GENETIC TESTING FOR INHERITED THROMBOPHILIA

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Description:

Inherited thrombophilias are a group of clinical conditions in which there is a genetic defect associated with a predisposition to thrombosis. However, not all individuals with a genetic predisposition to thrombosis will develop venous thromboembolism (VTE). The presence of inherited thrombophilia will presumably interact with other VTE risk factors to determine an individual’s VTE risk. Factor V Leiden mutation is the most common type of inherited thrombophilia accounting for up to 50% of the inherited thrombophilia syndromes. Inherited thrombophilias include the following conditions, which are defined by defects in the coagulation cascade:

- Activated protein C resistance (factor V Leiden [FVL] variant)
- Prothrombin gene variant (G20210A)
- Protein C deficiency
- Protein S deficiency
- Prothrombin deficiency
- Hyper-homocysteinemia (MTHFR variant)

Genetic testing is available for Factor V Leiden, Prothrombin gene and MTHFR gene. These tests include:

- eSensor® Thrombophilia Risk Test
- Factor II (Prothrombin) G20210A Kit
- Factor V Leiden Kit
- IMPACT Dx™ Factor V Leiden and Factor II Genotyping Test
- INFINITI™ System Assay for Factor II & Factor V
- Invader® Factor II, V, and MTHFR tests
- VeraCode® Genotyping Test for Factor V and Factor II
- Verigene® Factor F2, F5, and MTHFR Nucleic Acid Test
- Xpert® Factor II and Factor V Genotyping Assay

On April 6, 2017, the FDA permitted marketing of 23andMe® Personal Genome Service Genetic Health Risk (GHR) direct-to-consumer (DTC) tests for 10 diseases or conditions. The 23andMe GHR tests work by isolating DNA from a saliva sample which is then tested for more than 500,000 genetic variants. The presence or absence of some of these variants is associated with an increased risk for developing any 1 of 10 diseases or conditions. Testing for hereditary thrombophilia (2 variants in the F5 and F2 genes) is included.
GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Definitions:

Genetic Testing:
Analysis of DNA, RNA, chromosomes, proteins and certain metabolites in order to detect alterations related to an inherited disorder.

Gene:
A hereditary unit consisting of segments of DNA that occupies a specific location on chromosomes. Genes undergo mutation when their DNA sequence changes.

Genetic Counseling:
Instruction that provides interpretation of genetic tests and information about courses of action that are available for the care of an individual with a genetic disorder or for future family planning.

Affected Individual:
An individual displaying signs or symptoms characteristic of a suspected or specific inherited disorder.

Unaffected Individual:
An individual who displays no signs or symptoms characteristic of a suspected or specific inherited disorder.

Screening:
Genetic screening is the testing of an individual with no symptoms for a specific inherited disorder to determine if the individual carries an abnormal gene. Screening can be used to predict risk or potential risk for the individual or their offspring.

Criteria:

- Genetic testing and/or counseling of an **unaffected** individual, regardless of risk factors is considered **screening** and **not eligible for coverage**.

- Genetic testing and/or counseling of an **affected** individual to confirm a disease when confirmation of the diagnosis would not impact the care and/or management is considered **not medically necessary** and **not eligible for coverage**.
GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Criteria: (cont.)

- Genetic testing and/or counseling to determine the carrier status of the Factor V Leiden variant and/or Prothrombin 20210A variant for thrombophilia is considered **medically necessary** for an **affected individual** with documentation of **ANY** of the following:

  1. Venous thrombosis before age 50
  2. Venous thrombosis after age 50, except when active malignancy is present
  3. Venous thrombosis in unusual site (i.e., hepatic, mesenteric, and cerebral veins)
  4. Venous thrombosis in an individual with a strong family history of thrombotic disease
  5. Venous thrombosis in a pregnant woman
  6. Venous thrombosis in a woman taking oral contraceptives or hormone replacement therapy
  7. Venous thrombosis, recurrent
  8. Myocardial infarction in a female smoker under age 50

- Genetic testing and/or counseling to determine the carrier status of the Factor V Leiden variant and/or Prothrombin 20210A variant for an **affected individual** for all other indications not previously listed or if above criteria not met is considered **experimental or investigational** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  4. Insufficient evidence to support improvement outside the investigational setting.

- Genetic testing and/or counseling for MTHFR gene variants for inherited thrombophilia is considered **experimental or investigational** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.
GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Criteria: (cont.)

- If benefit coverage for maternity is available, preconception or prenatal genetic testing and/or counseling of the woman to determine the carrier status of the Factor V Leiden and/or Prothrombin 20210A variant for thrombophilia or plasminogen activator inhibitor-1 (PAI-1 4G/5G polymorphism) is considered medically necessary with documentation of ANY of the following:
  1. Two consecutive spontaneous abortions or miscarriages of unknown etiology within the first 18 weeks of gestation
  2. Unexplained severe pre-eclampsia
  3. Unexplained severe placental abruption
  4. Unexplained stillbirth

- Preconception or prenatal and/or infertility genetic testing and/or counseling of an affected individual to confirm a disease when confirmation of the diagnosis would not impact the care and/or management is considered not medically necessary and not eligible for coverage.

Resources:

Literature reviewed 06/07/17. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

Resources prior to 10/15/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.


GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Resources: (cont.)


Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Dii kwe’e atah nilinigii Blue Cross Blue Shield of Arizona haada yit’éego bina’idilkidgo éi doodago Háída bíjá aniyeedégií t’àadoo le’é yina’idilkidgo beeheaz’añii hólo díí t’àá hazaadk’ehjí háká a’dooowolgo bee haz’a doo bááh ilinigóó. Atá’ haine’iligíi kojí’ bich’í’ hodilníi 877-475-4799.

Chinese: 如果您，或是您正在幫助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thành viên dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعدك أسلحة بخصوص الضمورارية بلطفك من دون اية تكلفة للتحدث مع مترجم أتصل ب . 877-475-4799.
GENETIC TESTING FOR INHERITED THROMBOPHILIA (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay mga katarungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagsalain, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그에 대한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역관매기 위해서는 877-475-4799 로 전화해보십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если вы или лицо, которому вы помогаете, имеете вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799までお電話ください。

Farsi: 

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevoditeljem, nazovite 877-475-4799.

Thai: หากคุณ หรือคนที่คุณช่วยเหลืออยู่มีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้รับความช่วยเหลือและข้อมูลในภาษาของคุณได้โดยไม่เสียค่าใช้จ่าย ที่หมายเลข โทร. 877-475-4799