GENETIC TESTING WITH GENETIC PANELS

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 WITH GENETIC PANELS (cont.)

Description:
Genetic panel laboratory tests using next generation sequencing (NGS) technology have been investigated for the analysis of multiple genes at one time as opposed to sequential, individual mutations. This includes panels performed by next generation sequencing (NGS), massive parallel sequencing, and panels performed by microarray. Composition of the panels is variable, and different commercial products for the same condition may test a different set of genes. The make-up of the panels is determined by the specific lab that has developed the test. In addition, the composition of any individual panel is likely to change over time as new mutations are discovered and added to the existing panels.

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 GENETIC PANELS (cont.)

Criteria:

Although genetic testing with genetic panels are considered investigational, there may be individual components of the panel that are medically necessary. Testing for individual components of a genetic panel may be medically necessary in some clinical situations. Other Medical Coverage Guidelines may apply to these individual components.

For genetic testing with molecular panel testing of cancers to identify targeted therapies, see BCBSAZ Medical Coverage Guideline #O905, “Genetic Testing With Molecular Panel Testing of Cancers to Identify Targeted Therapies”.

For genetic testing with cancer susceptibility panels using next generation sequencing, see BCBSAZ Medical Coverage Guideline #O863, “Genetic Testing With Cancer Susceptibility Panels Using Next Generation Sequencing”.

- 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 with genetic panels, unless specifically addressed in a separate Medical Coverage Guideline, 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.

These panels include, but are not limited to:

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ AmHPR™ Helicobacter Pylori Antibiotic Resistance (NGS) Panel</td>
<td>American Molecular Laboratories, Inc.</td>
</tr>
<tr>
<td>▪ DetoxiGenomic™ Profile Test</td>
<td>Genova Diagnostics Inc.</td>
</tr>
<tr>
<td>▪ EndLeukemia Assay V1 Mutation Analysis</td>
<td>University of Texas MD Anderson</td>
</tr>
</tbody>
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GENETIC TESTING WITH GENETIC PANELS (cont.)

Criteria: (cont.)

➢ Genetic testing with genetic panels, unless specifically addressed in a separate Medical Coverage Guideline, is considered experimental or investigational based upon: (cont.)

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.

These panels include, but are not limited to: (cont.)

<table>
<thead>
<tr>
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<th>Laboratory</th>
</tr>
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<tbody>
<tr>
<td>GenArray&lt;sup&gt;SM&lt;/sup&gt;</td>
<td>GenPath&lt;sup&gt;SM&lt;/sup&gt; Diagnostics</td>
</tr>
<tr>
<td>Gram-Negative Bacillus Antimicrobial Resistance Genes, PCR Panel (Check-Points Check-MDR CT103XL)</td>
<td>Mayo Medical Laboratories</td>
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<tr>
<td>Focused Pharmacogenomics Panel</td>
<td>Mayo Medical Laboratories</td>
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<tr>
<td>MatePair Acute Myeloid Leukemia Panel</td>
<td>Mayo Medical Laboratories</td>
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<tr>
<td>MitoMED&lt;sup&gt;TM&lt;/sup&gt; Autism</td>
<td>MEDomics™</td>
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<tr>
<td>Monogenic Hypertension Evaluation Panel</td>
<td>Athena® Diagnostics</td>
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<tr>
<td>mRNA/RNA-Sequencing (by NGS OmniSec, Inc.)</td>
<td>Life Technologies Corporation</td>
</tr>
<tr>
<td>MyAML NGS Panel</td>
<td>LabPMM, Invivoscribe Technologies</td>
</tr>
<tr>
<td>NETest®</td>
<td>Wren</td>
</tr>
<tr>
<td>Oncogene panel mutation analysis UltraSEEK™ for solid tumor</td>
<td>Agena Bioscience, Inc.</td>
</tr>
<tr>
<td>OncoPlex Multiplexed Gene Sequencing Panel</td>
<td>University of Washington</td>
</tr>
<tr>
<td>PANEXIA®</td>
<td>Myriad</td>
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<tr>
<td>Periodic Fever Syndromes Panel</td>
<td>GeneDX</td>
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<td>Periodic Fever Syndromes Panel</td>
<td>ARUP Laboratories</td>
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<tr>
<td>ResponseDX&lt;sup&gt;SM&lt;/sup&gt; Lung</td>
<td>Response Genetics, Inc.</td>
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<tr>
<td>RightMed®</td>
<td>OneOme®, LLC</td>
</tr>
<tr>
<td>Spinocerebellar Ataxia Panel (SCAPN)</td>
<td>University of Washington</td>
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<tr>
<td>Tempus® xT assay</td>
<td>Tempus Labs</td>
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GENETIC TESTING WITH GENETIC PANELS (cont.)

Resources:

Literature reviewed 06/05/18. We do not include marketing materials, poster boards and non-published literature in our review.


GENETIC TESTING WITH GENETIC PANELS (cont.)

Resources: (cont.)


GENETIC TESTING WITH GENETIC PANELS (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 niilíngíí Blue Cross Blue Shield of Arizona haada yit’eego bíná’dííldígo éí doodago Háída biía aniyeedíííi t’áadoo le’é yina’dííldígo bee hazaad’ehdí háká a’doowolgí bee haza’ doo bąąh ilíngóó’o. Atá’ halne’ígíí kojí’ bích’ígí’ hodiilínih 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 thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك او أدى شخص تسامده أسئلة بخصوص الضرورية بلغتك من دون أي تكلفة. للتحدث مع مترجم التصل ب 877-475-4799.
GENETIC TESTING WITH GENETIC PANELS (cont.)

Multi-Language Interpreter Services: (cont.)

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

Korean: 만약 귀하 또는 귀하가 필요로 하는 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 통역사와 매기기 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: 
آگز شما، یا کسی که شما به یا کمک می‌پیشی‌گیری، سوالی که می‌زند، اطلاعاتی که به‌زبان خود را به‌طور رایگان دریافت نمی‌شود و 877-475-4799 خواهید بود.

Assyrian: 
Blue Cross Blue Shield of Arizona ئی چکا، یا خانمی، یا خانمی سوالی که می‌پیشی‌گیری، یا اطلاعاتی که به‌زبان خود را به‌طور رایگان دریافت نمی‌شود، 877-475-4799 خواهید بود.

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

Thai: หากคุณหรือคู่ค้าของคุณมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้ความช่วยเหลือและข้อมูลในภาษาของคุณได้โดยไม่พึงมีค่าใช้จ่าย โปรดโทรตาม โทร 877-475-4799.