

# HarmonyX<sup>®</sup> Test for Pain

## WHAT CAN THE TEST TELL US?

The HarmonyX<sup>®</sup> Test for Pain is a panel of clinical tests that provides information about the pharmacogenetic (gene-drug) relationship between the tested genes (*CYP2B6*, *CYP2D6*, *CYP2C9*, *CYP2C19*, *CYP3A4/A5*, *COMT*, *OPRM1*) and commonly prescribed pain medications.

Many factors influence patient response to medication. Pharmacogenetic testing yields patient-specific information about genetic factors associated with both drug metabolism and response. This testing does not yield information about other factors linked to medication metabolism or response, such as drug or food interactions, BMI, or comorbidities.

Our test results are color-coded to indicate exactly what you need to know. Guidance on dosing and side effect risk is also provided in your results report.

Try these medications as directed

Try these medications with caution

Try an alternative to these medications

(or consider dose adjustment with close monitoring)



The HarmonyX Test for Pain tests for the following medications:

buprenorphine	meloxicam
buprenorphine/naloxone	meperidine
carisoprodol	methadone
celecoxib	morphine
codeine	naloxone
diclofenac	naltrexone
fentanyl	naproxen
hydrocodone	oxycodone
hydromorphone	oxymorphone
ibuprofen	tramadol
ketorolac	

## Pharmacokinetics

The HarmonyX Test for Pain examines five key pharmacokinetic genes implicated in pain management: **CYP2B6** is partially responsible for methadone metabolism; **CYP2C9** is responsible for the metabolism of most NSAID pain medications; **CYP2C19** has been linked to the metabolism of carisoprodol, a skeletal muscle relaxant; **CYP2D6** has been shown to have a significant effect on the body's ability to metabolize the opioids codeine, oxycodone, and tramadol; and **CYP3A4/A5** affects the body's ability to metabolize fentanyl.

## Pharmacodynamics

The test also provides genotypes for **COMT** and **OPRM1**, two pharmacodynamic genes which have been linked to the therapeutic response of patients taking opioid medications.

# WHY IS TESTING IMPORTANT?



- **Pain affects more Americans than diabetes, heart disease, and cancer, combined.**<sup>1</sup> One in three Americans reports suffering from chronic pain.<sup>2</sup>
- Pain is the most common reason patients seek care in the United States. Acute pain, resulting from injuries, surgeries, or headaches, accounts for 40% of patient visits to primary care providers and more than 70% of emergency department visits.<sup>3</sup>
- Genetic testing provides the prescribing clinician with the ability to identify or predict the likelihood of efficacy and toxicity. Genotyping offers instructive data to improve the selection, dosing, and evaluation of analgesic therapy.<sup>4</sup>

## Black Box Warnings

In February 2008, the FDA issued a boxed warning for fentanyl to alert patients about potential adverse effects and abuse potential related to the medication. In February 2013, a boxed warning was issued for codeine, advising against use of the drug in children who are *CYP2D6* ultrarapid metabolizers.

### Fentanyl

**WARNING: RISK OF RESPIRATORY DEPRESSION, MEDICATION ERRORS, ABUSE POTENTIAL**  
See full prescribing information for complete boxed warning.

The concomitant use of Fentanyl with strong and moderate cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression.

### Codeine

**WARNING: DEATH RELATED TO ULTRARAPID METABOLISM OF CODEINE TO MORPHINE**  
See full prescribing information for complete boxed warning.

Respiratory depression and death have occurred in children who received codeine following tonsillectomy and/or adenoidectomy and had evidence of being ultrarapid metabolizers of codeine due to a *CYP2D6* polymorphism.

# WHO SHOULD BE TESTED?



## Adults Suffering from Chronic Pain

Patients who regularly use over-the-counter NSAIDs for mild to moderate pain conditions, and patients with moderate to severe chronic pain who regularly use opioids or skeletal muscle relaxants, will benefit from testing. Approximately 70% of people 65 years or older use NSAIDs at least once per week, increasing their risk for GI bleeds and other concentration-dependent side effects.<sup>3</sup> Pharmacogenetic testing can aid the prescriber in predicting more effective medication choices while minimizing the risk for side effects and toxicity.<sup>4</sup>

## Children Scheduled for Major or Minor Surgery

Due to concerns for respiratory depression and death associated with codeine and tramadol use in pediatric post-surgical patients, children should be tested prior to surgery in order to minimize risk associated with taking these medications.

## Patients for Whom Current Pain Treatment Is Not Effective

In order to determine a more effective treatment option, patients who are not responding as expected to their current treatment plan will benefit from testing.

<sup>1</sup>AAPM Facts and Figures on Pain. (n.d.) The American Academy of Pain Medicine. [www.painmed.org/patientcenter/facts\\_on\\_pain.aspx#chronic](http://www.painmed.org/patientcenter/facts_on_pain.aspx#chronic). Accessed February 26, 2015.

<sup>2</sup>Fleischer AB, Gardner EF, Feldman SR. Are patients' chief complaints generally specific to one organ system? *The American Journal of Managed Care*. 2001;7(3):299-305.

<sup>3</sup>Fine M. Quantifying the impact of NSAID-associated adverse events. *The American Journal of Managed Care*. 2013;19(14 suppl):S267-S272.

<sup>4</sup>Trescot AM, Faynboym S. A review of the role of genetic testing in pain medicine. *Pain Physician*. 2014;17(5):425-445.