2010 edition

PHYSICIAN UPDATE

PtProtect Pain Medication Management Program Monitors Patient Compliance

BENEFITS OF PROGRAM

- Monitors analgesic medication compliance to ensure patient safety and protect practices
- Uses lowest detection thresholds for most sensitive, comprehensive detection of opiates and opioids
- Offers highest testing specificity available
- Tests for more opiates/opioids than other laboratories, without relying on an initial screen
- Detects non-prescribed analgesic medication, reducing the possibility of adverse drug interactions
- Heroin metabolite (6-monoacetylmorphine) testing available on most panels
- Simplifies patient management with easy-to-understand interpretations
- Increases testing flexibility with multiple panel configurations

SUMMARY AND INDICATIONS

The PtProtect program offers pain medication management panels designed to improve monitoring of prescribed controlled substances. These panels will help you learn whether your patient is:

- Taking or potentially diverting the pain medications currently prescribed
- Taking pain medications that are not prescribed
- Using drugs of abuse

WHY CHOOSE US FOR YOUR PAIN MANAGEMENT TESTING?

With a decade of study behind it, the PtProtect program gives you the confidence and reliability you need to ensure successful pain medication monitoring. This complete suite of testing panels offers important features unique to our laboratories:

1. Detection thresholds

Results showing both the presence and absence of targeted opiate and opioid medications are crucial to an accurate assessment. Thresholds of detection as low as 2 and 5 ng/mL increase the ability to identify recent medication use. At the same time, that same low-threshold sensitivity can reveal an absence of expected medications which may indicate diversion, reduced dosages or non-compliance with the patient's prescribed medication regime.

2. Tandem mass spectrometry sets the gold standard

Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) is the most accurate and sensitive testing method for medication detection. Our anecdotal laboratory data shows that testing based on other methodologies can miss up to 30% of opiates/opioids present. Our panels use LC/MS/MS to test opiates and opioids without relying on an initial positive screen test with less sensitivity and poor specificity. This reduces turnaround time for test resulting and provides confirmatory sensitivity for all opiates/opioids included in the panels. Additional charges for initial screen tests are not incurred by you or your patients.

3. Reports with easy-to-read interpretive comments

The PtProtect report provides an "Interpretive Comment" section that allows you to quickly and accurately determine whether the test results are consistent or discrepant with patient prescription(s).

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PtProtect Program (Continued)

PATIENT SAFETY

The use and misuse of prescription medications continues to be a growing problem. A 2008 National Survey on Drug Use and Health report shows a steady increase in the number of primary admissions for opiate and opioid abuse, climbing from less than 20,000 in 1997 to over 80,000 in 2008.[1]

The possibility of adverse drug interactions makes this a significant patient and community safety issue, particularly if the patient is:

- Combining prescriptions from multiple prescribers or other sources
- Using controlled substances recreationally
- Diverting prescribed medications for financial gain

Since our program launched in 2008, our data suggests a 6-in-10 chance that a patient's urine drug test results will disclose information not explained by the patient's known pain medication prescriptions.

UNDERSTANDING TEST RESULTS

Determining whether a detected medication is from legitimate or illicit use can be difficult, and requires clinical correlation.

1. Why would a patient not have a drug present that was prescribed?

- Noncompliance
- Diversion
- Rapid or ultra-rapid metabolizer
- Drug-induced metabolism (e.g. rifampin)
- Poor drug absorption (e.g. celiac disease)
- Diluted urine

2. Why would a patient have a drug present that was not prescribed?

- Normal opiate and opioid metabolite from a legitimate prescription
- Opiate and opioid metabolite found when high doses of codeine or morphine are used
  - High-dose codeine can metabolize to hydrocodone
  - High-dose morphine can metabolize to hydromorphone
- Prescription from another physician
- Medication obtained from spouse or friend
- Illicit use of drug obtained without prescription

3. What is the relationship between heroin and morphine in my patient's results?

- Detection of 6-monoacetylmorphine is consistent with heroin use.
- Absence of 6-monoacetylmorphine does not rule out heroin use when morphine is present.
- Common reasons for the presence of morphine include a morphine prescription, codeine prescription (since codeine metabolizes to morphine), dietary poppy seeds and the use of heroin.

4. What is included in a report's interpretive comments?

PtProtect reports provide interpretive comments that are based on prescribed medications and the analytical test results. We compare medications prescribed, medications detected and the ratio of metabolite to parent substance to facilitate your understanding of the test data.

Examples may be found in the *Understanding Your Report* publication.

An interpretive comment will also be included even when prescription medication use is:

- Undisclosed on your requisition or order
- Unknown to you
- Not currently part of the patient's care plan under your supervision

5. Can I tell whether my patient has taken more (or less) than the dose of medication I prescribed?

Many aspects make it impractical to correlate urine drug concentration to a patient's dosage. Using urine concentrations to monitor therapeutic levels is unreliable.[8,9] Urine drug concentrations cannot determine:

- The amount of drug used
- Establish exactly when the last dose was taken
- Predict the source of the drug

6. What can I do if my patient's results are discrepant?

When a clinician receives results inconsistent with prescription history, he or she has several options to consider:

- Counseling the patient
- Modifying the patient's treatment plan
- Refering the patient to a substance abuse program
- Eliminating the patient from your practice

7. An instant test cup produced a negative result, while the PeaceHealth Laboratories test is positive. Why?

By nature, screens are limited in their specificity and sensitivity. Screens offer a generalized view of the existence of drugs that may be present in the patient. These limitations are particularly true when using instant cup drug screens, whether the indicators are on a dipstick or made part of the cup itself in some manner. For the highest accuracy and sensitivity, mass spectrometry testing should be used to verify all screen findings, whether positive or negative . See comparison of testing method sensitivities in Figure 1 below. All instant test cups should be returned to our laboratory for definitive testing.

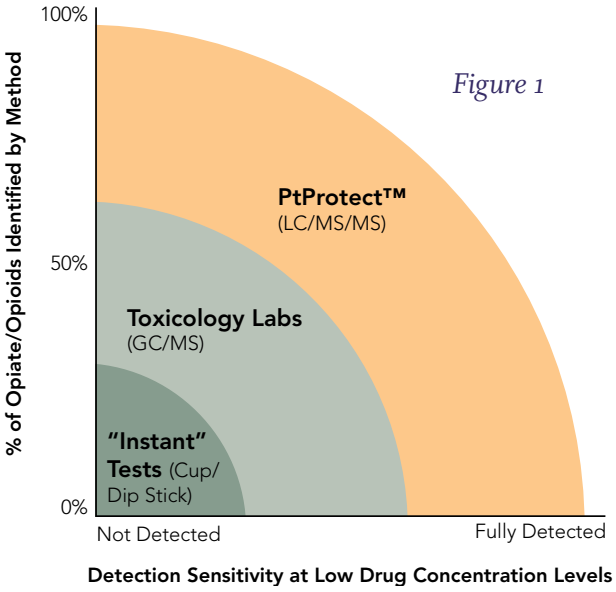

Figure 1

METABOLIC CONSIDERATIONS

Caution must be used in interpreting opiate and opioid results since commonly prescribed opiates (codeine) and opioids (hydrocodone and oxycodone) metabolize to active opiate and opioid drugs (codeine → morphine, hydrocodone → hydromorphone, and oxycodone → oxymorphone) which are also available by prescription.

In addition to the major metabolism that occurs in standard doses of opiate and opioids, when high doses of codeine or morphine are used in tolerant patients, "minor" metabolites can occur from commonly prescribed opioids (codeine → hydrocodone, and morphine → hydromorphone).

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PtProtect Program (Continued)

The complex biotransformation (metabolism) of opiates and opioids is shown in the accompanying diagram in *Figure 2*.

QUESTIONS?

Board-certified clinical toxicologists are available to answer questions and consult on the interpretation of test results.

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For an in-depth review of the PtProtect panel choices, please contact your account representative.

Frequently ordered tests can be added to your preprinted requisitions or added to your electronic interface ordering system.

MAJOR AND MINOR METABOLIC PATHWAYS FOR OPIATES AND OPIOIDS

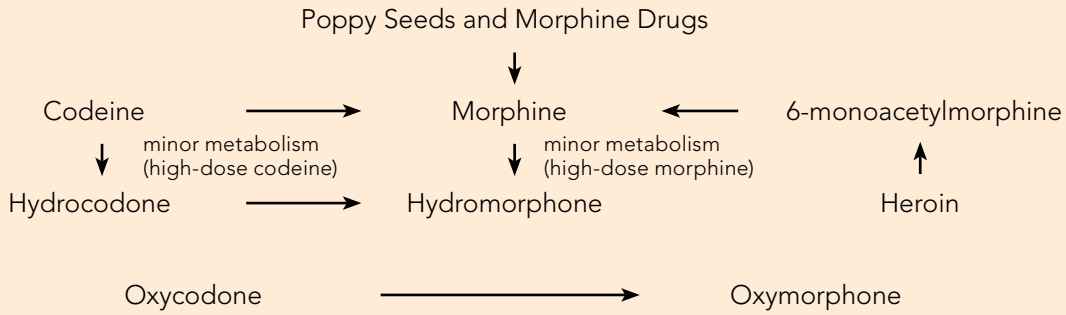

Figure 2

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PeaceHealth Laboratories

PtProtect™

Drug Detection and Retention Thresholds

Drug	Generic Name	Retention Time*	Threshold
Opiates/Opioids by LC/MS/MS			
6-monoacetylmorphine	Heroin metabolite	1–3 days	5 ng/mL
Codeine	Tylenol-3	1–3 days	5 ng/mL
Fentanyl	Duragesic, Actiq	1–2 days	2 ng/mL
Hydrocodone	Vicodin and others	1–3 days	5 ng/mL
Hydromorphone	Dilaudid	2–4 days	5 ng/mL
Meperidine	Demerol	1–2 days	5 ng/mL
Morphine	MS Contin, Roxanol	1–3 days	5 ng/mL
Norfentanyl	Fentanyl metabolite	1–4 days	2 ng/mL
Oxycodone	Oxycontin, Tylox, Percocet	1–3 days (SR 2–4 days)	5 ng/mL
Oxymorphone	Numorphan, Opana	1–3 days (SR 1–4 days)	5 ng/mL
Drug Screen by EIA and GC/MS			
Alcohol	Ethanol	2–14 hours	0.02/0.02 g/dL
Amphetamines	Amphetamine MDMA, MDA Methamphetamine	1–2 days	300/150 ng/mL
Barbiturates	Amobarbital Aprobarbital Butabarbital Butalbital Pentobarbital Phenobarbital Secobarbital	1–7 days 1–7 days 1–7 days 1–48 hours 1–24 hours 1–3 weeks 1–24 hours	200/200 ng/mL
Benzodiazepines	Alprazolam metabolite Chlordiazepoxide metabolite Clonazepam metabolite Clorazepate metabolite Diazepam metabolite Flunitrazepam metabolite Flurazepam metabolite Lorazepam Nordiazepam Oxazepam Temazepam	Therapeutic Dose: 3 days Extended Dosage: 4–6 weeks	200/100 ng/mL
Cocaine	Cocaine metabolite	1–2 days	300/150 ng/mL
Marijuana	THC metabolite	Heavy User: 4–6 weeks Moderate User: 2 weeks Light User: 0–4 days	20/15 ng/mL
Methadone	Methadone metabolite	3–11 days	150/100 ng/mL
Phencyclidine	Phencyclidine	8 days Chronic Use: up to 30 days	25/25 ng/mL
Propoxyphene	Propoxyphene metabolite	1–2 days	300/300 ng/mL
Misc by LC/MS/MS			
Carisoprodol & metabolite (meprobamate)	Soma	4 days	0.2 µg/mL
Tramadol & metabolite	Ultram, Ultracet, Ryzolt	3 days	50 ng/mL
Buprenorphine	Buprenex, Subutex, Suboxone	4 days	2 ng/mL

Understanding Your Report

INTERPRETIVE REPORT EXAMPLES

Example 1

When Vicodin (hydrocodone) is prescribed and both hydrocodone and hydromorphone (metabolite of hydrocodone) are detected in the urine and the ratio of hydromorphone to hydrocodone is consistent with hydromorphone coming from hepatic metabolism of hydrocodone, the "Interpretive Comment" would read:

Drug Class	Result	Interpretive Comment
Hydrocodone	864 ng/mL	Consistent with hydrocodone prescription
Hydromorphone	215 ng/mL	Hydromorphone source from hydrocodone metabolism

Example 2

When an opiate/opioid that is not prescribed is detected in the urine, for example oxycodone (Oxycontin), and the oxymorphone to oxycodone ratio indicates that oxymorphone (Opana) is also being used (but not prescribed), the "Interpretive Comment" would read:

Drug Class	Result	Interpretive Comment
Oxycodone	544 ng/mL	Discrepant result; oxycodone should be negative
Oxymorphone	317 ng/mL	Oxymorphone source from oxycodone metabolism and oxymorphone use

Example 3

An "Interpretive Comment" will also be provided when the requisition indicates that prescription use is "unknown" or not provided. If, for example, no prescription information is provided and codeine and morphine are positive in the urine; the morphine to codeine ratio indicates that morphine came from codeine metabolism. The "Interpretive Comment" would read as indicated below. Recent heroin use is likely excluded as the source of morphine since the 6-monoacetylmorphine test is negative. In addition, concentrations of codeine and morphine rule out poppy seeds as the source of morphine.

Drug Class	Result	Interpretive Comment
Codeine	327 ng/mL	Consistent with codeine use
Morphine	104 ng/mL	Morphine source from codeine metabolism

** Time estimate for drug/metabolite detection in urine following cessation of drug use; other considerations include patient's age, fluid intake, amount and frequency of drug used, and metabolic variables influenced by genetics or interactions with other medications. This is a general guideline.*