I. Off-Label Drug Use Description

The U.S. Food and Drug Administration (FDA) approves drugs for specific indications that are included in the drug’s labeling after proven to be safe and effective through review of supporting, well-designed clinical trials. Off-label or “unlabeled” drug use is the use of a drug approved by the FDA for uses other than those included in the approved drug labeling. Many off-label uses are effective drug therapeutic treatments, supported by peer-reviewed research literature and widely used. Off-label drug uses should be viewed as potentially medically necessary pending evaluation of their efficacy to determine whether the off-label use improves health outcomes in the absence of unacceptable toxicity.

- Part II of this guideline pertains to Medicare policy
- Part III of this guideline pertains to Non-Medicare policy

II. Medicare policy

II A. Medicare Position Statement

The Centers for Medicare & Medicaid Services (CMS) Medicare Benefit Policy; Pub 100-02 Transmittal 96, defines “compendium” as a comprehensive listing of FDA-approved drugs and biologicals or a comprehensive listing of a specific subset of drugs and biologicals in a specialty compendium. A compendium: (1) includes a summary of the pharmacologic characteristics of each drug or biological and may include information on dosage, as well as recommended or endorsed uses in specific diseases; (2) is indexed by drug or biological; and (3) effective January 1, 2010, pursuant to section 182(b) of the Medicare Improvements for Patients and Providers Act (MIPPA), has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.

Chapter 15 of the CMS Medicare Benefit Policy Manual (Covered Medical and Other Health Services) issues guidance for the determination of coverage for unlabeled uses of drugs and the off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen.

Pursuant to Chapter 15 section 50.4.2, FDA approved drugs used for indications other than what is indicated on the official label may be covered if it is determined that the use is medically accepted, taking into consideration major drug compendia, authoritative medical literature and/or accepted standards of medical practice.

In the case of drugs used in an anti-cancer chemotherapeutic regimen, off-label uses are reviewed pursuant to Chapter 15 section 50.4.5, as follows:
Drug Therapy Guidelines

Off-Label Drug Use

Last Review Date: 12/19

- When off-label, medically accepted* indications are supported in either one or more of the following Medicare-recognized compendia**:
  - American Hospital Formulary Service-Drug Information (AHFS-DI);
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium;
  - Micromedex DrugDex;
  - Clinical Pharmacology; and
  - Lexi-Drugs

*Uses are identified as being medically accepted if the indication is Category 1 or 2A in NCCN, Class I/IIa/IIb in DrugDex, narrative text in AHFS-DI or Clinical Pharmacology is supportive, or indication is listed in Lexi-Drugs as “Use: Off-Label” and rated as “Evidence Level A.”

**HealthNow will maintain subscriptions to the compendia listed.

- When off-label, medically accepted indications are supported in peer-reviewed medical literature when appearing in the regular editions of Medicare-recognized publications as outlined in Chapter 15 section 50.4.5. Literature will be evaluated in accordance with the guidance, taking into consideration the clinical relevance of the literature to the case at hand and the appropriateness of trial design and clinical outcomes.

- If warranted, HealthNow will request compendia documentation or peer-reviewed literature supporting the off-label use from the requesting physician.

- Exclusions
  - Uses are not medically accepted by a compendium if the following applies:
    - Category 3 in NCCN
    - Class III in DrugDex
    - Narrative text in AHFS-DI or Clinical Pharmacology is “not supportive”
    - Indication listed in Lexi-Drugs as “Use: Unsupported”
  - In-house publications of entities whose business relates to the manufacture, sale, or distribution of pharmaceutical products.
  - Abstracts/meeting abstracts.

II B. Medicare Procedure

Coverage for off-label, or unlabeled, drug uses not supported in a current National Coverage Determination (NCD)/Local Coverage Determination (LCD) will be reviewed in accordance with the guidance set forth in Chapter 15 sections 50.4.2 and 50.4.5 of the CMS Medicare Benefit Policy Manual.
III. Non-Medicare policy

III A. Non-Medicare Position Statement

Criteria in drug-specific policies (corporate Drug Therapy Guidelines) take precedence over the criteria listed in this policy. Therefore, drug-specific policies must be reviewed prior to applying the criteria listed below. However, this policy should be applied when a drug-specific policy is silent for an off-label use of a FDA approved drug or when developing drug specific medical policies. This policy shall not be construed to require coverage for any drug when the FDA has determined its use to be contraindicated. It is suggested that each unlabeled use of any drug be individually evaluated.

The literature must be provided with the prior authorization request along with other supporting documentation that may be relevant to the case.

III B. Non-Medicare Policy

Coverage for off-label, or unlabeled, drug uses will consider the following criteria to determine medical necessity:

- Drug must have an FDA-labeled indication, **AND**
- Drug must show positive impact or improve health outcome, **AND**
- Drug should improve the net health outcome as much as, or more than, established alternatives, **AND**
- Provider must demonstrate why established treatment alternatives cannot be utilized in the specific case being reviewed (by means of providing appropriate clinical rationale) **AND**
- The disease improvement must be attainable outside the investigational settings **AND**
- One of the following is true:
  - Requested drug indication is supported by one or more approved compendia **OR**
  - Requested drug use is supported by at least two peer-reviewed articles published in the medical literature:
    - The quality of the body of studies and the consistency of the results are considered in evaluating the evidence **AND**
    - The study must be at least a phase II clinical trial or higher **AND**
    - The clinical trial should include a sufficient number of subjects in relation to the incidence of the disease being treated **AND**
    - The outcomes of the study should support that the off-label use is generally safe in relation to the severity of the disease being treated and other existing treatment options **AND**
- The study outcomes should represent clinically meaningful outcomes experienced by patients.
- Exclusions
  - If the request is not supported by compendia or articles as listed above, then the request is not considered medically appropriate and will be denied as non FDA approved/experimental/investigational.
Case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

IV. Summary of Policy Changes

2/24/20: CP021 Off-Label Drug Use Policy and Procedure reformatted to fit Drug Therapy Guideline template

V. References


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.