

**Subject:** Genetic Testing: Hypercoagulability/Thrombophilia

**Medical Policy #:** 7.11

**Status:** Reviewed

**Original Effective Date:** 03-24-2021

**Last Review Date:** 03-20-2024

## Disclaimer

Refer to the member's specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in this Medical Policy.

## Description

Factor V Leiden thrombophilia, the most common inherited form of thrombophilia, is an inherited disorder of the F5 gene that results in resistance to activated protein C and a predisposition to venous thromboembolism.

Factor II Prothrombin thrombophilia, the second most common genetic risk factor for venous thromboembolism after factor V Leiden thrombophilia.

## Coverage Determination

**Prior Authorization is required. Logon to Pres Online to submit a request:** <https://ds.phs.org/preslogin/index.jsp>

### Coverage Determinations:

The following two germline hereditary mutation tests will be considered medically reasonable and necessary when performed for evaluation of venous thromboembolism.

- Factor II (F2 gene)
- Factor V (F5 gene)

### **For Commercial and Medicaid members:**

Presbyterian Health Plan follows MCG criteria (ACG: A-0600) for F5 Gene; and (ACG: A-0613) for F2 Gene coverage.

For non-coverage of Hyperhomocysteinemia -MTHFR Gene, see MCG criteria (A-0629).

Due to contractual restrictions, providers may not access the MCG website but may obtain a copy of the criteria from the Prior Authorization staff. For proprietary reasons, MCG criteria cannot be reproduced in this Medical Policy. Please contact Health Services for a copy of the MCG Guidelines® at (505) 923-5757 or 1-888- 923-5757, Monday through Friday from 8:00 a.m. to 5:00 p.m.

### **For Medicare members:**

Presbyterian Health Plan follows CMS Biomarkers Overview, LCD ([L35062](#)) and related article ([A56541](#)), for Factor II and for Factor V coverage.

- The Medicare benefit applies only to individuals with signs and symptoms of disease. There is no Medicare benefit for assessment of thrombosis risk in asymptomatic patients (aka screening for inherited thrombophilia) or in asymptomatic individuals whose relatives have documented inherited thrombophilia

For non-coverage of MTHFR see CMS, MolDX: Genetic Testing for Hypercoagulability/Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR), LCD ([L36400](#)) and related article ([A57571](#)).

### **Limitations:**

Testing for inherited thrombophilia in individuals who have experienced recurrent fetal loss or placental abruption is not covered because it is unclear if anticoagulation therapy reduces recurrence.

There is broad consensus in the medical literature that MTHFR genotyping (CPT 81291) has no clinical utility in any clinical scenario. This testing is considered investigational and is not a Medicare, Commercial or Medicaid benefit.

## Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.

CPT Codes	Description
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant

ICD-10 CODE	ICD-10 for Medicare ONLY
Refer to ICD-10 Code Group 1 in the related Local Coverage Article: Billing and Coding: Biomarkers Overview ( <a href="#">A56541</a> ).	

## Reviewed by / Approval Signatures

Population Health and Clinical Quality Committee (PHCQC): Gray Clarke MD

Medical Directory: Ana Maria Rael MD

Date Approved: 03-20-2024

## References

1. CMS, WPS, (LCD): MoIDX: Genetic Testing for Hypercoagulability Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR) (L36400), Revision date: 07/20/2023, R#7. Related policy article A57571, revision date 07/27/2023, R2. [Cited 02/15/2024]
2. MCG, 27<sup>th</sup> Edition, Factor V Leiden Thrombophilia – F5 Gene, (ACG: A-0600), last updated 9/21/2023. [Cited 02/15/2024]
3. MCG, 27<sup>th</sup> Edition, Prothrombin Thrombophilia – F2 Gene, ACG: A-0613, Last update 9/21/2023. [Cited 02/15/2024].
4. MCG, 27<sup>th</sup> Edition, Hyperhomocysteinemia – MTHFR Gene, (ACG: A-0629), Last Update: 9/21/2023. [Cited 02/15/2024]
5. ACOG Practice Bulletin, Inherited Thrombophilias in Pregnancy, Number 197, Vol.132, NO 1, July 2018, Reaffirmed 2022. [Cited 02/15/2024]
6. CMS, LCD Biomarkers Overview (L35062), Revision 22, revision date: 12/12/2021. Related policy article LCA A56541, Revised 08-03-2022 R6. [Cited 02/15/2024]
7. Hayes, MTHFR 2021. [Cited 02/15/2024]
8. Hayes, MTHFR Genetic Testing for Severe MTHFR Enzyme Deficiency, Clinical Utility Evaluation, Sep 29, 2023 | GERMLINE. [Cited 02/15/2024]
9. Hayes, MTHFR Genetic Testing for Hypertension, Clinical Utility Evaluation, Sep 29, 2023 | GERMLINE. [Cited 02/15/2024]
10. Hayes, MTHFR Genetic Testing for Pregnancy Complications, Clinical Utility Evaluation, Sep 29, 2023 | GERMLINE. [Cited 02/15/2024]
11. Hayes, Genetic Testing for Common Forms of Hereditary Thrombophilia in Pediatric Patients with Unprovoked Venous Thromboembolism, Clinical Utility Evaluation, Aug 1, 2019 | Annual Review: Jun 21, 2022 | GERMLINE. [Cited 02/15/2024]
12. Hayes, Genetic Testing for Common Forms of Hereditary Thrombophilia in Adults With Unprovoked Venous Thromboembolism, Clinical Utility Evaluation, May 21, 2019 | Annual Review: Jun 21, 2022 | GERMLINE. [Cited 02/15/2024]
13. Hayes, Genetic Testing for Factor V Leiden in Women with Unexplained Recurrent Pregnancy Loss, Clinical Utility Evaluation, Dec 19, 2019 | Annual Review: Oct 24, 2022 | GERMLINE. [Cited 02/15/2024]

## Publication History

- 03-24-21 New policy. Reviewed by PHP Medical Policy Committee on 02/10/2021. Thrombosis panel for risk assessment for venous thromboembolism was moved from MPM 7.1. Non-Medicare members will follow MCG A-0613 (for F-II) and MCG A-0600 (for F-V). Medicare will follow LCD L36400 and L35062. Set 81240 and 81241 to pay only for Medicare with those ICD-10 listed in CMS LCA A56541. Set 81291 to not pay due to investigational for all LOB because "There is broad consensus in the medical literature that MTHFR genotyping has no clinical utility in any clinical scenario."
- 03-23-22 Annual review: Reviewed by PHP Medical Policy Committee on 03-02-2022. No change. Continue Non-Medicare to follow MCG A-0613 (for F-II) and MCG A-0600 (for F-V). Medicare will continue to follow LCD L36400 and L35062. Continue with the configuration of 81240 and 81241 to link (111) ICD-10 codes listed in A56541 in Group 1 and continue PA requirement for 81240 and 81241. MTHFR genotyping (code 81291) will be

Not every Presbyterian health plan contains the same benefits. Please refer to the member's specific benefit plan and Schedule of Benefits to determine coverage [MPMPPC051001].

removed from PA grid and will be listed in the Investigative List (non-Covered Services), MPM 36.0, since it is still considered investigational.

- 03-22-23 Annual review: Reviewed by PHP Medical Policy Committee on 01/25/2023. No change to the overall policy regarding criteria. For non-Medicare section, added MCG (A-0629) to support non-coverage of MTHFR. Reformatted the policy. Previous config requested in CY 2021 for codes (81240 and 81241) to link to (111) ICD-10 listed in LCA (A56541) in Group 1 will be submitted. Continue previous configuration of 81291 to not pay due to investigational for all LOB. Continue the configuration to require prior authorization of 81240 and 81241, unless billed by a Hematology/Oncology provider. Removed code 81291, see MPM 36.0.
- 03-24-24 Annual review: Reviewed by PHP Medical Policy Committee on 02/15/2024. There is no change in coverage. Non-Medicare will continue to follow MCG for both covered and non-covered tests. For Medicare continue to follow both Novitas and WSP LCD and LCA for both covered and non-covered tests. Continue configuration of 81291 (MTHFR) to not pay for all LOB, since it is still considered investigational. Updated configuration to include UB claims for 81291. Continue current configuration for 81240 (F2) and 81241 (F5) to only pay for listed DX in Novitas LCA A56541 for ALOB. Updated config to include commercial and Medicaid for 81240/41 because it was not done. Continue prior authorization of 81240 and 81241, unless billed by a Hematology/Oncology provider.

*This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.*

*For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: [Click here for Medical Policies](#)*

**Web links:**

*At any time during your visit to this policy and find the source material web links has been updated, retired or superseded, PHP is not responsible for the continued viability of websites listed in this policy.*

*When PHP follows a particular guideline such as LCDs, NCDs, MCG, NCCN etc., for the purposes of determining coverage; it is expected providers maintain or have access to appropriate documentation when requested to support coverage. See the References section to view the source materials used to develop this resource document.*