GENETIC TESTING FOR LIMB-GIRDLE MUSCULAR DYSTROPHIES

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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Description:

The limb-girdle muscular dystrophies (LGMDs) are a genetically heterogeneous group of muscular dystrophies (MDs) characterized by predominantly proximal muscle weakness (pelvic and shoulder girdles), with normal sensory examination. Distal muscles may be involved, but usually to a lesser extent. Onset can be in childhood or adulthood. The degree of disability depends on the location and degree of weakness. Some LGMD subtypes are characterized by only mild, slowly progressive weakness, while others are associated with early-onset, severe disease with loss of ambulation.
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Description: (cont.)

LGMDs may be associated with cardiac dysfunction, cardiomyopathy (dilated or hypertrophic), respiratory depression, and dysphagia or dysarthria. Of particular note is the risk of cardiac complications, which is a feature of many but not all LGMDs. Most individuals have an elevated creatine kinase (CK) level. A large number of genetic variants have been associated with LGMD. Genetic testing is generally considered the criterion standard for diagnosis of a specific LGMD subtype. At least 9 autosomal dominant types and at least 23 autosomal recessive types have been identified. Subtypes vary in inheritance, pathophysiology, age of onset and severity.

Definitions:

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:
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.
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Criteria:

- Genetic testing and/or counseling for genes associated with limb-girdle muscular dystrophy (LGMD) is considered *medically necessary* for an **affected individual** to confirm a diagnosis when signs and symptoms of LGMD are present but a definitive diagnosis cannot be made without genetic testing with documentation of **ANY** of the following:
  1. Results of testing may lead to changes in clinical management that improve outcomes (e.g., confirming or excluding the need for cardiac surveillance)
  2. Genetic testing will allow the affected individual to avoid invasive testing, including muscle biopsy

- Genetic testing and/or counseling for genes associated with limb-girdle muscular dystrophy (LGMD) in the reproductive setting is considered *medically necessary* with documentation of **ALL** of the following:
  1. Diagnosis of LGMD in one or both of the parents
  2. Results of testing will allow informed reproductive decision making

- Targeted genetic testing for a known familial variant associated with limb-girdle muscular dystrophy (LGMD) for an **unaffected individual** to determine future risk of disease is considered *medically necessary* with documentation of **ALL** of the following:
  1. Individual has a close relative (i.e., first- or second-degree relative) with a known familial variant consistent with LGMD
  2. Results of testing will lead to changes in clinical management (e.g., confirming or excluding the need for cardiac surveillance)

- Genetic testing and/or counseling for genes associated with limb-girdle muscular dystrophy (LGMD) for an **unaffected individual** to determine future risk of disease is considered *medically necessary* with documentation of **ALL** of the following:
  1. Individual has a close relative (i.e., first- or second-degree relative) diagnosed with LGMD whose genetic status is unavailable
  2. Results of testing will lead to changes in clinical management (e.g., confirming or excluding the need for cardiac surveillance)
GENETIC TESTING FOR LIMB-GIRDLE MUSCULAR DYSTROPHIES (cont.)

Criteria: (cont.)

- Genetic testing and/or counseling for genes associated with limb-girdle muscular dystrophy (LGMD) 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
  4. Insufficient evidence to support improvement outside the investigational setting.

Resources:

Literature reviewed 05/23/17. 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.

GENETIC TESTING FOR LIMB-GIRDLE MUSCULAR DYSTROPHIES (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 nílínígíí Blue Cross Blue Shield of Arizona haada yít’éego bína’ídiłkidgo éí döodago Háída bijá aníyeedígíí t’aadoo le’e yína’ídiłkidgo beeheaz’ánnii hólo díí t’áá hazaadk’éhíí háká a’dooowolgo bee haza’ doo b’åą ilínígóó. Ata’halne’ígíí kójí ‘bich’í ji’hodïilínihí 877-475-4799.

Chinese: 如果您，或您正在協助的對象，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 thêm 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 لدى شخصكم أسلحة بالخصوص Blue Cross Blue Shield of Arizona الضرورة بلغكم من دون أية تكلفة، للتحدث مع مترجم النص، يرجى توجه مداريا 877-475-4799.
GENETIC TESTING FOR LIMB-GIRDLE MUSCULAR DYSTROPHIES (cont.)

Multi-Language Interpreter Services: (cont.)

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

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 얘기하기 위해서는 877-475-4799 로 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 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についての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:

آگر شما، یا کسی که شما به او کمک می‌کنید، سوال‌های باید مورد اطلاعات به زبان خود را به مراجع در دفتر نمایش کنید. 877-475-4799.

Assyrian:

Blue Cross Blue Shield of Arizona یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار، یارادیت یار.

Serbo-Croatian: Ukoiko 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: หากคุณ หรือคนที่คุณช่วยเหลือสามารถถามถึง Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้สิทธิ์ที่จะแชร์และขอความช่วยเหลือของคุณได้โดยไม่เก็บค่าใช้จ่าย โปรดโทรมา ที่ 877-475-4799.