GENETIC TESTING AND COUNSELING, OTHER

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 AND COUNSELING, OTHER (cont.)

Description:

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

Gene Expression:
The translation of the information encoded in a gene into messenger RNA (mRNA) which may or may not then be translated into a protein.

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.

Familial Assessment:
1st, 2nd, and 3rd degree relatives are blood relatives on the same side of the family (maternal or paternal).

- 1st Degree Relative: Blood-related sibling, parent or child.
- 2nd Degree Relative: Blood-related relative removed by one generation, e.g., grandparent, grandchild, aunt/uncle, niece/nephew or half siblings
- 3rd Degree Relative: Blood-related relative removed by two generations, e.g., great-grandparent, great-grandchild, great-aunt/uncle, grandniece/nephew or first cousin.
GENETIC TESTING AND COUNSELING, OTHER (cont.)

Criteria:

Other BCBSAZ Medical Coverage Guidelines may exist for diagnoses not addressed in this guideline.

Medullary Thyroid Cancer:

➢ Genetic testing and/or counseling to determine the carrier status of the RET proto-oncogene responsible for familial medullary thyroid cancer (FMTC) or multiple endocrine neoplasia (MEN) is considered medically necessary for an affected individual from a family with a known RET gene mutation.

SHOX-Related Short Stature:

➢ Genetic testing and/or counseling for SHOX-related short stature is considered medically necessary for an affected individual under 18 years of age with short stature (i.e., height more than two (2) standard deviations below the mean for age and sex) with documentation of ANY of the following:

1. Above average Body Mass Index (BMI)
2. Cubitus valgus (increased carrying angle)
3. Dislocation of the ulna at the elbow
4. Increased sitting height/height ratio
5. Madelung deformity of the forearm
6. Muscular hypertrophy
7. Reduce arm span/height ratio
8. Short or bowed forearm

➢ Genetic testing and/or counseling for SHOX-related short stature 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 COUNSELING, OTHER (cont.)

Criteria: (cont.)

All Other Indications:

- Genetic testing and counseling of an affected individual for all other conditions not previously listed is considered medically necessary ONLY with documentation of ALL of the following:

  1. The individual demonstrates signs or symptoms of a genetically linked inheritable disease
  2. The test results will directly impact the treatment decisions and clinical outcome
  3. The test is a proven method to identify a genetically linked inheritable disease and there is sufficient scientific evidence to support that this testing will impact the management/treatment of the affected individual's condition and result in an improvement of the net health outcome based on the test results

These tests include, but are not limited to:

- Canavan disease gene aspartoacylase (ASPA) for mental retardation of unknown cause with developmental delay in motor skills and hypotonia in children < 4 years of age of Ashkenazi Jewish descent
- CFTR gene to determine the G551D mutation in individuals with cystic fibrosis to select for treatment with ivacaftor (Kalydeco™)
- Familial Mediterranean fever (FMF)
- Hereditary hemorrhagic telangiectasia (HHT), also referred to as Oslo-Rendu-Weber disease, for individual who exhibits epistaxis, mucocutaneous telangiectasias in multiple sites, or visceral (pulmonary, cerebral, hepatic, spinal, gastrointestinal) arteriovenous malformations AND has a first degree relative who has been diagnosed with HHT
- Human papillomavirus (HPV) genotype testing
- Karyotype chromosome analysis
- Maturity onset diabetes of the young (MODY) for children and adolescents with fasting hyperglycemia and a family history of Non-Insulin Dependent Diabetes Mellitus or gestational diabetes, for which the diagnosis of Type I Insulin Dependent Diabetes Mellitus is not confirmed. Includes MODY subtype genetic testing to assist in the appropriate management of diabetes.
- Oral disease/disorder
- Prader-Willi syndrome gene (OCA2) for children under one year of age with feeding difficulty, failure to thrive, hypotonia, diminished/absent cry and somnolence OR children 1-6 years of age with hyperphagia, rapid weight gain, obesity, developmental delay and hypogonadism
- T-cell receptor gene rearrangement for evaluation of neutropenia
- Vysis CLL Fish Probe Kit
GENETIC TESTING AND COUNSELING, OTHER (cont.)

Criteria: (cont.)

All Other Indications: (cont.)

- Repeat genetic testing is **medically necessary** only when indicated for monitoring of treatment response to medication.

- Genetic testing and/or counseling is considered **screening, not medically necessary** and **not eligible for coverage** for ANY of the following:
  1. An **unaffected** individual, regardless of risk factors
  2. To confirm a disease when confirmation of the diagnosis would not impact the care and/or management of the affected individual
  3. The test itself is considered **experimental or investigational** and **not medically necessary** based upon:
     1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes,
     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.

**Experimental or investigational** and **not medically necessary** tests include, but are not limited to:

- Apolipoprotein E (Apo E) genotypes
- Biomarker genes for the detection of lymph node metastasis in breast cancer COL2A1
- CeliacPlus
- ColonSentry®
- Crohn’s Prognostic
- Cytochrome P450 genotyping of CYP2C19 to manage the treatment of H. pylori infection (includes AmpliChip™)
- DNA Methylation Pathway Profile
- DRD4 dopamine D4 receptor p450
- GI Effects® Comprehensive Stool Profile
- HLA gene subsets, including HLA-B27, HLA-B5701, HLA-DR, HLA-DQ
- ImmunoGenomic® Profile
- Morbid obesity related genes, including melanocortin-3-receptor (MC3R)
- OvaSure™
GENETIC TESTING AND COUNSELING, OTHER (cont.)

Criteria: (cont.)

All Other Indications: (cont.)

➢ Genetic testing and/or counseling is considered **screening, not medically necessary** and **not eligible for coverage** for ANY of the following: (cont.)

   *Experimental or investigational* and **not medically necessary** tests include, but are not limited to:

   (cont.)

   - Response DX Colon
   - SEPT9
   - TransPredict Fc gamma 3A

➢ Genetic testing for control and documentation of the handling of samples to decrease specimen provenance complications (SPC) is considered **not medically necessary**.

Tests include, but are not limited to:

- Know error®system DNA
- Specimen Provenance Assay

➢ Repeat genetic testing for all other indications not previously listed is considered **not medically necessary** and **not eligible for coverage**.

Resources:

Literature reviewed 08/15/17. 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 published prior to 2012 may be requested from the BCBSAZ Medical Policy and Technology Research Department.


GENETIC TESTING AND COUNSELING, OTHER (cont.)

Resources: (cont.)


GENETIC TESTING AND COUNSELING, OTHER (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: Díí kwe’é atah niiłíñíí Blue Cross Blue Shiel’d of Arizona haada yít’éego bíína’díilkidgo éí dodo de Háída bíá aniyeedííí t’áaado le’é yíná’díilkidgo beehaz’áaníí hóliq díí t’a’á hazaadk’e’ehjí háká a’doowolgo bee haz’a doo bąqą ilíngóó. Ata’ halne’ííí kojí’ bíchjí’ hodíílninh 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，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. Đê nói chuyển vợ một thông dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona الإضرورية بلغتك من دون أي تكلفة. للتحدث مع مرشح السجل ب 877-475-4799.
GENETIC TESTING AND COUNSELING, OTHER (cont.)

Multi-Language Interpreter Services: (cont.)

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

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관련해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 받을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799로 전화하십시오.

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 Doimetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются 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: اگر شما، یا کسی که شما به آن کمک می‌کنید، سوال در مورد آموزش آزمایش‌های ژنتیک Blue Cross Blue Shield of Arizona دارید، به شما اجازه خواهد داد تا با همکاران شما به زبان خود که بطور رایگان دریافت نمایید 877-475-4799، تماس حاصل نمایید.

Assyrian: Blue Cross Blue Shield of Arizona ئین خانە، یاسى، یەکەلیەکان، یەکەلیەکان، کەیەکە لە خەڵکی یاسى وە 877-475-4799. طەلافەکەیەکان، کەیەکە لە خەڵکی یاسى وە 877-475-4799.

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 prevodiocem, nazovite 877-475-4799.

Thai: หากคุณหรือคนที่คุณช่วยเหลอมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้รับความช่วยเหลือและข้อมูลในภาษาของคุณได้โดยไม่เสียค่าใช้จ่าย พบคุณที่ 877-475-4799