Presumptive (ie, immunoassay) Urine Drug Testing
In the outpatient pain management setting presumptive urine drug testing is used to verify treatment compliance, identify drug use or abuse that has not been reported, or to evaluate aberrant behavior such as lost prescriptions, repeated requests for early refills, prescriptions from multiple providers, unauthorized dose escalation, and apparent intoxication, or other unusual findings.

Presumptive Urine Drug testing is considered medically necessary as part of a routine monitoring for individuals who are:

- Being treated for chronic pain with prescription opioid or other potentially abused substances: OR
- Being treated or in a monitoring program for opioid addiction or substance abuse
  - Usual screening is 24 times per year

Presumptive Urine Drug testing is also considered medically necessary in the following situations:

- To evaluate an individual where the history or symptoms suggest use of non-prescribed medications or illegal substances; OR
- Upon initial evaluation and admission to a pain management program or substance abuse recovery program.

Definitive (ie, confirmatory) Urine Drug Testing
Definitive urine drug testing is considered medically necessary when ALL of the following criteria are met:
Presumptive urine drug testing was previously done for a medically necessary reason; AND The presumptive test was concerning in any of the following ways:

- Negative for prescribed medications,
- Positive for a prescription drug with abuse potential which was not prescribed, or Positive for an illegal drug (such as methamphetamine or cocaine or other), AND The specific definitive test(s) ordered are documented to be appropriate based on clinical chart notes that describe the rationale for each definitive test ordered; AND
- Chart notes describe how test results will guide clinical management AND
- Testing is for no more than 6 different drugs.

Not Medically Necessary Urine Drug Testing
Presumptive urine drug testing is considered not medically necessary when the criteria above are not met.
Definitive urine drug testing is considered **not medically necessary** when the criteria above are not met.

The use of presumptive or definitive testing panels is considered **not medically necessary** unless all components of the panel meet the medically necessary criteria listed above.

**Note:** A specific individual component of a panel may be considered **medically necessary** when criteria above are met.

The use of urine drug testing in the following settings is not subject to these guidelines:
- Testing done in the Emergency Room setting to diagnose or manage potential overdose or poisoning.
- Screening for commercial drivers licensing, or any other job related testing.
- State/legally mandated drug testing.

**Hair/Oral Fluid Drug Testing**
In outpatient pain management and substance abuse treatment, hair drug testing and oral fluid drug testing are considered **investigational**.

**Related Policies**

3.01.520  **Opioid Antagonists Under Heavy Sedation or General Anesthesia as a Technique of Opioid Detoxification**

**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](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 provider
- Unauthorized dose escalation
- 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 Opioid Risk Tool (ORT): Up to 1 per year
- Moderate risk by ORT: Up to 2 per year
- High risk or opioid dose >120 MED/d: Up to 3 to 4 per year
- Recent history of aberrant behavior. Each visit

Note that the ORT is a copyrighted instrument ([http://www.opioidrisk.com/node/884](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](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 Inter-Agency Guideline:

**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 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.”

The following table on interpreting unexpected results of urine drug tests was adapted from one developed by the Canadian National Opioid Use Guideline Group that was cited by ASIPP in their guideline on prescribing opioids for chronic noncancer pain.

<table>
<thead>
<tr>
<th>Unexpected Results</th>
<th>Possible Explanations</th>
<th>Possible Actions For the Physician</th>
</tr>
</thead>
</table>
| 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 a patient’s medication use for the |
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
- Monitor compliance with pill counts
- 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.

<table>
<thead>
<tr>
<th>Coding</th>
<th>CPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0006U</td>
<td>Prescription drug monitoring, 120 or more drugs and substances, definitive tandem mass spectrometry with chromatography, urine, qualitative report of presence (including quantitative levels, when detected) or absence of each drug or substance with description and severity of potential interactions, with identified substances, per date of service (new code effective 8/1/17)</td>
</tr>
<tr>
<td>0007U</td>
<td>Drug test(s), presumptive, with definitive confirmation of positive results, any number of drug classes, urine, includes specimen verification including DNA authentication in comparison to buccal DNA, per date of service (new code effective 8/1/17)</td>
</tr>
<tr>
<td>0011U</td>
<td>Prescription drug monitoring, evaluation of drugs present by LC-MS/MS, using oral fluid, reported as a comparison to an estimated steady-state range, per date of service including all drug comGermline disorders, gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood, report of specific gene rearrangement(s) pounds and metabolites (new code effective 8/1/17)</td>
</tr>
<tr>
<td>80184</td>
<td>Therapeutic drug assay (quantitative); phenobarbital</td>
</tr>
<tr>
<td>80300</td>
<td>Drug screen, any number of drug classes from Drug Class List A; any number of non-TLC devices or procedures, (eg, immunoassay) capable of being read by direct optical observation, including instrumented-assisted when performed (eg, dipsticks, cups, cards, cartridges), per date of service (code terminated 1/1/2017)</td>
</tr>
<tr>
<td>80301</td>
<td>Drug screen, any number of drug classes from Drug Class List A; single drug class method, by instrumented test systems (eg, discrete multichannel chemistry analyzers utilizing immunoassay or enzyme assay), per date of service (code terminated 1/1/2017)</td>
</tr>
<tr>
<td>80302</td>
<td>Drug screen, presumptive, single drug class from Drug Class List B, by immunoassay (eg, ELISA) or non-TLC chromatography without mass spectrometry (eg, GC, HPLC), each procedure (code terminated 1/1/2017)</td>
</tr>
<tr>
<td>80303</td>
<td>Drug screen, any number of drug classes, presumptive, single or multiple drug class method; thin layer chromatography procedure(s) (TLC) (eg, acid, neutral, alkaloid plate), per date of service (code terminated 1/1/2017)</td>
</tr>
<tr>
<td>80304</td>
<td>Drug screen, any number of drug classes, presumptive, single or multiple drug class method; not otherwise specified presumptive procedure (eg, TOF, MALDI, LDTD, DESI, DART), per date of service (code terminated 1/1/2017)</td>
</tr>
<tr>
<td>80305</td>
<td>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 (new code effective 1/1/2017)</td>
</tr>
<tr>
<td>80306</td>
<td>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 (new code effective 1/1/2017)</td>
</tr>
<tr>
<td>80307</td>
<td>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</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>-------------</td>
</tr>
<tr>
<td>80320</td>
<td>Alcohol biomarkers; 1 or 2</td>
</tr>
<tr>
<td>80321</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>80339</td>
<td>Antiepileptics, not otherwise specified; 1-3</td>
</tr>
<tr>
<td>80340</td>
<td>Antiepileptics, not otherwise specified; 4-6</td>
</tr>
<tr>
<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>
</tr>
<tr>
<td>80346</td>
<td>Benzodiazepines; 1-12</td>
</tr>
<tr>
<td>80347</td>
<td>Benzodiazepines; 13 or more</td>
</tr>
<tr>
<td>80353</td>
<td>Cocaine</td>
</tr>
<tr>
<td>80358</td>
<td>Methadone</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>80369</td>
<td>Skeletal muscle relaxants; 1 or 2</td>
</tr>
<tr>
<td>80370</td>
<td>Skeletal muscle relaxants; 3 or more</td>
</tr>
<tr>
<td>82542</td>
<td>Column chromatography/mass spectrometry (eg, GC/MS, or HPLC/MS), analyte not elsewhere specified; quantitative, single stationary and mobile phase</td>
</tr>
</tbody>
</table>

**HCPCS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0480</td>
<td>Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to, GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays (eg, IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (eg, alcohol dehydrogenase)), (2) stable isotope or other universally recognized internal standards in all samples (eg, to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (eg, to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day; 1-7 drug class(es), including metabolite(s) if performed</td>
</tr>
<tr>
<td>G0481</td>
<td>8-14 drug class(es), including metabolite(s) if performed</td>
</tr>
<tr>
<td>G0482</td>
<td>15-21 drug class(es), including metabolite(s) if performed</td>
</tr>
<tr>
<td>G0483</td>
<td>22 or more drug class(es), including metabolite(s) if performed</td>
</tr>
</tbody>
</table>

**Description**

Patients in pain management programs and substance abuse treatment may misuse prescribed opioids and/or may use nonprescribed drugs. Thus, patients in these settings are often assessed before treatment and monitored while they are receiving treatment. Urine drug screening is one 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, 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 patients in pain management and substance abuse treatment settings, 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,
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-Revisited (SOAPP-R), 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. 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 sampling are that it is readily available, and standardized techniques for detecting drugs in urine exist. Other biological specimens (e.g., 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 of oral fluids and hair.

**Urine Drug Testing**

The 2 primary categories of urine drug testing (UDT) are explained below.

**Immunoassay Testing (ie, Presumptive Testing, Screening)**

These tests 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, i.e., an antibody’s reactivity with a compound other than the target of the test, varies widely among immunoassays.

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

Immunoassays generally have a rapid turnaround time, within minutes for onsite tests and 1 to 4 hours for laboratory-based tests.(3)

**Specific Drug Identification (ie, Quantitative Testing, Confirmatory Testing)**

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 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 urine drug testing is the possibility of sample tampering to mask the presence of illegal drugs. A variety of products and techniques are available to patients, and can be as simple as drinking a large amount of water to dilute the sample. There are also commercial dilution and cleaning products, additives and urine substitutes. Some of these techniques can be detected by visual inspection of the sample e.g., color, or by onsite testing of sample characteristics including urine temperature, creatinine concentration, and specific gravity.
In addition, correct interpretation of urine drug testing 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 urine drug screening 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 urine drug screening 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 settings conduct 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 urine drug testing. 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 mass spectrometry (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 one-half 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 it 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, drug levels can be due to environmental exposure as well as use. In addition, variation in hair texture as well as cosmetic hair treatments can affect drug incorporation in 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 or 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 Act (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. The U.S. Food and Drug Administration 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 PCP. 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 Test Oral Specimen Collection Device (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.

**Scope**

Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

**Benefit Application**

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

**Rationale**
The policy was created in 2014 with a search of the MEDLINE database and updated with a literature review through October 25, 2016. The policy addresses urine drug testing 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

**Diagnostic Accuracy for Detecting Prescribed Opioids and/or Illicit Drugs**

Few studies have evaluated the accuracy of UDT outside of the research setting. One example of this type was published in 2011 by Manchikanti et al.(6) 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>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients prescribed morphine, hydrocodone, codeine, or hydromorphone</td>
<td>748</td>
<td>92.5% (90% to 94%)</td>
<td>89.6% (82% to 95%)</td>
</tr>
<tr>
<td>Patients prescribed oxycodone</td>
<td>134</td>
<td>80.0% (71% to 87%)</td>
<td>84.2% (60% to 96%)</td>
</tr>
<tr>
<td>Patients prescribed methadone</td>
<td>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.

A 2016 retrospective analysis by Johnson-Davis et al evaluated the diagnostic accuracy of an in-house urine drug screen panel at a national reference laboratory.(7) Samples were from routine clinical testing in consecutive patients. The panel tested for 9 drug classes using immunoassay testing. Specimens that screened positive underwent confirmatory testing with GC/MS or liquid chromatography with tandem-mass spectrometry (LC/MS/MS). A shared confirmatory panel was used for samples testing positive to opiates or oxycodone. A total of 8825 samples were tested. Of them, 2642 (30%) tested positive for opiates and 1215 (14%) tested positive for oxycodone. Confirmatory testing identified 898 (34%) false-positive tests for opiates and 23 (2%) false-positives tests for oxycodone. Authors did not include information on what drugs, if any, were prescribed to patients.

**Section Summary**

Few studies have evaluated the accuracy of UDT outside of the research setting, either for pain management or substance abuse treatment patients. One study found that diagnostic accuracy varied by drug type (eg, was higher for patients prescribed methadone than for those prescribed oxycodone). Another study of a urine drug panel found a relatively high false-positive rate.

**Clinical Utility for Chronic Pain Patients Treated With Opioids (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 urine drug testing (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.
Pain Management Treatment Setting

Managing Patients with Urine Drug Testing (UDT) versus without UDT

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. (8) Studies were eligible for inclusion in the review if they enrolled 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 was a RCT. Eight studies addressed UDT, 7 of the 8 interventions also involved treatment agreements. Studies used different protocols for UDT (eg, some used random screening, 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. Reviewers reported that 4 of 11 studies included a control or comparison group. (9-12) 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 by 7% before to 23% after intervention initiation 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. (9) 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 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 implementation ranged from 3% to 43%. There were 8 studies that included drug testing as a component of the intervention. The protocol and frequency of drug testing 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 UDS on patient management. (13) 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 etc. 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, published in 2000 by Schiller et al, was a study of routine drug screening in a psychiatric emergency center, a setting that is not addressed in this reference policy. 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: one of these 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, Manchikanti et al. 2006, (13) was included in the Starrels et al meta-analysis, (8) previously described. The authors of the 2014 systematic review did not pool study findings.

In 2016, Krishnamurthy et al published a retrospective cohort study comparing no-show and dropout rates in chronic pain patients who did and did not receive UDT. (14) Before each clinic visit, patients received a letter stating that their provider might monitor adherence to treatment, including UDT. UDTs were not preformed randomly; investigators used propensity score matching to adjust for potential selection bias and confounding.
The sample included 723 patients with a total of 4448 clinic visits (all patients had at least 2 visits). Results were that UDT in the first visit was significantly associated with a higher rate of no-shows at the second visit (odds ratio, 2.73; 95% confidence interval, 1.66 to 4.47; p<0.001). The no-show rate was 10.2% in patients without UDT and 23.8% in patients with UDT. Moreover, the no-show rate was higher in patients testing positive for illicit drugs (34.6%) than in those testing negative for illicit drugs (21.7%). In addition, the rate of dropout from treatment increased significantly with each additional UDT (95% CI of the hazard ratio, 1.54 to 2.61).

Managing Patients with Routine UDT versus selective UDT
No studies were identified that compared patient management decisions or health outcomes in patients managed using routine UDT compared with selective UDT.

Managing Patients with Routine Confirmation of Positive Qualitative Tests versus Selective Confirmation of Positive Qualitative Tests
No studies were identified that compared patient management decisions or health outcomes in patients managed using routine confirmation of positive qualitative tests versus selective confirmation of positive qualitative tests.

Section Summary
No RCTs were identified. There are several nonrandomized studies with comparison groups. In one of them, consumption of opioids was significantly higher in the intervention group (which signed a pain management contract, including the possibility of drug testing) than in the comparison group. In another study, the no-show rate was higher in patients who had UDT in a previous visit.

Clinical Utility Substance Abuse Treatment Setting
Managing Patients with UDT versus without UDT
One RCT was identified that suggests urine testing increases treatment compliance when receiving take-home methadone compared with no urine testing. In 2001, Chutuape et al. published finding 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.(15) 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; or
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 control group. 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).

In 2016, McDonell published an RCT evaluating a drug treatment intervention in primary care and that included analysis of whether UDT can detect underreporting of drug use.(16) The trial included 829 patients with self-reported nonprescribed drug use or illegal drug use in the past 90 days. UDT were performed at baseline and at 3, 6, 9, and 12 months. Investigators found that 331 (40%) participants denied drug use but had a positive drug screen during at least 1 of the 5 assessments. Patients who denied opioid use but whose UDT was positive were more likely to be older, female, and have a higher Addition Severity Index (ASI) drug composite score. This trial was not designed to compare treatment success rates in patients managed with and without UDT.

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.

**Section Summary**

No studies were identified that evaluated the accuracy of UDT compared with a valid reference standard in individuals undergoing substance abuse treatment. One RCT on UDT of patients in substance abuse treatment focused on the specific situation of testing to determine eligibility for take-home methadone. Another RCT found UDT identified drug use in a substantial number of patients who denied illicit usage; the impact on treatment success was not addressed.

**Oral Fluid Drug Testing**

**Diagnostic Accuracy of Oral Fluid Testing for Detecting Prescribed Opioids and/or Illicit Drugs Compared With UDT**

Several studies were identified that compared oral fluid testing 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. (17) A total of 164 pairs of urine and oral fluid samples, obtained 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 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 tetrahydrocannabinol. 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 Vindenes et al (2011), Using Urine Analysis as the Reference Standard

<table>
<thead>
<tr>
<th>Standard 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>NA (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>
<tr>
<td>NA: Not applicable</td>
<td></td>
<td></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. (18) 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 95%. 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 urine analysis as the reference standard (see Table 3).

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

<table>
<thead>
<tr>
<th>Standard 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 categories</td>
<td>76.1% (60.9% to 86.9%)</td>
<td>95.9% (92.0% to 98.0%)</td>
</tr>
<tr>
<td>Six drug categories</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 urine analysis in 153 paired samples from patients attending a pain management clinic. (19) 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 liquid chromatography-tandem mass spectrometry (LC/MS/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
No studies were identified that compared patient management decisions or health outcomes in patients managed using oral fluid drug testing versus urine drug testing or versus no drug testing.

Section Summary
The limited number of studies on the diagnostic accuracy of oral fluid testing compared with urine testing had variable findings. No studies were identified on the impact of oral fluid testing on health outcomes compared with UDT or no drug testing.

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

Hair tests revealed a higher prevalence of drug use than urine 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 to detect drug use anytime during the past several months and the urine analysis detected drug use in the past several days.

Clinical Utility
No studies were identified that compared patient management decisions or health outcomes in patients managed using testing of hair versus UDT or no drug testing.

Section Summary
Hair testing cannot detect recent drug use (ie, in the past few days). One study looked at this longer time frame in patients starting psychiatric treatment. It found a higher prevalence of drug use with hair testing versus UDT testing for most drugs; however, the implications of study findings for patients in pain management or substance abuse treatment is unclear. No studies were identified on the diagnostic accuracy of hair testing versus urine testing in patients with chronic pain or substance abuse. In addition, no studies were identified on the clinical
utility of hair testing in pain management or substance abuse treatment.

Summary of Evidence

**Urine Drug Testing**
For individuals who have chronic pain who receive urine drug testing (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 limited strength evidence on whether UDT in the pain management setting improves patient 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.

Based on the available evidence and clinical input, urine drug testing may be considered medically necessary under specific conditions listed in the policy statements.

**Oral Fluid Drug Testing**
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.

**Hair Drug Testing**
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. 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.

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 5.

<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>On-site Evaluation of Substances Consumption on Opiate Maintenance (ESUB-MG)</td>
<td>400</td>
<td>Sept 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
Clinical Input Received through Physician Medical 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 5 physician specialty societies and 8 academic medical centers while this policy was under review in 2014. There was near-consensus among reviewers that, in outpatient pain management, presumptive (ie, qualitative) urine drug testing may be considered medically necessary for patients who meet the stated criteria and that the frequency of repeat drug testing should depend on the risk level of the individual. There was also near-consensus among reviewers that, in substance abuse treatment, baseline presumptive 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 presumptive drug testing that may be considered medically necessary during the maintenance phase of substance abuse treatment. In addition, clinical input was mixed on confirmatory definitive (ie, quantitative) drug testing and particularly on whether definitive drug testing should only be performed on a drug-specific basis.

Practice Guidelines and Position Statements

Pain Management Treatment Setting

In 2014, Nuckols et al. published a systematic review of guidelines that addressed management opioid use for chronic pain.(21) 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.

Centers for Disease Control and Prevention

In 2016, Centers for Disease Control and Prevention (CDC) guidelines on opioids for chronic pain were published.(22) The guidelines included the following recommendation on UDT: “When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.”

American Society of Interventional Pain Physicians (ASIPP)

In 2012, the ASIPP issued guidelines on responsible opioid prescribing for chronic noncancer pain.(23) The guidelines included the following recommendations on UDT:

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Comprehensive assessment and documentation is recommended before initiating opioid therapy.”</td>
<td>Good</td>
</tr>
<tr>
<td>“Despite limited evidence for reliability and accuracy, screening for opioid use is recommended, as it will identify opioid abusers and reduce opioid abuse.”</td>
<td>Limited</td>
</tr>
<tr>
<td>“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.”</td>
<td>Good</td>
</tr>
</tbody>
</table>

LOE: level of evidence.

The evidence behind the above recommendations was not clearly described in either the guidance document or the accompanying evidence assessment document.(1)

American Pain Society and American Academy of Pain Medicine In 2009, the APS and AAPM jointly published clinical guidelines on use of opioid therapy in chronic noncancer pain.(24) The guidelines do not address urine drug testing or other forms of monitoring adherence.
**American College of Occupational and Environmental Medicine (ACOEM)**

In 2011, the ACOEM issued guidelines on the chronic use of opioids with the following recommendations on UDT (25):

> “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.

**National Opioid Use Guideline Group**

The National Opioid Use Guideline Group issued guidelines in Canada in 2010 on the Safe and effective use of opioids for chronic noncancer pain that included the following recommendation on urine drug screening(4): “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 guidelines also stated that there was no “compelling evidence” to guide physicians on identifying patients who should have UDS, or on how often they should be tested. The document stated 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 VA and DoD issued clinical practice guidelines for managing opioid therapy for chronic pain treatment.(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 include 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 (SOAPP).

The guideline included the following specific recommendations regarding urine drug testing:

1. Inform patients that drug testing is a routine procedure for all patients starting or on opioid therapy, 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 (eg, past SUD, 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 (ie, 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, this group issued interagency guidelines on opioid dosing for chronic noncancer pain. (26) The guidelines included recommendations on urine drug testing. Recommendations on testing frequency differed depending on patient risk of opioid addiction and opioid dosage, as listed below (also see Policy Guidelines):

- Low risk: Periodic screening (up to once per year)
- Moderate risk: Regular screening (up to 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 (ASAM)**

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.(27) As stated therein, it is ASAM policy 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.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References

Appendix

N/A

History

<table>
<thead>
<tr>
<th>Date</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>04/24/15</td>
<td>Annual Review. Revised last bullet point under quantitative UDT from “Testing is for no more than for 6 substances” to “Testing is for no more than 6 different drugs”. Policy updated with literature review through January, 2015. Reference 15 added; others renumbered. Policy statement clarified as noted. Related policy 2.01.30 removed. Coding update. The following codes were deleted</td>
</tr>
</tbody>
</table>

effective 12/31/14, notation made: 80100-80104, 80154, 82101, 82145, 82205, 82520, 82646, 82654, 82742, 83805, 80840, 83925 and 84022. The following codes were added and are effective as of 1/1/15: 80300-80304, 80320-80326, 80339-80347, 80353, 80358, 80361-80364, 80369-80370.

03/09/16 Annual Review. Policy updated with literature review through November 30, 2015; references added. Statement added that, in outpatient pain management and substance abuse treatment, hair drug testing and oral fluid drug testing are considered investigational. “Urine” deleted from title.

05/04/16 Update Related Policies. Policy 3.01.02 was deleted and replaced with policy 3.01.520.

02/14/17 Annual review. Policy updated with literature review through October 25, 2016; references 7, 14, 16, and 22 added. In policy statements and policy guidelines, “qualitative” changed to “presumptive” and “quantitative” changed to “definitive”. Coding update; removed terminated CPT and HCPCS codes. Added HCPCS codes G0480-G0483.

10/01/17 Coding update. Added new CPT codes 0006U, 0007U, and 0011U (effective 8/1/17).

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

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Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5992, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at:
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at:

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).
Premera Blue Cross has a disability program that allows members who are deaf to pay for healthcare services through direct deposit or a personal check. If you need help, please call 800-722-1471 (TTY: 800-842-5357).