# Medical Policy

**Title:** Drug Testing in Pain Management and Substance Abuse Treatment

<table>
<thead>
<tr>
<th>Professional</th>
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<tr>
<td>Original Effective Date: May 21, 2015</td>
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<td>Current Effective Date: July 25, 2016</td>
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**DESCRIPTION**

**Summary**
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 they are 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.

**Background**
According to an evidence assessment by the American Society of Interventional Pain Physicians (ASIPP), approximately one-third of chronic pain patients do not use opioids as prescribed or may abuse them.\(^1\) Moreover, studies have found that a substantial proportion of chronic pain patients inaccurately report nonadherence to prescribed medications and use of illicit drugs.\(^2\)

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 (ORT), 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.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With chronic pain treated with opioids</td>
<td>• Urine drug testing</td>
<td>• No urine drug testing</td>
<td>• Test accuracy</td>
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<tr>
<td>Individuals:</td>
<td></td>
<td></td>
<td>• Test validity</td>
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<tr>
<td>• With a drug addiction and are in substance</td>
<td></td>
<td></td>
<td>• Health status measures</td>
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<tr>
<td>abuse treatment</td>
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<td>• Resource utilization</td>
</tr>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With chronic pain treated with opioids or</td>
<td>• Oral fluid or hair drug testing</td>
<td>• No testing</td>
<td>• Test accuracy</td>
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<tr>
<td>with a drug addiction in substance abuse</td>
<td></td>
<td></td>
<td>• Test validity</td>
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<td>treatment</td>
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<td>• Health status measures</td>
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<td>• Resource utilization</td>
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</table>
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 biological specimens for the presence or absence of drugs. Currently, urine is the most commonly used biological substance. Advantages of urine drug testing (UDT) are that it is readily available, and standardized techniques for detecting drugs in urine exist. Other biological specimens (eg, blood, oral fluids, hair and 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 Testing**
Immunoassay testing, also called qualitative testing or screening, can be performed either 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. 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.⁴

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 UDT 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 healthcare 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 qualitative versus quantitative tests. Some of these involve conducting routine confirmation of positive qualitative tests with quantitative testing. Others use selective confirmation of positive qualitative tests, such as when an unexpected immunoassay result is not adequately explained by the patient. There is also
a mixed approach, with routine conformation of qualitative 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.5

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 or not saliva stimulation methods were used. Several collection devices are commercially available in the United States and these 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; these 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 (GC/MS) 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.

A CLIA waiver is available for use of certain point-of-care immunoassays. Tests eligible for a CLIA waiver are those considered to be simple, with low risk of error and low potential for harm. FDA is tasked with approving manufacturers’ applications for test system waivers. There are commercially available CLIA-waived tests for drugs such as cocaine, methadone, morphine/opiates, and oxycodone. There are also commercially available hair testing tests such as Quest Diagnostics ELISA tests for amphetamines, opiates, cocaine, marijuana metabolites, and phencyclidine. In addition, Omega Laboratories offers hair drug screening for cocaine and cocaine metabolites.

Several oral fluid drug test collection devices have been cleared for marketing by FDA through the 510(k) process. They include:

- 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)

In addition to the oral fluid collection devices, FDA has cleared a number of assays for analysis of oral samples. For example, there are FDA-cleared assays for 9 drugs collected with the Intercept device. These are amphetamines, methamphetamine, cocaine/metabolite, opiates, marijuana/THC, phencyclidine, barbiturates, benzodiazepines, and methadone.
POLICY
A. In outpatient pain management, qualitative (ie, immunoassay) urine drug testing may be considered medically necessary for:
   1. Baseline screening before initiating treatment or at the time treatment is initiated, when the following conditions are met:
      a. An adequate clinical assessment of patient history and risk of substance abuse is performed
      b. Clinicians have knowledge of test interpretation
      c. There is a plan in place regarding how to use test findings clinically
   2. Subsequent monitoring of treatment at a frequency appropriate for the risk-level of the individual patient (see Policy Guidelines section).

B. In outpatient substance abuse treatment, in-office or point-of-care qualitative (ie, immunoassay) urine drug testing may be considered medically necessary 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 the following conditions are met:
      a. An adequate clinical assessment of patient history and risk of substance abuse is performed
      b. Clinicians have knowledge of test interpretation
      c. There is a plan in place regarding how to use test findings clinically
   2. Stabilization phase – targeted weekly qualitative screening for a maximum of 4 weeks (see Policy Guidelines section)
   3. Maintenance phase – targeted qualitative screening once every 1 to 3 months (see Policy Guidelines section)

C. Quantitative (ie, confirmatory) urine drug testing, in outpatient pain management or substance abuse treatment, may be considered medically necessary under the following circumstances:
   1. When immunoassays for the relevant drug(s) are not commercially available
   2. In specific situations for which quantitative drug levels are required for clinical decision making (see Policy Guidelines section)

D. In outpatient pain management and outpatient substance abuse treatment, urine drug testing is considered not medically necessary when the above criteria are not met including but not limited to routine qualitative or quantitative urine drug testing (eg, testing at every visit, without consideration for specific patient risk factors or without consideration for whether quantitative testing is required for clinical decision making)
E. In outpatient pain management and substance abuse treatment, hair drug testing and oral fluid drug testing are considered experimental / investigational.

Policy Guidelines

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

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 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 qualitative 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 Quantitative (Confirmatory) Testing
Specific situations for quantitative drug testing may include, but are not limited to the following:

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

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):

a. 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.”

b. 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.”

c. 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...
American Society of Interventional Pain Physicians in its guideline on prescribing opioids for chronic noncancer pain:

Table PG1. Interpreting Unexpected Urine Drug Tests Results

<table>
<thead>
<tr>
<th>Unexpected Result</th>
<th>Possible Explanations</th>
<th>Possible Actions for the Physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test is negative for prescribed opioid</td>
<td></td>
<td></td>
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<tr>
<td>▪ False negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Noncompliance</td>
<td></td>
<td></td>
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<tr>
<td>▪ Diversion</td>
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<tr>
<td>▪ Conduct confirmatory testing, specifying the drug of interest (eg, oxycodone often missed by immunoassay)</td>
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<td></td>
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<tr>
<td>▪ 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)</td>
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<tr>
<td>▪ Ask patients if they’ve given the drug to others</td>
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<td></td>
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<tr>
<td>▪ Monitor compliance with pill counts</td>
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<td></td>
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<tr>
<td>Test is positive for nonprescribed opioid or benzodiazepines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ False positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Patient acquired opioids from other sources (double-doctoring, “street”)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Repeat urine drug testing regularly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Ask patients if they accessed opioids from other sources</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Assess for opioid misuse/addiction</td>
<td></td>
<td></td>
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<tr>
<td>▪ Review/revise treatment agreement</td>
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<tr>
<td>UDS positive for illicit drugs (eg, cocaine, cannabis)</td>
<td></td>
<td></td>
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<tr>
<td>▪ False positive</td>
<td></td>
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<tr>
<td>▪ Patient is occasional user or addicted to the illicit drug</td>
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<td></td>
</tr>
<tr>
<td>▪ Cannabis is positive for patients taking certain medications (eg, dronabinol)</td>
<td></td>
<td></td>
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<tr>
<td>▪ Repeat urine drug test regularly</td>
<td></td>
<td></td>
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<tr>
<td>▪ Assess for abuse/addiction and refer for addiction treatment as appropriate</td>
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</tbody>
</table>

UDS: urine drug screen.

RATIONALE
The evidence review has been updated with a literature review through November 30, 2015. The evidence review addresses urine drug testing (UDT) as a component of pain management and substance abuse treatment. For each of these settings, the literature search focused on the accuracy of testing and on the clinical utility of testing (ie, the impact of test results on patient management and/or on health outcomes). When published studies were not identified, relevant national and regional clinical practice guidelines were sought. In January 2016, testing oral fluids and hair was added to the review.

Urine Drug Testing

Accuracy of UDT for Detecting Prescribed Opioids and/or Illicit Drugs
Few studies have evaluated the accuracy of UDT outside of the research setting. One example of a study of this type was published in 2011 by Manchikanti et al. The investigators evaluated in-office immunoassay testing and used gas chromatography/mass spectrometry (GC/MS) as the criterion standard comparison. The study was prospective and included consecutive patients recruited from a single pain management practice. Urine samples were tested for opioids and for illicit drugs. A total of 1000 patients had both the immunoassay and confirmatory tests; both tests were performed on the same urine sample. Personnel analyzing the tests were blinded to the results of the other test and to patient demographics. The study’s primary findings for the
diagnostic accuracy of in-office immunoassays for detecting opioids compared with the reference standard are shown in Table 1.

Table 1: Diagnostic Accuracy Findings in Manchikanti et al (2011)

<table>
<thead>
<tr>
<th>Group</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients prescribed morphine, hydrocodone, codeine, or hydromorphone (n=748)</td>
<td>92.5% (90% to 94%)</td>
<td>89.6% (82% to 95%)</td>
</tr>
<tr>
<td>Patients prescribed oxycodone (n=134)</td>
<td>80.0% (71% to 87%)</td>
<td>84.2% (60% to 96%)</td>
</tr>
<tr>
<td>Patients prescribed methadone (n=46)</td>
<td>97.8% (88% to 99%)</td>
<td>100% (2% to 100%)</td>
</tr>
</tbody>
</table>

CI: confidence interval.

The most commonly identified illicit drugs were marijuana and amphetamines. The sensitivity and specificity of the immunoassay for detecting marijuana were 90.9% and 98.0%, respectively. Similar statistics for amphetamines were 47.0% and 99.1%, respectively. There were too few data to reliably report diagnostic accuracy of other illicit drugs.

Clinical Utility (ie, Impact on Patient Management Decisions and/or Health Outcomes)

The preferred study design is a randomized controlled trial (RCT) comparing treatment decisions and/or health outcomes in patients managed with and without use of UDT. When multifaceted interventions are used, it may be difficult to isolate the impact of drug testing from that of other components of the intervention. In that case, the preferred study design would include 1 arm with the full intervention and another arm with the same intervention but without UDT missing. In the absence of RCTs, the next most preferred study design is a nonrandomized controlled trial that adjusts findings for potential confounding factors.

Clinical Utility: Pain Management

Managing Patients With UDT Versus Without UDT

No RCTs or nonrandomized controlled studies adjusting for potential confounders were identified. A systematic review of the available literature on UDT in the chronic pain management setting, alone or as part of a treatment agreement, was published in 2010 by Starrels et al. Studies were considered eligible for inclusion in the review if they included patients with chronic noncancer pain who were treated in an outpatient setting and measured opioid misuse outcomes after intervention implementation. Eleven studies met eligibility criteria; none were RCTs. Eight studies addressed UDT, 7 of the 8 interventions also involved treatment agreements. Studies used different protocols for UDT; eg, some used random screening and others screened on a regular basis. Three studies stated that drug screening was done at a minimum frequency (ie, at enrollment and/or annually), with additional testing if deemed necessary by the physician. Five studies described the type of testing used; 4 of them included confirmatory GC/MS testing.

The review authors reported that 4 of 11 studies included a control or comparison group. On closer inspection, 2 of the 4 studies labeled as controlled used historic comparison groups and 1 was a prospective single-arm study. Starrels et al did not pool findings of the 4 studies. In the individual studies, opioid misuse was reduced after intervention initiation from 7% to 23%, compared with preintervention or historic controls.

Only 1 of the studies included in the systematic review used a concurrent comparison group. The study, by Goldberg et al, retrospectively reviewed data from a medical center database on 91
patients with a documented pain management contract.\(^8\) By signing the contract, the patient agreed to 8 provisions, 1 of which was “lab tests may be used to check opioid use.” Among the other 7 provisions was an agreement not to use illegal drugs and not to share or sell any medication and an agreement that the patient would receive opioid medication only from a single primary care or pain clinic physician. The comparison group consisted of 224 similar patients without pain management contracts. Consumption of opioids was significantly higher in the intervention group than the comparison group. For example, the intervention group consumed an average of 91 units of opioids quarterly and the comparison group consumed an average of 81 units (\(p<0.05\); an opioid unit was defined as equivalent to 1 systematic administration of 10-mg morphine sulfate). Some of the data presented in the article were contradictory. For example, a table showed significantly greater number of emergency department visits among patients in the pain contract group than the comparison group, but the text stated that there were not more emergency department visits among patients in the pain contract group.

In the uncontrolled studies included in the systematic review, the proportion of patients with opioid misuse after intervention initiation ranged from 3% to 43%. There were 8 studies that included UDT as a component of the intervention. The protocol and frequency of UDT varied in these studies. In 3 studies, there was a minimum baseline frequency, at the time of enrollment, annually, or both, with additional testing performed according to the judgment of the treating clinician. One study performed testing at baseline and on a monthly basis. In the remaining 4 studies, the frequency was not specified explicitly, but was described as “regular” or “random.” In 2014, Dupouy et al published a systematic review of literature on the impact of UDT on patient management.\(^12\) All study designs and clinical settings were eligible for inclusion. Other article inclusion criteria were that the urine drug screens were conducted using the enzyme immunoassay technique and, for controlled studies, the comparison arm was patient management in the absence of urine testing. In addition, some type of medical management outcome needed to be reported (eg, reassessment of treatment, referral for specialist visits, hospitalization). Eight studies met the review’s inclusion criteria. Five were rated as poor quality and 3 as fair quality. The studies consisted of 1 RCT, 2 quasi-randomized studies, 1 observational cohort study, and 4 cross-sectional studies. The RCT was a study of routine drug screening in a psychiatric emergency center, a setting that is not addressed in this evidence review. Most of the other studies were also conducted in settings that fall outside of the scope of the policy. However, 2 studies evaluated relevant populations: 1 was an uncontrolled evaluation of UDT of opioid-addicted patients and the other was a quasi-randomized study conducted in U.S. pain centers. The latter study, by Manchikanti et al,\(^10\) was included in the Starrels et al 2010 meta-analysis,\(^7\) previously described. The authors of the 2014 systematic review (Dupouy et al) did not pool study findings.

*Managing Patients With Routine UDT Versus Selective UDT*

No studies were identified.

*Managing Patients With Routine Confirmation of Positive Qualitative Tests Versus Selective Confirmation of Positive Qualitative Tests*

No studies were identified.
Clinical Utility: Substance Abuse Treatment

Managing Patients With UDT Versus Without UDT
One RCT was identified that suggests UDT increases treatment compliance when receiving take-home methadone compared with no UDT. In 2001, Chutuape et al published findings of a study that included patients in a methadone treatment program who had submitted fewer than 80% positive opiate and/or cocaine-positive urine samples during a 5-week baseline period. These patients then participated in a methadone take-home program and were randomized to 1 of 3 groups: (1) continued permission to take-home methadone was contingent on 1 negative urine sample, randomly selected each week; (2) continued permission to take-home methadone was contingent on 1 negative urine sample, randomly selected each month; or (3) permission to take-home methadone was not based on results of urine testing (control group). After participating in the intervention, the rate of sustained (8 or more weeks) opiate and cocaine abstinence was significantly higher in the groups receiving UDT. The percentage of patients with sustained (8 or more weeks) opiate and cocaine abstinence was 56.6%, 38.9%, and 10.5% in the weekly, monthly, and control groups, respectively (p<0.002).

Managing Patients With Routine UDT Versus Selective UDT
No studies were identified.

Managing Patients With Routine Confirmation of Positive Qualitative Tests Versus Selective Confirmation of Positive Qualitative Tests
No studies were identified.

Oral Fluid Drug Testing

Accuracy of Oral Fluid Testing for Detecting Prescribed Opioids and/or Illicit Drugs Compared With UDT
Several studies were identified that compared oral fluid and UDT using paired samples collected concurrently. In 2011, Vindenes et al in Norway published a study comparing drug detection in oral fluid and urine samples in the drug treatment setting. A total of 164 pairs of urine and oral fluid samples, collected at the same time, were collected from 45 opioid-dependent patients participating in a drug treatment program. Oral fluid samples were collected using the Intercept device and analyzed using a liquid chromatography tandem mass spectrometry (LC/MS/MS) method developed in Norway. Urine samples were screened using immunoassays and confirmed using LC/MS/MS. All patients were being treated with buprenorphine or methadone, so it was expected that 1 of these drugs would be detected in each sample. Other than these 2 drugs, those most commonly detected were 7-aminoflunitrazepam (metabolite of flunitrazepam), amphetamine, and THC. The sensitivity and specificity of the oral fluid samples compared with urine results were calculated. Key findings are shown in Table 2.
Table 2: Sensitivity and Specificity of Oral Fluid Samples in Vinden et al (2011), Using Urinalysis as the Reference Standard

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>75%</td>
<td>Not applicable (analytic problems)</td>
</tr>
<tr>
<td>7-aminoflunitrazepam</td>
<td>76%</td>
<td>97%</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>THC</td>
<td>82%</td>
<td>98%</td>
</tr>
<tr>
<td>6-MAM (heroin)</td>
<td>95%</td>
<td>80%</td>
</tr>
</tbody>
</table>

A 2012 study by Heltsley et al included 133 patients undergoing pain management treatment who consented to provide oral fluid and urine samples.15 Oral samples were collected with the Quantisal device and specimens were analyzed by LC/MS/MS. Urine specimens were screened by immunoassay procedures and non-negative samples were confirmed by MS. Samples were tested for 34 drugs or drug metabolites, although in some instances different analyses were performed on urine and oral fluid specimens. A total of 1544 paired tests were performed. Of these, 329 (21.3%) were positive and 984 (63.7%) were negative in both matrices, for an overall agreement of 85%. Eighty-three (5.4%) findings were positive in oral fluid only and 148 (9.6%) were positive in urine only. The authors conducted several analyses of the sensitivity and specificity of oral fluid samples using urinalysis as the reference standard (see Table 3).

Table 3: Sensitivity and Specificity of Oral Fluid Samples in Heltsley et al (2012), Using Urinalysis as the Reference Standard

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All drugs</td>
<td>69.0% (64.6% to 73.1%)</td>
<td>92.2% (90.4% to 93.7%)</td>
</tr>
<tr>
<td>Four drug categoriesa</td>
<td>76.1% (60.9% to 86.9%)</td>
<td>95.9% (92.0% to 98.0%)</td>
</tr>
<tr>
<td>Six drug categoriesb</td>
<td>82.3% (75.0% to 87.9%)</td>
<td>92.2% (88.7% to 94.7%)</td>
</tr>
</tbody>
</table>

CI: confidence interval.

a Categories include amphetamines, cannabis, cocaine, and opiates.
b Includes the above categories plus hydrocodone and oxycodone.

In 2014, Conermann et al compared findings of oral fluid and urinalysis in 153 paired samples from patients attending a pain management clinic.16 This study focused on confirmation that a treatment drug was being taken and did not report the sensitivity and specificity of oral fluid samples compared with urine samples. Oral fluid samples were collected with the Quantisal device. All specimens were screened with immunoassays and presumptive positive findings were confirmed using LC/MS. A total of 136 of the 153 paired samples (89%) tested positive for 1 or more treatment drugs (ie, opioids or benzodiazepines) in 1 or both matrices. After excluding 4 paired samples due to missing data, 101 of 132 positive specimen pairs had exact drug class matches (76.5%). In another 21 paired samples, there was at least 1 drug class match (15.9%). Thus, there was an overall agreement between samples of 92.4%. Two analyses were positive in oral fluid only and 8 were positive in urine only.

Clinical Utility (ie, Impact on Patient Management Decisions and/or Health Outcomes)
No studies were identified that compared patient management decisions or health outcomes in patients managed using oral fluid drug testing versus UDT or versus no drug testing.
Hair Testing

Accuracy of Hair Testing for Detecting Prescribed Opioids and/or Illicit Drugs Compared With UDT

No studies were identified that compared the accuracy of hair and urine testing using paired samples collected concurrently in the pain management setting or drug abuse treatment setting. One study using paired samples of urine and hair was identified. It was published by Musshoff et al in 2006 and was conducted in Germany.\textsuperscript{17} Patients underwent drug testing as part of the intake process for psychiatric treatment. Urine and hair samples (both head hair and pubic hair) from known drug users were analyzed. Fifty-one patients were included; all provided urine samples, 47 provided head hair samples (1-3 segments), and 36 provided pubic hair samples. Hair samples were washed, dried, and cut into pieces about 1 mm long. Drug analysis was done using GC-MS methods. The hair test was considered positive if any segment had a positive finding. Urine samples were analyzed using standard immunoassays; positive findings were not confirmed. Prevalence rates of drugs identified in hair and urine samples, as well as self-report of drug use, are shown in Table 4.

Table 4: Prevalence Rates of Drug Use in Musshoff et al (2006) (N=47)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Self-report</th>
<th>Cocaine</th>
<th>Methadone</th>
<th>Cannabinoids</th>
<th>Amphetamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiates</td>
<td>42 (89%)</td>
<td>18 (38%)</td>
<td>15 (32%)</td>
<td>26 (55%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>33 (70%)</td>
<td>13 (28%)</td>
<td>14 (30%)</td>
<td>21 (45%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Methadone</td>
<td>38 (81%)</td>
<td>26 (55%)</td>
<td>23 (49%)</td>
<td>15 (32%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>26 (55%)</td>
<td>21 (45%)</td>
<td>15 (32%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Amphetamines</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%).

Hair tests revealed a higher prevalence of drug use than UDT for most drugs, with the exception of cannabinoids. The prevalence of amphetamines was too low to make meaningful comparisons. Cannabinoids are known to be excreted slowly in urine and to have a low incorporation rate into hair. It is important to note that the hair analysis was used to detect drug use anytime during the past several months and the urine analysis to detect drug use in the past several days.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02345655</td>
<td>Impact of On-site Evaluation of Substances Consumption on Opiate Maintenance in the Context of Family Practice</td>
<td>400</td>
<td>Jan 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

Summary of Evidence

The evidence for urine drug testing (UDT) in individuals who have chronic pain treated with opioids or who have a drug addiction and are in substance abuse treatment includes 1 well-conducted diagnostic accuracy study and 1 study on eligibility for take-home methadone. Relevant outcomes are test accuracy and validity, health status measures, and resource utilization. Few studies have evaluated the accuracy of UDT outside of the research setting. One study identified evaluated diagnostic accuracy of urine testing compared with a valid reference standard with individuals in a pain management setting; no studies assessed individuals undergoing substance abuse treatment. In terms of clinical utility, for pain management patients,
there are no randomized controlled trials (RCTs) that isolate the potential effect of UDT on patient management or health outcomes. One RCT was identified on UDT of patients in substance abuse treatment; that trial focused on the specific situation of testing to determine eligibility for take-home methadone. The current published evidence does not permit conclusions on the impact of UDT on clinical outcomes.

The evidence for oral fluid and hair drug testing in individuals who have chronic pain treated with opioids or who have a drug addiction and are in substance abuse treatment includes several diagnostic accuracy studies. Relevant outcomes include test and validity, health status measures, and resource utilization. Two studies of pain management patients and 1 of substance abuse treatment patients have evaluated diagnostic accuracy of oral fluid testing compared with urine testing. The studies reported sensitivities in the range of 75% to 100%, with variability in the sensitivity by type of drug. The reported specificities are higher, generally greater than 90% across different drugs. No studies were identified on the clinical utility of oral fluid testing in pain management or substance abuse treatment. 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 urine testing in either of these settings. 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 current published evidence does not permit conclusions on the impact of hair or oral fluid drug testing on clinical outcomes.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 8 academic medical centers and 5 physician specialty societies while this policy was under review in 2014. There was near-consensus among reviewers that, in outpatient pain management, qualitative urine drug testing (UDT) may be considered medically necessary for patients who meet the stated criteria and that the frequency of repeat drug testing should be dependent on the risk level of the individual. There was also near-consensus among reviewers that, in substance abuse treatment, baseline qualitative drug testing may be considered medically necessary for patients who meet the stated criteria and that targeted weekly qualitative screening for a maximum of 4 weeks may be considered medically necessary during the stabilization phase. There was mixed input on the frequency of qualitative drug testing that may be considered medically necessary during the maintenance phase of substance abuse treatment. In addition, clinical input was mixed on confirmatory quantitative drug testing and particularly on the issue of whether quantitative drug testing should only be performed on a drug-specific basis.
Practice Guidelines and Position Statements

Pain Management

In 2014, Nuckols et al published a systematic review of guidelines that addressed management of opioid use for chronic pain. The authors included guidelines from national organizations and specialty societies, as well as guidelines from state agencies and specific health systems. The authors identified 9 guidelines with recommendations on UDT. The recommendations varied widely; 2 guidelines recommended mandatory testing for all patients, 1 recommended testing only patients at increased risk of medication abuse, and 2 stated that testing patients at low risk of abuse is not cost-effective. If UDT is used, the recommended frequency of follow-up testing was at least quarterly in 1 guideline, at least yearly in 1 guideline, and randomly in 2 guidelines.

American Society of Interventional Pain Physicians

In 2012, the American Society of Interventional Pain Physicians issued guidelines for responsible opioid prescribing for chronic noncancer pain. The guidelines include the following recommendations on UDT:

- “Comprehensive assessment and documentation is recommended before initiating opioid therapy....” (Evidence: good)
- “Despite limited evidence for reliability and accuracy, screening for opioid use is recommended, as it will identify opioid abusers and reduce opioid abuse.” (Evidence: limited)
- “Urine drug testing 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 abuse or illicit drug use when patients are in chronic pain management therapy.” (Evidence: good)

The evidence behind these recommendations was not clearly described in either the guidance document or the accompanying evidence assessment document.

American Pain Society and American Academy of Pain Medicine

In 2009, the American Pain Society and American Academy of Pain Medicine jointly published clinical guidelines on use of opioid therapy in chronic noncancer pain. The guidelines do not address UDT or other forms of monitoring adherence.

American College of Occupational and Environmental Medicine

In 2011, the American College of Occupational and Environmental Medicine issued updated guidelines (from 2008) on the chronic use of opioids, which contained the following recommendations on UDT:

“Routine use of urine drug screening for patients on chronic opioids is recommended, as there is evidence that urine drug screens can identify aberrant opioid use and other substance use that otherwise is not apparent to the treating physician.” Evidence (C): “The intervention is recommended for appropriate patients. There is limited evidence that the intervention may improve important health and functional benefits.”
Screening is recommended for all patients at baseline, and then randomly at least twice and up to 4 times a year, and at termination. Screening should also be performed if the provider suspects abuse of prescribed medication.

**Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain**

A guideline was issued in 2010 and includes the following recommendation on urine drug screening⁴: “When using urine drug screening (UDS) to establish a baseline measure of risk or to monitor compliance, be aware of benefits and limitations, appropriate test ordering and interpretation, and have a plan to use results. (Grade C).” The guideline also states that there is no “compelling evidence“ to guide physicians on identifying patients who should have UDS, or on how often they should be tested. The document states that the following factors should be considered when deciding whether to order a urine drug screen:

- patient’s risk for opioid misuse and addiction
- aberrant drug-related behaviors
- testing availability (note: this may be a Canadian-specific issue)

**Veterans Affairs and Department of Defense**

In 2010, the Department of Veterans Affairs and Department of Defense issued clinical practice guidelines for managing opioid therapy for treatment of chronic pain.⁵ The recommendations on assessing adherence to prescribed opioids includes, with patient consent, obtaining a urine drug test before initiating opioid therapy and randomly at follow-up to confirm appropriate use. Other strategies recommended including clinical assessment and screening aids such as random pill counts, adherence checklists, and standardized instruments such as the Screener and Opioid Assessment for Patients with Pain.

The guideline included the following specific recommendations on UDT:

**RECOMMENDATIONS**

1. Inform patients that drug testing is a routine procedure for all patients starting or on opioid therapy [OT], and is an important tool for monitoring the safety of their treatment.
2. With patient consent, obtain a UDT in all patients prior to initiation of OT.
3. With patient consent, monitor all patients on OT with periodic random UDTs to confirm adherence to the treatment plan. Increase the frequency of UDTs based on risk level for aberrant drug-related behaviors and following each dose increase.
4. Take into consideration a patient’s refusal to take a UDT as part of the ongoing assessment of the patient’s ability to adhere to the treatment plan and the level of risk for adverse outcomes.
5. When interpreting UDT results take into account other clinical information (e.g., past SUD [substance use disorder], other risk factors, aberrant drug-related behaviors, and other conditions indicating risk.)
6. Understanding of lab methods for drug testing and reporting are necessary to interpret UDT results (i.e., screen versus confirmatory test, substances tested, cut-off levels for tests). Maintain a close working relationship with the clinical laboratory to answer any questions about the UDT or for confirming the results.”

**Washington State Agency Medical Directors’ Group**

In 2015, the Washington State Agency Medical Directors’ Group issued updated interagency guidelines on opioid dosing for chronic noncancer pain.²²
The guideline included recommendations on UDT. Recommendations on testing frequency differed depending on patient risk of opioid addiction and opioid dosage, and are summarized next:

- Low risk: Once per year
- Moderate risk: Twice per year
- High risk or opioid dose over 120 mg MED/d: 3-4 times per year
- Aberrant behavior: Each visit

No pain management guidelines were identified that had recommendations on oral fluid or hair testing.

Substance Abuse Treatment

American Society of Addiction Medicine

In 2010, the American Society of Addiction Medicine (ASAM) issued an updated policy statement (from 2005) on drug testing in the substance abuse treatment programs. As stated in this document, it is ASAM policy of ASAM that: “Urine drug testing is a key diagnostic and therapeutic tool that is useful for patient care and in monitoring of the ongoing status of a person who has been treated for addiction. As such, it is a part of medical care, and should not face undue restrictions.” The document did not have specific statements on oral fluid or hair testing.

U.S. Preventive Services Task Force Recommendations

Not applicable.

CODING

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

CPT/HCPCS

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

80320 Alcohols
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>80321</td>
<td>Alcohol biomarkers; 1 or 2</td>
</tr>
<tr>
<td>80322</td>
<td>Alcohol biomarkers; 3 or more</td>
</tr>
<tr>
<td>80323</td>
<td>Alkaloids, not otherwise specified</td>
</tr>
<tr>
<td>80324</td>
<td>Amphetamines; 1 or 2</td>
</tr>
<tr>
<td>80325</td>
<td>Amphetamines; 3 or 4</td>
</tr>
<tr>
<td>80326</td>
<td>Amphetamines; 5 or more</td>
</tr>
<tr>
<td>80327</td>
<td>Anabolic steroids; 1 or 2</td>
</tr>
<tr>
<td>80328</td>
<td>Anabolic steroids; 3 or more</td>
</tr>
<tr>
<td>80329</td>
<td>Analgesics, non-opioid; 1 or 2</td>
</tr>
<tr>
<td>80330</td>
<td>Analgesics, non-opioid; 3-5</td>
</tr>
<tr>
<td>80331</td>
<td>Analgesics, non-opioid; 6 or more</td>
</tr>
<tr>
<td>80332</td>
<td>Antidepressants, serotonergic class; 1 or 2</td>
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<tr>
<td>80333</td>
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<td>80334</td>
<td>Antidepressants, serotonergic class; 6 or more</td>
</tr>
<tr>
<td>80335</td>
<td>Antidepressants, tricyclic and other cyclicals; 1 or 2</td>
</tr>
<tr>
<td>80336</td>
<td>Antidepressants, tricyclic and other cyclicals; 3-5</td>
</tr>
<tr>
<td>80337</td>
<td>Antidepressants, tricyclic and other cyclicals; 6 or more</td>
</tr>
<tr>
<td>80338</td>
<td>Antidepressants, not otherwise specified</td>
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<tr>
<td>80339</td>
<td>Antiepileptics, not otherwise specified; 1-3</td>
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<td>80340</td>
<td>Antiepileptics, not otherwise specified; 4-6</td>
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<td>80341</td>
<td>Antiepileptics, not otherwise specified; 7 or more</td>
</tr>
<tr>
<td>80342</td>
<td>Antipsychotics, not otherwise specified; 1-3</td>
</tr>
<tr>
<td>80343</td>
<td>Antipsychotics, not otherwise specified; 4-6</td>
</tr>
<tr>
<td>80344</td>
<td>Antipsychotics, not otherwise specified; 7 or more</td>
</tr>
<tr>
<td>80345</td>
<td>Barbiturates</td>
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<td>Benzodiazepines; 1-12</td>
</tr>
<tr>
<td>80347</td>
<td>Benzodiazepines; 13 or more</td>
</tr>
<tr>
<td>80348</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>80349</td>
<td>Cannabinoids, natural</td>
</tr>
<tr>
<td>80350</td>
<td>Cannabinoids, synthetic; 1-3</td>
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<tr>
<td>80351</td>
<td>Cannabinoids, synthetic; 4-6</td>
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<tr>
<td>80352</td>
<td>Cannabinoids, synthetic; 7 or more</td>
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<td>80353</td>
<td>Cocaine</td>
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<td>80354</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>80355</td>
<td>Gabapentin, non-blood</td>
</tr>
<tr>
<td>80356</td>
<td>Heroin metabolite</td>
</tr>
<tr>
<td>80357</td>
<td>Ketamine and norketamine</td>
</tr>
<tr>
<td>80358</td>
<td>Methadone</td>
</tr>
<tr>
<td>80359</td>
<td>Methyleneoxyamphetamine (MDA, MDEA, MDMA)</td>
</tr>
<tr>
<td>80360</td>
<td>Methylphenidate</td>
</tr>
<tr>
<td>80361</td>
<td>Opiates, 1 or more</td>
</tr>
<tr>
<td>80362</td>
<td>Opioids and opiate analogs; 1 or 2</td>
</tr>
<tr>
<td>80363</td>
<td>Opioids and opiate analogs; 3 or 4</td>
</tr>
<tr>
<td>80364</td>
<td>Opioids and opiate analogs; 5 or more</td>
</tr>
<tr>
<td>80365</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>80366</td>
<td>Pregabalin</td>
</tr>
<tr>
<td>80367</td>
<td>Propoxyphene</td>
</tr>
<tr>
<td>80368</td>
<td>Sedative hypnotics (non-benzodiazepines)</td>
</tr>
</tbody>
</table>
80369  Skeletal muscle relaxants; 1 or 2
80370  Skeletal muscle relaxants; 3 or more
80371  Stimulants, synthetic
80372  Tapentadol
80373  Tramadol
80374  Phencyclidine (PCP)

G0477  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

G0478  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

G0479  Drug test(s), presumptive, any number of drug classes; any number of devices or procedures by instrumented chemistry analyzers utilizing immunoassay, enzyme assay, TOF, MALDI, LTD, DESI, DART, GHPC, GC mass spectrometry), includes sample validation when performed, per date of service

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

Contains Public Information
ICD-9 Diagnoses

Any of a large number of diagnosis codes might apply to this policy, the following are examples

304.01 Opioid type dependence, continuous
304.02 Opioid type dependence, episodic
304.03 Opioid type dependence, in remission
304.11 Sedative, hypnotic or anxiolytic dependence, continuous
304.12 Sedative, hypnotic or anxiolytic dependence, episodic
304.13 Sedative, hypnotic or anxiolytic dependence, in remission
304.21 Cocaine dependence, continuous
304.22 Cocaine dependence, episodic
304.23 Cocaine dependence, in remission
304.31 Cannabis dependence, continuous
304.32 Cannabis dependence, episodic
304.33 Cannabis dependence, in remission
304.41 Amphetamine and other psychostimulant dependence, continuous
304.42 Amphetamine and other psychostimulant dependence, episodic
304.43 Amphetamine and other psychostimulant dependence, in remission
304.51 Hallucinogen dependence, continuous
304.52 Hallucinogen dependence, episodic
304.53 Hallucinogen dependence, in remission
304.61 Other specified drug dependence, continuous
304.62 Other specified drug dependence, episodic
304.63 Other specified drug dependence, in remission
304.71 Combinations of opioid type drug with any other drug dependence, continuous
304.72 Combinations of opioid type drug with any other drug dependence, episodic
304.73 Combinations of opioid type drug with any other drug dependence, in remission
305.01 Nondependent alcohol abuse, continuous
305.02 Nondependent alcohol abuse, episodic
305.03 Nondependent alcohol abuse, in remission
305.21 Nondependent cannabis abuse, continuous
305.22 Nondependent cannabis abuse, episodic
305.23 Nondependent cannabis abuse, in remission
305.31 Nondependent hallucinogen abuse, continuous
305.32 Nondependent hallucinogen abuse, episodic
305.33 Nondependent hallucinogen abuse, in remission
305.41 Nondependent sedative hypnotic or anxiolytic abuse, continuous
305.42 Nondependent sedative, hypnotic or anxiolytic abuse, episodic
305.43 Nondependent sedative, hypnotic or anxiolytic abuse, in remission
305.51 Nondependent opioid abuse, continuous
305.52 Nondependent opioid abuse, episodic
305.53 Nondependent opioid abuse, in remission
305.61 Nondependent cocaine abuse, continuous
305.62 Nondependent cocaine abuse, episodic
305.63 Nondependent cocaine abuse, in remission
305.71 Nondependent amphetamine or related acting sympathomimetic abuse, continuous
305.72 Nondependent amphetamine or related acting sympathomimetic abuse, episodic
305.73 Nondependent amphetamine or related acting sympathomimetic abuse, in remission
305.81 Nondependent antidepressant type abuse, continuous
305.82 Nondependent antidepressant type abuse, episodic
305.83 Nondependent antidepressant type abuse, in remission
305.91 Other, mixed, or unspecified nondependent drug abuse, continuous
305.92 Other, mixed, or unspecified nondependent drug abuse, episodic
305.93 Other, mixed, or unspecified nondependent drug abuse, in remission
338.0 Central pain syndrome
338.11 Acute pain due to trauma
338.12 Acute post-thoracotomy pain
338.18 Other acute postoperative pain
338.19 Other acute pain
338.21 Chronic pain due to trauma
338.22 Chronic post-thoracotomy pain
338.28 Other chronic postoperative pain
338.29 Other chronic pain
338.3 Neoplasm related pain (acute) (chronic)
338.4 Chronic pain syndrome
338.0 Central pain syndrome

ICD-10 Diagnoses (Effective October 1, 2015)

Any of a large number of diagnosis codes might apply to this policy, the following are just examples

F11.10 Opioid abuse, uncomplicated
F11.120 Opioid abuse with intoxication, uncomplicated
F11.121 Opioid abuse with intoxication delirium
F11.122 Opioid abuse with intoxication with perceptual disturbance
F11.14 Opioid abuse with opioid-induced mood disorder
F11.150 Opioid abuse with opioid-induced psychotic disorder with delusions
F11.151 Opioid abuse with opioid-induced psychotic disorder with hallucinations
F11.181 Opioid abuse with opioid-induced sexual dysfunction
F11.182 Opioid abuse with opioid-induced sleep disorder
F11.188 Opioid abuse with other opioid-induced disorder
F11.19 Opioid abuse with unspecified opioid-induced disorder
F11.20 Opioid dependence, uncomplicated
F11.21 Opioid dependence, in remission
F11.220 Opioid dependence with intoxication, uncomplicated
F11.221 Opioid dependence with intoxication delirium
F11.222 Opioid dependence with intoxication with perceptual disturbance
F11.23 Opioid dependence with withdrawal
F11.24 Opioid dependence with opioid-induced mood disorder
F11.250 Opioid dependence with opioid-induced psychotic disorder with delusions
F11.251 Opioid dependence with opioid-induced psychotic disorder with hallucinations
F11.281 Opioid dependence with opioid-induced sexual dysfunction
F11.282 Opioid dependence with opioid-induced sleep disorder
F11.288 Opioid dependence with other opioid-induced disorder
F11.29  Opioid dependence with unspecified opioid-induced disorder
F11.90  Opioid use, unspecified, uncomplicated
F11.920 Opioid use, unspecified with intoxication, uncomplicated
F11.921 Opioid use, unspecified with intoxication delirium
F11.922 Opioid use, unspecified with intoxication with perceptual disturbance
F11.93  Opioid use, unspecified with withdrawal
F11.94  Opioid use, unspecified with opioid-induced mood disorder
F11.950 Opioid use, unspecified with opioid-induced psychotic disorder with delusions
F11.951 Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations
F11.981 Opioid use, unspecified with opioid-induced sexual dysfunction
F11.982 Opioid use, unspecified with opioid-induced sleep disorder
F11.988 Opioid use, unspecified with other opioid-induced disorder
F11.99  Opioid use, unspecified with unspecified opioid-induced disorder
F14.10  Cocaine abuse, uncomplicated
F14.120 Cocaine abuse with intoxication, uncomplicated
F14.121 Cocaine abuse with intoxication with delirium
F14.122 Cocaine abuse with intoxication with perceptual disturbance
F14.14  Cocaine abuse with cocaine-induced mood disorder
F14.150 Cocaine abuse with cocaine-induced psychotic disorder with delusions
F14.151 Cocaine abuse with cocaine-induced psychotic disorder with hallucinations
F14.180 Cocaine abuse with cocaine-induced anxiety disorder
F14.181 Cocaine abuse with cocaine-induced sexual dysfunction
F14.182 Cocaine abuse with cocaine-induced sleep disorder
F14.188 Cocaine abuse with other cocaine-induced disorder
F14.19  Cocaine abuse with unspecified cocaine-induced disorder
F14.20  Cocaine dependence, uncomplicated
F14.21  Cocaine dependence, in remission
F14.220 Cocaine dependence with intoxication, uncomplicated
F14.221 Cocaine dependence with intoxication delirium
F14.222 Cocaine dependence with intoxication with perceptual disturbance
F14.23  Cocaine dependence with withdrawal
F14.24  Cocaine dependence with cocaine-induced mood disorder
F14.250 Cocaine dependence with cocaine-induced psychotic disorder with delusions
F14.251 Cocaine dependence with cocaine-induced psychotic disorder with hallucinations
F14.280 Cocaine dependence with cocaine-induced anxiety disorder
F14.281 Cocaine dependence with cocaine-induced sexual dysfunction
F14.282 Cocaine dependence with cocaine-induced sleep disorder
F14.288 Cocaine dependence with other cocaine-induced disorder
F14.29  Cocaine dependence with unspecified cocaine-induced disorder
F14.90  Cocaine use, unspecified, uncomplicated
F14.920 Cocaine use, unspecified with intoxication, uncomplicated
F14.921 Cocaine use, unspecified with intoxication delirium
F14.922 Cocaine use, unspecified with intoxication with perceptual disturbance
F14.929 Cocaine use, unspecified with intoxication, unspecified
F14.94  Cocaine use, unspecified with cocaine-induced mood disorder
F14.950 Cocaine use, unspecified with cocaine-induced psychotic disorder with delusions
F14.951 Cocaine use, unspecified with cocaine-induced psychotic disorder with hallucinations
F14.98  Cocaine use, unspecified with other specified cocaine-induced disorder
F14.980  Cocaine use, unspecified with cocaine-induced anxiety disorder
F14.981  Cocaine use, unspecified with cocaine-induced sexual dysfunction
F14.982  Cocaine use, unspecified with cocaine-induced sleep disorder
F14.988  Cocaine use, unspecified with other cocaine-induced disorder
F14.99  Cocaine use, unspecified with unspecified cocaine-induced disorder
F16.10  Hallucinogen abuse, uncomplicated
F16.120 Hallucinogen abuse with intoxication, uncomplicated
F16.121 Hallucinogen abuse with intoxication with delirium
F16.122 Hallucinogen abuse with intoxication with perceptual disturbance
F16.14  Hallucinogen abuse with hallucinogen-induced mood disorder
F16.150 Hallucinogen abuse with hallucinogen-induced psychotic disorder with delusions
F16.151 Hallucinogen abuse with hallucinogen-induced psychotic disorder with hallucinations
F16.180 Hallucinogen abuse with hallucinogen-induced anxiety disorder
F16.183 Hallucinogen abuse with hallucinogen persisting perception disorder (flashbacks)
F16.188 Hallucinogen abuse with other hallucinogen-induced disorder
F16.19  Hallucinogen abuse with unspecified hallucinogen-induced disorder
F16.20  Hallucinogen dependence, uncomplicated
F16.21  Hallucinogen dependence, in remission
F16.220 Hallucinogen dependence with intoxication, uncomplicated
F16.221 Hallucinogen dependence with intoxication with delirium
F16.24  Hallucinogen dependence with hallucinogen-induced mood disorder
F16.250 Hallucinogen dependence with hallucinogen-induced psychotic disorder with delusions
F16.251 Hallucinogen dependence with hallucinogen-induced psychotic disorder with hallucinations
F16.280 Hallucinogen dependence with hallucinogen-induced anxiety disorder
F16.283 Hallucinogen dependence with hallucinogen persisting perception disorder (flashbacks)
F16.288 Hallucinogen dependence with other hallucinogen-induced disorder
F16.29  Hallucinogen dependence with unspecified hallucinogen-induced disorder
F16.90  Hallucinogen use, unspecified, uncomplicated
F16.920 Hallucinogen use, unspecified with intoxication, uncomplicated
F16.921 Hallucinogen use, unspecified with intoxication with delirium
F16.94  Hallucinogen use, unspecified with hallucinogen-induced mood disorder
F16.950 Hallucinogen use, unspecified with hallucinogen-induced psychotic disorder with delusions
F16.951 Hallucinogen use, unspecified with hallucinogen-induced psychotic disorder with hallucinations
F16.980 Hallucinogen use, unspecified with hallucinogen-induced anxiety disorder
F16.983 Hallucinogen use, unspecified with hallucinogen persisting perception disorder (flashbacks)
F16.988 Hallucinogen use, unspecified with other hallucinogen-induced disorder
F16.99  Hallucinogen use, unspecified with unspecified hallucinogen-induced disorder
F45.42  Pain disorder with related psychological factors
G89.21  Chronic pain due to trauma
G89.22  Chronic post-thoracotomy pain
G89.28  Other chronic postprocedural pain
G89.29  Other chronic pain
G89.3 Neoplasm related pain (acute) (chronic)
G89.4 Chronic pain syndrome

**REVISED**

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<td>05-21-2015</td>
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<tr>
<td>07-25-2016</td>
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<td>Description section updated</td>
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<td>- Added Item E “In outpatient pain management and substance abuse treatment,</td>
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<td>hair drug testing and oral fluid drug testing are considered experimental/</td>
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<td>- Updated Policy Guidelines</td>
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<td><strong>Rationale section updated</strong></td>
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<td>- Added CPT Codes: 80370, 80371, 80372, 80373, 80374</td>
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<td>- Added HCPCS Codes: G0477, G0478, G0479, G0480, G0481, G0482, G0483</td>
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**REFERENCES**


