



Policy	PHARM-0063
Effective Date	07/01/2025
Reviewed/Revised Date	03/09/2026
Next Review Date	03/09/2027
Origination Date	06/02/2015
Origination Department	Pharmacy

Off-Label Coverage Policy

Purpose

To define the conditions under which off-label drug use may be covered.

Definition

- Off-label drug use is the use of an approved drug by the U.S. Food and Drug Administration (FDA) for uses in treatment that have not been included in the drug information labeling.
- The FDA approves drugs for specific indicated use(s) that are listed in the drug labeling. Off-label uses of the drug may be considered effective and well-documented in the literature.
- Unapproved treatment uses of the drugs are used in a variety of situations, from being completely un- or understudied to having been investigated, and the FDA hasn't been asked to include this in the approval. Approved uses have proven to be safe and effective by the FDA after review, showing that the studies are adequate and have also gone through the clinical trials process.

Prior Authorization Criteria

1. Rare or orphan diseases will be reviewed case by case with the Medical or Pharmacy Director. A rare disease is defined as a condition that affects fewer than 200,000 people in the US and is recognized by NORD (National Organization for Rare Disorders).
 - 1.1 See <https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-disease>
2. All of the following criteria must be met for off-label drug use to be considered medically necessary. Documentation must be provided.
 - 2.1 Coverage options such as clinical trials and expanded use have been exhausted
 - a) See <https://www.fda.gov/news-events/public-health-focus/expanded-access;ClinicalTrials.gov>
 - 2.2 The drug is approved by the FDA

2.3 The patient has tried and failed, or has a contraindication to ALL of the following, if applicable:

- a) Drugs labeled by the FDA for requested condition
- b) Recommended therapies per Clinical Guidelines

2.4 The requested off-label use is supported by at least one of the following:

- a) Thomson Mircomedex Drugdex® meeting one of the following:
 - i. Strength of Recommendation Class I or IIa and
 - ii. Strength of Evidence Category A or B and
 - iii. Efficacy Class I or IIa
- b) Lexicomp
- c) National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™ Category of Evidence and Consensus 1, 2A, or 2B
- d) Qualified articles from major scientific or medical peer-reviewed journals. Qualified articles include at least one large, multi-centered and prospective, double-blinded and randomized trial OR at least three small high-quality trials with appropriate controls when a large multi-center study is not possible. Articles must include validating and uncontested data supporting the proposed safety and efficacy for the use of the drug in the requested disease state.
 - i. Examples of accepted journals include, but are not limited to: American Journal of Medicine, Clinical Cancer Research, Journal of American Medical Association, Journal of Clinical Oncology, and New England Journal of Medicine.

Exclusions/Contraindications

- The prior use of samples will not be considered in the determination of a member's eligibility for coverage for this medication.
- Requests that do not meet the above criteria are considered experimental and investigational and are not a covered benefit (see plan benefit documents or applicable policy).

References

- Anthem Blue Cross Blue Shield. Off-Label Drug and Approved Orphan Drug Use. Available at: <https://www.bcbsks.com/medical-policies/label-approved-orphan-and-expanded-access-compassionate-use-drugs> Updated 08/8/2023. Accessed 03/13/2024.
- DrugDex® System [online database]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/>. Accessed 03/13/2024.
- Lexi-Drugs Off-Label Uses Policy <https://www.wolterskluwer.com/en/solutions/uptodate/about/notices/lexidrug-off-label-uses-policy>. Accessed 03/13/2024

- National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™. Available at: <https://www.nccn.org>. Accessed 03/13/2024
- U.S Food and Drug Administration. 'Off-Label' and Investigational Use of Marketed Drugs, Biologics, and Medical Devices. Available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/label-and-investigational-use-marketed-drugs-biologics-and-medical-devices>. Accessed 03/13/2024
- Wellmark Blue Cross Blue Shield. Off-Label Drug Use. Available at: https://www.wellmark.com/-/media/sites/public/files/medical-policies/off-label-drug-use.pdf?sc_lang=en&hash=FDf058C93DE30C25B8A5B0C2847E56D0 . Accessed 03/13/2024
- The National Organization for Rare Disorders <https://rarediseases.org/>

Vendors
<ul style="list-style-type: none"> • RealRx • Wipro/Health Plan Services • Personify Health

Review/Revision/Approval History	
Date	Description
06/02/2015	Policy created
04/06/2016	Policy reviewed and approved by P&T Committee
01/25/2017	Policy reviewed and approved by P&T Committee
04/18/2018	Policy reviewed and approved by P&T Committee
05/06/2019	Policy sent to P&T Committee for review
05/09/2019	Policy reviewed and approved by P&T Committee
05/12/2020	Added Lexicomp as a reference. Added the definition to orphan/rare disease and NORD as a reference.
06/01/2020	Policy reviewed and approved by P&T Committee
01/28/2021	Updated Lines of Business
05/11/2021	<ul style="list-style-type: none"> • Updated Rare diseases website • Removed Facts and Comparisons as a reference to guide use as there is not access to Facts and Comparisons with current U of U subscriptions. • Added Lexicomp as a reference • Clarified language defining the requirements for medical literature that may be considered to allow off-label use.
05/19/2021	Policy reviewed and approved by P&T Committee. Effective 06/01/2021
01/01/2022	Removed University of Utah Health Plans (Healthy U, Healthy U Integrated) from Lines of Business to create Healthy U specific policy. Removed Medicare Advantage from University of Utah Health Insurance Plans to create Medicare Advantage specific policy.
05/11/2022	Completed annual review of policy. Removed: Case reports, case series without control cohort, letters, posters, and abstracts are not qualified articles but may be considered for rare or orphan diseases as indicated above

	Added: Requests that do not meet the above criteria are considered experimental and investigational and are not a covered benefit (see plan benefit documents or applicable policy)
05/18/2022	Policy reviewed and approved by the P&T Committee. Policy effective 06/01/2022
03/13/2024	Completed annual review of policy
03/27/2024	Policy reviewed and approved by the P&T Committee. Policy effective 04/01/2024
02/03/2025	Clerical update to include: or applicable policy under exclusions/contraindications
06/02/2025	Completed annual review of policy
06/11/2025	Policy reviewed and approved by the P&T Committee. Policy effective 07/01/2025
3/09/2026	Approved by Mountain Health CO-OP Policy Committee

Disclaimer	
<ul style="list-style-type: none"> • The plan reserves the right to modify, revise, change, apply, and interpret this policy at its sole discretion, and the exercise of this discretion shall be final. The plan also revises and updates Pharmacy Coverage Policies annually, or more frequently if new evidence becomes available that suggests needed revisions. Policies are subject to change in accordance with Federal and State notice requirements. 	
<ul style="list-style-type: none"> • Services requiring prior authorization may not be covered if the prior authorization is not obtained. 	
<ul style="list-style-type: none"> • This Pharmacy Coverage Policy does not guarantee coverage or payment of the service. The Plan may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member, and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. 	
<ul style="list-style-type: none"> • The service must be a benefit in the member's plan, and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy. 	
<ul style="list-style-type: none"> • Pharmacy Coverage Policies have been developed for determining coverage for plan benefits, and when published, are available to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a member's benefit document and in coordination with the member's physician(s). The plan makes coverage decisions on a case-by-case basis, considering the individual member's health care needs. 	