Clover Health

Policy Title	Pharmacogenomic (PGx) Testing Clinical Policy
Policy Department	Utilization Management
Effective Date	3/26/26
Revision Date(s)	N/A

Disclaimer:

Clover Utilization Management applies CMS criteria and guidelines, National Coverage Determinations (NCD), Local Coverage Determinations (LCD), Clover Policies, and MCG for determining medical necessity. Clover Policies are intended to provide a standard guideline but are not used to preempt providers' judgment in rendering services. Providers are expected to provide care based on best practices and use their medical judgment for appropriate care.

Policy:

- PGx testing is medically necessary when a member is prescribed a medication with actionable pharmacogenomic markers, exhibits polypharmacy with high-risk agents, or presents clinical patterns where genotype-guided therapy is likely to improve outcomes. Clover administers PGx testing globally across prioritized populations to optimize medication safety, therapeutic effectiveness, and total cost of care.

1. Purpose:

- This policy defines the global criteria, workflows, and clinical governance for administering pharmacogenomic (PGx) testing to ensure safe, effective, and

cost-efficient prescribing of medications. The intent is to standardize when and how PGx testing is used, ensuring consistent, evidence based application across eligible populations.

2. Clinical Rationale:

- Pharmacogenomic variation significantly affects drug metabolism, treatment response, and safety profiles. FDA guidelines indicate actionable metabolizer phenotypes influenced by genes such as CYP2D6, CYP2C19, CYP3A4/5, SLCO1B1, etc.

  The use of PGx testing reduces:
  - Ineffective therapy and prolonged trial-and-error prescribing.
  - Dose-dependent toxicity and adverse drug events.
  - Avoidable emergency visits and hospitalizations.
  - Inappropriate use of high-cost specialty or newer agents.

3. Procedure: Global Eligibility Criteria

PGx testing may be administered based on drug-level, condition-level, or population-level criteria.

3.1 Tier 1: Drug-Based Indications (Automatic Approval)

PGx testing is clinically indicated for members prescribed medications with well-established CPIC guidelines or supported by FDA labeling or FDA pharmacogenomic tables. Below are examples of medications implicated in Pharmacogenomic testing, but a full list of active ingredients can be found here

CNS / Behavioral Health

- SSRIs/SNRIs (citalopram, escitalopram, sertraline, fluoxetine, paroxetine, venlafaxine, duloxetine)
- TCAs (amitriptyline, nortriptyline)
- Antipsychotics (risperidone, aripiprazole, haloperidol)

- Stimulants influenced by CYP2D6

Pain & Neurology
- Codeine
- Tramadol
- Hydrocodone, oxycodone
- Tapentadol

Cardiology
- Clopidogrel
- Warfarin

Oncology / Specialty
- Thiopurines (azathioprine, mercaptopurine)
- Fluoropyrimidines (5-FU, capecitabine)

Metabolic & Endocrine
- Statins

3.2 Tier 2: Condition-Based, Polypharmacy and Medication Effect related Indications

PGx testing is recommended for members with:
- Polypharmacy (≥8 active medications)
- Recurrent ADEs or intolerance to medications
- Treatment-resistant depression/anxiety
- Chronic or neuropathic pain with multiple trial failures
- High-risk cardiovascular profiles (e.g., recent PCI)

4. Operational Protocol

4.1 Identification

Eligible members are identified through:
- Claims data (pharmacy; medical)
- EMR medication lists (Athena, Canvas)
- High-risk registry and risk stratification engines

4.2 Consent Education
Members will receive:

- Clear explanation of purpose and risks
- Privacy protections (HIPAA)
- Documentation of verbal or written consent

4.3 Sample Collection

- Buccal swab kits are used across all populations, unless another specimen type is clinically appropriate and accepted by the performing CLIA-certified laboratory.
- All laboratories must be CLIA-certified
- Chain-of-custody is logged end-to-end

4.4 Result Interpretation
Pharmacists evaluate:

- Metabolizer status (Ultra Rapid vs Poor Metabolizer)
- Drug-gene and drug-drug interactions
- Dose adjustment recommendations (per CPIC)
- Alternative medication options
- Safety concerns (QT interval prolongation, sedation, bleeding risk)

4.5 Follow-Up

- Patients not enrolled in IHC will be followed by their PCP in accordance with consult recommendations.
- Patients enrolled in IHC will have consults reviewed and addressed by the IHC provider.

4.6 Urgent Notification

- Urgent or clinically significant findings will be communicated promptly to the responsible provider

5. Exclusions:

PGx testing is not indicated when:

- Repeat testing of the same germline genetic content for the same genetic information, when prior results are available and remain applicable to current medication management (unless prior results cannot be obtained or additional, non-duplicative genetic content is needed for current medication management).

- There is no active or planned drug with PGx relevance
- The member declines testing
- Member is in hospice care (unless PGx testing is medically necessary for medication management and is consistent with Original Medicare hospice coverage rules (including when related to the hospice plan of care or for conditions unrelated to the terminal illness))

6. Expected Clinical Impact

6.1 Clinical Impact

- Reduction in adverse drug events
- Reduced polypharmacy burden
- Improved symptom control and stability
- Increased adherence and patient engagement
- More predictable prescribing outcomes
- Reduced time to therapeutic value

References

- Table of Pharmacogenomic Biomarkers in Drug Labeling