GUIDELINES
This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

DESCRIPTION
Drug efficacy and toxicity vary substantially between individuals. Drugs and doses are typically adjusted to meet individual requirements as needed by using trial and error, therefore clinical consequences may include a prolonged time to optimal therapy and serious adverse events. It has been found that inherited DNA sequence variation (polymorphisms) in genes for drug-metabolizing enzymes may have a significant effect on the efficacy or toxicity of a drug. This field of research is referred to as pharmacogenomics.

It has been proposed that genotype testing for certain genes to detect polymorphisms will allow physicians to predict side effects to drugs and to tailor a drug regimen based on an individual’s genetic make-up. It may be that genotype testing will improve the choice of drug, or the dose of the drug, when the drug in question has a narrow therapeutic dose range, when the consequences of treatment failure are severe, and/or when serious adverse reactions are more likely in individuals with certain polymorphisms.

Pharmacogenetic testing has been proposed to predict individual response to a variety of CYP2C19-metabolized drugs including clopidogrel, proton pump inhibitors, and tricyclic antidepressants, among others. In certain scenarios, an individual patient may benefit from genetic testing in determining dosage and likely response to specific medications.

Pharmacogenetic testing has been proposed to predict individual response to a variety of CYP2D6-metabolized drugs including tamoxifen, antidepressants, opioid analgesics, and tetrabenazine for chorea, among others. In certain scenarios, an individual patient may benefit from this genetic testing in determining dosage and likely response to specific medications.

The impact of polymorphisms has been the focus of study with a wide variety of drugs and for many diseases and conditions. The use of this type of science is just starting to be investigated, and its impact on actual medical practice is not yet fully understood.

POLICY
CYP2C19 (81225) and CYP2D6 (81226) genotyping requires prior authorization for all product lines.

Refer to PG0390 Genetic Testing for Warfarin Dose for CYP2C9 and VKORC1 genotyping.

HMO, PPO, Individual Marketplace, Elite, Advantage
CYP2C19 genotyping is considered medically necessary to determine the drug-metabolizer status of individuals who meet either of the following criteria:
- The individual is currently undergoing treatment with clopidogrel (Plavix) and has not been tested; OR
- The use of clopidogrel (Plavix) is being proposed

Repeat CYP2C19 genotyping has no proven value, and therefore is limited to once per lifetime.

CYP2D6 genotyping is considered medically necessary when the following criteria are met:
- FDA approved test; AND
- Individual has been diagnosed with Gaucher type I disease; AND
- Prior to initiation of eliglustat (Cerdelga)

CYP2D6 genotyping is considered medically necessary to guide medical treatment and/or dosing for individuals for whom initial therapy is planned with:
- Amitriptyline or nortriptyline for treatment of depressive disorders; OR
• Tetrabenazine (Xenazine) doses greater than 50 mg/day, or re-initiation of therapy with doses greater than 50 mg/day for the treatment of chorea associated with Huntington’s disease.

Repeat CYP2D6 genotyping has no proven value, and therefore is limited to once per lifetime.

CYP2C19 and CYP2D6 genotyping is considered investigational at this time for the following medications including, but may not be limited to, the following:
• Proton pump inhibitors
• Antidepressants other than those listed above
• Antipsychotics
• Antiepileptics
• Donepezil or Galantamine for Alzheimer’s disease
• Tamoxifen
• Warfarin

CYP2C19 and CYP2D6 genotyping for any indications other than those listed above are considered investigational and not medically necessary including, but may not be limited to, the following:
• General population screening

CODING/BILLING INFORMATION
The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>Description</th>
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<tbody>
<tr>
<td>81225</td>
<td>CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)</td>
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TAWG REVIEW DATES: 05/24/2018

REVISION HISTORY EXPLANATION
05/24/18: CYP2C19 (81225) and CYP2D6 (81226) genotyping requires prior authorization for all product lines. Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

REFERENCES/RESOURCES
Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid http://jfs.ohio.gov/
American Medical Association, Current Procedural Terminology (CPT®) and associated publications and services
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.