



MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 02/08/11
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE: 02/06/18
ARCHIVE DATE:

OFF LABEL, UNLABELED AND ORPHAN DRUG USE

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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OFF LABEL, UNLABELED AND ORPHAN DRUG USE (cont.)

Description:

Off Label and Unlabeled Drugs:

Off label or unlabeled drug use is the use of a U.S. Food & Drug Administration (FDA)-approved drug for other uses or in treatment regimens or a population that is not included in the approved labeling by the drug's manufacturer.

Unapproved or unlabeled uses include a variety of situations ranging from completely unstudied to thoroughly investigated drug uses where the FDA has not been asked for approval.

Orphan Drugs:

The Orphan Drug Act defines an orphan drug as a drug or biological product for the diagnosis, treatment or prevention of a rare disease or condition. A rare disease is one that affects less than 200,000 people in the U.S. or one that affects greater than 200,000 people but for which there is no reasonable expectation that the cost of developing the drug and making it available will be recovered from the sales of that drug in the U.S.

Orphan drugs may be approved or still experimental. If an orphan drug has been approved for marketing, it can be obtained via usual pharmaceutical methods. If not approved, it may be available on a compassionate use basis by the sponsor (generally the manufacturer).

Criteria:

Off Label and Unlabeled Drug Use:

- Off label or unlabeled use of prescription drugs may be reviewed for medical necessity under the following circumstances:
 1. When a Medical Coverage Guideline currently exists for the requested drug.
 2. If during the course of review of medical information BCBSAZ discovers that a medication is for an off label or unlabeled use, the Pharmacy and Medical Coverage Guidelines may be referenced, when available, to guide benefit coverage even if the purpose of the review was not specifically to review a specific medication. If the medication under review does not have a Pharmacy or Medical Coverage Guideline to address the off label or unlabeled use, BCBSAZ will determine at the time of benefit coverage if there is sufficient medical literature, including medical literature supplied by the provider, to establish safety and efficacy and therefore benefit coverage¹.



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OFF LABEL, UNLABELED AND ORPHAN DRUG USE (cont.)

Criteria: (cont.)

Off Label and Unlabeled Drug Use: (cont.)

- Off label or unlabeled use of prescription drugs may be considered **medically necessary** when positive health outcomes result based upon **ALL** of the following:
 1. Sufficient scientific evidence to permit conclusions concerning the effect on health outcomes
 - The evidence consists of well-designed and well-conducted investigations published in United States major peer-review journals. The quality of the body of studies and the consistency of the results are considered in evaluating the evidence for safety and efficacy.
 - The evidence should demonstrate that the technology can measure or alter the physiological changes related to a disease, injury, illness, or condition. In addition, there should be evidence or a convincing argument based on established medical facts that such measurement or alteration affects the health outcomes.
 - Opinions and evaluations by national medical associations, consensus panels, or other technology evaluation bodies are evaluated according to the scientific quality of the supporting evidence and rationale.
 2. Sufficient evidence to support improvement of the net health outcome
 - The technology's beneficial effects on health outcomes should outweigh any harmful effects on health outcomes
 3. Sufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives
 4. Sufficient evidence to support improvement outside the investigational setting
 - When used under the usual conditions of medical practice, the technology should be reasonably expected to satisfy criteria 2 and 3

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OFF LABEL, UNLABELED AND ORPHAN DRUG USE (cont.)

Criteria: (cont.)

Orphan Drugs:

- Use of an orphan drug for an FDA-approved for marketing orphan indication is considered **medically necessary**.
 - Drug resources that may be used by Blue Cross Blue Shield of Arizona include the following:
 1. FDA²: <http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm>
 2. Drug Facts & Comparisons®³
 3. Compendia-Based Drug Bulletin (Oncology)
 4. Drug Topics®
 5. Red Book™
 6. Physicians' Desk Reference (PDR)
 - Use of an orphan drug for a use not FDA-approved for marketing for an orphan indication is considered a **benefit plan exclusion** and **not eligible for coverage** even if the FDA allows orphan drugs to be sold on a compassionate use basis.
- ¹ Physicians may legally prescribe drugs for off label uses. This Medical Coverage Guideline does not attempt to preclude all off label drug uses; it is intended to provide guidance for benefit coverage. All other plan limitations and requirements apply; including precertification, age and quantity limits, etc.
- ² The orphan drug must have FDA Orphan Designation **and** FDA Orphan Approved Status for that specific orphan indication.
- ³ Orphan drugs listed in the drug resource Drug Facts & Comparisons are found in the Keeping Up section of that resource. Those that have been approved for marketing are denoted by the footnote a.

Resources:

Literature reviewed 02/06/18. 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.

1. 5.01.01 BCBS Association Medical Policy Reference Manual. Off-Label Drug Use. Re-issue date 12/08/2011, issue date 12/01/1995.
2. Drug Facts & Comparisons®. Orphan Drugs. 09/2008 2008.
3. FDA. Office of Orphan Products Development (OOPD) Frequently Asked Questions. Accessed 10/16/2003 and 12/17/2008.



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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 nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idííkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idííkidgo beehaz'áanii hólg díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilínígóó. Ata' halne'ígíí kojí' bich'í' hodíilnih 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 thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، ف لديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.

