GENE EXPRESSION PROFILING AND PROTEIN BIOMARKERS FOR PROSTATE CANCER MANAGEMENT

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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GENE EXPRESSION PROFILING AND PROTEIN BIOMARKERS FOR PROSTATE CANCER MANAGEMENT (cont.)

**Description:**

Gene expression profile analysis and protein biomarkers has been investigated as a means to risk-stratify individuals with low risk prostate cancer. These tests are intended to be used either on prostate needle biopsy, or post radical prostatectomy to guide treatment decisions.

Gene expression profiling tests which use archived tumor specimens as the mRNA source, include Prolaris® and Oncotype Dx® Prostate Cancer Assay. Prolaris is used to quantify expression levels of 31 cell cycle progression (CCP) genes and 15 housekeeper genes to generate a CCP score. Oncotype Dx Prostate Cancer Assay is used to quantify expression levels of 12 cancer-related and 5 reference genes to generate a Genomic Prostate Score (GPS). In the final analysis, the CCP score or GPS are combined in proprietary algorithms with clinical risk criteria (PSA, Gleason grade, tumor stage) to generate new risk categories (i.e., reclassification) intended to reflect biological inactivity or aggressiveness of individual lesions, and thus inform management decisions.

Decipher® is a tissue-based tumor 22-biomarker gene expression profile test that is intended to guide the use of radiation after radical prostatectomy. This test classifies individuals as low risk, who can delay or defer radiation after prostatectomy, or high risk, as those who would potentially benefit from early radiation. The gene expression classifier is a continuous risk score between 0 and 1, with higher risk scores indicating a greater probability of metastasis.

A protein biomarker test, Promark™ is an automated quantitative imaging method to measure protein biomarkers by immunofluorescent staining in defined areas in intact formalin-fixed paraffin-embedded biopsy tissue, in order to provide independent prognostic information to aid in the stratification of individuals with prostate cancer to active surveillance or therapy.

**Definitions:**

**Gene Expression:**
The translation of the information encoded in a gene into messenger RNA (mRNA) which may or may not then be translated into a protein.

**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.
Definitions: (cont.)

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.

Criteria:

For genetic and protein biomarkers for the diagnosis and assessment of prostate cancer, see BCBSAZ Medical Coverage Guideline #O768, “Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer”.

- 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.

- Gene expression profile analysis and protein biomarkers for prostate cancer management 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.

These tests include, but are not limited to:

- Decipher
- Oncotype Dx Prostate Cancer Assay
- Prolaris
- Promark
### GENE EXPRESSION PROFILING AND PROTEIN BIOMARKERS FOR PROSTATE CANCER MANAGEMENT (cont.)

**Resources:**

Literature reviewed 12/06/16. 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.

GENE EXPRESSION PROFILING AND PROTEIN BIOMARKERS FOR PROSTATE CANCER MANAGEMENT (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 kwéé atah niliníí Blue Cross Blue Shield of Arizona haada yit’éego bina’díl dikgo éí doocdago Háida bijá aniyeedígíí t’áadoo le’é yina’díl dikgo beehaz’áanii hólo díí t’áa hazaad’éhí háhá a’doowolgí bee haz’a doo báah nilinío. Ata’ halne’igíí koj’ bích’íj’ hodiliiní 877-475-4799.

Chinese: 如果您，或是您在協助的對象，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 người dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعده أسلحة بخصوص الضرورية بلغتك من دون أي تكلفة للتحدث مع مترجم أصله ب. 877-475-4799.
GENE EXPRESSION PROFILING AND PROTEIN BIOMARKERS FOR PROSTATE CANCER MANAGEMENT (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tunang, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatang para magiisang siling sa isang talaan at imponaryo sa iyong wika ng walang gastos. Upang makausap ang isang talaan, 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 문구와 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 함으로써 하기 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 у вас есть право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: あなたも、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:

ارگ شما، یا کسی که شما به آنکه می‌کنید، سوال در مورد اطلاعات به باید دو مورد را یکی به طور رایگان دریافت نمایید 877-475-4799.

Assyrian:

Blue Cross Blue Shield of Arizona یاری یا سوالات شما را می‌گیرد.


Thai: หากคุณหรือผู้ที่คุณช่วยเหลือมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถติดต่อได้โดยไม่มีค่าใช้จ่าย ที่หมายเลข โทร 877-475-4799