# Clinical Policy: Off-Label Drug Use

Reference Number: HIM.PA.154
Effective Date: 02.01.21
Last Review Date: 01.21 Revision Log
Line of Business: HIM

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
This policy defines the responsibility of the prescriber when requesting prior authorization (PA) for approval consideration of a non-Preferred Drug List (PDL) medication for an off-label use.

Off-label drug use is the use of a drug, approved by the U.S. Food and Drug Administration (FDA), for other indications, treatment regimens, or patient populations that are not included in approved labeling. When a drug is used for an indication other than those specifically included in the FDA labeling, it is referred to as an off-label use. Many off-label uses are effective, well-documented in the literature, and widely used.

Prescribers requesting PA approval of a non-PDL medication for an off-label use must submit specified documentation. PA requests that do not meet established criteria for off-label uses will not be approved. Other PA criteria may be enforced prior to approval of a non-PDL medications, despite the prescriber meeting the specifications listed (i.e. PDL guidelines require trial and failure of two or more PDL medications prior to approval of non-PDL agents). Please refer to EPS.PHARM.03B for any exceptions to the policy (California Senate Bill No. 583).

**FDA Approved Indication(s)**
Varies by drug product.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that all medical necessity determinations for off-label uses be considered on a case-by-case basis by a physician, pharmacist or ad hoc committee, using the guidance provided within this policy.

The clinical pharmacist working in the prior authorization department may consider approval of a prior authorization request for a non-PDL drug for an off-label use if the prescriber submits all of the following information:

**I. Initial Approval Criteria**
**A. Requests for Off-Label Use** (must meet all)**:**
1. Use must be diagnosis specific as defined by ICD-9 or ICD-10 code(s);
2. Off-labeled use must be supported by one major multi-site study or three smaller studies (enrolling at least 50 subjects) published in Journal of the American Medical

Association (JAMA), New England Journal of Medicine (NEJM), The Lancet or similarly reputable medical journals; or peer reviewed specialty medical journals such as Journal of Cardiology;
   a. Articles submitted from the above referenced journals must support the current accepted medical standards of the specified diagnosis/disease state; AND
   b. Off-label use must have a specified dosage regimen, supported by primary clinical literature referenced above; AND
   c. Off-labeled use must have a specified duration of treatment, supported by primary clinical literature referenced above; AND
   d. The off-labeled use must show clear and significant clinical or economic advantage over existing approved drug regimens;
3. Failure of an adequate trial of or clinically significant adverse effects to two generics* (each from a different manufacturer) or the preferred biosimilar(s) of the requested brand name drug, if available, unless one of the following is met (a or b):
   a. Member has contraindications to the excipients in all generics/biosimilars;
   b. Request is for a biologic product for Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix D*).

**If a second generic of the requested brand name drug is not available, member must try a formulary alternative that is FDA-approved or supported by standard pharmacopeias (e.g., DrugDex) for the requested indication, provided that such agent exists*

**Approval duration: 12 months**

## II. Continued Therapy

**A. Requests for Off-Label Use** (must meet all)**:**

1. Currently receiving medication via Centene benefit;
2. Member has previously met initial approval criteria;
3. Member is responding positively to therapy;
4. If request is for a non-preferred biologic product, one of the following (a or b):
   a. Member must use the preferred biosimilar product(s), unless contraindicated or clinically significant adverse effects are experienced;
   b. Request is for Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix D*);
5. If request is for a dose increase (quantity or frequency), member has been titrated up from the lower dose with documentation of partial improvement, and the new dose does not exceed dosing guidelines recommended by the product information label or clinical practice guidelines and/or medical literature.

**Approval duration: 12 months**

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Indications or diagnoses in which the drug has been shown to be unsafe or ineffective.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration

*Appendix B: Therapeutic Alternatives*
Varies by drug product

*Appendix C: Contraindications/Boxed Warnings*
Varies by drug product

*Appendix D: States with Regulations against Redirections in Stage IV or Metastatic Cancer*

| State | Step Therapy Prohibited? | Notes |
|---|---|---|
| FL | Yes | For stage 4 metastatic cancer and associated conditions. |
| GA | Yes | For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness. |
| IA | Yes | For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA. |
| LA | Yes | For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy. |
| OH | Yes | For stage 4 metastatic cancer and associated conditions |
| PA | Yes | For stage 4 advanced, metastatic cancer |
| TN | Yes | For advanced metastatic cancer and associated conditions |
| TX | Yes | For stage 4 advanced, metastatic cancer and associated conditions |

## V. Dosage and Administration
Varies by drug product

## VI. Product Availability
Varies by drug product

## VII. References
1. Utah Department of Health. Administration of Off-Label Drug use Policy. The Amber Sheet. 2006 Aug; 14:3.
2. BlueShield of Northeastern New York. Drug Therapy Guidelines: Off-Label Drug Use Policy. P&T Newsletter. 2007 Nov.
3. BlueCross BlueShield of Minnesota. Off-Label Use of Phosphodiesterase-5 Inhibitors. Behavioral Health Policy II-67. 2007 May.
4. EPS.PHARM.03B State Specific Addendum

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created. | 12.18.20 | 01.21 (ad hoc) |
| Added redirection to generic/biosimilar products, with bypass allowed for states with regulations against redirections in stage IV or metastatic cancer. | 03.15.21 | |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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