



Manual: IU Health Plans
Department: Utilization Management
Policy # MP064
Effective Date: 10/01/22
Last revision: 12/12/2021

Health Plans

Medicare Advantage

X Commercial

Plavix (Clopidogrel) Metabolism Genetic Test Policy

I. Purpose

Indiana University Health Plans (IU Health Plans) considers clinical indications when making a medical necessity determination for Plavix (Clopidogrel) Metabolism Genetic Test.

II. Scope

This policy applies to all IU Health Plans and Utilization Management staff having decision making responsibilities where authorization is required for Fully insured and Self-insured commercial plans

III. Exceptions

- A. Members are limited to one test per lifetime. Genotype test results are valid life-long making repeat genetic testing for clopidogrel (Plavix) metabolism of no proven value.
- B. Genetic testing for the CYP2C19 gene is considered investigational at this time for all other indications including, but not limited to the following medications:
 - 1. Amitriptyline
 - 2. Proton pump inhibitors
 - 3. Selective serotonin reuptake inhibitors
 - 4. Warfarin

IV. Definitions

Clopidogrel bisulfate (Plavix)- widely prescribed medication to/for:

- 1. Prevent blood clots in patients with acute coronary syndrome (ACS),
- 2. Other cardiovascular (CV) disease-related events,
- 3. Undergoing percutaneous coronary intervention.

CYP2C19 - one of the principal enzymes involved in the metabolism of clopidogrel (Plavix). The presence of CYP2C19*2, a gene variant, can cause poor metabolism of the drug which can lead to increased risk for adverse cardiovascular events. Genetic testing is available to identify a patient's CYP2C19 genotype (including the presence of gene variants) which can be used in determining the therapeutic strategy for treatment with Clopidogrel (Plavix). Examples of test names are: AccuType® CP, AccuType,™ and clopidogrel CYP2C19 genotyping.

V. Policy Statements

IU Health Plans considers **Plavix (Clopidogrel) Metabolism Genetic Test** medically necessary for members meeting **all of the following** indications:

1. Clopidogrel (Plavix) being considered for treatment
2. Test completed before treatment begins
3. No previous genetic testing for clopidogrel (Plavix) has been done

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
Covered CPT Code	
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g. drug metabolism), gene analysis, common variants (e.g. *2,*3,*4,*8,*17)
ICD-10 codes covered if selection criteria are met:	
I20.0-I20.9	Angina Pectoris
I21.01-I21.4	ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I22.0-I22.9	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I24.0-I24.9	Acute ischemic heart diseases
I25.10-I25.9	Chronic ischemic heart disease
I63.00-I63.9	Occlusions and stenosis of cerebral/precerebral arteries resulting in cerebral infarction
I65.29	Occlusion and stenosis of unspecified carotid artery
I66.01-I66.9	Occlusions and stenosis of cerebral arteries , not resulting in cerebral infarction
I73.89-I73.9	Other specified peripheral vascular diseases/ Peripheral vascular disease, unspecified

VI. Procedures

None

VII. References/Citations

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): Biomarkers Overview L35062. Revision Effective Date: 12/12/2021. [LCD - Biomarkers Overview \(L35062\) \(cms.gov\)](#)
2. Hayes Clinical Utility Evaluation. (Annual Review September 30, 2021). CYP2C19 Pharmacogenomic Phenotyping to Direct Clopidogrel Therapy in Adult Patients Undergoing Percutaneous Coronary Intervention (PCI). [Hayes Knowledge Center | symplr\(hayesinc.com\)](#)
3. Hayes Clinical Utility Evaluation. (Annual Review September 30, 2021). CYP2C19 Pharmacogenomic Genotyping To Direct Clopidogrel Therapy For Secondary Prevention In Patients With A History Of Stroke And/or Transient Ischemic Attack (TIA). [Hayes Knowledge Center | symplr \(hayesinc.com\)](#)
4. Mohammad, A. M., & Al-Allawi, N. (2018). CYP2C19 Genotype is an Independent Predictor of Adverse Cardiovascular Outcome in Iraqi Patients on Clopidogrel After Percutaneous Coronary

Intervention. *Journal of cardiovascular pharmacology*, 71(6), 347–351.

<https://doi.org/10.1097/FJC.0000000000000577>

5. Raman, G., Chang, L., Gaylor, J. M., Avendano, E., Wallace, B., Ramon, I., & Lau, J. (2012). *Update on Mapping the Landscape of Genetic Tests for Non-Cancer Diseases/Conditions*. Agency for Healthcare Research and Quality (US).
6. Solomon, H. V., Cates, K. W., & Li, K. J. (2019). Does obtaining CYP2D6 and CYP2C19 pharmacogenetic testing predict antidepressant response or adverse drug reactions?. *Psychiatry research*, 271, 604–613. <https://doi.org/10.1016/j.psychres.2018.12.053>
7. Trubiano, J.A., Crowe, A., Worth, L.J., Thursky, K.A., & Slavin, M.A. (2015, April). Putting CYP2C19 genotyping to the test: utility of pharmacogenomic evaluation in a voriconazole-treated haematology cohort, *Journal of Antimicrobial Chemotherapy*, Volume 70, Issue 4, April 2015, Pages 1161–1165, <https://doi.org/10.1093/jac/dku529>

VIII. Forms/Appendices

None

IX. Responsibility

Medical Director

This Policy is proprietary and confidential. No part of this Policy may be disclosed in any manner to a third party without the prior written consent of IU Health Plans, Inc.