

Drug Testing in Pain Management or Substance Use Disorder Treatment

MEDICAL POLICY NUMBER: 15

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INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ Commercial

☒ Medicaid/OHP*

☐ Medicare**

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

Diagnostic Guideline Note 23

**Medicare Members

This Company policy may be applied to Medicare Plan members only when directed by a separate Medicare policy. Note that investigational services are considered “**not medically necessary**” for Medicare members.

COVERAGE CRITERIA

Urine Drug Testing

Note: Please see Providence Health Plans Reimbursement Policy 12, Urine Drug Testing, for additional payment and coding restrictions.

Presumptive Urine Drug Testing

- I. Presumptive urine drug testing using codes: 80305, 80306, or 80307 (see Billing Guideline Section), may be considered **medically necessary**, for pain management or substance use treatment, when **all** of the following (A.-C.) criteria are met:
 - A. Drug misuse, use or diversion is suspected; **and**
 - B. Clinical documentation indicates how test results will impact treatment planning; **and**
 - C. Testing is ordered by the treating provider.
- II. Presumptive urine drug testing is considered **not medically necessary** when criterion I., above is not met.

Definitive Urine Drug Testing

- III. Definitive urine drug testing using codes G0480 (see Billing Guideline Section) may be considered **medically necessary** when **all** of the following (A.-E.) criteria are met:
 - A. Drug misuse or use is suspected; **and**

- B. Test results will impact clinical decision making and treatment planning; **and**
- C. Testing is ordered by the treating provider; **and**
- D. An unexpected presumptive test warrants further, specific definitive testing; **and**
- E. Definitive testing must be performed within 48 hours after the aberrant presumptive test.

IV. Definitive urine drug testing is considered **not medically necessary** when criterion III. above is not met.

V. Definitive urine drug testing of more than 7 drug classes, or broad-spectrum definitive testing, (e.g., 0051U, G0481, G0482, G0483, G0659) is considered **not medically necessary**.

Non-Covered Services

VI. The following urine drug testing is considered **not medically necessary**:

- A. Mandated drug testing (e.g., testing required by a court-order, employment drug screening, or screening for a commercial driver's license)
- B. Residential monitoring
- C. Specimen validity testing

VII. The use of oral fluid or hair samples for drug testing is considered **not medically necessary** for all indications.

Link to [Evidence Summary](#)

POLICY CROSS REFERENCES

None

The full Company portfolio of current Medical Policies is available online and can be [accessed here](#).

POLICY GUIDELINES

Background

According to the Centers for Disease Control and Prevention, 91 Americans die every day from an opioid overdose and this number has quadrupled since 1999.¹ Furthermore, the American Society of Intervention Pain Physicians (ASIPP) estimates that one-third of chronic pain patients misuse or use prescription opioids. Several societies and guidelines recommend monitoring patients in pain management and substance use programs. Testing biological substances, most commonly urine, for the presence or absence of drugs is the most common strategy for monitoring these patients.

Urine Drug Testing (UDT)

Urine drug testing is performed to detect the use of prescription medication and illegal substances of

concern for use. Urine drug testing should not routinely include a panel of all drugs of use. Testing should focus on the detection of specific drugs. Testing should be done at the lowest level to detect the presence of drugs.

Presumptive Versus Definitive Testing

Drugs or classes of drugs are commonly assayed by presumptive testing. Presumptive, UDT identifies if a particular substance (analyte) is present in the specimen.² Presumptive test may be followed by confirmation with a second method (definitive), only if there is a positive finding.

Definitive UDT identifies how much (the quantity) of an analyte is present. “After the presence of an analyte has been established (which may involve a second, confirmatory test), the amount of the analyte present in the sample then may be measured. For example, you could test for the presence of alcohol in the blood (presumptive), and/or may test for the actual blood alcohol level (definitive).”² Immunoassay, the measurement of the presence of a molecule in a solution, is the most common analytic method for presumptive UDT. Chromatography is the most common analytic mechanism for confirmatory UDT. This process involves passing a dissolved mixture that is in a mobile phase through a stationary phase; thus isolating different molecules by type. These isolated molecules can then be identified and measured.

All urine drug testing should be performed on a frequency appropriate for clinical needs. Adherence to substance use treatment is best measured through random testing rather than scheduled testing.

Table 1. Comparison of Presumptive and Definitive Urine Drug Testing³

	Presumptive	Definitive
Analytic Technique	Immunoassay	Gas Chromatography-Mass Spectrometry (GC-MS) or High Performance Liquid Chromatography (HPLC)
Sensitivity	Low or none when testing for semi-synthetic or synthetic opioids	High
Specificity	Varies based on assay used- can result in false positives and false negatives	High
Use	Presumptive analysis; detects classes of drugs	Definitive analysis; identifies the quantity of a specific drug

Oral Fluid Drug Testing

Oral fluid drug testing utilizes saliva samples as a means for therapeutic or substance use monitoring.⁴ The use of these tests has increased considerably due to their quick and non-invasive approach, and the ability to conduct them outside of the lab. Additionally, the use of screening cartridges and devices that provide an instantaneous electronic readout are available and widely used.

Hair Sample Drug Testing

A hair follicle drug test involves the removal of a small amount of hair to evaluate drug use in the last 90 days.⁵ Enzyme-linked immunosorbent assay is used first, and if a positive result is seen, confirmatory

testing is performed. The sampling can be taken in a health care setting, workplace, or at home, but the analysis must be performed in the lab.

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

Several studies were identified which evaluated the analytic validity (i.e., sensitivity and specificity) of urine drug testing.⁶⁻¹⁸ However, no studies were identified which assessed the clinical utility of urine drug testing for monitoring patients in pain management and substance use programs. Therefore, no reliable conclusions can be drawn regarding urine drug testing and its possible impact on health outcomes in these patient populations.

CLINICAL PRACTICE GUIDELINES

Oregon Health Evidence Review Commission (HERC)

In 2018, HERC published a coverage guidance for urine drug testing. The coverage guidance recommended the following:

“Urine drug testing (UDT) using presumptive testing is recommended for coverage (weak recommendation) when the results will affect treatment planning.

Definitive testing is recommended for coverage as a confirmatory test only when the result of the presumptive testing is inconsistent with the patient’s history, presentation, or current prescribed medication plan, and the results would change management.

Definitive testing other than to confirm the results of a presumptive test as specified above is not recommended for coverage (weak recommendation), unless the clinician suspects use of a substance that is inadequately detected by presumptive UDT (e.g., fentanyl).

Definitive testing is recommended for coverage for no more than seven substances per day.

In patients receiving treatment for a substance use disorder, random UDT is recommended for coverage (weak recommendation). Up to 36 presumptive tests and 12 definitive tests are recommended per year. These limits must be applied in accordance with mental health parity law.

In patients receiving chronic opioid therapy for chronic pain, random UDT is recommended for coverage (weak recommendation), with frequency of testing depending on the patient's risk level (using a validated opioid risk assessment tool). Definitive testing should be conducted only for confirmatory purposes as described above and should not exceed 12 tests per year:

- Low Risk: Random presumptive testing up to two times per year
- Moderate Risk: Random presumptive testing up to four times per year
- High Risk: Random presumptive testing up to 12 times per year

In patients with unexplained alteration of mental status and when knowledge of drug use is necessary for medical management (e.g., emergency department evaluation for altered mental status), UDT (presumptive and confirmatory definitive testing, if indicated) is recommended for coverage not subject to the above limitations (weak recommendation)."¹⁹

The HERC coverage guidance gives no recommendation for drug testing using oral fluid or hair samples.

Department of Veterans Affairs/Department of Defense (VA/DoD)

The 2022 VA/DoD evidence-based guideline for opioid therapy for chronic pain gave the following recommendation:

"Risk mitigation: We suggest urine drug testing for patients on long-term opioids. (Weak recommendation).

"We suggest urine drug testing (UDT) for patients on long-term opioids to decrease the risk of self-directed violence. The Work Group acknowledges that standard of care includes many risk mitigation strategies, despite the insufficient evidence confirming their usefulness. For most risk mitigation strategies, predictive modeling, and risk assessment tools, little evidence exists to suggest improved safety for patients on long-term opioids or those who are being considered for opioids for chronic pain. The Work Group sought to find studies that investigated the effectiveness or comparative effectiveness of informed consent, risk assessment instruments, pill counts or limited pills per prescription, use of abuse deterrent formulations, diversion prevention interventions, pharmacogenetic testing, random call-backs, monitoring for aberrant or high risk behaviors, or naloxone prescription to improve outcomes, but evidence was lacking for most strategies...

"The Work Group systematically reviewed evidence related to this recommendation (203-207) and considered the assessment of evidence put forth in the 2017 VA/DoD Opioids CPG.(175) Therefore, this is a Reviewed, New-replaced recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including small sample sizes and a lack of evidence on many of the interventions that are typically considered part of risk mitigation strategies.(203-206) The potential benefits of risk mitigation strategies (some improvement in aberrant

behaviors and COMM and ABC scores as well as decreased risk of suicide attempt) (175, 204, 206) were balanced with the potential harms of utilizing risk mitigation strategies, such as time and stigma. Patient values and preferences were somewhat varied because of stigma and level of effort associated with increased monitoring and appointment frequency. Thus, the Work Group decided upon a Weak for recommendation.”

Washington State Department of Labor Industries

The 2013 Washington State Department of Labor Industries guideline for prescribing opioids to treat pain in injured workers gave the following recommendations for urine drug testing:

“Use of chronic opioid therapy requires regular monitoring and documentation, such as screening for risk of co-morbid conditions with validated tools, checking the Prescription Monitoring Program database, assessing clinically meaningful improvement in function and administering random urine drug tests.”²⁰

The 2015 Washington State Agency Medical Directors’ Group (AMDG) Interagency Guideline on Prescribing Opioids for Pain gave the following considerations regarding urine drug testing for specific classes of drugs²¹:

- *Opioids or “Opiates”—Natural (from opium)*
 - Immunoassays for “opiates” are responsive for morphine and codeine but do not distinguish which is present. Confirmatory testing is required to reliably identify drug(s) present. Since codeine is metabolized to morphine and small quantities to hydrocodone, these drugs may be found in the urine. Also, morphine may metabolize to produce a small amount (<10%) of hydromorphone.
- *Opioids—Semisynthetic (derived from opium)*
 - “Opiates” immunoassays may also detect semisynthetic opioids depending on their cross-reactivity pattern. However, a negative result does not exclude use of semisynthetic opioids. Confirmatory testing (GC/MS or LC/MS/MS) is required to verify compliance with the prescribed semisynthetic opioid(s).
 - Since hydrocodone is metabolized in small amounts to hydromorphone, both may be found in the urine. Likewise, oxycodone is metabolized to oxymorphone, so these may both be present in the urine of oxycodone users. However, the reverse is not true. In other words, hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively.
- *Synthetic Opioids*
 - Current “opiates” immunoassays do not detect synthetic opioids. Thus confirmatory testing (GC/MS or LC/MS/MS) is needed to identify these drugs. If the purpose is to document compliance with treatment, the laboratory can be instructed to remove the cutoff concentration so that the presence of lower concentrations can be identified.

The guideline gives no recommendation for drug testing using oral fluid or hair samples.

Centers for Disease Control and Prevention (CDC)

The 2022 evidence-based CDC guideline for prescribing opioids for chronic pain recommended the following:

“When prescribing opioids for chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances (recommendation category: B, evidence type: 4).”²²

A category B recommendation is defined as “(i)ndividual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.”²² Type 4 evidence is defined as “(c)linical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.”²²

American Pain Society/College on Problems of Drug Dependence (APS/CPDD)

The 2014 APS/CPDD evidence-based clinical practice guideline for methadone safety recommended the following regarding urine drug testing:

- The panel recommends that clinicians obtain urine drug screens prior to initiating methadone and at regular intervals in patients prescribed methadone for opioid addiction (strong recommendation, low-quality evidence).
- The panel recommends that patients prescribed methadone for chronic pain who have risk factors for drug use undergo urine drug testing prior to initiating methadone and at regular intervals thereafter; it recommends that clinicians consider urine drug testing in all patients regardless of assessed risk status (strong recommendation, low-quality evidence).²³

The guideline gives no recommendation for drug testing using oral fluid or hair samples.

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American Society of Interventional Pain Physicians (ASIPP)

The 2006 (revised 2012) ASIPP evidence-based guideline for responsible opioid prescribing in chronic non-cancer pain gave the following recommendations:

Regarding the initial steps of opioid therapy, ASIPP states:

“Urine drug testing (UDT) must be implemented from initiation along with subsequent adherence monitoring, in an in office setting with immunoassay and confirmation for accuracy with chromatography in select cases, to identify patients who are non-compliant or abusing prescription drugs or illicit drugs, and urine drug testing may decrease prescription drug use or illicit drug use when patients are in chronic pain management therapy. (Evidence: good)”²⁴

Regarding adherence monitoring, ASIPP states:

“In order to reduce prescription drug use and doctor shopping, adherence monitoring by urine drug testing and PMDPs (prescription drug monitoring programs) provide evidence that is essential to the identification of those patients who are non-compliant or abusing prescription drugs or illicit drugs. (Evidence: fair)”²⁵

The guideline gives no recommendation for drug testing using oral fluid or hair samples.

American Society of Addiction Medicine (ASAM)

In 2013, ASAM published a white paper which, “describes the uses of drug testing as a primary prevention, diagnostic, and monitoring tool to identify the presence or absence of drugs of use or therapeutic agents related to addiction management in multiple settings.”²⁶ The guidelines note the following regarding presumptive and definitive testing:

“POC (point-of-care) testing, relying on IA (automated Immunoassay) technology, is currently limited to a relatively narrow range of drug classes and a few specific drugs (usually 15 or less) and to urine and oral fluid samples. IA drug tests are incapable of distinguishing among specific drugs within a class (e.g. amphetamines, barbiturates, benzodiazepines, opioids), are variably reactive with drugs within a class, and are vulnerable to cross-reactivity with other, sometimes unrelated, molecules. Laboratory-based immunoassays are available for scores of drugs, but because the technology requires an antibody and not all drugs elicit an antibody response (i.e. small molecules such as alcohol or ethyl sulfate), immunoassays are not available for all drugs.

Confirmation of presumptive positive results (and at times presumptive negative results) from laboratory or POC immunoassay tests is sometimes performed, potentially by GC-MS. Gas chromatography separates the different drugs or metabolites in a specimen, and mass spectrometry definitively identifies specific drugs or metabolites. GC-MS analysis typically focuses on a select group of related compounds and to achieve this selectivity may involve cumbersome and time-consuming extraction and chemical derivatization processes.”

The ASAM guidelines cautioned against over-testing:

“Today, it is important not to let the best in drug testing become the enemy of the good, and to not embrace technologies merely because they are available and before their potential for improving patient care has been fully assessed. ***The most important challenge in drug testing today is not the identification of every drug that we are technologically capable of detecting, but to do medically necessary and accurate testing for those drugs that are most likely to impact clinical decisions.*** Choices of technology should be based on the clinical situation and patient risk. Cost must be considered in the choice of drug testing in balance with the clinical goals for each patient. The major need today is the wider and smarter use of the currently available drug testing technologies and practices.”

In 2017, ASAM published consensus guidelines which focused on when, where, and how often it is appropriate to perform drug testing to identify risk in patients with addiction.²⁷ The guideline indicated the following:

- “Before choosing the type of test and matrix, providers should determine the questions they are seeking to answer and familiarize themselves with the benefits and limitations of each test and matrix.
- Drug testing panels should be based on the patient’s drug(s) of choice and prescribed medications, and drugs commonly used in the patient’s geographic location and peer group.
- 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 (eg, treatment transition, changes in medication therapies, changes in legal status).
- 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 guideline gives no recommendation for drug testing using oral fluid or hair samples.

EVIDENCE SUMMARY

The evidence is insufficient to establish the clinical utility of urine drug testing for monitoring patients in pain management and substance use programs. However, several clinical practice guidelines agree that urine drug testing, both presumptive and definitive, is necessary to mitigate risk, monitor adherence to prescribed treatments, and prevent adverse effects in these patient populations. Therefore, presumptive and/or definitive urine drug testing may be considered medically necessary when criteria are met.

There is insufficient evidence to establish the analytic validity and clinical utility of other methodologies used for drug testing, including hair and oral fluid samples. Additionally, no clinical practice guidelines recommend the use of hair or oral fluid samples for drug testing. Therefore, these drug testing methodologies are considered investigational.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online [here](#).

BILLING GUIDELINES AND CODING

- The following laboratory codes are not to be used for testing of drug analytes and are therefore NOT appropriate to use for urine drug testing:
 - 82541 - 82544
 - 83789
- The following codes may not be billed individually, as this is not the least costly alternative for drug screening:
 - 80323 - 80335
 - 80337 - 80350
 - 80352 - 80374

Presumptive Testing

- Presumptive testing must precede definitive testing. Definitive testing must be performed within 48 hours after the aberrant presumptive test.
- Only 1 of the 3 presumptive tests may be billed per day.
- Only 1 unit per date of service may be billed.

Definitive Testing

- Definitive testing should be used to confirm an aberrant presumptive test and should be specific and targeted to each patient's clinical scenario. Therefore, broad-spectrum definitive testing of more than 7 classes of drugs is not medically necessary and is not covered.
- Only 1 unit per date of service may be billed.

CODES*		
Presumptive Urine Drug Testing		
CPT	80305	Drug test(s), presumptive, any number of drug classes, any number of devices or procedures (eg, immunoassay); capable of being read by direct optical observation only (eg, dipsticks, cups, cards, 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 (eg, immunoassay); read by instrument assisted direct optical

		observation (eg, dipsticks, cups, cards, 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 Urine Drug Testing		
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 (eg, 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)
Miscellaneous Codes		
HCPCS	0007U	Drug test(s), presumptive, with definitive confirmation of positive results, any number of drug classes, urine, includes specimen verification including DNA authentication in comparison to buccal DNA, per date of service
	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
	0051U	Prescription drug monitoring, evaluation of drugs present by liquid chromatography tandem mass spectrometry (LC-MS/MS), urine or blood, 31 drug panel, reported as quantitative results, detected or not detected, per date of service
	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
	0093U	Prescription drug monitoring, evaluation of 65 common drugs by LC-MS/MS, urine, each drug reported detected or not detected
	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
	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

	0603U	Drug assay, presumptive, 77 drugs or metabolites, urine, liquid chromatography with tandem mass spectrometry (LC-MS/MS), results reported as positive or negative
	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
	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 (eg, 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 (eg, 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; 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 (eg, 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; 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 (eg, IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (eg, 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
	H0003	Alcohol and/or drug screening; laboratory analysis of specimens for presence of alcohol and/or drugs
	80299	Quantitation of therapeutic drug, not elsewhere specified

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- See the non-covered and prior authorization lists on the Company [Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website](#) for additional information.
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Centers for Disease Control and Prevention: Opioid Overdose- Understanding the Epidemic. <https://www.cdc.gov/overdose-prevention/about/understanding-the-opioid-overdose-epidemic.html>. Accessed 10/25/2025.
2. American Academy of Professional Coders: Qualitative vs. Quantitative Drug Testing. <https://www.aapc.com/blog/19170-qualitative-vs-quantitative-drug-testing/>. Published 2012. Accessed 10/26/2025.
3. Opioid Risk: Screening vs. Confirmatory Tests. <https://www.opioidrisk.com/node/489>. Accessed 10/25/2025.
4. Drummer OH. Drug testing in oral fluid. *Clin Biochem Rev.* 2006;27(3):147-159. <https://www.ncbi.nlm.nih.gov/pubmed/17268583>
5. Eske J. What to know about hair follicle drug tests. <https://www.medicalnewstoday.com/articles/325013>. Published 2024. Accessed 10/25/2025.
6. Barnes AJ, Young S, Spinelli E, Martin TM, Klette KL, Huestis MA. Evaluation of a homogenous enzyme immunoassay for the detection of synthetic cannabinoids in urine. *Forensic science international.* 2014;241:27-34.
7. Blum K, Han D, Femino J, et al. Systematic evaluation of "compliance" to prescribed treatment medications and "abstinence" from psychoactive drug abuse in chemical dependence programs: data from the comprehensive analysis of reported drugs. *PLoS one.* 2014;9(9):e104275.

8. Bodor GS. Quantitative, Multidrug Pain Medication Testing by Liquid Chromatography: Tandem Mass Spectrometry (LC-MS/MS). *Methods in molecular biology* (Clifton, NJ). 2016;1383:223-240.
9. Castaneto MS, Scheidweiler KB, Gandhi A, et al. Quantitative urine confirmatory testing for synthetic cannabinoids in randomly collected urine specimens. *Drug testing and analysis*. 2015;7(6):483-493.
10. Colby JM, Wu AH, Lynch KL. Analysis of codeine positivity in urine of pain management patients. *Journal of analytical toxicology*. 2015;39(5):407-410.
11. Dickerson JA, Laha TJ, Pagano MB, O'Donnell BR, Hoofnagle AN. Improved detection of opioid use in chronic pain patients through monitoring of opioid glucuronides in urine. *Journal of analytical toxicology*. 2012;36(8):541-547.
12. Donroe JH, Holt SR, O'Connor PG, Sukumar N, Tetrault JM. Interpreting quantitative urine buprenorphine and norbuprenorphine levels in office-based clinical practice. *Drug and alcohol dependence*. 2017;180:46-51.
13. Doyle K, Strathmann FG. Cost and Efficacy Assessment of an Alternative Medication Compliance Urine Drug Testing Strategy. *Pain medicine* (Malden, Mass). 2017;18(2):307-315.
14. Gasparini M, Curatolo M, Assini W, Bozzoni E, Tognoli N, Dusi G. Confirmatory method for the determination of nandrolone and trenbolone in urine samples using immunoaffinity cleanup and liquid chromatography-tandem mass spectrometry. *Journal of chromatography A*. 2009;1216(46):8059-8066.
15. Knezevic NN, Khan OM, Beiranvand A, Candido KD. Repeated Quantitative Urine Toxicology Analysis May Improve Chronic Pain Patient Compliance with Opioid Therapy. *Pain physician*. 2017;20(2s):S135-s145.
16. Kwong TC, Magnani B, Moore C. Urine and oral fluid drug testing in support of pain management. *Critical reviews in clinical laboratory sciences*. 2017;54(6):433-445.
17. Krock K, Pesce A, Ritz D, et al. Lower Cutoffs for LC-MS/MS Urine Drug Testing Indicates Better Patient Compliance. *Pain physician*. 2017;20(7):E1107-e1113.
18. Saleem M, Martin H, Tolya A, Coates P. Do all screening immunoassay positive buprenorphine samples need to be confirmed? *Annals of clinical biochemistry*. 2017;54(6):707-711.
19. Health Evidence Review Commission. Health Evidence Review Commission (HERC) Coverage Guidance: Urine Drug Testing. Approved 8/9/2018. <https://www.oregon.gov/oha/HPA/DSI-HERC/EvidenceBasedReports/CG%20Urine%20Drug%20Testing.pdf>. Accessed 10/6/2025.
20. National Guideline C. Guideline for prescribing opioids to treat pain in injured workers. 2013. <https://www.guideline.gov/summaries/summary/43745/guideline-for-prescribing-opioids-to-treat-pain-in-injured-workers?q=urine+drug+testing>
21. Washington State Agency Medical Directors' Group. Interagency Guideline on Prescribing Opioids for Pain. June 2015. <http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf>. Accessed 10/6/2025.
22. Center for Disease Control. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. 2022. <https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm>
23. National Guideline C. Methadone safety: a clinical practice guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. 2014. <https://www.guideline.gov/summaries/summary/49245/methadone-safety-a-clinical-practice-guideline-from-the-american-pain-society-and-college-on-problems-of-drug-dependence-in-collaboration-with-the-heart-rhythm-society?q=urine+drug+testing>
24. National Guideline C. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: part 2 - guidance. Agency for

- Healthcare Research and Quality (AHRQ).
<https://www.guideline.gov/summaries/summary/38257/american-society-of-interventional-pain-physicians-asipp-guidelines-for-responsible-opioid-prescribing-in-chronic-noncancer-pain-part-2--guidance?q=urine+drug+testing>. Published 2012. Accessed
25. Manchikanti L, Abdi S, Atluri S, et al. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance. *Pain physician*. 2012;15(3 Suppl):S67-116.
 26. American Society of Addiction Medicine (ASAM). Drug Testing: A White Paper of the American Society of Addiction Medicine (ASAM).
<https://www.cmm.com.au/files/uploads/resources/20170817102442drug-testing-a-white-paper-by-asam.pdf>. Published 2013. Accessed 10/25/2025.
 27. Jarvis M, Williams J, Hurford M, et al. Appropriate Use of Drug Testing in Clinical Addiction Medicine. *Journal of addiction medicine*. 2017;11(3):163-173.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
7/2023	Marked several codes as termed.
12/2023	Annual update. No changes to criteria.
12/2024	Annual update. Updated criterion III.B
12/2025	Annual update. No changes to criteria.
1/2026	Q1 2026 code set update. One new code added.