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Drug Testing in Pain Management and Substance Abuse Treatment

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I. Description

Patients in pain management programs and substance abuse treatment may misuse prescribed opioids and/or may use nonprescribed drugs. Thus, these patients are often assessed before treatment and monitored while receiving treatment. Urine drug testing (UDT) can be part of this monitoring strategy; it is most often used as part of a multifaceted intervention that includes other components such as patient contracts.

For individuals who have chronic pain treated with opioids who receive UDT, the evidence includes nonrandomized comparative studies and a systematic review. Relevant outcomes are test accuracy and validity, health status measures, and resource utilization. There is insufficient evidence on diagnostic accuracy. No randomized controlled trials (RCTs) evaluating clinical utility were identified. Several nonrandomized comparative studies have provided inconclusive evidence on whether UDT in the pain management setting improves patient outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a drug addiction who are in substance abuse treatment who receive UDT, the evidence includes 2 RCTs. Relevant outcomes are test accuracy and validity, health status measures, and resource utilization. No studies were identified that evaluated the accuracy of UDT compared with a valid reference standard in individuals undergoing substance abuse treatment. One RCT focused specifically on testing to determine eligibility for take-home methadone. The second RCT found that UDT identified drug use in a substantial number of patients who denied illicit usage; the impact on treatment success was not addressed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2014 indicated that UDT is standard of care, and supported the medical necessity of UDT under certain circumstances. Thus, UDT may be considered medically necessary in selected situations.

For individuals who have chronic pain treated with opioids or with a drug addiction in substance abuse treatment who receive oral fluid drug testing, the evidence includes diagnostic accuracy studies using UDT as the reference standard. Relevant outcomes are test accuracy and validity, health status measures, and resource utilization. The limited number of studies on diagnostic

accuracy of oral fluid testing compared with UDT had variable findings. No studies were identified assessing the impact of oral fluid testing on health outcomes compared with UDT or no drug testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have chronic pain treated with opioids or with a drug addiction in substance abuse treatment who receive hair drug testing, the evidence includes 1 diagnostic accuracy study in the psychiatric treatment setting. Relevant outcomes are test accuracy and validity, health status measures, and resource utilization. Hair testing cannot detect recent drug use (ie, in the past few days) and thus has limited applicability to pain management or substance abuse treatment settings, except, perhaps, for initial intake. There are no studies comparing the diagnostic accuracy of hair testing compared to UDT in either setting. However, 1 relatively small study tested the hair and urine of known drug users recruited from a psychiatric clinic. The study looked for drug use over the past several months rather than the shorter timeframe generally needed in pain management or drug treatment settings. No studies were identified on the clinical utility of hair testing in pain management or substance abuse treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

II. Criteria/Guidelines

A. In outpatient **pain management**, **presumptive** (ie, immunoassay) urine drug testing is covered for:

1. **Baseline screening** before initiating treatment or at the time treatment is initiated, when the clinical records document an adequate clinical assessment of patient history and assessment of risk of substance abuse.
2. **Subsequent monitoring** of treatment at a frequency appropriate for the risk level of the individual patient as follows:
   a) Low risk using an instrument such as Opioid Risk Tool (ORT): Once a year
   b) Moderate risk: Twice a year
   c) High risk or opioid dose >120 mg Morphine Equivalent Dose (MED)/d: 3-4 times a year
   d) Recent history of aberrant behavior: Each visit (a maximum of one visit per week)

B. In outpatient **substance abuse treatment**, in-office or point-of-care **presumptive** (ie, immunoassay) urine drug testing is covered under the following conditions:

1. **Baseline screening** before initiating treatment or at the time treatment is initiated (ie, induction phase), 1 time per program entry, when clinical records document an adequate clinical assessment of patient history and risk of substance abuse is performed; or
2. **Stabilization phase** – targeted weekly presumptive screening for a maximum of 4 weeks; or
3. **Maintenance phase** – targeted presumptive screening once every 1 to 3 months.

C. **Definitive** (ie, confirmatory) urine drug testing, in outpatient pain management or substance abuse treatment is covered under the following circumstances:

1. Medical records document that immunoassays for the relevant drug(s) are not commercially available.
2. In specific situations for which medical records document that definitive drug levels are required for clinical decision making:

a. Unexpected positive test inadequately explained by the patient
b. Unexpected negative test (suspected medication diversion)
c. Need for quantitative levels to compare with established benchmarks for clinical decision making

III. Limitations

A. Urine drug testing is not covered when the above criteria are not met including but not limited to routine presumptive or definitive urine drug testing (eg, testing at every visit, without consideration for specific patient risk factors or without consideration for whether definitive testing is required for clinical decision making).
B. Hair drug testing and oral fluid drug testing are not covered because they are not known to improve health outcomes.
C. Drug testing for a panel of compounds using definitive testing methods are not covered because they are not known to improve health outcomes.
D. Definitive drug testing is covered only for those compounds that could have contributed to the positive preliminary result.

IV. Administrative Guidelines

Precertification is not required for a urine drug test. Supporting documentation should be legible, maintained in the patient's medical record and available to HMSA upon request. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

CPT Codes	**Description**
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	;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., GC, HPLC), and mass spectrometry either with or without chromatography, (e.g., DART, DESI, GC-MS/MS, LC-MS, LC-MS/MS, LDTD, MALDI, TOF) includes sample validation when performed, per date of service
80320-80377	Definitive drug testing code range (testing may also be reported with the appropriate code from the chemistry code range)
HCPCS Codes	**Description**
G0480	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 and excluding immunoassays [e.g., IA, EIA, ELISA, EMIT, FPIA] and enzymatic methods]e.g., alcohol dehydrogenase]); qualitative or quantitative, all sources(s), includes specimen validity testing, per day, 1-7 drug class(es), including metabolite(s) if performed
G0481	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 and excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase); qualitative or quantitative, all sources(s), includes specimen validity testing, per day, 8-14 drug class(es), including metabolite(s) if performed
G0482	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 and excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase); qualitative or quantitative, all sources(s), includes specimen validity testing, per day, 15-21 drug class(es), including metabolite(s) if performed
G0483	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 and excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase); qualitative or quantitative, all sources(s), 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 (new code 01/01/17)

V. Background

According to an 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. Moreover, studies have found that a substantial proportion of chronic pain patients inaccurately report nonadherence to prescribed medications and use of illicit drugs.

Various strategies are available to monitor pain management and substance abuse 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 (eg, taking medication as prescribed) and not engage in (eg, 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.

Another strategy for monitoring patients is testing of biologic specimens for the presence or absence of drugs. Currently, urine is the most commonly used biologic substance. Advantages of urine drug testing (UDT) are that it is readily available and standardized techniques for detecting drugs in urine exist. Other biologic specimens (eg, blood, oral fluids, hair, sweat) can also be tested and may gain in popularity over time as techniques for collecting and analyzing these specimens become more standardized. In addition to urine testing, this review will address testing for oral fluids and hair.

URINE DRUG TESTING

There are 2 primary categories of UDT: immunoassay and specific drug identification.

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 to an opiate immunoassay can be due to morphine or hydromorphone. The degree of crossreactivity (ie, 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 onsite tests, and 1 to 4 hours for laboratory-based tests.

Specific Drug Identification

Confirmatory tests are always performed in a laboratory. Gas chromatography/mass spectrometry (GC/MS) is considered to be the criterion standard for confirmatory testing. This technique involves using GC 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 generally requires 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 testing.

An issue with both types of 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 (eg, color) or by onsite testing of sample characteristics including urine temperature, creatinine concentration, and specific gravity.

In addition, 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 have this degree of hydrocodone if high amounts of oxycodone were also present.

There are various approaches to incorporating UDT into pain management and substance abuse 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 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. As stated in a joint U.S. Veterans Affairs/Department of Defense guideline, patients' refusal to consent to urine testing should be considered as 1 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- naso-pharyngeal secretions, and cellular debris. The mixture of fluids obtained varies depending on the collection method used (eg, spitting, suctioning, draining, or collection on some type of absorbent material). In addition, drug concentrations can be affected by the collection method, as well as by whether saliva stimulation methods were used. Several collection devices are commercially available in the United States and they generally involve collection on absorbent material (eg, foam pad). Pads are then placed in a container with a stabilizing buffer solution. Drug concentrations may also vary depending on how the oral fluid is recovered from the collection device (eg, by centrifugation or by applying pressure). Another issue is that drug concentrations may not reflect blood levels because of residual amounts of 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 tend to 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 liquid chromatography-mass spectrometry (LC-MS) methods.

A practical advantage of oral fluid collection compared with urine is that samples can be obtained under 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 the pain management or substance abuse treatment settings, particularly when substitution or tampering with urine drug samples is suspected.

HAIR TESTING

Hair is made up of protein that traps chemicals in the blood at the time the hair was made in the hair follicle. Hair on the human head grows at the rate of approximately 0.5 inch per month. Thus, a 1.5-inch hair sample could be used to reveal drug use during the previous 90 days. Potential advantages of hair as a drug testing source include that its collection is noninvasive; it is easy to

collect, store, and ship; sufficient samples are generally available for testing and retesting; and it is difficult to substitute or adulterate. Potential disadvantages are that hair analysis cannot detect recent drug use (ie, within past 7 days), it is difficult to detect very light drug use (eg, a single episode), and the fact that drug levels can be due to environmental exposure as well as drug use. 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 sought (eg, preemployment screening, post-drug-treatment verification of relapse).

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Gas chromatography/mass spectrometry tests and some immunoassays are performed in laboratory settings. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of this test.

PAIN MANAGEMENT/ FREQUENCY OF TESTING

Opinions vary on the optimal frequency of urine drug screening to monitor patients on opioid therapy for chronic pain. Screening frequency using a risk-based approach, as recommended by the Washington State interagency guideline (Washington State Agency Medical Directors' Group, 2015) is as follows:

- Low risk by ORT: Once a year
- Moderate risk by ORT: Twice a year
- High risk or opioid dose >120 mg MED/d: 3-4 times a year
- Recent history of aberrant behavior: Each visit

Note that the ORT is a copyrighted instrument (http://www.opioidrisk.com/node/884). The Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain does not include specific screening frequencies but states that an individual patient's risk for opioid misuse and addiction should be considered when deciding when to order a urine drug screen (http://nationalpaincentre.mcmaster.ca/opioid).

SUBSTANCE ABUSE

Stabilization phase: Most patients are expected to be on a stable dose of opioid medication within 4 weeks of initiating treatment. In some complicated patients, the stabilization phase may last longer than 4 weeks.

Maintenance phase: For most patients, targeted presumptive screening once every 1 to 3 months is sufficient during the maintenance phase of treatment. More frequent testing may be appropriate for some complicated patients.

GUIDANCE ON DEFINITIVE (CONFIRMATORY) TESTING

Specific situations for definitive drug testing may include, but are not limited to the following:

- Unexpected positive test inadequately explained by the patient
- Unexpected negative test (suspected medication diversion)
- Need for quantitative levels to compare with established benchmarks for clinical decision making.

There may not be commercially available tests for certain synthetic or semisynthetic opioids.

The following information on immunoassay availability and diagnostic capacity is included in the Washington State interagency guideline (Washington State Agency Medical Directors' Group, 2015):

Natural opioids (eg, codeine, morphine)

"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."

Semisynthetic Opioids (eg, hydrocodone, hydromorphone, oxycodone, oxymorphone)

"'Opiates' immunoassays may also detect semisynthetic opioids depending on their crossreactivity pattern. However, a negative result does not exclude use of semisynthetic opioids. Confirmatory testing (GC/MS [gas chromatography/mass spectrometry] or LC/MS/MS [liquid chromatography tandem mass spectrometry]) 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 (eg, fentanyl, meperidine, methadone, propoxyphene)

"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."

Table PG1, on interpreting unexpected results of urine drug tests, was adapted from a table developed by the Canadian National Opioid Use Guideline Group that was cited by the American Society of Interventional Pain Physicians in its guideline on prescribing opioids for chronic noncancer pain.

Table PG1. 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 (eg, oxycodone often missed by immunoassay) • Take a detailed history of patient's medication use for the preceding 7 d (eg, 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
Unexpected Result	**Possible Explanations**	**Possible Actions for the Physician**
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 (eg, 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

UDS: urine drug screen.

RISK ASSESSMENT

The risk level for an individual patient should include 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, a 24-item tool (http://painedu.org/soapp.asp?gclid=CPvLjOeFl7oCFY1FMgodzQ4ANA).

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

A. multiple lost prescriptions,
B. multiple requests for early refill,
C. obtained opioids from multiple providers,
D. unauthorized dose escalation, and
E. apparent intoxication during previous visits.

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References

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