MedStar Health, Inc.
POLICY AND PROCEDURE MANUAL

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MP.119.MH – CYP2D6 Gene Analysis

This policy applies to the following lines of business:
- ✓ MedStar Employee (Select)
- ✓ MedStar MA – DSNP – CSNP
- ✓ MedStar CareFirst PPO

MedStar Health considers **CYP2D6 Gene Analysis** medically necessary for the following indications:

CYP2D6 Gene Analysis for tetrabenazine (Xenazine) treatment is indicated for all of the following:
1. Testing should be done once when needed in the decision making process of member's clinical management. (Repeat CYP2D6 genotyping has no proven value.)
2. Member has been prescribed doses of Tetrabenazine doses greater than 50 mg/day, or re-initiation of therapy with doses greater than 50 mg/day

CYP2D6 Gene Analysis for eliglustat (Cerdelga) treatment is indicated once to determine the appropriate dosing of this medication.

Limitations
1. Any other use of the CYP2D6 Gene Analysis than listed above is considered not medically necessary.
2. The test should be performed in a Clinical Laboratory Improvement Amendments (CLIA) approved laboratory.
3. There is insufficient evidence to demonstrate that genetic testing for the CYP2D6 gene improves clinical outcomes for the following medications. Consequently, genetic testing for the CYP2D6 gene is considered investigational for the following:
    a. Antidepressants other than those listed above
    b. Antipsychotics
    c. Codeine
    d. Donepezil
    e. Galantamine
    f. Tamoxifen

Background
Cytochrome P450 2D6 (CYP2D6) is an enzyme that is encoded by the CYP2D6 gene in humans. CYP2D6 is one of the most important polymorphic enzymes active in

metabolizing medications and is responsible for metabolizing 25% of commercially available drugs. The effect that this gene will potentially have on the metabolism of a medication is based on particular combinations of variants within the gene, specifically the number of positive variants.

The four CYP2D6 phenotypes include poor, intermediate, extensive and ultra-rapid metabolizers. The frequency of the poor metabolizer phenotype varies by ethnicity with 7-10% in Caucasians, 1.9-7.3% in African- Americans, and ≤1% in most Asian populations studied. The extensive metabolizer phenotype, observed in 50% of Caucasians, is the most common in this population. Genetic variation, as well as drug-drug interactions, can influence the classification of CYP2D6 metabolism into one of the above phenotypes. In addition, chronic dosing of a CYP2D6 drug can inhibit its own metabolism over time as the concentration of the drug approaches a steady state. Poor metabolizers tend to accumulate higher drug levels in their blood and likely require lower doses to achieve therapeutic effects and may be at increased risk of drug toxicity. One the other hand, ultra-rapid metabolizers may require higher doses because of faster elimination.

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.

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
81226	CYP2D6 Gene Analysis
ICD-9 codes covered if selection criteria are met:	
272.7	Gaucher disease (Lipidoses)
333.4	Huntington’s chorea
ICD-10 codes covered if selection criteria are met:	
E75.22	Gaucher disease
G10	Huntington’s disease

References

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MedStar Health reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.