline #: CG-LAB-09 **Publish Date:** 01/03/2024
Status: Reviewed **Last Review Date:** 11/09/2023

Description

This document addresses the use of drug testing (using urine, blood, saliva, sweat or hair) in the outpatient setting for adherence monitoring in the following situations:

- controlled substance use as part of the management of chronic pain
- individuals undergoing treatment for opioid addiction and/or substance use disorder.

Note: This document **does not address** the use of urine drug testing in the following circumstances:

- Emergency department testing, including for the detection of potential overdose or poisoning.
- Screening for commercial drivers licensing, or any other job-related testing.
- State/legally mandated drug testing.

Note: Drug testing or screening for employment issues may be addressed in the member certificate. Please refer to the member's benefits for further information.

Note: Sample validation is a method that is sometimes needed to assure source integrity. Quality assurance to assure sample integrity is part of expected clinical laboratory test management.

Note: For more information about pain biomarker urine testing, please see:

- LAB.00048 Pain Management Biomarker Analysis

Clinical Indications

Medically Necessary:

Presumptive urine drug testing (UDT) to verify compliance with treatment, identify undisclosed drug use or abuse, or evaluate aberrant* behavior is considered **medically necessary** up to 24 times per year, beginning at the start of treatment, as part of a monitoring program tailored to the unique needs of individuals who are:

A. Receiving treatment for chronic pain with prescription opioid or other potentially abused medications;**or**
B. Undergoing treatment for, or monitoring for relapse of, opioid addiction or substance use disorder.

Presumptive urine drug testing is also considered **medically necessary** for the following:

A. To assess an individual when clinical evaluation suggests use of non-prescribed medications or illegal substances;**or**
B. On initial entrance into a pain management program or substance use disorder recovery program.

Definitive urine drug testing to verify compliance with treatment, identify undisclosed drug use or abuse, or evaluate aberrant* behavior is considered **medically necessary** up to 24 times per year, beginning at the start of treatment, as part of a monitoring program tailored to the unique needs of individuals whose requests meet criteria *both* A and B below:

A. Testing indications- *either* 1 or 2 below must be present:
    1. Receiving treatment for chronic pain with prescription opioid or other potentially abused medications;**or**
    2. Undergoing treatment for, or monitoring for relapse of, opioid addiction or substance use disorder;
    and
B. Testing scenarios- *either* 1 or 2 below have been met:
    1. Definitive testing following prior presumptive testing:
        a. The *presumptive* urine drug testing was done for a medically necessary reason;**and**
        b. The *presumptive* test was positive for an illegal drug (for example, but not limited to methamphetamine or cocaine), positive for a prescription drug with abuse potential which was not prescribed, or negative for prescribed medications; **and**
            i. The specific *definitive* test(s) ordered are supported by documented rationale for each test ordered;**and**
            ii. Clinical documentation reflects how the results of the test(s) will be used to guide clinical care;
            or
    2. Definitive testing without prior presumptive testing:
        a. *Presumptive* urine drug tests are not available for the drug in question (examples may include, opioids and their metabolites such as fentanyl, meperidine, tramadol, and tapentadol, muscle relaxants and their metabolites such as carisoprodol, synthetic cannabinoids and their metabolites, as well as cathinones ["Bath Salts"] and their metabolites); **and**
        b. The specific *definitive* test(s) ordered are supported by documented rationale for each test ordered;**and**
        c. Clinical documentation reflects how the results of the test(s) will be used to guide clinical care.

*Aberrant behavior includes, but is not limited to, lost prescriptions, repeated requests for early refills, prescriptions from multiple providers, unauthorized dose escalation, and apparent intoxication.

Note: Each definitive test request must be based on the tested individual's diagnosis, substance use patterns, results of presumptive testing and other clinical factors documented in the medical record. Community patterns of illicit drug use must not be imputed to an individual without a documented rationale. UDT monitoring of prescribed drugs is not a clinically appropriate way to estimate the therapeutic effectiveness of prescribed drugs. Definitive testing for more than 7 classes of drugs (including metabolites) would be unusual for most individuals. For a list of drug classes, see the Appendix below.

The use of *blood* samples as an alternative to urine for drug testing is considered **medically necessary** when the use of urine is not feasible (for example, when an individual has advanced kidney failure).

Not Medically Necessary:

The use of *presumptive* urine drug testing is considered **not medically necessary** when the criteria above are not met.

The use of *definitive* urine drug testing is considered **not medically necessary** when the criteria above are not met.

The use of presumptive or definitive testing panels is considered **not medically necessary** unless all components of the panel have been determined to be medically necessary based on the criteria above. However, individual components of a panel may be considered medically necessary when criteria above are met.

The use of blood samples for drug testing is considered **not medically necessary** in all other circumstances, including when the criteria above have not been met.

The use of saliva, sweat, or hair samples for drug testing is considered **not medically necessary** in all circumstances.

The use of any of the following for *definitive* drug testing of urine or blood samples is considered **not medically necessary** in all circumstances:

A. Reflex testing; **or**
B. Standing orders; **or**
C. Blanket orders.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
	Presumptive Drug Class Screening codes:
80305	Drug test(s), presumptive, any number of drug classes, any number of devices or procedures; capable of being read by direct optical observation only (eg, utilizing immunoassay [eg, dipsticks, cups, cards, or cartridges]) includes sample validation when performed, per date of service
80306	Drug test(s), presumptive, any number of drug classes, any number of devices or procedures; read by instrument assisted direct optical observation (eg, utilizing immunoassay [eg, dipsticks, cups, cards, or cartridges]), includes sample validation when performed, per date of service
80307	Drug test(s), presumptive, any number of drug classes, any number of devices or procedures; by instrument chemistry analyzers (eg, utilizing immunoassay [eg, EIA, ELISA, EMIT, FPIA, IA, KIMS, RIA]), chromatography (eg, GC, HPLC), and mass spectrometry either with or without chromatography, (eg, DART, DESI, GC-MS, GC-MS/MS, LC-MS, LC-MS/MS, LDTD, MALDI, TOF) includes sample validation when performed, per date of service
	Definitive Drug Testing codes:
80320	Alcohols
80321	Alcohol biomarkers; 1 or 2
80322	Alcohol biomarkers; 3 or more
80323	Alkaloids, not otherwise specified
80324	Amphetamines; 1 or 2
80325	Amphetamines; 3 or 4
80326	Amphetamines; 5 or more
80327	Anabolic steroids; 1 or 2
80328	Anabolic steroids; 3 or more
80329	Analgesics, non-opioid, 1 or 2
80330	Analgesics, non-opioid, 3-5
80331	Analgesics, non-opioid, 6 or more
80332	Antidepressants, serotonergic class; 1 or 2
80333	Antidepressants, serotonergic class; 3-5
80334	Antidepressants, serotonergic class; 6 or more
80335	Antidepressants, tricyclic and other cyclicals; 1 or 2
80336	Antidepressants, tricyclic and other cyclicals; 3-5
80337	Antidepressants, tricyclic and other cyclicals; 6 or more
80338	Antidepressants, not otherwise specified
80339	Antiepileptics, not otherwise specified; 1-3
80340	Antiepileptics, not otherwise specified; 4-6
80341	Antiepileptics, not otherwise specified; 7 or more
80342	Antipsychotics, not otherwise specified; 1-3
80343	Antipsychotics, not otherwise specified; 4-6
80344	Antipsychotics, not otherwise specified; 7 or more
80345	Barbiturates
80346	Benzodiazepines; 1-12
80347	Benzodiazepines; 13 or more
80348	Buprenorphine
80349	Cannabinoids, natural
80350	Cannabinoids, synthetic; 1-3
80351	Cannabinoids, synthetic; 4-6
80352	Cannabinoids, synthetic; 7 or more
80353	Cocaine
80354	Fentanyl

80355	Gabapentin, non-blood
80356	Heroin metabolite
80357	Ketamine and norketamine
80358	Methadone
80359	Methylenedioxyamphetamines
80360	Methylphenidate
80361	Opiates, 1 or more
80362	Opioids and opiate analogs; 1 or 2
80363	Opioids and opiate analogs; 3 or 4
80364	Opioids and opiate analogs; 5 or more
80365	Oxycodone
80366	Pregabalin
80368	Sedative hypnotics (non-benzodiazepines)
80369	Skeletal muscle relaxants; 1 or 2
80370	Skeletal muscle relaxants; 3 or more
80371	Stimulants, synthetic
80372	Tapentadol
80373	Tramadol
80374	Stereoisomer (enantiomer) analysis, single drug class
80375	Drug(s) or substance(s), definitive, qualitative or quantitative, not otherwise specified; 1-3
80376	Drug(s) or substance(s), definitive, qualitative or quantitative, not otherwise specified; 4-6
80377	Drug(s) or substance(s), definitive, qualitative or quantitative, not otherwise specified; 7 or more
83992	Phencyclidine (PCP)
0328U	Drug assay, definitive, 120 or more drugs and metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS), includes specimen validity and algorithmic analysis describing drug or metabolite and presence or absence of risks for a significant patient adverse event, per date of service CareView360; NewStar Medical Laboratories

HCPCS

G0480	Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays [e.g., IA, EIA, ELISA, EMIT, FPIA] and enzymatic methods [e.g., alcohol dehydrogenase]), (2) stable isotope or other universally recognized internal standards in all samples (e.g., to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (e.g., to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day, 1-7 drug class(es), including metabolite(s) if performed
G0481	Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays [e.g., IA, EIA, ELISA, EMIT, FPIA] and enzymatic methods [e.g., alcohol dehydrogenase]), (2) stable isotope or other universally recognized internal standards in all samples (e.g., to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (e.g., to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day, 8-14 drug class(es), including metabolite(s) if performed
G0482	Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays [e.g., IA, EIA, ELISA, EMIT, FPIA] and enzymatic methods [e.g., alcohol dehydrogenase]), stable isotope or other universally recognized internal standards in all samples (e.g., to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (e.g., to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day, 15-21 drug class(es), including metabolite(s) if performed
G0483	Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays [e.g., IA, EIA, ELISA, EMIT, FPIA] and enzymatic methods [e.g., alcohol dehydrogenase]), stable isotope or other universally recognized internal standards in all samples (e.g., to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (e.g., to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day, 22 or more drug class(es), including metabolite(s) if performed
G0659	Drug test(s), definitive, utilizing drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including but not limited to GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem), excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase), performed without method or drug-specific calibration, without matrix-matched quality control material, or without use of stable isotope or other universally recognized internal standard(s) for each drug, drug metabolite or drug class per specimen; qualitative or quantitative, all sources, includes specimen validity testing, per day, any number of drug classes

ICD-10 Diagnosis

All diagnoses

When services are Not Medically Necessary:

For the procedure codes listed above when criteria are not met or for situations designated in the Clinical Indications section as not medically necessary.

When services are also Not Medically Necessary:
For the following procedure codes, or when the code describes a procedure designated in the Clinical Indications section as not medically necessary.

CPT	
0011U	Prescription drug monitoring, evaluation of drugs present by LC-MS/MS, using oral fluid, reported as a comparison to an estimated steady-state range, per date of service including all drug compounds and metabolites Cordant CORE™; Cordant Health Solutions
0082U	Drug test(s), definitive, 90 or more drugs or substances, definitive chromatography with mass spectrometry, and presumptive, any number of drug classes, by instrument chemistry analyzer (utilizing immunoassay), urine, report of presence or absence of each drug, drug metabolite or substance with description and severity of significant interactions per date of service NextGen Precision™ Testing, Precision Diagnostics, Precision Diagnostics LBN Precision Toxicology, LLC
0093U	Prescription drug monitoring, evaluation of 65 common drugs by LC-MS/MS, urine, each drug reported detected or not detected ComplyRX, Claro Labs
0116U	Prescription drug monitoring, enzyme immunoassay of 35 or more drugs confirmed with LC-MS/MS, oral fluid, algorithm results reported as a patient-compliance measurement with risk of drug to drug interactions for prescribed medications Snapshot Oral Fluid Compliance, Ethos Laboratories
0227U	Drug assay, presumptive, 30 or more drugs or metabolites, urine, liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, includes sample validation Comprehensive Screen, Aspenti Health
HCPCS	
P2031	Hair analysis (excluding arsenic)
ICD-10 Diagnosis	
	All diagnoses

Discussion/General Information

Urine Drug Testing (UDT)

The use of UDT in individuals with a substance use disorder or undergoing opioid treatment for chronic pain conditions is common and serves several purposes. According to the American College of Physicians (ACP, 2008), the reasons for UDT include:

- Enhancing patient care.
- Providing objective documentation of an individual's compliance with the treatment plan and opioid agreement.
- Reducing the risk of an unrecognized drug misuse/abuse problem.
- Serving as an adjunct to self-reports of drug/substance use.
- Proving or disproving abuse/addiction of illicit or non-prescribed licit drugs.
- Justifying continuation of chronic opioid analgesic therapy in individuals who adhere to the treatment plan and have acceptable urine drug tests.
- Providing a rationale to change the treatment plan in individuals with unacceptable urine drug tests and justifying referral to addiction specialists.

The American Pain Society (APS) and American Academy of Pain Medicine (AAPM) joint guidelines panel released their opioid treatment guidelines titled *Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Non-cancer Pain* in 2009 (Chou, 2009). In this document, the AAPM addressed the monitoring of controlled substances use via UDT as part of a chronic opioid treatment (COT) program. The guideline section on monitoring (Section 5) states:

> 5.1 Clinicians should reassess patients on COT periodically and as warranted by changing circumstances. Monitoring should include documentation of pain intensity and level of functioning, assessments of progress toward achieving therapeutic goals, presence of adverse events, and adherence to prescribed therapies (strong recommendation, low-quality evidence).
> 5.2 In patients on COT who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the COT plan of care (strong recommendation, low-quality evidence).
> 5.3 In patients on COT not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the COT plan of care (weak recommendation, low-quality evidence). Clinicians should periodically reassess all patients on COT. Regular monitoring of patients once COT is initiated is critical because therapeutic risks and benefits do not remain static.

In 2017, the American Society of Addition Medicine (ASAM) published a document titled *Appropriate Use of Drug Testing in Clinical Addiction Medicine* (Jarvis, 2017). The ASAM provided an array of recommendations related to UDT and other drug testing procedures. The document included the following recommendations regarding presumptive and definitive testing:

- Presumptive testing should be a routine part of initial and ongoing patient assessment.
- Presumptive testing should be used when it is a priority to have more immediate (although less accurate) results.
- Definitive testing techniques should be used whenever a provider wants to detect specific substances not identified by presumptive methods, quantify levels of the substance present, and refine the accuracy of the results.
- Definitive testing should be used when the results inform clinical decisions with major clinical or non-clinical implications for the patient (e.g. treatment transition, changes in medication therapies, changes in legal status).
- If a patient disputes the findings of a presumptive test, a definitive test should be done.
- When ordering a definitive test, providers should advise the testing laboratory if the presence of any particular substance or group of substances is suspected or expected.

The ASAM document also addressed testing frequency:

- For people in addiction treatment, frequency of testing should be dictated by patient acuity and level of care.
- Providers should look to tests' detection capabilities and windows of detection to determine the frequency of testing.
- Providers should understand that increasing the frequency of testing increases the likelihood of detection of substance use, but there is insufficient evidence that increasing the frequency of drug testing has an effect on substance use itself.
- Drug testing should be scheduled more frequently at the beginning of treatment; test frequency should be decreased as recovery progresses.
- During the initial phase of treatment, drug testing should be done at least weekly. When possible, testing should occur on a random schedule.
- When a patient is stable in treatment, drug testing should be done at least monthly. Individual consideration may be given for less frequent testing if a patient is in stable recovery. When possible, testing should occur on a random schedule.

Finally, ASAM recommended the following related to UDT:

- Urine should be considered the most well-established and well-supported biological matrix for presumptive detection of substance use in a clinical setting.
- Urine should be considered the best established matrix for POCTs.*

*Point of care tests.

In 2019 ASAM published a document titled *Public Policy Statement on the Ethical Use of Drug Testing in the Practice of Addiction Medicine*. This document contained important statements regarding the ethical use of drug testing, including:

2. Drug testing should be used only when clinically necessary. Tests should be selected based on an individualized clinical assessment of the patient and performed after informed consent whenever possible.
    a. Clinicians should document the rationale for the drug tests they order and document the clinical decisions they make based on those tests. The use of drug screening panels that test for multiple classes of drugs or multiple compounds within a drug class is a pragmatic approach that can be helpful especially in primary care practices. Drug testing panels may be pragmatic for new patients in addiction treatment programs, but follow-up testing should be individualized to the patient's history, needs, initial test results, and drugs commonly used in the patient's geographic location and peer group. (This may not be possible where an external entity such as a governmental agency requires routine testing drug panels to be performed periodically on a set time frame.)
    b. The use of drug testing panels which apply to every patient at every testing time regardless of the patient's individual clinical history and needs may not be appropriate because this can result in over- or underutilization of diagnostic services.
3. Presumptive testing should be a routine part of initial and ongoing patient assessment. Definitive testing may be used to detect specific substances not identified by presumptive methods and to refine the accuracy of the test results. Definitive testing may be used when the results are needed to inform clinical decisions where the results will alter the care plan.
    a. Clinical decisions may be made based on drug test results or on patient self-report of use. Patient self-report of negative use is often unreliable and positive self-report is complicated by purchasing of illicit drugs that are not consistent or reliable in their components.
    b. It is inappropriate to order definitive testing for all analytes in every drug test conducted on a patient and to do so repeatedly, without regard to the results from previous tests or the patient's overall response to addiction treatment interventions. Ethical use of drug testing requires that the scope of the analyte panel and the frequency of testing be justified by the patient's clinical status and the ordering clinician's need for information.

The exact frequency and pattern of urine drug screening is individualized based on the risk for abuse. The Washington State Agency Medical Directors' Group (AMGD) published an Interagency Guideline on opioid dosing for pain. This guideline and related expert commentary support low-risk individuals having 1 UDTs up to once per year, moderate-risk up to 2 UDTs per year, high-risk individuals up to 3-4 UDTs per year. Individuals exhibiting aberrant behaviors should be tested at the time of the office visit. The American Pain Society guidelines (Chou, 2009) state that for individuals at low risk for adverse outcomes, quarterly or semi-annual monitoring is sufficient. For very high-risk individuals, weekly monitoring may be reasonable. However, the AMGD states that there is insufficient evidence to support this recommendation. This observation is reiterated in a review article by McMillin and colleagues (2013), where they comment that there is a lack of detailed guidelines addressing the appropriate use of DUT to support chronic pain management. The ASAM white paper does not recommend an upper limit for testing. However, in the context of abuse, the McMillin review recommends testing no less than once weekly at first then once monthly once abstinence is established. Such limits apply to both presumptive and definitive testing. There is insufficient clinical reasoning to support the use of definitive testing at a frequency greater than for presumptive testing.

The American College of Obstetricians and Gynecologists (ACOG) recommends a screening interview for substance use be completed on the first prenatal visit as part of comprehensive obstetric care (2017). ACOG recommends following up with UDT to detect or confirm suspected substance use when the individual consents.

The risk for abuse may be measured using standard tools, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP®; PainEdu.org, 2013) and the Revised Opioid Risk Tool (ORT-R or ORT-OUD; Cheatle, 2019). These tools aid clinicians in assessing the suitability of long-term opioid therapy for individuals with chronic pain, and help differentiate those who may require more or less clinician monitoring while on long-term opioid therapy. The SOAPP tool is available for free and can be accessed at https://www.mcstap.com/docs/SOAPP-5.pdf . Four different versions are available to allow for varying levels of evaluation. All versions of the SOAPP tool may be self-administered at or prior to an office visit or can be completed as part of an interview with a nurse, physician or psychologist. The ORT was developed by Webster (2005) and was modified by Cheatle in 2019 (ORT-R/ORT-OUD). Like the SOAPP, it may be self-administered or used as part of a clinical evaluation. The ORT-R/ORT-OUD can be accessed for free at https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-resources/opioid-risk-tool-oud-ort-oud.

Presumptive versus Definitive Testing

Presumptive testing is intended to identify the use or non-use of a drug or class of drugs. Definitive tests are more specific and allow for the detection of specific drugs or metabolites of interest. In most cases presumptive testing is used because it is quick, fairly accurate, and easily accessible in a wide variety of settings. Definitive testing may be needed when presumptive results alone are not sufficient to guide clinical care. However, in most situations, the identification or quantification of a specific drug of interest may not result in a different treatment plan. Definitive testing, particularly when performed repeatedly, must be clinically meaningful and documentation must support the specific necessity of each definitive assay performed as well as how that test result will affect clinical management.

Drug Testing of Blood, Saliva, Sweat, or Hair Samples

The 2017 ASAM recommendations (Jarvis, 2017) address the use of alternate sample matrices in the following statements:

- The relevance of blood testing in addiction treatment is limited mostly to emergency situations where there is a need to assess intoxication or impairment.
- No statements about the appropriateness of breath testing were endorsed by the Expert Panel.
- Oral fluid testing is appropriate for presumptive detection of substance use in addiction treatment settings.
- There is insufficient evidence to support the use of sweat testing in addiction treatment. More research is needed before sweat testing can be recommended over urine testing in clinical settings.
- Hair testing in addiction treatment can detect long-term patterns of use. Routine use of hair testing is not appropriate for addiction treatment.

These recommendations support the use of oral fluid testing for presumptive detection; however, the evidence cited in the guideline discussion consists of low-quality references including reviews and a study that evaluates the volume of oral fluid needed for an appropriate sample. The recommendations reference a Committee Opinion from the American College of Obstetricians and Gynecologists (ACOG) on ethical issues in relation to alcohol abuse and other substance use disorders. ACOG recommends routine screening with validated questionnaires or conversations and does not recommend routine laboratory testing of biologic samples for substance use disorders (ACOG, 2015). ASAM does suggest that oral fluid testing might be useful in some cases, but further research on which specific drugs and metabolites oral fluid testing might best detect is recommended (Jarvis, 2017).

The U.S. Department of Health and Human Services (DHHS) Substance Abuse and Mental Health Services Administration (SAMHSA) has published two documents that address drug testing for individuals in primary care and substance abuse disorder treatment programs (SAMHSA, 2012, 2014). In these documents, the benefits and drawbacks of drug testing using alternative sample sources is evaluated. However, in their primary care document (2012) SAMHSA clarifies that urine is the most widely used and studied source. This was reiterated in their 2014 Treatment Improvement Protocol (TIP) for opioid addiction programs.

The use of samples other than urine, including blood, hair, saliva, and sweat, is not recommended by most authoritative organizations that provide guidance on drug testing, including the ACP (Kirschner, 2014), the American Pain Society (APS) and the American Academy of Pain Medicine (AAPM, Chou, 2010) and the Washington State Agency Medical Directors' Group (AMGD, 2015). The American Society of Transplantation recommends urine drug testing in individuals when needed to identify abuse and diversion and to guide treatment (Jowsey-Gregoire, 2022). The use of UDT is not possible in some circumstances. Individuals with renal failure who are on dialysis or those with bladder control impairments may be unable to provide a sample. In these limited circumstances, UDT may need to be replaced by blood tests.

There is growing support for the use of saliva testing, especially in cases where a urine sample is unobtainable, when such results may be unreliable, or when there is a history of urine sample tampering. However, as noted above, there is little evidentiary support for this approach.

In summary, the use of blood, hair, saliva, and sweat is not widely recommended and these matrices each have significant drawbacks to their use when compared to UDT.

Testing Panels

Many commercial laboratories market multi-test panels for the presence of various prescription and illicit drugs and their metabolites. While the use of some individual tests included in these test panels may be reasonable under specific circumstances, the use of all the tests within a panel is rarely justified unless there is clinical evidence that an individual has used or been exposed to multiple substances, and knowledge of such exposure provides information that leads to meaningful impact on treatment.

Reflex testing, Standing orders, and Blanket orders

The use of reflex testing, standing orders, and blanket orders for definitive testing of urine or blood samples is contrary to good clinical practice, which is based on clinical decision-making as to the necessity of specific laboratory tests. In the case of these types of tests, they are done in the absence of the requisite clinical decision-making process and are based solely on automated processes devoid of clinical judgment. They do not meet the requirement for there to be documentation of a specific rationale for each ordered test and documentation of how the test will be used to modify treatment for the tested individual.

Definitions

Blanket order: A test request that is not for a specific individual, but it is an identical order for all individuals in a clinician’s practice. Such orders do not take the clinical situation of each individual into consideration at the time of request, or during each visit.

Definitive testing: A type of testing that is more specific than presumptive testing, and allows for the detection of specific drugs or metabolites.

Drug class: Drugs, medications or illicit substances (including metabolites of each member of the class) that share similar essential aspects of their chemical structure and at least one similar mechanism of action (i.e., bind to the same biological target). For example, opioids interact with one or more opioid receptor. Drugs associated with substance use disorders, including alcohol and inhalants, are thought to directly activate the brain reward system as a common mode of action.

Drug diversion: Prescription drugs provided to an individual other than the one to whom the drugs were prescribed.

Drug testing panel: A type of test that involves tests for more than one type of drug and may test for a pre-defined set of drug classes or metabolites of specific drugs or drug classes.

Member-specific profile: This term refers to the specific characteristics of an individual being treated for chronic pain or an individual undergoing treatment for opioid addiction and substance use disorder, which may be used to help guide treatment. These characteristics may include current and past alcohol and drug use patterns and clinical findings such as slurred speech, hallucinations or pin-point pupils that tend to be specific to a drug or drug class. Use of member-specific profiles assist in guiding the selection of the specific tests for drugs and their metabolites.

Planned testing: Testing being conducted at a time previously scheduled and known to the individual being tested.

Presumptive testing: A type of testing that is intended to identify the use or non-use of a drug or general class of drugs.

Random testing: Testing being conducted at a time not previously scheduled and not known to the individual being tested.

Reflex Testing: A laboratory test that is performed "reflexively" after an initial or presumptive test result suggests the need for further diagnostic information. This type of testing is not based on a specific clinical situation and provider's order, but is built into the testing process. Testing performed as a step necessary to complete the request of physician responsible for a members care and provided by

an order is not considered reflex testing.

Standing order: A test request for a specific individual representing: 1) repetitive testing to monitor a condition or disease, or 2) individualized orders for repetitive automatic testing for certain individuals for pre-determined tests based on historical use, risk, and community trend patient profiles. Definitive drug testing standing orders are not consistent with ordering laboratory testing based upon clinical findings, nor are they sensitive to the individual's history of drug use and community patterns of drug use.

Testing panel: A type of laboratory procedure where multiple tests are automatically run on a single sample to detect the presence of a variety of substances or class of substances.

References

Peer Reviewed Publications:

1. Cheatle MD, Compton PA, Dhingra L, et al. Development of the revised opioid risk tool to predict opioid use disorder in patients with chronic nonmalignant pain. J Pain. 2019; 20(7):842-851.
2. Christo PJ, Manchikanti L. Ruan X, et al. Urine drug testing in chronic pain. Pain Physician. 2011; 14(2):123-143.
3. Owen GT, Burton AW, Schade CM, Passik S. Urine drug testing: current recommendations and best practices. Pain Physician. 2012; 15(3 Suppl):ES119-ES133.
4. Melanson SE. The utility of immunoassays for urine drug testing. Clin Lab Med. 2012; 32(3):429-447.
5. Melanson SE, Ptolemy AS, Wasan AD. Optimizing urine drug testing for monitoring medication compliance in pain management. Pain Med. 2013; 14(12):1813-1820.
6. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med. 2005; 6(6):432-442.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American College of Obstetricians and Gynecologists (ACOG). Committee opinion.
    - Committee Opinion No. 633: Alcohol abuse and other substance use disorders: ethical issues in obstetric and gynecologic practice. Obstet Gynecol. 2015; 125(6):1529-1537. Reaffirmed 2021.
    - Committee Opinion No. 711: Opioid Use and Opioid Use Disorder in Pregnancy. Obstet Gynecol. 2017; 130(2):e81-e94. Reaffirmed 2021.
2. American Society of Addiction Medicine (ASAM).
    - The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. 2020; 14(2S Suppl 1):1-91. Erratum in: J Addict Med. 2020; 14(3):267.
    - Public Policy Statement on the Ethical Use of Drug Testing in the Practice of Addiction Medicine. April 3, 2019. Available at: https://www.asam.org/docs/default-source/public-policy-statements/2019-ethical-use-of-drug-testing-in-the-practice-of-addiction-medicine.pdf?sfvrsn=75bb4bc2_4#search="drug testing". Accessed on October 14, 2023.
3. Chou R, Fanciullo GJ, Fine PG, et al.; American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain. 2009. 10(2):113-130.
4. Centers of Medicare and Medicaid, Complying with documentation requirements for laboratory services. August 2018. Available at: Complying with Laboratory Services Documentation Requirements (cms.gov). Accessed on October 14, 2023.
5. Jarvis M, Williams J, Hurford M, et al. Appropriate Use of Drug Testing in Clinical Addiction Medicine. J Addict Med. 2017; 11(3):163-173.
6. Jowsey-Gregoire S, Jannetto PJ, Jesse MT, et al. Substance use screening in transplant populations: Recommendations from a consensus workgroup. Transplant Rev (Orlando). 2022; 36(2):100694.
7. Manchikanti L, Kaye AM, Knezevic NN, et al. Responsible, safe, and effective prescription of opioids for chronic non-cancer pain: American Society of Interventional Pain Physicians (ASIPP) guidelines. Pain Physician. 2017; 20(2S):S3-S92.
8. McMillin GA, Slawson MH, Marin SJ, Johnson-Davis KL. Demystifying analytical approaches for urine drug testing to evaluate medication adherence in chronic pain management. J Pain Palliat Care Pharmacother. 2013; 27(4):322-339.
9. New Hampshire Medical Society. New Hampshire Opioid Prescribing Risk. Opioid risk screening tools and articles. 2016. Available at: Opioid Risk Screening - New Hampshire Medical Society (nhms.org) Accessed on October 14, 2023.
10. PainEDU.org. Screener and Opioid Assessment for Patients with Pain- Revised (SOAPP® -R) . Available at: https://d1li5256ypm7oi.cloudfront.net/colospine/2016/08/SOAPP-R-Screener-and-Opioid-Assessment-for-Patients-with-Pain-Revised-160816-57b258fc9a277.pdf . Accessed on October 14, 2023.
11. U.S. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration (SAMHSA).
    - Clinical Drug Testing in Primary Care. Technical Assistance Publication Series 32. 2012. Available at: https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4668.pdf. Accessed on October 14, 2023.
    - Federal Guidelines for Opioid Treatment Programs. January 2015. https://store.samhsa.gov/sites/default/files/d7/priv/pep15-fedguideotp.pdf. Accessed on October 14, 2023.
    - Medication-assisted treatment for opioid addiction in opioid treatment programs. A treatment improvement protocol TIP 43. 2014 Available at: https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4108.pdf. Accessed on October 14, 2023.
    - Medications for Opioid use Disorder. A treatment improvement protocol TIP 63. Updated 2021. Available at: https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf. Accessed on October 14, 2023.
12. Washington State Agency Medical Directors' Group. Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An educational aid to improve care and safety with opioid therapy. 2015 Update. Available at: https://agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf. Accessed on October 14, 2023.

Index

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action

Reviewed	11/09/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Discussion/General Information and References section.
	06/28/2023	Updated Coding section with 07/01/2023 CPT changes; removed 0143U, 0144U, 0145U, 0146U, 0147U, 0148U, 0149U, 0150U, codes deleted as of 07/01/2023.
Reviewed	11/10/2022	MPTAC review. Updated Description, Discussion and References section.
	06/29/2022	Updated Coding section with 07/01/2022 CPT changes; added 0328U.
Reviewed	11/11/2021	MPTAC review. Updated Discussion and References section.
	01/07/2021	Corrected date error in History section.
Reviewed	11/05/2020	MPTAC review. Updated Reference sections. Reformatted Coding section and updated with 01/01/2021 CPT changes, added PLA code 0227U.
Revised	05/14/2020	MPTAC review. Revised note in Clinical Indications section in relation to drug classes. Added Appendix section with drug class table. Updated Rationale and References sections. Updated Coding section; added codes 80329, 80330, 80331.
	04/01/2020	Updated Coding section with 04/01/2020 CPT changes; removed 0006U deleted 03/31/2020.
Reviewed	11/07/2019	MPTAC review. Updated Rationale and References sections. Updated Coding section with 01/01/2020 CPT changes; added codes 0143U, 0144U, 0145U, 0146U, 0147U, 0148U, 0149U, 0150U.
	10/01/2019	Updated Coding section with 10/01/2019 CPT changes; added 0116U, revised descriptor for 0082U.
	06/27/2019	Updated Coding section with 07/01/2019 CPT changes; added 0093U.
Revised	01/24/2019	MPTAC review. Clarified MN statement for presumptive testing. Expanded MN statement regarding definitive testing. Added note regarding number of drug classes tested for during definitive testing. Updated Rationale and References sections.
	12/27/2018	Updated Coding section with 01/01/2019 CPT changes; added 0082U.
	06/28/2018	Updated Coding section with 07/01/2018 CPT changes; revised descriptor for code 0006U.
Reviewed	03/22/2018	MPTAC review.
Reviewed	02/23/2018	Behavioral Health Subcommittee review. Updated References section.
	12/27/2017	The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Coding section with 01/01/2018 CPT descriptor changes for codes 80305-80307.
Revised	08/03/2017	MPTAC review.
Revised	07/21/2017	Behavioral Health Subcommittee review. Updated formatting in Clinical Indications section. Added new NMN statement regarding reflex testing, standing orders, and blanket orders. Updated Description, Discussion, and References sections. Updated Coding section with 08/01/2017 CPT changes; added 0006U and 0011U.
	01/01/2017	Updated Coding section with 01/01/2017 CPT and HCPCS changes; removed codes 80300, 80301, 80302, 80303, 80304, G0477, G0478, G0479 deleted 12/31/2016.
Reviewed	08/04/2016	MPTAC review.
Reviewed	07/29/2016	Behavioral Health Subcommittee review. Updated Discussion and References sections.
Revised	02/04/2016	MPTAC review.
Revised	01/29/2016	Behavioral Health Subcommittee review. Revised title to change “Substance Abuse” to “Substance Use Disorder”. Added the use of blood, saliva, sweat, or hair to position statement. Revised Background, Coding and References sections.
	01/01/2016	Updated Coding section with 01/01/2016 HCPCS changes, removed codes G0431, G0434, G6031, G6040, G6041, G6042, G6043, G6044, G6045, G6046, G6048, G6051, G6052, G6053, G6056, G6057, G6058 deleted 12/31/2015; also removed ICD-9 codes.
Revised	02/05/2015	MPTAC review.
Revised	01/30/2015	Behavioral Health Subcommittee review. Revised clinical indications section to address “presumptive” and “definitive” testing. Clarified the limit of 24 tests per calendar year to be a rolling 24 year. Updated Discussion, Definitions, and References sections.
	01/01/2015	Updated Coding section with 01/01/2015 CPT and HCPCS changes; removed deleted codes and codes 80184, 82491, 82492, 82541, 82542, 82543, 82544 (no longer applicable).
Revised	02/13/2014	MPTAC review.
Revised	02/07/2014	Behavioral Health Subcommittee review. Added not medically necessary statement addressing the use of testing panels. Updated Discussion, Definitions, and References sections.
New	11/14/2013	MPTAC review. Initial document development.

Appendix

The following table lists drugs and their metabolites in drug classes based on Generic Product Index level 2 classifications (GPI2), the FDA’s National Drug Classifications (NDC), PubChem classifications, and the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), but does not include every drug and metabolite. Metabolites not listed in the table should be categorized with their parent drug.

Drug Class	Drugs and Metabolites	Reference
Alcohols	Ethyl Glucuronide	PubChem
	Ethyl Sulfate	PubChem
	ETOH	PubChem
	Methanol	PubChem
Analgesics, NonNarcotic	Acetaminophen	GPI2, PubChem
	Diclofenac	DSM-5, NDC

	Ibuprofen	DSM-5, NDC
	Ketoprofen	DSM-5, NDC
	Naproxen	DSM-5, NDC
Androgens, Anabolic	Anabolic Steroids	PubChem
	Clostebol	PubChem
	Danazol	GPI2, PubChem
	Methyltestosterone	GPI2, PubChem, NDC
Anticonvulsants	Carbamazepine	GPI2, PubChem, NDC
	Cannabidiol	GPI2, PubChem
	Gabapentin	GPI2, PubChem
	Lamotrigine	GPI2, PubChem, NDC
	Phenytoin	GPI2, PubChem, NDC
	Pregabalin	GPI2, PubChem
	Primidone	GPI2, PubChem
	Topiramate	GPI2, PubChem, NDC
	Valproic Acid	GPI2, PubChem
	Zonisamide	GPI2, PubChem
Antidepressants	Amitriptyline	GPI2, PubChem, NDC
	Amoxapine	GPI2, PubChem
	Bupropion	GPI2, PubChem, NDC
	Citalopram	GPI2, PubChem
	Desipramine	GPI2, PubChem, NDC
	Desvenlafaxine	GPI2, PubChem, NDC
	Doxepin	GPI2, PubChem, NDC
	Duloxetine	GPI2, PubChem, NDC
	Fluvoxamine	GPI2, PubChem
	Fluoxetine	GPI2, PubChem
	Escitalopram	GPI2, PubChem, NDC
	Imipramine	GPI2, PubChem, NDC
	Mirtazapine	GPI2, PubChem
	Nefazodone	GPI2, PubChem
	Nortriptyline	GPI2, PubChem, NDC
	Paroxetine	GPI2, PubChem, NDC
	Phenelzine	GPI2, PubChem
	Selegiline	PubChem, NDC
	Sertraline	GPI2, PubChem, NDC
	Tranylcypromine	GPI2, PubChem, NDC
	Trazodone	GPI2, PubChem, NDC
	Venlafaxine	GPI2, PubChem, NDC
	Vilazodone	GPI2, PubChem
	Vortioxetine	GPI2, PubChem
Antipsychotics/Antimanic Agents	Aripiprazole	GPI2, PubChem, NDC
	Cariprazine	GPI2, PubChem
	Chlorpromazine	GPI2, PubChem, NDC
	Clozapine	GPI2, PubChem, NDC
	Haloperidol	GPI2, PubChem, NDC
	Lurasidone	GPI2, PubChem
	Olanzapine	GPI2, PubChem, NDC
	Paliperidone	GPI2, PubChem, NDC
	Perphenazine	GPI2, PubChem, NDC
	Risperidone	GPI2, PubChem, NDC
	Thioridazine	GPI2, PubChem, NDC
	Ziprasidone	GPI2, PubChem, NDC
Barbiturates and Barbituate-Like Drugs	Amobarbital	GPI2, PubChem, DSM-5
	Butabarbital	GPI2, PubChem, DSM-5
	Butalbital	DSM-5, PubChem, NDC
	Glutethimide	DSM-5, PubChem
	Meprobamate	DSM-5, PubChem
	Pentobarbital	GPI2, PubChem, DSM-5
	Phenobarbital	GPI2, PubChem, DSM-5
	Secobarbital	GPI2, PubChem, DSM-5
Benzodiazepine and Benzodiazepine-Like Drugs	Alprazolam	GPI2, PubChem, DSM-5, NDC
	Chlordiazepoxide	GPI2, PubChem, DSM-5, NDC
	Clonazepam	GPI2, PubChem, DSM-5, NDC
	Clorazepate	GPI2, PubChem, DSM-5
	Diazepam	GPI2, PubChem, DSM-5, NDC
	Eszopiclone	GPI2, PubChem, DSM-5
	Flumazenil	GPI2, PubChem, DSM-5, NDC
	Lorazepam	DSM-5, PubChem, NDC
	Oxazepam	GPI2, PubChem, DSM-5
	Temazepam	GPI2, PubChem, DSM-5, NDC
	Zaleplon	GPI2, PubChem, DSM-5
	Zolpidem	DSM-5, PubChem
Cannabinoids	Dronabinol	PubChem
	K2/Spice	PubChem

	Marijuana	DSM-5
	Marinol	PubChem
	THC	PubChem
Cathinones	Bath salts	DSM-5, PubChem
	Kratom	DSM-5, PubChem
Hallucinogen-Related Disorders, Other Hallucinogen Use Disorder	Atropine	PubChem
	Dimethyltryptamine (DMT)	DSM-5, PubChem
	DOM	DSM-5, PubChem
	Jimson weed	DSM-5, PubChem
	LSD (Ergolines)	DSM-5, PubChem
	Mescaline (Phenylalkylamines)	DSM-5, PubChem
	MDA	DSM-5, PubChem
	MDEA	DSM-5, PubChem
	MDMA	DSM-5, PubChem
	Morning Glory Seeds	DSM-5, PubChem
	Phenethylamine	PubChem
	Psilocybin (Indoleamines)	DSM-5, PubChem
	Salvia Divinorum	DSM-5, PubChem
	Salvinorin	PubChem
	Scopolamine	PubChem
Hallucinogen-Related Disorders, Phencyclidine Use Disorder	Phencyclidine	DSM-5, PubChem
	Ketamine (Including Esketamine)	DSM-5, PubChem
	Cyclohexamine (1-Phenylcyclohexylamine)	DSM-5, PubChem
	Dizocilpine	DSM-5, PubChem
	Norketamine	PubChem
Musculoskeletal Therapy Agents	Baclofen	GPI2, PubChem
	Carisoprodol	GPI2, PubChem, NDC
	Cyclobenzaprine	GPI2, PubChem, NDC
	Metaxalone	GPI2, PubChem
	Methocarbamol	GPI2, PubChem, NDC
	Orphenadrine	GPI2, PubChem, NDC
	Tizanidine	GPI2, PubChem
Opioids	6-Acetylmorphine (6-MAM)	PubChem
	Acetylcodeine	PubChem
	Acetylfentanyl	PubChem
	Actiq	GPI2, PubChem
	Alfentanil	GPI2, PubChem, NDC
	Belbuca	GPI2, PubChem
	Bunavail	GPI2, PubChem
	Buprenorphine (for example, Subutex and others)	GPI2, PubChem, NDC
	Butorphanol	GPI2, PubChem, NDC
	Butrans	GPI2, PubChem
	Codeine	GPI2, PubChem, NDC
	Desomorphine	PubChem
	Dextromethorphan	PubChem
	Dextrophan	PubChem
	Diacetylmorphine (commonly known as heroin)	PubChem
	Diamorphine (commonly known as heroin)	PubChem
	Dihydrocodeine	GPI2, PubChem, NDC
	EDDP	PubChem
	Fentanyl	GPI2, PubChem
	Heroin	PubChem
	Hydrocodone	GPI2, PubChem, NDC
	Hydromorphone	GPI2, PubChem, NDC
	Kratom	PubChem
	Levorphanol	GPI2, PubChem
	Meperidine	GPI2, PubChem, NDC
	Methadone	GPI2, PubChem, NDC
	Mitragynine	PubChem
	Morphine	GPI2, PubChem, NDC
	Naloxone	GPI2, PubChem, NDC
	Naltrexone	GPI2, PubChem, NDC
	Norfentanyl	PubChem
	Noroxycodone	PubChem
	Norpropoxyphene	PubChem
	O-Desmethyltramadol	PubChem
	Oxycodone	GPI2, PubChem, NDC
	Oxymorphone	GPI2, PubChem, NDC
	Pentazocine	GPI2, PubChem, NDC
	Probuphine	GPI2, PubChem, NDC

	Propoxyphene	GPI2, PubChem
	Sublocade	GPI2, PubChem
	Suboxone	GPI2, PubChem
	Subutex	PubChem
	Sufentanil	PubChem
	Tapentadol	GPI2, PubChem
	Tramadol	GPI2, PubChem, NDC
	Ultram	GPI2, PubChem, NDC
	Zubsolv	GPI2, PubChem, NDC
Other Drugs or Metabolites	Drugs or Metabolites Not Otherwise Specified	N/A
Other (or Unknown) Substance Use Disorder	Cortisol	DSM-5
	Nitrous Oxide (“Laughing Gas”)	DSM-5
	Amyl-, Butyl, Isobutyl-Nitrites	DSM-5
	Betel Nut	DSM-5
	Kava	DSM-5
Stimulants, Amphetamine-Type Substance	Amphetamine	DSM-5, PubChem, NDC
	D/L Isomer Analysis	DSM-5, PubChem
	Dextroamphetamine	DSM-5, PubChem, NDC
	Lisdexamfetamine	DSM-5, PubChem
	Methamphetamine	DSM-5, PubChem, NDC
	Methylphenidate	DSM-5, PubChem, NDC
	Phentermine	DSM-5, PubChem, NDC
	Phenylpropanolamine	DSM-5, PubChem
	Pseudoephedrine	PubChem
	Ritalinic Acid	PubChem
Stimulants, Cocaine	Benzoylecgonine	DSM-5, PubChem
	Cocaine	DSM-5, PubChem
	Ecgonine Methyl Ester	DSM-5, PubChem
Tobacco Use Disorder	Cotinine	DSM-5, PubChem
	Nicotine	DSM-5, PubChem