Drug Testing in Pain Management and Substance Use Disorder Treatment

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DESCRIPTION

Patients in pain management programs and substance use disorder treatment may misuse prescribed opioids and/or may use nonprescribed drugs. Thus, these patients are often assessed before treatment and monitored while receiving treatment. Drug testing can be part of this monitoring strategy and the collection and analysis of body fluids, especially urine samples, is commonly performed in support of addiction treatment services. The detection of drugs such as alcohol, opiates, benzodiazepines, or their metabolites, and other illegal substances, can provide evidence of ongoing substance abuse and assist in directing treatment. Urine drug testing (UDT) to detect the parent drug and/or its metabolite(s) to demonstrate use of prescription medications and illegal substances of concern for medical treatment purposes are considered beneficial.

According to a 2012 evidence assessment by the American Society of Interventional Pain Physicians, approximately one-third of chronic pain patients do not use opioids as prescribed or may abuse them. In 2016, the International Narcotics Control Board reported that between 1999 and 2010, the number of deaths related to the use of prescription opioid painkillers increased 5-fold among U.S. women and increased by a factor of 3.6 among U.S. men. Additionally, studies have found that a substantial proportion of chronic pain patients inaccurately report nonadherence to prescribed medications and the use of illicit drugs.

Substance use, abuse, and addiction involving numerous prescription and illicit drugs is also a serious social and medical problem. Addiction is a primary, chronic disease of brain reward, motivation, memory, and related circuitry and is manifested by the individual pathologic pursuit of reward and/or relief by substance use and other behaviors.

Various strategies are available to monitor pain management and substance use disorder treatment patients, and multicomponent interventions are often used. Many settings require patients to sign a contract before they are given a prescription for opioids. The contracts generally involve obtaining patients' agreement on behaviors they will engage in during the treatment period (e.g., taking medication as prescribed) and not engage in (e.g., selling prescribed medication and/or obtaining additional prescriptions from other physicians).

Confirming whether patients follow these behavioral guidelines can be a challenge. Risk-assessment screening instruments, such as the Screener and Opioid Assessment for Patients with Pain, and the Opioid Risk Tool, can aid in the assessment of patients' risk for inappropriate drug use. In addition, the presence of "aberrant behaviors" can be used as a marker for patients who are at high-risk for deviating from treatment protocols. Aberrant behaviors include multiple lost prescriptions, obtaining prescriptions from other practitioners, and displaying evidence of acute intoxication during office visits.

Urine Drug Testing (UDT)

There are 2 primary categories of urine drug testing (UDT): presumptive testing (immunoassay) and confirmatory testing (specific drug identification).

Presumptive (Immunoassay) Testing

Immunoassay testing (also called presumptive testing or qualitative testing or screening) can be performed in a laboratory or at point-of-service. Immunoassay tests are based on the principle of competitive binding and use antibodies to detect a particular drug or drug metabolite in a urine sample. With competitive binding, a fixed amount of a labeled drug is added to the urine sample, and the drug or metabolite in the sample competes with the labeled drug for binding sites on the antibody. The amount of labeled antigen that binds with the antibody is inversely proportional to the amount of the drug or metabolite in the sample.

Immunoassay tests vary in the type of compounds they can detect. Some detect specific drugs and may fail to recognize similarly structured drugs within the same class. Other immunoassays identify only classes of drugs and thus results cannot be used to determine which drug a patient is taking. For example, a positive result of an opiate immunoassay can be due to morphine or hydromorphone. The degree of cross reactivity (i.e., an antibody's reactivity with a compound other than the target of the test) varies widely among immunoassays.

Immunoassay findings are generally reported qualitatively as either positive (drug level above a prespecified threshold) or negative (drug level below a prespecified threshold). Raising or lowering the threshold thus changes the proportion of positive tests. A negative test is interpreted as a level below the threshold and does not necessarily mean that the drug or metabolite is absent.

Immunoassays generally have a rapid turnaround time, to within minutes for on-site tests, and 1 to 4 hours for laboratory-based tests

Confirmatory (Specific Drug Identification)
Confirmatory tests are always performed in a laboratory. Gas chromatography/mass spectrometry (GC/MS) and liquid chromatography/mass spectrometry (LC/MS) are considered to be the criterion standard for confirmatory testing. These techniques involve using GC or LC to separate the analytes in a specimen and for MS to identify the specific molecular structures of the drug and its metabolites. The tests are able to quantify the amount of drug or metabolite present in the urine sample. Definitive quantitative tests can be used to confirm the presence of a specific drug identified by a screening test and can identify drugs that cannot be isolated by currently available immunoassays. Results are reported as the specific levels of substances detected in the urine. GC/MS and LC/MS generally require the specification of the drug or drugs to be identified. Alternatively, "broad-spectrum screens" can be conducted. There is a several-day turnaround time for GC/MS and LC/MS testing.

An issue with both types of urine drug testing (UDT) is the possibility of sample tampering to mask the presence of illegal drugs. A variety of products and techniques are available to patients and can be as simple as drinking a large amount of water to dilute the sample. There are also commercial dilution and cleaning products, additives, and urine substitutes. Some of these techniques can be detected by visual inspection of the sample (e.g., color) or by on-site testing of sample characteristics including urine temperature, creatinine concentration, and specific gravity.

The correct interpretation of UDT results is very important. Knowledge of drug metabolites is essential for accurate interpretation. Accurate interpretation of test results also requires knowledge of the drug manufacturing process. For example, due to manufacturing impurities, a small amount of hydrocodone may be present in urine samples from patients prescribed oxycodone. Thus, it would be acceptable to detect a small amount of hydrocodone if high amounts of oxycodone were also present.

There are various approaches to incorporating UDT into pain management and substance use disorder treatment settings. Most commonly, patients undergo urine drug screening before beginning treatment to verify current drug use. Some clinicians believe that UDT should be routinely used to establish baseline information about substance use, but the optimal frequency and interval of testing remains uncertain. A universal approach to screening may uncover more inappropriate use and may reduce patients' sense that testing is being performed due to a lack of trust. However, routine universal screening may place an unnecessary burden on the health care system and on the doctor-patient relationship. An alternative approach is selective testing of patients who are judged to be at increased risk for drug misuse.

Existing protocols vary for the use of presumptive versus definitive tests. Some involve conducting routine confirmation of positive presumptive tests with definitive quantitative testing. Others use selective confirmation of positive presumptive tests, such as when an unexpected immunoassay result is not adequately explained by the patient. There is also a mixed approach, with routine confirmation of presumptive tests only for drugs with poor-performing immunoassays.

Full informed consent is a requirement before UDT. Patients should be informed of the specific drug testing protocol before treatment and should provide written agreement with the plan for monitoring. A patients' refusal to consent to urine testing should be considered a factor in the overall assessment of patients' ability to adhere to treatment

Oral Fluid Drug Testing

Oral fluid (liquid samples obtained from the oral cavity) can potentially be used to test for drug use. Oral fluid contains secretions from several different sources, including secretions from the 3 pairs of major salivary glands (parotid, sublingual, and submandibular), secretions from the minor salivary glands, oro-nasopharyngeal secretions, and cellular debris. The mixture of fluids obtained varies depending on the collection method used (e.g., spitting, suctioning, draining, or collection on some type of absorbent material). Drug concentrations can be affected by the collection method and by the use of saliva stimulation methods. Several collection devices are commercially available in the U.S., and they generally involve collection on an absorbent material, such as foam pads; pads are then placed in a container with a stabilizing buffer solution. Drug concentrations may also depend on how the oral fluid is recovered from the collection device (e.g., by centrifugation or by applying pressure). Drug concentrations may not reflect blood levels because of residual amounts of a drug (specifically those ingested or smoked) remaining in the oral cavity after recent use.

Analysis techniques must be able to detect drugs present in low concentration and in a small volume of fluid (often <1 mL). Immunoassay techniques are available to detect drugs in oral fluid; they require a small sample volume (»25 µL). Immunoassays tend to be relatively sensitive techniques, but they have low specificity. Confirmation analysis is generally performed using MS-based methods. In recent years, advancements have been

made in MS analysis techniques, including the development of multianalyte LC/MS methods.
A practical advantage of oral fluid collection compared with urine collection is that samples can be obtained under the direct supervision and without loss of privacy. It has been used in situations where urine sampling is impractical, such as testing drivers during traffic stops. Oral fluid sampling also has the potential to be useful in pain management or substance use disorder treatment settings, particularly when substitution or tampering with urine drug samples is suspected.

Hair Testing
Hair is composed of protein that traps chemicals in the blood at the time the hair develops in the follicle. Hair on the human head grows at approximately 0.5 inches per month. Thus, a 1.5-inch hair sample could be used to detect drug use during the previous 90 days. Potential advantages of hair as a drug testing source include noninvasive collection; ease of collection, storage, and shipping; availability of samples for testing and retesting; and difficulty in tampering. Potential disadvantages include recent drug use (i.e., within the past 7 days) cannot be detected; difficulty in detecting very light drug use (e.g., a single episode); and drug levels can be affected by environmental exposure. In addition, variation in hair texture as well as cosmetic hair treatments can affect drug incorporation into hair and the accuracy of drug tests on hair samples. As with other types of samples, hair can be initially tested using immunoassay techniques, with confirmation by MS-based methods. Hair testing has been used in a variety of situations where detection of drug use during the previous several months is desired (e.g., pre-employment screening, post-drug-treatment verification of relapse). There is insufficient evidence in the published peer-reviewed scientific literature to establish the role of hair analysis for clinical drug testing. Further, there is a lack of professional society support as evidenced by published consensus guidelines to establish hair analysis as a standard of care for drug testing.

Drug Testing Indications and Treatment Setting
Indications for drug testing depend upon the treatment setting and clinical purpose. According to a consensus statement from the American Society for Addiction Medicine (ASAM) on the appropriate use of drug testing in clinical addiction medicine, drug testing is recommended as a therapeutic tool for evidence-based addiction treatment and can be used in all addiction treatment settings. Treatment providers should include drug testing at intake to assist in a patient's initial assessment and treatment planning. Using a variety of laboratory methods, clinical drug testing may be presumptive or definitive and may be used to detect prescription drugs of abuse, illicit drugs and other substances. Drug testing in a physician supervised treatment setting may be appropriate when there is a high suspicion or concern of drug abuse or misuse for the individual being tested. This may include testing of one or more metabolites of a prescribed drug to assure actual compliance with the drug regimen rather than diversion. The results of testing should be necessary for treatment planning. Clinical records should support the need for testing for the specific drug(s) or substance(s) of interest by documentation regarding the diagnosis, history and physical examination and/or behavior of the individual being tested. Records should also reflect how results of testing will impact the treatment plan.

Specimen Source
Drug testing using urine has been evaluated rigorously and is the most common biological substance used in the addiction treatment setting.

Specimen Adulteration
SAMHSA (2012) has established specific requirements for urinary specific gravity, pH, and creatinine concentration for a specimen to be considered valid for drug testing. Individuals may attempt to undermine drug testing using several methods, including dilution and adulteration. Large amounts of water may be ingested or added to a urine specimen with the intent to dilute the level of a drug below a detectable threshold. Masking agents, such as hydrastis canadensis tea or niacin may be consumed with the intent to hide the presence of a misused or abused drug. Other adulterants including ammonia, bleach, hydrogen peroxide, liquid soaps, vinegar, and radish and mustard seed extracts may be added to the urine specimen. Some individuals may substitute a drug-free urine specimen or submit a sample of synthetic urine in an attempt to prevent the detection of the drug(s) or substance of abuse. According to ASAM, if there is suspicion that a sample had been tampered with, it should be tested for specimen validity including creatinine concentration, pH level, specific gravity, and adulterants.

Specimen Verification
DNA analysis and other methods have been proposed to ensure that the source of a specimen for testing is the same as the individual for whom testing is intended. Specimen verification is considered part of the quality assurance process for laboratory test management and is not a separately reimbursable service.

Rationale
Guidelines with evidence reviews of published peer-reviewed scientific literature suggest that evidence of benefit on health outcomes for drug testing for both patients in chronic pain using opioids and patients with substance use disorder is limited and usually confounded with drug testing as part of a multifaceted intervention of risk mitigation or contingency management. There is also no clear evidence in the literature regarding the most effective frequency of testing.

Notwithstanding the lack of evidence, clinical input and guidelines indicate that drug testing is standard of care. Therefore, a rigorous study comparing drug testing to no drug testing and following patients for health outcomes is unlikely to be performed.

Thus, a traditional evidence review will not be performed, and relevant national and regional clinical practice guidelines were sought to inform the review.

Summary of Evidence
For individuals who have chronic pain treated with opioids who receive drug testing, there is limited peer-reviewed scientific literature to guide drug testing strategies; however, guidelines indicate that drug testing is standard of care. Guidelines from

Centers for Disease Control and Prevention, American Society of Interventional Pain Physicians, American Pain Society and American Academy of Pain Medicine, American College of Occupational and Environmental Medicine, Department of Veterans Affairs and Department of Defense have recommended drug testing and consider the frequency of testing to be at the discretion of the health care provider, based on an assessment of the patient's risk for misuse or addiction.

For individuals who have a drug addiction who are in substance use disorder treatment who receive drug testing, there is limited peer-reviewed scientific literature to guide drug testing strategies; however, guidelines indicate that drug testing is standard of care. Guidelines from the American Society of Addiction Medicine have recommended drug testing and consider the frequency of testing to be at the discretion of the health care provider, based on an assessment of the patient's risk and substance(s) used.

There may be certain threshold for the number of tests that are approved without review with subsequent tests requiring medical review. Patients who have unusually high numbers of tests ordered need medical review to confirm that the tests meet medical necessity.

Appropriate frequency of testing depends on many factors:

- Tests' detection capabilities and windows of detection
- Patient factors such as severity and chronicity of addiction
- Substance(s) used
- Phase of treatment
    - During the stabilization phase, drug testing may be scheduled more frequently
    - During the maintenance phase, drug testing may be scheduled less frequently

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 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.

Practice Guidelines and Position Statements

American Academy of Family Physicians (AAFP)

In 2019, the American Academy of Family Physicians (AAFP) published recommendations concerning ordering and interpreting urine drug tests which states the following:

- Several federal and state regulations have been enacted that recommend or require urine drug testing in patients receiving long-term opioid therapy. Similar guidance may apply to patients receiving long-term benzodiazepine or stimulant therapy.
- The frequency of urine drug testing depends on individual risk factors and is ultimately left to the attending physician; however, they do state a recommended frequency for urine drug testing given in the table below:

Recommended Frequency for Urine Drug Testing

Level of Misuse Risk	Frequency to Testing
Low (no risk factors)	Every 6 to 12 months
Moderate	Every 3 to 6 months
High (mental health disorder, substance use disorder, prior opioid misuse, aberrant behavior*) or opioid dosage >120 morphine milligram equivalents	Every 1 to 3 months

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

American Academy of Pain Medicine (AAPM)

In 2018, the American Academy of Pain Medicine (AAPM) published a consensus statement on urine drug monitoring (UDM) in patients with chronic pain who are prescribed opioids. The expert panel recommended that definitive UDM is the most clinically useful method for assessing baseline opioid use and misuse in patients with chronic pain. The panel suggested the following strategies to determine UDM frequency:

- a physical examination to obtain patient history and behaviors that can be used to predict opioid misuse should be conducted
- validated tools to assess the risk for aberrant medication-taking behavior, opioid misuse, opioid use disorder, and the potential for respiratory depression/overdose should be used
- prescription drug monitoring programs (PDMPs) along with previous UDM results should be checked

Additionally, AAPM recommended that low-risk patients should be tested at least annually, moderate risk patients should be tested two or more times per year, and high-risk patients should be tested three or more times per year. Additional monitoring can be performed as frequently as necessary according to clinical judgment.

American Society of Addiction Medicine (ASAM)

In 2017, the American Society of Addiction Medicine (ASAM) published a consensus statement on the appropriate use of drug testing in clinical addiction. The ASAM stated that drug testing assists with monitoring adherence and abstinence in treatment and can improve patient outcomes. Therefore, drug testing should be used in addiction treatment settings. The guidelines included the following recommendations regarding the frequency of testing:

- 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.
- During the initial phase of treatment, drug testing should be done at least weekly.
- When a patient is stable in treatment, drug testing should be done at least monthly.
- Increasing the frequency of testing does not result in decreased substance use.

In 2019, the American Society of Addiction Medicine (ASAM) published a public policy statement on the ethical use of drug testing in the practice of addiction medicine. The statement included the following recommendations:

- Drug testing is recommended as a therapeutic tool in evidence-based addiction treatment.
- Drug testing should be used only when clinically necessary.
- Presumptive testing should be a routine part of initial and ongoing patient assessment.
- Definitive testing may be used when the results will alter the care plan.
- It is inappropriate to order definitive testing for all analytes in every drug test conducted on a patient.
- Clinicians should ensure that drug test results remain confidential.
- Clinicians ordering drug tests should be aware of the costs of different testing methods and the financial burden that the patient and society may incur.
- If clinicians responsible for making clinical decisions based on drug test results do not have training in toxicology, collaboration should occur with a toxicologist or an individual with Medical Review Officer certification
- It is unethical to provide or receive incentives for the use of drug testing independent of a clinical rationale.

In 2020, the American Society of Addiction Medicine (ASAM) published a National Practice Guideline for the Treatment of Opioid Use Disorder. The guideline noted that urine drug testing can be used during assessment and diagnosis to validate patient self-reported information and to identify poly-substance use. Additionally, testing can be used to monitor patients for adherence to medication and for use of illicit and controlled substances during treatment. The frequency of drug testing is determined by a number of factors including the stability of the patient, type of treatment and treatment setting. The guideline also notes that no further clarification was found in the literature related to urine drug testing and this is considered a gap in literature.

American Society of Interventional Pain Physicians (ASIPP)
In 2017, the American Society of Interventional Pain Physicians (ASIPP) issued a guideline for Responsible, Safe, and Effective Prescription of Opioids for Chronic Non-Cancer Pain, which noted that presumptive urine drug testing (UDT) is implemented from initiation along with subsequent adherence monitoring, using in-office point of service testing, followed by confirmation with chromatography/mass spectrometry for accuracy in select cases, to identify patients who are non-compliant or abusing prescription drugs or illicit drugs. Urine drug testing may decrease prescription drug abuse or illicit drug use when patients are in chronic pain management therapy.

Regulatory Status
The U.S. Food and Drug Administration (FDA) regulates drugs of abuse tests that are sold to consumers or health care professionals in the U.S. The FDA reviews many of these tests before they are sold for use. In its review, the FDA evaluates the design and performance of tests and sample collection systems to help ensure that they produce accurate results. The FDA does not review drugs of abuse tests intended for employment and insurance testing provided they include a statement in their labeling that the device is intended solely for use in employment and insurance testing. The FDA review does not include test systems intended for federal drug testing programs (eg, programs run by the Substance Abuse and Mental Health Services Administration, the Department of Transportation, and the U.S. military.)

The FDA has cleared assays for urine testing of drugs of abuse a
s well as oral fluid specimen collection devices and assays for analysis of oral fluid for drugs of abuse through the 510(k) regulatory pathways. Several collection devices are commercially available in the U.S., and they generally involve collection on an absorbent material, such as foam pads; pads are then placed in a container with a stabilizing buffer solution. Immunoassays of urine specimens have previously been cleared by the FDA and are used as the predicates for the oral fluid immunoassays.

Several oral fluid drug test collection devices have been cleared for marketing by FDA through the 510(k) process include but are not limited to the following:

- Intercept™ Oral Fluid Drug Testing System (OraSure Technologies, Bethlehem, PA)
- Oral-Eze Saliva Collection System (Quest Diagnostics, Madison NJ)
- Quantisal® Oral Fluid Collection Device (Alere, Waltham, MA

PRIOR APPROVAL

Not applicable.

POLICY

Presumptive Urine Drug Testing (UDT)

Presumptive urine drug testing (UDT) (80305, 80306, 80307) to verify compliance with treatment, identify undisclosed drug use or abuse or evaluate aberrant* behavior may be considered **medically necessary**, beginning at the start of treatment, as part of a monitoring program tailored to the unique needs of the individual who are:

- Receiving treatment for chronic pain with prescription opioid or other potentially abused medication; **or**
- Undergoing treatment for, or monitoring for relapse of, opioid addiction or substance abuse disorder.

*Aberrant behavior defined by **one or more** of the following:

- Lost prescriptions
- Requests for early refills
- Obtained opioids from multiple providers
- Unauthorized dose escalation
- Apparent intoxication.

Presumptive urine drug testing (UDT) (80305, 80306, 80307) may be considered **medically necessary** for the following:

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

Definitive Urine Drug Testing (UDT)

Definitive urine drug testing (UDT) (G0480, G0481, G0482, G0483, G0659) to verify compliance with treatment, identify undisclosed drug use or abuse, or evaluate aberrant* behavior may be considered **medically necessary** beginning at the start treatment, as part of a monitoring program tailored to the unique needs of individuals who meets below criteria:

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

One of the Following Testing Scenarios:

- Definitive testing following prior presumptive testing:
    - The presumptive urine drug testing (UDT) was done for a medically necessary reason; **and**
    - The presumptive urine drug test (UDT) 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 medication; **and**
        - The specific definitive test(s) ordered are supported by documented rationale for each test ordered; and

    - Clinical documentation reflects how the results of the test(s) will be used to guide clinical care; **OR**

- Definitive testing without prior presumptive testing:
    - Presumptive urine drug tests (UDTs) 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**
    - The specific definitive test(s) ordered are supported by documented clinical rationale for each test ordered; **and**
    - Clinical documentation reflects how the results of the test(s) will be used to guide clinical care.

*Aberrant behavior defined by **one or more** of the following:

- Lost prescriptions
- Requests for early refills
- Obtained opioids from multiple providers
- Unauthorized dose escalation
- Apparent intoxication.

The use of blood samples as an alternative to urine for drug testing (UDT) may be considered **medically necessary** when the use of urine is not feasible (for example, when an individual has advanced kidney failure and on dialysis or an individual with shy bladder).

The testing of presumptive and definitive testing at the same time is considered **not medically necessary,** unless the criteria above is met regarding definitive testing without prior presumptive testing because presumptive testing is not available for the drug in question, as the results of presumptive testing should guide the clinician when definitive testing is required.

Note: Frequency

The frequency of drug testing should be individualized to the treatment plan. Frequency shall not exceed every seven days at any time during the treatment process for both presumptive and definitive testing.

- *Baseline screening before initiating treatment or at the time treatment is initiated, 1 time per program entry.*
- *Stabilization phase - targeted weekly screening for a maximum of 4 weeks.*

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

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

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

The use of DNA analysis to ensure that the source of a specimen for testing is the same as the individual for whom testing is intended is considered **not medically necessary** as specimen verification is considered part of the quality assurance process for laboratory test management.

The use of any of the following for drug testing is considered **not medically,** including but not limited to:

- Routine testing or testing completed due to any of the following (due to non-individualized treatment):
  - Standing orders
  - Blanket orders
- Reflex testing
- Testing for non-medical purposes
- When the patient is not in an active phase of treatment (maintenance) or participating in a chronic pain program

Panel Drug Testing
The use of presumptive or definitive drug testing panels is considered **not medically necessary.** 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 in guiding clinical management of the individual.

Policy Guidelines

Documentation Requirements
Medical records should support the need for testing for the specific substance(s) of interest by documentation regarding the diagnosis, history, and physical examination and/or behavior of the patient. Medical records should also justify the test that is being used and describe how results of testing will guide medical decision-making.

Pain Management
The risk level for an individual patient should include both a global assessment of risk factors and monitoring for the presence of aberrant behavior. Standardized risk-assessment tools are available, such as the 5-item Opioid Risk Tool (ORT). Another screening instrument is the Screener and Opioid Assessment for Patients in Pain, which is a 24-item tool.

Aberrant behavior is defined by one or more of the following:

- multiple lost prescriptions,
- multiple requests for early refill,
- obtained opioids from multiple providers,
- unauthorized dose escalation, and
- apparent intoxication during previous visits.

Presumptive Test Availability

There may not be commercially available tests for certain synthetic or semisynthetic opioids. The below table describes limitations on availability of presumptive tests.

Limitations in Availability of Presumptive Immunoassays

Drug Type	**Potential limitations in availability of or sensitivity of presumptive immunoassays for certain drugs in urine**
Benzodiazepines	• Clonazepam and lorazepam are detected with varying sensitivity by different assays. • Therapeutic doses of benzodiazepines are generally not detected
Semisynthetic Opioids	• Oxycodone and oxymorphone (a metabolite of oxycodone) are detected in a few but not most standard opiate immunoassays depending on the antibodies used by the manufacturer. • Hydrocodone and hydromorphone (a metabolite of hydrocodone) are also detected in most standard opiate immunoassays.
Synthetic opiates	• Meperidine, methadone, buprenorphine, and fentanyl will not be detected in a standard opiate immunoassay and require their own definitive test for detection.
Natural opioids	• Morphine and codeine (which is metabolized to morphine) are detected by standard immunoassays for opiates but presumptive testing does not distinguish specific drug present. • Heroin is unable to be specifically detected by presumptive tests due to rapid metabolism to 6-MAM and subsequently to morphine.

Interpreting Unexpected Urine Drug Tests Results

Unexpected Result	Possible Explanations	Possible Actions for the Physician
Test is negative for prescribed opioid	• False-negative • Noncompliance • Diversion	• Conduct confirmatory testing, specifying the drug of interest (e.g., oxycodone often missed by immunoassay) • Take a detailed history of patient's medication use for the preceding 7 days (e.g., could learn that patient ran out several days before test) • Ask patients if they've given the drug to others • Monitor compliance with pill counts
Test is positive for nonprescribed opioid or benzodiazepines	• False-positive • Patient acquired opioids from other sources (double doctoring, "street")	• Repeat urine drug testing regularly • Ask patients if they accessed Opioids from other sources • Assess for opioid misuse/addiction • Review/revise treatment agreement
UDS positive for illicit drugs (e.g., cocaine, cannabis)	• False-positive • Patient is occasional user or addicted to the illicit drug • Cannabis is positive for patients taking certain medications (eg, dronabinol)	• Repeat urine drug test regularly • Assess for abuse/addiction and refer for addiction treatment as appropriate

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.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 80305 Drug test(s), presumptive, any number of drug classes, any number of devices or procedures (e.g., immunoassay); capable of being read by direct optical observation only (e.g., 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 (e.g., immunoassay); read by instrument assisted direct optical observation (e.g., 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 (e.g., utilizing immunoassay [e.g., EIA, ELISA, EMIT, FPIA, IA, KIMS, RIA]), chromatography (e.g., GC, HPLC), and mass spectrometry either with or without chromatography, (e.g., DART, DESI, GC-MS, GC-MS/MS, LC-MS, LC-MS/MS, LDTD, MALDI, TOF) includes sample validation when performed, per date of service
- 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)), (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 (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; 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

- P2031 Hair analysis (excluding arsenic)
- 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. For the ToxProtect Test from Genotox Lab
- 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. For the Cordant CORE test by Cordant Health Solutions
- 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. For the UCompliDX test by Elite Medical Labs
- 0054U Prescription drug monitoring, 14 or more classes of drugs and substances, definitive tandem mass spectrometry with chromatography, capillary blood, quantitative report with therapeutic and toxic ranges, including steady-state range for the prescribed dose when detected, per date of service. For the AssuranceRX Micro Serum test by Firsttox Lab
- 0079U Comparative DNA analysis using multi selected single-nucleotide polymorphisms (SNP's), urine and buccal DNA, for specimen identity verification. For the ToxLok test from InSource Diagnostics
- 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. For the NextGen Precision test by Precision Diagnostics
- 0093U Prescription drug monitoring, evaluation of 65 common drugs by LC-MS/MS, urine, each drug reported detected or not detected. For the ComplyRX test by 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
- 0143U Drug assay, definitive, 120 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. CareViewRx Plus, Newstar Medical Laboratories [when specified as related to chronic pain, opioid addiction and substance use disorder]
- 0144U Drug assay, definitive, 160 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using

multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. CareViewRx Plus, Newstar Medical Laboratories [when specified as related to chronic pain, opioid addiction and substance use disorder]

- 0145U Drug assay, definitive, 65 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. PainViewRx, Newstar Medical Laboratories, LLC

  0146U Drug assay, definitive, 80 or more drugs or metabolites, urine, by quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. PainViewRx, Newstar Medical Laboratories, LLC
- 0147U Drug assay, definitive, 85 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. RiskViewRx, Newstar Medical Laboratories, LLC
- 0148U Drug assay, definitive, 100 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. RiskViewRx, Newstar Medical Laboratories, LLC
- 0149U Drug assay, definitive, 60 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. PsychViewRx, Newstar Medical Laboratories, LLC
- 0150U Drug assay, definitive, 120 or more drugs or metabolites, urine, quantitative liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring (MRM), with drug or metabolite description, comments including sample validation, per date of service. PsychViewRx, Newstar Medical Laboratories, LLC
- 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
- 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 (CareView 360, Newstar Medical Laboratories LLC.)

SELECTED REFERENCES

- Substance Abuse and Mental Health Services Administration (US); 2006 Urine Collection and Testing Procedures and Alternative Methods for Monitoring Drug Use. (Treatment Improvement Protocol (TIP) Series, No. 47.)
- Substance Abuse and Mental Health Services Administration (US); 2009 Screening and Assessing Adolescents for Substance Use Disorders. (Treatment Improvement Protocol (TIP) Series, No. 31.)
- Substance Abuse and Mental Health Services Administration (US); 1999 Treatment of Adolescents with Substance Use Disorders. (Treatment Improvement Protocol (TIP) Series, No. 32.)
- ASAM Policy Statement. Drug Testing As A Component Of Addiction Treatment and Monitoring Programs and in Other Clinical Settings July 1, 2002; rev. October 1, 2010.
- The American Psychiatric Publishing Textbook of Substance Abuse Treatment, 4th Edition. Edited by Marc Galanter, Herbert Kleber. 2009.
- Principles of Addiction Medicine, 4th Edition. Edited by Richard Ries, David Fiellin, Schannon Miller, Richard Saitz. 2009.
- American Psychiatric Association guidelines for treatment of substance use disorders, American Journal of Psychiatry. 2007 Apr;164(4 Suppl):5-123.
- Manchikanti L, Manchukonda R, Pampati V et al. Does random urine drug testing reduce illicit drug use in chronic pain patients receiving opioids? Pain Physician 2006; 9(2):123-9
- Manchikanti L, Atluri S, Trescot AM et al. Monitoring opioid adherence in chronic pain patients: tools, techniques, and utility. Pain Physician 2008; 11(2 Suppl):S155-80.
- 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 I—evidence assessment. Pain Physician 2012; 15(3 Suppl):S1-65.
- American Society of Addiction Medicine (ASAM). Public Policy Statement On Drug Testing as a Component of Addiction Treatment and Monitoring Programs and in other Clinical Settings.
- 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 treatment.
- Hamill-Ruth RJ, Larriviere K, McMasters MG. Addition of objective data to identify risk for medication misuse and abuse: the inconsistency score. Pain Medicine. 2013 Dec;14(12):1900-1907.
- Opioid Risk Tool (ORT).
- Dupouy J, Memier V, Catala H, et al. Does urine drug abuse screening help for managing patients? A systematic review. Drug Alcohol Depend. Mar 1 2014;136:11-20. PMID 24417964

- American Academy of Child and Adolescent Psychiatry (AACAP). Practice parameter for the assessment and treatment of children and adolescents with substance use disorders. Published June 2015
- PubMed Health. Drug names and classes. Published August 2015.
- UpToDate, Inc. Screening for unhealthy use of alcohol and other drugs in primary care. Updated July 2016.
- UpToDate, Inc. Substance use disorder: principles for recognition and assessment in general medical care. Updated July 2016.
- UpToDate, Inc. Testing for drugs of abuse (DOA). Updated July 2016.
- 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. Feb 2017;20(2S):S3-S92. PMID 28226332
- Jarvis M, Williams J, Hurford M, et al. Appropriate use of drug testing in clinical addiction medicine. J Addict Med. May/Jun 2017;11(3):163-173. PMID 28557958
- Bertholf RL, Sharma R, Reisfield GM. Predictive value of positive drug screening results in an urban outpatient population. J Anal Toxicol. Nov 2016;40(9):726-731. PMID 27550994
- Snyder ML, Fantz CR, Melanson S. Immunoassay-based drug tests are inadequately sensitive for medication compliance monitoring in patients treated for chronic pain. Pain Physician. Feb 2017;20(2S):SE1-SE9. PMID 28226337
- American Society of Addiction Medicine (ASAM). Public Policy Statement on the Ethical Use of Drug Testing in the Practice of Addiction Medicine. 2019 Apr 3.
- Argoff CE, Alford DP, Fudin J, et al. Rational Urine Drug Monitoring in Patients Receiving Opioids for Chronic Pain: Consensus Recommendations. Pain Med. Jan 01 2018; 19(1): 97-117. PMID 29206984
- UpToDate Testing for drugs of abuse (DOAs). Robert J Hoffman M.D., Topic last updated September 21, 2022. Also available at https://www.uptodate.com
- UpToDate Urine drug testing for patients with chronic pain. Gogan Mahajan M.D., Topic last updated September 17, 2021. Also available at https://www.uptodate.com

POLICY HISTORY

Date	Reason	Action
October 2022	Annual Review	Policy Renewed
October 2021	Annual Review	Policy Revised
October 2020	Annual Review	Policy Revised
November 2019	Annual Review	Policy Revised
October 2018	Annual Review	Policy Revised
October 2017	Annual Review	Policy Renewed
October 2016	Annual Review	Policy Revised
October 2015	Annual Review	Policy Renewed

November 2014		New Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

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Medical Policy Analyst
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