GENETIC TESTING WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING

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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(cont.)

**Description:**

Invasive prenatal (fetal) testing refers to direct testing of fetal tissue, typically by chorionic villus sampling (CVS) or amniocentesis. Chromosomal microarray (CMA) testing and molecular diagnosis of single-gene disorders have been used to confirm the presence of a pathogenic fetal abnormality after it has been determined that the fetus is at increased risk for one of these conditions.

Chromosomal microarray (CMA) testing increases the chromosomal resolution to detect genomic imbalances that are too small to be detectable by conventional karyotyping (e.g., microdeletions and microduplications). Next-generation sequencing (NGS) rapidly sequences large portions of DNA and has been investigated for multigene panels and whole exome and genome sequencing.

**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.
GENETIC TESTING WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING (cont.)

Criteria:

MATERNITY COVERAGE IS DEPENDENT UPON BENEFIT PLAN LANGUAGE. REFER TO MEMBER’S SPECIFIC BENEFIT PLAN BOOKLET TO VERIFY BENEFITS.

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

➢ If benefit coverage for maternity is available, genetic testing and/or counseling of an unaffected individual, regardless of risk factors is considered screening and not eligible for coverage.

➢ If benefit coverage for maternity is available, 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.

➢ If benefit coverage for maternity is available, genetic testing and/or counseling of an affected individual with chromosome microarray (CMA) or karyotyping in individuals undergoing invasive diagnostic prenatal (fetal) testing is considered medically necessary.

➢ If benefit coverage for maternity is available, genetic testing and/or counseling of the affected fetus during the current pregnancy is considered medically necessary with documentation of ANY of the following:

1. Congenital malformation(s) determined in utero
2. Intrauterine fetal growth retardation (estimated weight of fetus is below the 10th percentile for its gestational age)

➢ If benefit coverage for maternity is available, amniocentesis or chorionic villous sampling is considered medically necessary with documentation of ANY of the following:

1. Advanced maternal age (35 years or older)
2. Congenital malformation(s) determined in utero
3. Two consecutive spontaneous abortions or miscarriages of unknown etiology within the first 18 weeks of gestation
GENETIC TESTING WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING
(cont.)

Criteria: (cont.)

➢ If benefit coverage for maternity is available, genetic testing with invasive diagnostic prenatal (fetal) testing for molecular analysis for single-gene disorders is considered medically necessary with documentation of ALL of the following:

1. The natural history of the disease is well understood, and there is a reasonable likelihood that the disease is one with high morbidity in the homozygous or compound heterozygous state,
2. The disease has high penetrance
3. The genetic test has adequate sensitivity and specificity to guide clinical decision making and residual risk is understood,
4. Association of the marker with the disorder has been established
5. ANY of the following high-risk identifiers:
   • For autosomal dominant conditions, at least one parent has a known pathogenic mutation
   • For autosomal recessive conditions, ONE of the following:
     a. Both parents are suspected or known to be carriers OR
     b. One parent is clinically affected and the other parent is a suspected or a known carrier
   • For X-linked conditions: A parent is a suspected or a known carrier.

➢ If benefit coverage for maternity is available, genetic testing and/or counseling with invasive diagnostic prenatal (fetal) testing for molecular analysis for single-gene disorders for all other indications 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.

➢ If benefit coverage for maternity is available, the use of next-generation sequencing in the setting of invasive prenatal testing 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 WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING (cont.)

**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 WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING (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) 864-2298, 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 niliníí Blue Cross Blue Shield of Arizona haada yit’ęgo bina’ídiłkidgo éi doodago Háida bijá aniyleedíí t’áadoo le’é yina’iídiłkidgo beehaz’áanii hóól díí t’áá hazaad’ehji háká a’dowolgo be haz’a doo baq’áñi ilinígód. Atá’ halne’igii kojí’ bich’í’ hodilííníh 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. Đề nghị chuyển với một thống dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعد أسهلة بخصوص Blue Cross Blue Shield of Arizona، فإن الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أي تكلفة للتحدث مع مترجم أفضل بـ 877-475-4799.
GENETIC TESTING WITH INVASIVE PRENATAL (FETAL) DIAGNOSTIC TESTING (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 makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 도와드릴 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관련해서 질문이 있다면 귀하가 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 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 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، سوال در مورد Blue Cross Blue Shield of Arizona داشته باشید یا اطلاعات به زبان خود را به طور رایگان دریافت نیاز دارید، 877-475-4799 تماس حاصل نمایید.

Assyrian:

خانمه معاونت‌دار، مادربزرگ، که شما یا کسی که به شما کمک می‌کند سوالاتی در مورد Blue Cross Blue Shield of Arizona داشته باشید و 877-475-4799 تماس حاصل نمایید.

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: หากคุณ หรือคุณที่ช่วยเหลือคนเฝ้าคุณคุณต้องการข้อมูลเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถขอได้จากเจ้าหน้าที่ที่ทำงานอยู่ที่ 877-475-4799.