

## Medical Policy Manual

**Approved Revised Policy: Do Not Implement Until 8/30/25**

### **Pharmacogenetic Testing for Pain Management**

#### **DESCRIPTION**

While multiple pharmacologic therapies are available for the management of acute and chronic pain, there is a high degree of heterogeneity in pain response, particularly in the management of chronic pain. Testing for genetic variants that are relevant to pharmacokinetics or pharmacodynamics of analgesics is proposed to assist in selecting and dosing drugs affected by these genetic variants.

Pharmacogenetic testing combines pharmacology and genomics with the intent of discovering effective and safe medications and doses tailored to a person's genetic makeup. Commercially available panel tests (e.g., GeneSight® Analgesic, Proove® Opioid Risk Panel, Pain Medication DNA Insight™, Millennium PGT™, IDgenetix®) have been proposed as an aid in pain management.

Individual or panel tests relevant to pharmacogenetics could include testing of the following genes:

- 5HT2C (serotonin receptor gene)
- 5HT2A (serotonin receptor gene)
- SLC6A4 (serotonin transporter gene)
- DRD1 (dopamine receptor gene)
- DRD2 (dopamine receptor gene)
- DRD4 (dopamine receptor gene)
- DAT1 or SLC6A3 (dopamine transporter gene)
- DBH (dopamine beta-hydroxylase gene)
- COMT (catechol O-methyltransferase gene)
- MTHFR (methylenetetrahydrofolate reductase gene)
- γ-aminobutyric acid (GABA) A receptor gene
- OPRM1 (μ-opioid receptor gene)
- OPRK1 (κ-opioid receptor gene)
- UGT2B15 (uridine diphosphate glycosyltransferase 2 family, member 15)
- Cytochrome p450 genes: *CYP2D6*, *CYP2C19*, *CYP2C9*, *CYP3A4*, *CYP2B6*, *CYP1A2*

The standard of care for assessing opioid use disorder (OUD) currently includes structured clinician assessments. Recently in the U.S., there are tests (e.g., AvertD™, AutoGenomics, Inc.) now made available and being proposed to assess the risk of OUD. They consist of a panel involved in the brain reward pathway and could include the following:

- 5-HT2A C>T (serotonin 2A receptor)
- COMT G>A (catechol-o-methyltransferase)
- DRD1 A>G (dopamine D1 receptor)
- DRD2 G>A (dopamine D2 receptor)
- DRD4 T>C (dopamine D4 receptor)
- DAT1 A>G (dopamine transporter)
- DBH C>T (dopamine beta hydroxylase)
- MTHFR C>T (methylene tetrahydrofolate reductase)
- OPRK1 G>T (kappa Opioid Receptor)

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- GABA C>A (gamma-Aminobutyric Acid [GABA])
- OPRM1 A>G (mu Opioid Receptor)
- MUOR G>A (mu Opioid Receptor)
- GAL T>C (galanin)
- DOR G>A (delta Opioid Receptor)
- ABCB1 C>T (ATP binding cassette transporter I [ABCB1])

### POLICY

- Pharmacogenetic testing for the treatment of pain is considered *investigational*.
- Pharmacogenetic testing to assess the risk of developing opioid use disorder is considered *investigational*.

### IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g. statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

### ADDITIONAL INFORMATION

No high-quality studies were found in the published literature that validates the use of pharmacogenetic testing for pain management. At present, the clinical utility of pharmacogenetic testing in pain management is poorly defined.

### SOURCES

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**EFFECTIVE DATE** 8/30/2025

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