# Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

## Title: Off-Label, Approved Orphan, and Expanded Access (Compassionate Use) Drugs

**Professional**
Original Effective Date: July 30, 2012
Revision Date(s): July 30, 2012; September 25, 2013; December 7, 2015; May 10, 2017
Current Effective Date: December 7, 2015

**Institutional**
Original Effective Date: July 30, 2012
Revision Date(s): July 30, 2012; September 25, 2013; December 7, 2015; May 10, 2017
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**State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.**

**The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.**

**The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.**

**If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.**

## DESCRIPTION

Off-label or "unlabeled" drug use is the use of a drug approved by the U.S. Food and Drug Administration (FDA) for other uses that are not included in approved labeling.

The FDA approves drugs for specific indications that are included in the drug's labeling. When a drug is used for an indication other than those specifically included in the labeling, it is referred to as an off-label use. Many off-label uses are effective, well documented in the literature, and widely used.

An "orphan drug" is a product that treats a rare disease (e.g., affecting fewer than 200,000 Americans). Products have FDA orphan drug approval when they meet the

orphan drug criteria established by the FDA. The intent of the Orphan Drug Act (ODA) is to stimulate the research, development, and approval of products that treat rare diseases. Orphan designation can be obtained prior to submission of a marketing application. The safety and efficacy of the drug must be established through clinical studies. If the designated product meets the standard FDA regulatory requirements and process for obtaining marketing approval, it is given an FDA approved orphan drug designation status (i.e., "Designated/Approved"). Over 1,400 drugs and biologics have been designated as orphan drugs and over 250 have been approved for marketing.

Expanded access refers to the use of an investigational new drug (IND) outside of a clinical trial by patients with serious or life-threatening conditions who do not meet the enrollment criteria for the clinical trial in progress. This type of access may be available, in accordance with United States Food and Drug Administration (FDA) regulations, when it is clear that patients may benefit from the treatment, the therapy can be given safely outside the clinical trial setting, no other alternative therapy is available, and the drug developer agrees to provide access to the drug. The FDA refers to such a program as an expanded access program (EAP). [1] EAPs can be used in a wide range of therapeutic areas including HIV/AIDS and other infectious diseases, cancer, rare diseases, and cardiovascular diseases.

There are several types of EAPs allowed in the United States. Treatment protocols and treatment INDs provide large numbers of patients access to investigational drugs. A single-patient IND is a request from a physician to the FDA that an individual patient be allowed access to an investigational drug on an emergency or compassionate use basis.

## POLICY

### I. Off-Label Drug Use

A. Off-label use of **cancer drugs**:

1. By state mandate (40-2, 168 article 2 General Provisions), off-labeled use of an FDA approved prescription drug for cancer treatment **is covered** "if the prescription drug is recognized for treatment of the indication in one of the standard reference compendia or in substantially accepted peer reviewed medical literature. The prescribing physician shall submit to the insurer documentation supporting the proposed off-label use or uses if requested by the insurer."
(History: I. 1999, ch. 128, and Mark 2; May 6.)

2. For experimental / investigational chemotherapy drugs (not FDA approved), deny as **experimental / investigational**.

B. Off-label drug use for **non-cancer drugs** is considered **medically necessary** when ONE of the following conditions is met:

1. ALL of the following:
   a. The drug is approved by the U.S. Food and Drug Administration
   **AND**
   b. The use of the prescribed drug is for an indication that is supported by compendia. (NCCN Compendium™ level of evidence 1, 2A, or 2B, AHFS (American Hospital Formulary Service), DrugDex, Clinical Pharmacology) or the prescriber has submitted additional documentation supporting the requested therapeutic use

   **OR**

2. Sufficient evidence from published studies from major scientific or medical peer-reviewed journals that support the proposed use for the specific medical condition as safe and effective (Accepted study designs include, but are not limited to, randomized, double blind, placebo controlled clinical trials.)

### II. Orphan Drug Use

A. Use of an orphan drug is considered **medically necessary** when it receives FDA Orphan Drug designation and marketing approval ("Designated/Approved")

B. A product may have an orphan drug designation but fail to meet the criteria to have FDA marketing approval. Use of a product with orphan drug designation alone without FDA marketing approval is considered **not medically necessary.**

## III. Expanded Access (Compassionate Use) Drugs

Expanded Access (Compassionate Use) Drugs (e.g. when a single patient IND (investigational new drug) request is approved by the FDA on a compassionate use basis) are considered **experimental / investigational** but may be covered if Research Urgent or Off-Label Drug use requirements (I. A. 1.) are met.

**Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

## REVISIONS

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|---|---|
| 07-30-2012 | Policy added to the bcbsks.com web site. |
| 09-25-2013 | Description reviewed with no changes |
| | References updated |
| 12-07-2015 | Policy published 11-06-2015. Effective 12-07-2015. |
| | In Policy section:<br>Revised I B From:<br>"B. Off-label drug use for non-cancer drugs is considered medically necessary when the following conditions are met:<br>1. The drug is approved by the U.S. Food and Drug Administration AND<br>2. The prescribed drug use is supported in any one of the following:<br>a. Thomson Healthcare Inc. DrugPoints® meeting each of the following:<br>▪ Strength of Recommendation Class I or IIa; and<br>▪ Strength of Evidence Category A or B; and<br>▪ Efficacy Class I or IIa; OR<br>b. Sufficient evidence from published studies from major scientific or medical peer-reviewed journals that support the proposed use for the specific medical condition as safe and effective (Accepted study designs include, but are not limited to, randomized, double blind, placebo controlled clinical trials.)"<br>To:<br>"B. Off-label drug use for non-cancer drugs is considered medically necessary when ONE of the following conditions is met:<br>1. ALL of the following:<br>a. The drug is approved by the U.S. Food and Drug Administration AND<br>b. The use of the prescribed drug is for an indication that is supported by compendia. (NCCN Compendium™ level of evidence 1, 2A, or 2B, AHFS (American Hospital Formulary Service), DrugDex, Clinical Pharmacology) or the prescriber has submitted additional documentation supporting the requested therapeutic use OR<br>2. Sufficient evidence from published studies from major scientific or medical peer-reviewed journals that support the proposed use for the specific medical condition as safe and effective (Accepted study designs include, but are not limited to, randomized, double blind, placebo controlled clinical trials.)" |
| | References updated to include removal of Other References section. |

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| 05-10-2017 | Policy reviewed with no changes. |

## REFERENCES

1. Kansas Statute 40-2,168. http://www.ksrevisor.org/statutes/chapters/ch40/040_002_0168.html Accessed 04-24-2017.
2. U.S. Food and Drug Administration (FDA). Off-label and investigational use of marketed drugs, biologics, and medical devices. Available at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm Accessed 04-24-2017.
3. U.S. Food and Drug Administration (FDA). Orphan Product Designations and Approval Search. Available at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm Accessed 04-24-2017.
4. *National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™ (electronic version). Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp
5. *American Hospital Formulary Service (AHFS) (electronic version). Available at: http://www.ahfsdruginformation.com/
6. *DrugDex (electronic version). Available at: http://micromedex.com/compendia
7. *Clinical Pharmacology (electronic version). Available at: https://www.clinicalpharmacology.com/forms/login.aspx

*Reference requires subscription.