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Implementing a Prescription Drug Monitoring Protocol to Ensure Responsible Opioid Prescribing

Faculty

Jeremy A. Adler, MS, PA-C
Senior Pain Management PA
Chief Operating Officer
Pacific Pain Medicine Consultants
Encinitas, California

W. Clay Jackson, MD, DipTh, FAAFP
Clinical Assistant Professor
Departments of Family Medicine and Psychiatry
The University of Tennessee College of Medicine
Memphis, Tennessee

Introduction

Opioid therapy may be an effective strategy for the treatment of chronic moderate to severe pain that is not responsive to other measures.[1] However, the potential risk for abuse, misuse, and diversion of opioid analgesics poses unintended dangers to patient health, and may expose prescribers to professional liability.[2,3] The inherent risks in prescribing controlled substances underscore the need for appropriate monitoring for most patients receiving chronic prescription opioid therapy.[4,5]

Guidelines

Government and professional organizations, such as the CDC, American Pain Society, and American Academy of Pain Medicine (AAPM), as well as expert consensus panels have released guidelines to provide clinicians with strategies for responsible opioid prescribing.[1,4,5] These programs help practitioners identify appropriate candidates for chronic opioid therapy, ensure the safe and informed use of the product, and monitor for adverse outcomes.

Guidelines assert a preference for nonopioid therapy for chronic pain.[1,4] If opioids are deemed appropriate, guidelines recommend developing written opioid treatment agreements; shared decision making to develop treatment goals; and discussing the benefits and risks of opioid therapy, the risk for and consequences of misuse, and responsibilities, including opioid medication management and monitoring (Table 1).[1,4,5]

Risk Stratification and Monitoring

Stratifying risk is important to identify patients at high risk for opioid abuse, misuse, or diversion for whom more intensive monitoring may be appropriate.[1,5] Examples of validated screening instruments for risk stratification include the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) and the Opioid Risk Tool (ORT).[6,7] The ORT assigns each factor a point value, with higher total scores indicating greater risk.[7]

Adherence monitoring is essential during chronic opioid therapy, and there is no substitute for vigilance. Components of monitoring should include:

- A focused clinical history and physical examination at every visit with intermittent corroboration by family or significant others;
- Periodically checking the state-based Prescription Drug Monitoring Program (PDMP) for prescribing and dispensing data of controlled substances for each patient to help avoid dangerous drug interactions and identify "doctor shopping" behaviors; and
- Urine drug monitoring (UDM) (Table 1).[1,4,5,8]

Urine Drug Monitoring

Studies show that UDM identifies more nonadherent patients compared with behavior monitoring or self-reporting alone,[9] and most guidelines recommend the use of UDM for patients at the start of chronic opioid therapy and periodically throughout treatment, necessitating the implementation of a consistent protocol.[4,5] The mere expectation of a UDM may act as a deterrent to illicit drug use.[10]

An AAPM-commissioned expert panel has published consensus recommendations based on formal risk assessment to help guide the frequency and type of UDM (Table 2).[5] Furthermore, because patients may change behaviors when they expect a test, other groups recommend occasional unscheduled (vs scheduled) urine drug screens.[11]

The UDM Process

Drug testing procedures are divided into presumptive and definitive testing.

Although some practitioners support definitive-only testing, generally, best practice in UDM comprises both presumptive and definitive testing (Table 3)[4,5,12]:

1. Presumptive drug tests are used to identify possible use or non-use of a drug or a drug class. Examples of presumptive testing include laboratory instrument chemistry immunoassays (IA) and analyzers, as well as point of care (POC) devices.[12]
2. Definitive drug testing is used to confirm presumptive results by identifying the drugs and/or drug metabolites present. Mass spectrometry (MS) is typically utilized for definitive drug testing.[12]

Prescribers can use presumptive methods to test for, and thus rule out, multiple drug classes before conducting more expensive definitive tests to confirm presumptive-positive or unexpected presumptive-negative results. Therefore, the 2-step process has the potential to balance clinical care with cost by reducing overtesting.[4,12]

Table 1. Key Elements of a Prescription Drug Monitoring Protocol

1. Establish which individuals to monitor (eg, patients who receive prescription opioids for chronic therapy [≥30 days]).
2. Evaluate risk factors for opioid-related harm such as potential for abuse, misuse, or diversion, including obtaining patient history and intermittent input from family members.
3. Review the state-based PDMP database to identify controlled substances prescribed by other providers, avoid dangerous drug interactions, and identify "doctor shopping" behaviors. The CDC recommends that clinicians review PDMP data when starting opioid therapy for chronic pain and periodically during therapy from every prescription to every 3 months.
4. Present a written opioid treatment agreement in a collaborative, patient-centered manner to gain alignment and establish a clinician–patient partnership.
5. Discuss the benefits of opioid therapy and the risk for and consequences of misuse.
6. Review responsibilities, including opioid medication management and monitoring.
7. Stratify opioid risk with validated tools (eg, ORT) to determine frequency of UDM.
8. Conduct baseline UDM for prescribed, unprescribed, and illicit substances based on patient history and community usage. Common drug class tests may include, but are not limited to alcohol, amphetamines, barbiturates, benzodiazepines, cocaine, fentanyl, heroin, marijuana, methadone, opiates (eg, codeine, hydrocodone, hydromorphone, morphine), and oxycodone.
9. Conduct periodic UDM throughout the duration of therapy based on risk status.

ORT, Opioid Risk Tool; **PDMP,** prescription drug monitoring program; **UDM,** urine drug monitoring

Based on references 1, 4, 5, 8, 16, and 17.

Presumptive Testing

Presumptive tests are limited to certain classes of drugs, such as amphetamines, cocaine, marijuana, opioids, phencyclidine, methamphetamine, barbiturates, and benzodiazepines.[12] A presumptive test result equal to or greater than an established cutoff value indicates the possible presence of a drug or drug class, and results are expressed qualitatively as either negative or presumptive positive.[12] However, presumptive tests are not definitive, do not identify specific drugs and metabolites, cannot distinguish true-positive from false-positive results, and may be false negative due to sensitivity limitations.[12] In addition, presumptive testing may not be available for some of the commonly used and potentially abused medications, such as tramadol and tapentadol.[12] Although there is now an available IA for fentanyl,[13] most IAs do not detect synthetic opioids,[4] which are increasingly abused in the United States and frequently identified in lethal overdoses.[2]

Presumptive IA testing is limited to possible identification of the classes of drugs and not specific drugs or drug metabolites, and thus does not allow clinicians to discern between a prescribed and unprescribed opioid. In laboratory settings, presumptive IA methods can be modified with lower cutoff values that enhance sensitivity to aid in the identification of drug classes, such as benzodiazepines and opioids.[12] Presumptive testing helps prescribers clarify discrepancies between the clinical regimen and patient use, and indicates when a definitive test is warranted.[4]

POC tests are inexpensive, produce results within minutes, and require definitive confirmation.[4,12,14] POC presumptive test devices detect possible use or non-use of certain classes of drugs, and unlike some laboratory-based tests, are limited by high cutoff values that cannot be modified to enhance detection of commonly used substances, such as benzodiazepines and opiates.[12,14] In addition, POC methodology exhibits variable sensitivity and specificity across drug class (eg, 0%-50% missed positives and 11%-100% erroneously identified positives).[15]

Definitive Testing

Definitive tests with gas chromatography/MS or liquid chromatography (LC)/tandem MS provide specific and sensitive identification of drugs and drug metabolites.[14] Definitive test results are expressed as qualitative identification or as quantitative identification (presence/nonpresence) and concentration of the drug. Definitive testing is necessary to[12]:

- confirm presumptive positive results by identifying present drugs and drug metabolites;
- rule out false-positive presumptive results;
- rule out false-negative results when presumptive testing lacks sensitivity;
- minimize false results from specimen tampering by specifically identifying metabolites of drugs instead of just parent drugs (eg, norhydrocodone is a metabolite of hydrocodone); and
- use as the only test option when presumptive testing is not available (eg, tapentadol).

Table 2. Recommendations for Frequency of UDM Based on Risk Assessment

Patient Risk Group	Baseline Testing	Frequency (random or as clinically indicated)
Low	Prior to initiation of chronic opioid therapy	1-2 times per year
Moderate		1-2 times every 6 months
High		1-3 times every 3 months

UDM, urine drug monitoring
Based on references 5 and 12.

Table 3. Presumptive and Definitive Urine Drug Monitoring

	Presumptive		Definitive (GC/MS or LC/MS)
	Point of Care	Reference Laboratory IA	
Advantages	• Rapid results • Low cost • Results help guide prescriber–patient discussion • Identifies possible drug class	• Low cost • Lower cutoff values enhance sensitivity • Results help guide prescriber–patient discussion • Reduces over-testing • Identifies possible drug class	• Highly sensitive • Highly specific • Confirms presumptive results • Rules out false-positive presumptive results • Rules out false-negative presumptive results • Detects specific drugs and metabolites • Can be used as the only option when presumptive testing is not available • Potentially easier to interpret
Disadvantages	• High cutoff values that cannot be modified • Variable sensitivity • Variable specificity • Cannot identify specific drug or drug metabolite • Results are not definitive • Cannot distinguish true-positive from false-positive results	• Results are not immediate • Cannot identify specific drug or drug metabolite • Results are not definitive • Cannot distinguish true-positive from false-positive results	• Results are not immediate • Higher cost

GC/MS, gas chromatography/mass spectrometry; **IA,** immunoassay; **LC/MS,** liquid chromatography/mass spectrometry
Based on references 4, 12, 14, and 15.

Implementing a Prescription Drug Monitoring Protocol

Clinicians who prescribe controlled substances should develop and implement a prescription drug monitoring protocol that is tailored to the needs of their patients. There are many examples of prescription drug monitoring protocols.[5,14] Table 1 lists key elements that clinicians may incorporate into protocols to manage those patients receiving controlled medications who require monitoring.[1,4,5,8,16,17]

Conclusion

UDM is an essential component of care for most patients receiving chronic prescription opioid therapy, which warrants a consistent protocol to ensure its safety and success.[4,5] Components of responsible prescribing include assessing data from PDMPs and implementing UDM both at the start of opioid prescribing and periodically throughout treatment.[1,4,5] Rational use of presumptive testing and the subsequent conduct of definitive tests only to confirm presumptive positive results reduces patient and health system costs.[4,12]

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Disclosures: Mr Adler reported that he is a consultant to Collegium Pharmaceutical, Depomed, Egalet, Millennium Health, and Quest Diagnostics. He also is on the speakers bureau for AstraZeneca, Daiichi-Sankyo, Pernix Therapeutics, and St. Jude Medical (Abbott). Dr Jackson reported that he is a consultant to Otsuka Pharmaceutical.

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