BlueCross BlueShield of New Mexico

Reimbursement Policy

Policy Number: RPLAB058	**Policy Title:** Venous and Arterial Thrombosis Risk Testing
Approval Date: May 15, 2026	**Effective Date:** Sept. 4, 2026

Policy Disclaimer

If a conflict arises between a Reimbursement Policy and any Plan document under which a member is entitled to covered services, the Plan document will govern. If a conflict arises between a reimbursement policy and any provider contract pursuant to which a provider participates in and/or provides covered services to eligible member(s) and/or plans, the provider's contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, Benefit Booklets, Summary Plan Descriptions, and other coverage documents. Blue Cross and Blue Shield of New Mexico may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM has full and final discretionary authority for their interpretation and application to the extent provided under any applicable Plan documents.

Providers are responsible for submitting accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology (CPT®) Assistant, Healthcare Common Procedure Coding System, ICD-10-CM and ICD-10-PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare & Medicaid Services National Correct Coding Initiative Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services and procedures billed. Claim submissions are subject to claim review, including but not limited to, any terms of benefit coverage, provider contract language, medical policies, and reimbursement policies, as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Description

The Plan has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information

1. For individuals without recurrent venous thromboembolism (VTE) risk factors (e.g., surgery, prolonged immobilization, collagen vascular disease, malignancy, certain hematologic disorders), plasma testing for protein C deficiency, protein S deficiency, and antithrombin III deficiency (See **Notes 1 and 2**) **may be reimbursable** in any of the following situations:
    a. For individuals less than 50 years of age who have experienced any deep venous thrombosis/DVT or pulmonary embolism/PE.
    b. For individuals who have experienced a DVT in unusual sites (e.g., hepatic, mesenteric, or cerebral veins).
    c. For individuals who have experienced a DVT and who have a strong family history of thrombotic disease.
    d. For individuals who have experienced a DVT and who are pregnant or who are taking oral contraceptives (OCs).
    e. For first-and second-degree relatives (See **Note 3**) of individuals who have experienced a deep venous thrombosis before 50 years of age.
    f. Before the administration of oral contraceptives, targeted testing of individuals with a personal or family history of DVT.
    g. For pediatric individuals who have suffered from a pediatric arterial ischemic stroke.

2. For individuals with warfarin-induced skin necrosis or for infants who develop neonatal purpura fulminans, plasma testing for protein C deficiency and protein S deficiency (**See Note 1) may be reimbursable.**

3. Venous thrombosis risk testing for superficial venous thrombosis (including superficial thrombophlebitis and varicosities) **is not reimbursable**.

4. For all situations, all activated protein C/aPC resistance assay **is not reimbursable.**

5. DVT risk testing as part of a pre-transplant evaluation test **is not reimbursable**.

Note 1: Plasma testing for protein C deficiency, protein S deficiency and antithrombin III deficiency should be performed at least six weeks after the acute thrombotic event and while the patient is not taking anticoagulants.

Note 2: In addition to plasma testing (protein C deficiency, protein S deficiency, antithrombin III deficiency), risk factor testing for individuals suspected of having a hereditary and/or acquired thrombophilia should include genetic testing for Factor V Leiden and Prothrombin gene G20210A mutations.

Note 3: First-degree relatives include parents, full siblings, and children of the individual. Second-degree relatives include grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings of the individual.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Code	Description
85300	ANTITHROMBIN III ACTIVITY
85301	ANTITHROMBIN III ANTIGEN
85302	CLOT INHIBIT PROT C ANTIGEN
85303	CLOT INHIBIT PROT C ACTIVITY
85305	CLOT INHIBIT PROT S TOTAL
85306	CLOT INHIBIT PROT S FREE
85307	ASSAY ACTIVATED PROTEIN C

References

1. Stevens SM, Woller SC, Bauer KA, et al. Guidance for the evaluation and treatment of hereditary and acquired thrombophilia. *J Thromb Thrombolysis*. 2016;41:154-64. doi:10.1007/s11239-015-1316-1
2. Bartholomew JR. Update on the management of venous thromboembolism. *Cleveland Clinic journal of medicine*. Dec 2017;84(12 Suppl 3):39-46. doi:10.3949/ccjm.84.s3.04
3. Herrmann J. *Clinical Cardio-Oncology*. Elsevier; 2018.
4. Bauer KA, Lip GY. Overview of the causes of venous thrombosis in adults. Updated March 18, 2026. https://www.uptodate.com/contents/overview-of-the-causes-of-venous-thrombosis-in-adults
5. Byrnes JR, Wolberg AS. Red blood cells in thrombosis. *Blood*. Oct 19 2017;130(16):1795-1799. doi:10.1182/blood-2017-03-745349
6. Bauer KA. Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity. Updated January 16, 2026. https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-the-nonpregnant-adult-with-suspected-deep-vein-thrombosis-of-the-lower-extremity

7. Thompson BT, Kabrhel, Christopher. Overview of acute pulmonary embolism in adults. Updated October 09, 2025. https://www.uptodate.com/contents/overview-of-acute-pulmonary-embolism-in-adults
8. Crous-Bou M, Harrington LB, Kabrhel C. Environmental and genetic risk factors associated with venous thromboembolism. *Semin Thromb Hemost*. Nov 2016;42(8):808-20. doi:10.1055/s-0036-1592333
9. Middeldorp S. Factor V Leiden and activated protein C resistance. Updated April 23, 2025. https://www.uptodate.com/contents/factor-v-leiden-and-activated-protein-c-resistance
10. Bauer KA. Protein S deficiency. Updated December 5, 2025. https://www.uptodate.com/contents/protein-s-deficiency
11. Bauer KA. Prothrombin G20210A. Updated May 30, 2025. https://www.uptodate.com/contents/prothrombin-g20210a
12. Bauer KA. Protein C deficiency. Updated January 29, 2026. https://www.uptodate.com/contents/protein-c-deficiency
13. Connors JM. Thrombophilia Testing and Venous Thrombosis. *N Engl J Med*. 2017;377(23):2298. doi:10.1056/NEJMc1713797
14. Bauer KA, Stevens SM. Evaluation for thrombophilia and occult malignancy in adults with venous thromboembolism. Updated December 15, 2025. https://www.uptodate.com/contents/evaluation-for-thrombophilia-and-occult-malignancy-in-adults-with-venous-thromboembolism
15. Kujovich JL. Factor V Leiden thrombophilia. *Genet Med*. Jan 2011;13(1):1-16. doi:10.1097/GIM.0b013e3181faa0f2
16. Carroll BJ, Piazza G. Hypercoagulable states in arterial and venous thrombosis: When, how, and who to test? *Vasc Med*. Aug 2018;23(4):388-399. doi:10.1177/1358863x18755927
17. Kujovich JL. Factor V Leiden Thrombophilia. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews((R))*. University of Washington, Seattle; 2018.
18. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. *Blood Transfus*. Apr 2011;9(2):120-38. doi:10.2450/2010.0066-10
19. NATF. Genetic Risk Factors for Blood Clots and the Role of Genetic Testing. Updated July 21, 2022. https://thrombosis.org/patients/patient-articles/genetic-risk-factors-for-blood-clots-and-the-role-of-genetic-testing
20. Raffini L. Thrombophilia testing in children and adolescents. Updated July 15, 2025. https://www.uptodate.com/contents/thrombophilia-testing-in-children-and-adolescents
21. Curtis C, Mineyko A, Massicotte P, et al. Thrombophilia risk is not increased in children after perinatal stroke. *Blood*. May 18 2017;129(20):2793-2800. doi:10.1182/blood-2016-11-750893
22. Ferriero DM, Fullerton HJ, Bernard TJ, et al. Management of Stroke in Neonates and Children: A Scientific Statement From the American Heart Association/American Stroke Association. *Stroke*. 2019;50(3)doi:10.1161/str.0000000000000183
23. Lehman LL, Beaute J, Kapur K, et al. Workup for Perinatal Stroke Does Not Predict Recurrence. *Stroke*. 2017;48(8):2078-2083. doi:10.1161/STROKEAHA.117.017356
24. de Moerloose P, Reber G, Perrier A, Perneger T, Bounameaux H. Prevalence of factor V Leiden and prothrombin G20210A mutations in unselected patients with venous

thromboembolism. *Br J Haematol*. Jul 2000;110(1):125-9. doi:10.1046/j.1365-2141.2000.02039.x
25. Mäkelburg AB, Veeger NJ, Middeldorp S, et al. Different risk of deep vein thrombosis and pulmonary embolism in carriers with factor V Leiden compared with non-carriers, but not in other thrombophilic defects. Results from a large retrospective family cohort study. *Haematologica*. Jun 2010;95(6):1030-3. doi:10.3324/haematol.2009.017061
26. Murphy CH, Sabath DE. Comparison of Phenotypic Activated Protein C Resistance Testing With a Genetic Assay for Factor V Leiden. *Am J Clin Pathol*. Feb 4 2019;151(3):302-305. doi:10.1093/ajcp/aqy142
27. Chiasakul T, De Jesus E, Tong J, et al. Inherited Thrombophilia and the Risk of Arterial Ischemic Stroke: A Systematic Review and Meta-Analysis. *J Am Heart Assoc*. Oct 2019;8(19):e012877. doi:10.1161/jaha.119.012877
28. Ordieres-Ortega L, Demelo-Rodríguez P, Galeano-Valle F, Kremers BMM, ten Cate-Hoek AJ, ten Cate H. Predictive value of D-dimer testing for the diagnosis of venous thrombosis in unusual locations: A systematic review. *Thrombosis Research*. 2020/05/01/ 2020;189:5-12. doi:10.1016/j.thromres.2020.02.009
29. Linkins LA, Takach Lapner S. Review of D-dimer testing: Good, Bad, and Ugly. *Int J Lab Hematol*. May 2017;39 Suppl 1:98-103. doi:10.1111/ijlh.12665
30. Algahtani FH, Stuckey R. High factor VIII levels and arterial thrombosis: illustrative case and literature review. *Ther Adv Hematol*. 2019;10:2040620719886685. doi:10.1177/2040620719886685
31. Bank I, Libourel EJ, Middeldorp S, et al. Elevated levels of FVIII:C within families are associated with an increased risk for venous and arterial thrombosis. *J Thromb Haemost*. Jan 2005;3(1):79-84. doi:10.1111/j.1538-7836.2004.01033.x
32. Lee EJ, Dykas DJ, Leavitt AD, et al. Whole-exome sequencing in evaluation of patients with venous thromboembolism. *Blood advances*. Jul 11 2017;1(16):1224-1237. doi:10.1182/bloodadvances.2017005249
33. Segal JB, Brotman DJ, Emadi A, et al. Outcomes of genetic testing in adults with a history of venous thromboembolism. *Evidence report/technology assessment*. Jun 2009;(180):1-162.
34. Onda S, Furukawa K, Haruki K, et al. d-dimer-based screening for early diagnosis of venous thromboembolism after hepatectomy. *Langenbeck's Archives of Surgery*. 2021/05/01 2021;406(3):883-892. doi:10.1007/s00423-020-02058-9
35. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. *Stroke*. Jul 2021;52(7):e364-e467. doi:10.1161/str.0000000000000375
36. Kang BE, Zhang S, Lesmana H, et al. Venous thromboembolism laboratory testing (factor V Leiden and factor II c.∗97G>A), 2025 revision: A technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*. 2025;27(8)doi:10.1016/j.gim.2025.101466
37. Zhang S, Taylor AK, Huang X, et al. Venous thromboembolism laboratory testing (factor V Leiden and factor II c.*97G>A), 2018 update: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. Dec 2018;20(12):1489-1498. doi:10.1038/s41436-018-0322-z

38. Hickey SE, Curry CJ, Toriello HV. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. *Genet Med*. Feb 2013;15(2):153-6. doi:10.1038/gim.2012.165
39. Bashford MT, Hickey SE, Curry CJ, et al. Addendum: ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. *Genetics in Medicine*. 2020/12/01 2020;22(12):2125-2125. doi:10.1038/s41436-020-0843-0
40. ASH. ASH - Testing for thromboembolism | Choosing Wisely. Choosing Wisely https://www.hematology.org/education/clinicians/guidelines-and-quality-care/choosing-wisely
41. Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. *Blood advances*. 2018;2(22):3226. doi:10.1182/bloodadvances.2018024828
42. Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. *Blood advances*. 2020;4(19):4693-4738. doi:10.1182/bloodadvances.2020001830
43. Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. *Blood advances*. Nov 28 2023;7(22):7101-7138. doi:10.1182/bloodadvances.2023010177
44. King H, Kelley TP, Shatzel JJ. Gender-affirming hormone therapy in the transgender patient: influence on thrombotic risk. *Hematology*. 2024;2024(1):652-663. doi:10.1182/hematology.2024000592
45. ACOG. ACOG Practice Bulletin No. 138: Inherited thrombophilias in pregnancy. *Obstetrics and gynecology*. Sep 2013;122(3):706-17. doi:10.1097/01.AOG.0000433981.36184.4e
46. ACOG. ACOG Practice Bulletin No. 197 Summary: Inherited Thrombophilias in Pregnancy. *Obstetrics and gynecology*. Jul 2018;132(1):249-251. doi:10.1097/aog.0000000000002705
47. EGAPP. Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. *Genet Med*. Jan 2011;13(1):67-76. doi:10.1097/GIM.0b013e3181fbe46f
48. Gupta A, Sarode R, Nagalla S. Thrombophilia Testing in Provoked Venous Thromboembolism: A Teachable Moment. *JAMA Internal Medicine*. 2017;177(8):1195-1196. doi:10.1001/jamainternmed.2017.1815
49. Barnes G. Thrombophilia Testing for Provoked VTE. American College of Cardiology; 2017;2019(02/13/2019). https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2017/06/05/12/46/thrombophilia-testing-in-provoked-venous-thromboembolism
50. Barnes GD. Thrombophilia Testing and Venous Thrombosis. American College of Cardiology; 2017. https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2017/10/20/11/18/thrombophilia-testing-and-venous-thrombosis.
51. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management

of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Respir J*. Sep 2019;54(3)doi:10.1183/13993003.01647-2019
52. Mazzolai L, Ageno W, Alatri A, et al. Second consensus document on diagnosis and management of acute deep vein thrombosis: updated document elaborated by the ESC Working Group on aorta and peripheral vascular diseases and the ESC Working Group on pulmonary circulation and right ventricular function. *European Journal of Preventive Cardiology*. 2022;doi:10.1093/eurjpc/zwab088
53. De Backer J, Haugaa KH, Hasselberg NE, et al. 2025 ESC Guidelines for the management of cardiovascular disease and pregnancy: Developed by the task force on the management of cardiovascular disease and pregnancy of the European Society of Cardiology (ESC)Endorsed by the European Society of Gynecology (ESG). *European Heart Journal*. 2025;46(43):4462-4568. doi:10.1093/eurheartj/ehaf193
54. WHO. Medical eligibility criteria for contraceptive use: web annex: development of updated recommendations and Grading of Recommendations Assessment, Development and Evaluation (GRADE) tables, 6th ed. https://doi.org/10.2471/B09566
55. NICE. Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. Updated August 2, 2023. https://www.nice.org.uk/guidance/ng158/chapter/Recommendations
56. Kirsch J, Wu CC, Bolen MA, et al. ACR Appropriateness Criteria® Suspected Pulmonary Embolism: 2022 Update. *J Am Coll Radiol*. Nov 2022;19(11s):S488-s501. doi:10.1016/j.jacr.2022.09.014
57. Thrombosis Canada. Pulmonary Embolism (PE): Diagnosis. Updated April 30, 2025. https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=PULMONARYEMBOLISMDIAGNOSISANDM
58. Thrombosis Canada. Deep Vein Thrombosis: Diagnosis. Updated May 7, 2025. https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=DEEPVEINTHROMBOSISDIAGNOSIS
59. Thrombosis Canada. Thrombophilia: Deficiencies in Protein C, Protein S and Antithrombin. Updated November 10, 2025. https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=DEFICIENCIESINPROTEINCPROTEINS
60. Thrombosis Canada. Thrombophilia: Factor V Leiden and Prothrombin Gene Mutation. Updated April 30, 2025. https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=THROMBOPHILIAFACTORVLEIDENANDP
61. Thrombosis Canada. Pregnancy: Diagnosis of DVT and PE. Updated January 6, 2026. https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=83
62. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2017;102(11):3869-3903. doi:10.1210/jc.2017-01658

Policy History

Approval Date	Description
05/15/2026	09/04/2026; Document updated with literature review. The following changes were made to Reimbursement Information: Removed #1f as it is no longer included as a recommended condition for thrombophilia risk testing in ACMG guidelines; #1d edited for clarity. Removed "Assays for clotting inhibitors amount and function should be performed prior to any molecular testing" from Note 1 for clarity. References revised.
04/08/2025	08/08/2025; Document updated with literature review. Minor revisions made to Reimbursement Information for clarity; no changes to intent of reimbursement information. References revised.
10/30/2024	01/15/2025: Document updated with literature review. The following changes were made to Reimbursement Information: Added pulmonary embolism to 1.a; added #2 For individuals with warfarin-induced skin necrosis or for infants who develop neonatal purpura fulminans, plasma testing for protein C deficiency and protein S deficiency (See Note 1) may be reimbursable. References revised.
11/01/2023	11/01/2023: Document updated with literature review. Reimbursement information revised for clarity. Added: For all situations, all activated protein C (aPC) resistance assay is not reimbursable. References revised; some added, others removed.
11/1/2022	11/1/2022: New policy