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
Thrombophilia (or hypercoagulability) is the propensity to develop thrombosis due to either an acquired or inherited defect in the coagulation system. The major clinical manifestation of thrombophilia is venous thromboembolism. Acquired thrombophilia risk factors include but are not limited to advancing age (> 50), trauma, malignancy, chemotherapy, major surgery, immobilization, pregnancy, estrogen, inflammation, antiphospholipid antibody syndrome, myeloproliferative disorders, heparin-induced thrombocytopenia, liver disease, nephrotic and prolonged air travel. Inherited thrombophilia risk factors include deficiencies in antithrombin, Protein C, Protein S, mutation in Factor V Leiden and prothrombin, and dysfibrinogenemias. Mixed or unknown risk factors include hyperhomocysteinemia, elevated levels of Factor VIII, acquired Protein C resistance in the absence of Factor V Leiden, and elevated levels of Factors IX and XI.

Genetic testing is available for a number of types of inherited thrombophilia, including mutations in the Factor V Leiden (FVL) gene, the Factor II Prothrombin (PT) gene and the MTHFR (methyltetrahydrofolate reductase) gene. However, the clinical utility of testing is uncertain. The clinical utility of genetic testing depends on the ability of testing results to change management that results in improved clinical outcomes. The clinical utility of genetic testing for thrombophilia is based on the overall risk of thromboembolism and the risk/benefit ratio of treatment, primarily with anticoagulants.

There is insufficient evidence in the published peer-reviewed scientific literature to determine how testing for mutations in the MTHFR gene would guide decisions in the clinical setting related to disease treatment, management or prevention. Furthermore, it is not known whether health outcomes are improved as a result of clinical decision-making based on this gene test. Consequently, genetic testing for inherited thrombophilia, specifically testing for MTHFR mutations are considered investigational.

POLICY
Genetic testing for hereditary thrombophilia (81240, 81241) requires prior authorization for HMO, PPO, Individual Marketplace, & Elite.

MTHFR (methyltetrahydrofolate reductase) gene testing (81291) is non-covered for HMO, PPO, Individual Marketplace, & Elite.

Genetic testing for hereditary thrombophilia (81240, 81241, 81291) requires prior authorization for Advantage.

Genetic testing for hereditary thrombophilia is considered medically necessary for an individual who is not otherwise receiving anticoagulant prophylaxis for the following indications:

- Pregnant woman who has a personal history of venous thromboembolism associated with a non-recurrent (transient) risk factor (e.g., fracture, surgery, prolonged immobilization)
- Individual who has a first-degree relative with Factor V Leiden or Factor II Prothrombin thrombophilia and ONE of the following:
  - surgery is planned
  - pregnant
- A significant family history, in first degree family members, of recurrent thromboembolic events or of a hypercoagulable state, prior to surgery, planned pregnancy or starting oral contraceptives

Genetic testing for hereditary thrombophilia for ANY of the following indications is considered not medically necessary (this list may not be all-inclusive):

- General population screening
- Routine screening during pregnancy or prior to the use of oral contraceptives, hormone replacement therapy (HRT), or selective estrogen receptor modulators (SERMs)
- Newborn testing, or routine testing in an asymptomatic child
- Routine initial testing in an individual with arterial thrombosis
- Testing of an asymptomatic first-degree relative of an individual with proven symptomatic VTE and a proven coagulation Factor V Leiden or Factor II Prothrombin mutation, for the purpose of considering primary prophylactic anticoagulation
- Neonate or child with asymptomatic central venous catheter-related thrombosis

Note: A first-degree relative is defined as a blood relative with whom an individual shares approximately 50% of his/her genes, including the individual’s parents, full siblings, and children.

**HMO, PPO, Individual Marketplace, Elite**
MTHFR (methyltetrahydrofolate reductase) gene testing is considered investigational and not medically necessary for all indications.

**Advantage**
MTHFR (methyltetrahydrofolate reductase) gene testing may be covered with prior authorization following the criteria listed above per the Ohio Department of Medicaid guidelines.

**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 CODES</th>
<th>Description</th>
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<tbody>
<tr>
<td>81240</td>
<td>F2 (prothrombin, coagulation factor II)(e.g., hereditary hypercoagulability) gene analysis, 20210G&gt;A variant</td>
</tr>
<tr>
<td>81241</td>
<td>F5 (coagulation Factor V)(e.g., hereditary hypercoagulability) gene analysis, Leiden variant</td>
</tr>
<tr>
<td>81291</td>
<td>MTHFR (5, 10-methylenetetrahydrofolate reductase)(e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)</td>
</tr>
</tbody>
</table>

**TAWG REVIEW DATES:** 04/22/2016, 11/14/2017, 02/22/2018

**REVISION HISTORY EXPLANATION**
04/22/16: Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
11/14/17: Genetic testing for hereditary thrombophilia (81240, 81241) is now covered with prior authorization for HMO, PPO, Individual Marketplace, & Elite. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
02/22/18: Updated indications to include: a significant family history, in first degree family members, of recurrent thromboembolic events or of a hypercoagulable state, prior to surgery, planned pregnancy or starting oral contraceptives. Policy reviewed and updated 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/
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.