GENETIC TESTING FOR RETT SYNDROME

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 RETT SYNDROME (cont.)

Description:

Rett syndrome (RTT), a neurodevelopmental disorder, is usually caused by pathogenic variants in the MECP2 (methyl-CpG-binding protein 2) gene. Genetic testing is available to determine whether a pathogenic variant exists in Rett syndrome-associated genes (e.g., MECP2, FOXG1 or CDLK5) in an individual with clinical features of RTT, or in an individual’s family member. RTT is a neurodevelopmental disorder primarily affecting girls with an incidence of 1:10,000 female births, making it one of the most common genetic causes of intellectual disability in girls. It is characterized by apparent normal development for the first 6 to 18 months of life, followed by the loss of intellectual functioning, loss of acquired fine and gross motor skills and the ability to engage in social interaction. Purposeful use of the hands is replaced by repetitive stereotyped hand movements, sometimes described as hand-wringing. Other clinical manifestations include seizures, disturbed breathing patterns with hyperventilation and periodic apnea, scoliosis, growth retardation and gait apraxia.

There is wide variability in the rate of progression and severity of the disease. In addition to the classical form of RTT, there are a number of recognized atypical variants. Three distinct atypical variants have been described; preserved speech, early seizure, and congenital variants. Rett syndrome occurring in males is also considered a variant type and is associated with somatic mosaicism or Klinefelter (XXY) syndrome. A small number of RTT cases in males arising from the MECP2 exon 1 mutation have been reported. The required diagnostic criteria for typical (or classic) RTT and atypical (or variant) RTT have been established. For typical RTT, a period of regression followed by recovery or stabilization and fulfillment of all main criteria are required to meet the diagnostic criteria for classic RTT. For atypical RTT, a period of regression followed by recovery or stabilization, at least 2 out of the 4 main criteria plus 5 out of 11 supportive are required to meet the diagnostic criteria of variant RTT.

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 TESTING FOR RETT SYNDROME (cont.)

Definitions: (cont.)

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.

Infertility:
Inability of a couple to conceive after one year of unprotected intercourse.

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.

- Preconception or prenatal and/or infertility genetic testing and/or counseling of an unaffected individual, regardless of risk factors for Rett syndrome variants 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 counseling for Rett syndrome-associated genes (e.g., MECP2, FOXG1, or CDKL5) to confirm a diagnosis of Rett syndrome is considered medically necessary in a child with developmental delay and signs/symptoms of Rett syndrome, when a definitive diagnosis cannot be made without genetic testing.
GENETIC TESTING FOR RETT SYNDROME (cont.)

Criteria: (cont.)

- Genetic testing and/or counseling for Rett syndrome-associated genes (e.g., MECP2, FOXG1, or CDKL5) 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.

Resources:

Literature reviewed 06/19/18. 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.

Resources prior to 01/21/14 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

GENETIC TESTING FOR RETT SYNDROME (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 interprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah niiłíngíí Blue Cross Blue Shield of Arizona haada yit’éegí bina’idíldíigdo éí doodago Háída biibá aniłeeééíííí tí’áádo le’é yína’idíldíigdo beežah’ááníííí hóóló díí t’áá hazaak’ehíí hí háká a’dooowolgó bee haz’á doo bááh ilínígóó. Ata’háalné’iíííí kojí’ bich’í’ hodiíííih 877-475-4799.

Chinese: 如果您，或是您正在协助的对象，有关于插入项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权免费以您的母语得到帮助和讯息。洽询一位翻译员，请拨电话，在此插入数字 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 thống dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو أدى شخص تسلمه أسئلة بخصوص الخدمات الضرورية بلغتك من دون أي تكلفة. للتحدث مع مترجم الصلة ب 877-475-4799.
GENETIC TESTING FOR RETT SYNDROME (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutuiangan, 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 makeasap ang isang tagsalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 들고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 무담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 매기기 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 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々でも、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:

انگر شما، یا کسی که شما به آنکه می‌گوید، سوال در مورد اطلاعات به زبان خود را به طور رایگان درآورید؟ 877-475-4799

Assyrian:

Blue Cross Blue Shield of Arizona 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 dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคุณ หรือคนที่คุณช่วยเหลือสอบถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้รับความช่วยเหลือและข้อมูลในภาษาของคุณโดยไม่เสียค่าใช้จ่าย ที่หมายเลข 877-475-4799