GENETIC TESTING FOR NEUROFIBROMATOSIS

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 NEUROFIBROMATOSIS (cont.)

Description:

The neurofibromatoses are autosomal dominant genetic disorders associated with tumors of the peripheral and central nervous systems. There are 3 clinically and genetically distinct forms: neurofibromatosis (NF) type 1 (NF1), NF type 2 (NF2) and schwannomatosis.

Neurofibromatosis 1 Diagnosis:
NF1 is caused by dominant loss-of-function mutations in the NF1 gene. The clinical diagnosis of NF1 should be suspected in individuals with the diagnostic criteria for NF1 developed by the National Institute of Health (NIH). The criteria are met when an individual has 2 or more of the following features:

- Six or more café-au-lait macules over 5 mm in greatest diameter in prepubertal individuals and over 15 mm in postpubertal individuals
- Two or more neurofibromas of any type of one plexiform neurofibroma
- Freckling in the axillary or inguinal regions
- Optic glioma
- Two or more Lisch nodules (raised, tan-colored hamartomas of the iris)
- A distinctive osseous lesion such as sphenoid dysplasia or tibial pseudarthrosis
- A first degree relative with NF1 as defined by the above criteria

For evaluation of NF1, testing for a variety of pathogenic variants of NF1, preferably through a multistep mutation detection protocol, is indicated. If no NF1 pathogenic variants are detected in individuals with suspected NF1, testing for SPRED1 variants is reasonable.

Neurofibromatosis 2 Diagnosis:
NF2 is caused by dominant loss-of-function mutations in the NF2 gene. The diagnosis of NF2 is usually made on clinical findings. Modified NIH diagnostic clinical criteria are one of the following:

- Bilateral vestibular schwannomas
- A first degree relative with NF2 AND
  - Unilateral vestibular schwannoma OR
  - Any 2 of: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities
- Multiple meningiomas AND
  - Unilateral vestibular schwannoma OR
  - Any 2 of: schwannoma, glioma, neurofibroma, cataract

Schwannomatosis:
Schwannomatosis is a rare condition that is defined as multiple schwannomas without vestibular schwannomas that are diagnostic of NF2. Individuals with schwannomatosis may develop intracranial, spinal nerve root, or peripheral nerve tumors.
GENETIC TESTING FOR NEUROFIBROMATOSIS (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.

1\textsuperscript{st} Degree Relative:
Blood-related sibling, parent or child.

2\textsuperscript{nd} Degree Relative:
A relative removed by one generation, e.g., grandparent, grandchild, aunt/uncle, niece/nephew or first cousin.

3\textsuperscript{rd} Degree Relative:
A relative removed by two generations, e.g., great-grandparent, great-grandchild, great-aunt/uncle, grandniece/nephew or second cousin.
GENETIC TESTING FOR NEUROFIBROMATOSIS (cont.)

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 and/or counseling for neurofibromatosis when the diagnosis is clinically suspected due to signs of disease, but a definitive diagnosis cannot be made without genetic testing and the diagnosis would impact the care and/or management (i.e., referrals to specialists, treatment of manifestations and surveillance) is considered medically necessary.

- Genetic testing for neurofibromatosis 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.

Resources:

Literature reviewed 02/20/18. 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.

GENETIC TESTING FOR NEUROFIBROMATOSIS (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 níllinií Blue Cross Blue Shield of Arizona haada yít’ éego bina’ídilkidgo éi doodago Háida bída anilyeeedííi t’áado le’ é yina’ídilkidgo bee hazaá aho dií t’áá hazaadk’ehíi háká a’doowolgo bee haza’ doo bąqil ilínigóó. Aña’ halné’ígíi kójí bích’į’ hodílíníh 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. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic: 
إن كان لديك أو أدى شخص تساعدك أسلحة بخصوص الضرورية بلغتك من دون أية تكلفة، للتحدث مع مترجم اتصل ب 877-475-4799.
GENETIC TESTING FOR NEUROFIBROMATOSIS (cont.)

Multi-Language Interpreter Services: (cont.)

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

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하의 그룹은 귀하의 언어로 이용 부담없이 알 수 있는 권리가 있습니다. 그룹에 문의하기 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 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 имеет 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。通訳をお願いする場合、877-475-4799 までお電話ください。

Farsi:

آگر شما، یا کسی که شما به او کمک می‌کنید، سوال‌های مربوط به Blue Cross Blue Shield of Arizona را داشته باشید، حق داشته باشید دومانی را درباره آن را دریافت نمایید. 877-475-4799.

Assyrian:

ارگ شما، یا کسی که شما به او کمک می‌کنید، سوال‌های مربوط به Blue Cross Blue Shield of Arizona را داشته باشید، حق داشته باشید دومانی را درباره آن را دریافت نمایید. 877-475-4799.

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

Thai: หากคุณ หรือคนที่คุณช่วยเหลือมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ที่จะได้ความช่วยเหลือและข้อมูลในภาษาของคุณโดยไม่มีค่าใช้จ่าย ติดต่อตาม โทร 877-475-4799.