



Harmony Behavioral Health, Inc.

Harmony Behavioral Health of Florida, Inc.

Harmony Health Plan of Illinois, Inc.

HealthEase of Florida, Inc.

*'Ohana Health Plan, a plan offered by
WellCare Health Insurance of Arizona, Inc.*

WellCare Health Insurance of Illinois, Inc.

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WellCare Prescription Insurance, Inc.

Genetic Testing for Factor V Leiden

Policy Number: HS-056

Original Effective Date: 11/6/2008

**Revised Date(s): 11/11/2009;
11/12/2010; 10/6/2011**

DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

BACKGROUND

Factor V Leiden thrombophilia is an inherited disorder of blood clotting. Factor V Leiden is the name of a specific mutation that results in thrombophilia, or an increased tendency to form abnormal blood clots in blood vessels. People who have the factor V Leiden mutation are at somewhat higher than average risk for a type of clot that forms in veins, such as the deep veins of the legs (deep venous thrombosis), or a clot that travels through the bloodstream and lodges in the lungs (pulmonary embolism). Most people with the factor V Leiden mutation never develop abnormal blood clots, however. Factor V Leiden is the most common inherited form of thrombophilia. Between 3 percent and 8 percent of the Caucasian (white) population in the United States and Europe carry one copy of the factor V Leiden mutation in each cell, and about 1 in 5,000 people have two copies of the mutation. The mutation is less common in other populations.

F5 Gene

Mutations in the **F5** gene cause factor V Leiden thrombophilia. The F5 gene plays a critical role in the formation of blood clots in response to injury. The protein made by the F5 gene, coagulation factor V, is involved in a series of chemical reactions that hold blood clots together. A molecule called activated protein C (APC) prevents blood clots from growing too large by inactivating factor V. The term "factor V Leiden" refers to the specific G-to-A substitution at nucleotide 1691 in the gene for factor V that predicts a single amino acid replacement (R506Q) at one of three APC cleavage sites in the factor Va molecule. In people with the factor V Leiden mutation, APC is unable to inactivate factor V normally. As a result, the clotting process continues longer than usual, increasing the chance of developing abnormal blood clots.

Other factors also increase the risk of blood clots in people with the factor V Leiden mutation. These factors include increasing age, obesity, trauma, surgery, smoking, the use of oral contraceptives (birth control pills) or hormone replacement therapy, and pregnancy. The combination of the factor V Leiden mutation and mutations in other genes involved in blood clotting can also influence risk.

POSITION STATEMENT

Genetic Testing for Factor V Leiden thrombophilia is considered medically necessary if ANY of the following criteria are met:

- Members are aged < 50 years with any venous thrombosis; **OR**,
- Member has venous thrombosis in unusual sites (such as hepatic, mesenteric, and cerebral veins); **OR**,
- Member has recurrent venous thrombosis; **OR**,
- Member has venous thrombosis and a strong family history of thrombotic disease; **OR**,
- Member is female, has venous thrombosis and is pregnant or taking oral contraceptives; **OR**,
- Member has relatives with venous thrombosis under age 50; **OR**,
- Member is a female smoker under the age of 50 with myocardial infarction; **OR**,
- Female members who have experienced recurrent pregnancy loss

Genetic Testing for Factor V Leiden thrombophilia is NOT medically necessary and NOT a covered benefit in the following situations:

- Random screening of the general population; **OR**,
- Routine screening during pregnancy; **OR**,
- Routine screening prior to use of oral contraceptives, hormone replacement therapy, or selective estrogen receptor modulators; **OR**,
- Prenatal or newborn testing; **OR**,
- Routine testing in asymptomatic children; **OR**,
- Routine initial testing in members with arterial thrombosis.

CODING

CPT®* Codes

83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (DNA or RNA)
83892	Molecular diagnostics; enzymatic digestion, each enzyme treatment
83896	Molecular diagnostics; nucleic acid probe, each
83898	Molecular diagnostics; amplification of patient nucleic acid
83908	Molecular diagnostics; amplification, signal, each nucleic acid sequence
83909	Molecular diagnostics; separation and identification by high resolution technique, each nucleic acid preparation
83912	Molecular diagnostics; interpretation and report
83914	Mutation identification by enzymatic ligation or primer extension, single segment, each segment (OLA,SBCE,ASPE)

ICD-9-CM Procedure Codes No applicable codes.

Covered HCPCS Code

S3843*	DNA analysis of the F5 gene for susceptibility to Factor V Leiden thrombophilia *Note: S-Codes are NON COVERED FOR MEDICARE -For Medicare, bill the appropriate CPT code listed above.
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Covered ICD-9-CM Diagnosis Codes - This list may not be all inclusive

434.0	Cerebral Artery Thrombosis
453.0	Hepatic Vein Thrombosis; Budd-Chiari Syndrome
453.2	Vena Cava Thrombosis
453.3	Renal Vein Thrombosis
453.40	DVT - Venous embolism and thrombosis of unspecified deep vessels of lower extremities
453.41	DVT – Venous embolism and thrombosis of deep vessels of proximal lower extremity
453.42	DVT – Venous embolism and thrombosis of deep vessels of distal lower extremity
453.8	DVT of other specified veins
646.33	Habitual Aborter, Complication of Pregnancy Elsewhere classified

Non-Covered ICD-9-CM Diagnosis Codes

433.00 – 433.91	Pre-Cerebral Arterial Thrombosis or Occlusions
434.00 – 434.91	Cerebral Artery Thrombosis or Occlusions
V28.9	Antenatal Screening, Unspecified
V78.8	Screening for other disorders of blood and blood forming organs
V82.71	Screening for genetic disease carrier status
V82.79	Other genetic screening

*Current Procedural Terminology (CPT) 2011 American Medical Association: Chicago, IL.®©

REFERENCES

Peer Reviewed

1. Coppens, M., Kaandorp, S.P., & Middeldorp, S. (2006). Inherited thrombophilias. *Obstetrics and Gynecology of North America*, 33(3), 357-374.
2. Grody, W.W., Griffin, J.H., Taylor, A.K., Korf, B.R., Heit, J.A., & American College of Medical Genetics Factor V Leiden Working Group. (2001). American College of Medical Genetics consensus statement on Factor V Leiden mutation testing. *Genetic Medicine*, 3(2), 139-148.
3. Ornstein, D.L. & Cushman, M. (2003). Factor V Leiden. *Journal of the American Heart Association*, 107, e94-e97.
4. Press, R.D., Bauer, K.A., Kujovich, J.L., & Heit, J.A. (2002). Clinical utility of Factor V Leiden (R506Q) testing



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for the diagnosis and management of thromboembolic disorders. *Archives of Pathology and Laboratory Medicine*, 126(11), 1304-1318.

Government Agencies, Professional and Medical Organizations

N/A

HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none">• New template design approved by MPC.
10/6/2011	<ul style="list-style-type: none">• Approved by MPC.• Reformatted references; no major changes.