BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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OFF LABEL, UNLABELED AND ORPHAN DRUG USE

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.

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.

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 indications 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.

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

Description: (cont.)

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 coverage*.

* Physicians may legally prescribe drugs for off label indications. 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.

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

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. FDA**: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm
  2. Drug Facts & Comparisons® ***
  3. Compendia-Based Drug Bulletin (Oncology)
  4. Drug Topics®
  5. Red Book™
  6. Physicians' Desk Reference (PDR)

- Use of an orphan drug for an indication 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.

** The orphan drug must have FDA Orphan Designation **and** FDA Orphan Approved Status for that specific orphan indication.

*** 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:

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.