Clinical Policy: No Coverage Criteria/Off-Label Use Policy

Reference Number: PA.CP.PMN.53
Effective Date: 01/18
Last Review Date: 04/19
Line of Business: Medicaid

Coding Implications
Revision Log

Description
The intent of this policy is to provide coverage criteria when a request for a preferred agent is received for:

- Use in an FDA-approved indication where no previously-approved coverage criteria exist specifically addressing that indication
- Use in an off-label indication (i.e. utilization of an FDA-approved drug for uses other than those listed in the FDA-approved labeling or in treatment regimens or populations that are not included in approved labeling

Policy/Criteria
** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria **

It is the policy of Pennsylvania Health and Wellness® that the off-label use of a non-specialty drug is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Labeled Use without Coverage Criteria (must meet all)**:**

1. Request is for a drug without custom coverage criteria;
   **All requests for non- preferred drug list (PDL) drugs, under the pharmacy or medical benefit, should be reviewed against CP.PMN.16 - Request for Medically Necessary Drug Not on the PDL.*
2. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist, at maximum indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
3. If request is for combination product or alternative dosage form or strength of existing drugs (except combination HIV antiretrovirals), medical justification* supports inability to use the individual drug products concurrently or alternative dosage forms or strengths (e.g., contraindications to the excipients of all alternative products);
   **Use of a copay card or discount card does not constitute medical necessity*
4. Member has no contraindications to prescribed agent per the product information label;
5. If applicable, prescriber has taken necessary measures to minimize any risk associated with a boxed warning in the product information label;
6. Treatment is not for a benefit-excluded purpose (e.g., cosmetic);
7. Dose does not exceed the FDA-approved maximum recommended dose for the relevant indication.

Approval duration: duration of request or 6 months (whichever is less)

B. Off-label Use (i.e. utilization of an FDA-approved drug for uses other than those listed in the FDA-approved labeling or in treatment regimens or populations that are not included in approved labeling) (must meet all)**:**

1. There are no pharmacy and therapeutic committee approved off-label use criteria for the diagnosis;
2. Request meets one of the following (a, b, or c):
   a. Use is supported by the National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1, 2A, and 2B (*see Appendix D*)
   b. Evidence from at least two high-quality, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i-iv):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes as a result of the drug therapy in question;
      iv. Appropriate experimental design and method to address research questions (*see Appendix E for additional information*);
   c. Micromedex DrugDex® with strength of recommendation Class I or IIa (*see Appendix D*);
   d. Micromedex DrugDex® with strength of recommendation Class IIb (*see Appendix D*), provided that the request meets the following (i and ii):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
3. Treatment is not for a benefit-excluded purpose (e.g., cosmetic);
4. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist, at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has no contraindications to prescribed agent per the product information label;
6. If applicable, prescriber has taken necessary measures to minimize any risk associated with a boxed warning in the product information label;
7. Requested dosage regimen and duration is within dosing guidelines recommended by clinical practice guidelines and/or medical literature.

Approval duration: duration of request or 6 months (whichever is less)

II. Continued Therapy

A. Labeled Use without Coverage Criteria/Off-Label Use (must meet 1 or 2-4)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit, or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies and documentation supports positive response to therapy;

2. Use is supported by one of the following (a, b, or c):
   a. The NCCN Drug Information and Biologics Compendium level of evidence 1, 2A, or 2B (*see Appendix D);*
   b. Evidence from at least two, high-quality, published studies in peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes as a result of the drug therapy in question;
      iv. Appropriate experimental design and method to address research questions (*see Appendix E for additional information*);
   c. Micromedex DrugDex with strength of recommendation Class I or IIa (*see Appendix D*);
   d. Micromedex DrugDex® with strength of recommendation Class IIb (*see Appendix D*), provided that the request meets the following (i and ii):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
3. Member is responding positively to therapy;
4. 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 product information label or clinical practice guidelines and/or medical literature.

Approval duration: duration of request or 12 months (whichever is shorter)

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

IV. Appendices/General Information
Appendix A: Abbreviation Key
FDA: Food and Drug Administration
HIV: human immunodeficiency virus
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
Varies by drug product

Appendix C: Contraindications/Boxed Warnings
Varies by drug product

Appendix D: General Information
- These criteria are to be used only when specific prior authorization criteria do not exist.
- The U.S. FDA approves drugs for specific indications included in the drug's product information label. The approval by the FDA means that the company can include the information in their package insert. Omission of uses for a specific age group or a

specific disorder from the approved label means that the evidence required by law to allow their inclusion in the label has not been submitted to the FDA. Off-label, or "unlabeled," drug use is the utilization of an FDA-approved drug for indications, treatment regimens, or populations other than those listed in the FDA-approved labeling. Many off-label uses are effective and well-documented in the peer-reviewed literature, and they are widely used even though the manufacturer has not pursued the additional indications. Refer to the drug's FDA-approved indication(s) and labeling (varies among drug products).

- NCCN Categories of Evidence and Consensus:
  - Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
  - Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
  - Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
  - Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.
- Micromedex DrugDex Strength of Evidence, Strength of Recommendation, and Efficacy Definitions (Tables 1, 2, and 3):

Table 1. Strength of Recommendation		
Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases
Class IIb	Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test, or treatment is not useful, and should be avoided.
Class Indeterminate	Evidence Inconclusive	Not applicable

Table 2. Strength of Evidence	
Category A	Category A evidence is based on data derived from: Meta-analyses of randomized controlled trials with homogeneity with regard to the directions and degrees of results between individual studies. Multiple, well-done randomized clinical trials involving large numbers of patients
Category B	Category B evidence is based on data derived from: Meta-analyses of randomized controlled trials with conflicting conclusions with regard to the directions and degrees of results between individual studies. Randomized controlled trials that involved small numbers of patients or had significant methodological flaws (e.g., bias, drop-out rate, flawed analysis, etc.). Nonrandomized studies (e.g., cohort studies, case-control studies, observational studies)

Table 2. Strength of Evidence	
Category C	Category C evidence is based on data derived from: Expert opinion or consensus, case reports or case series
No Evidence	Not applicable

Table 3. Efficacy		
Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence Favors Efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is Inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.
Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective.

Appendix E: Appropriate Experimental Design Methods
Randomized, controlled* trials are generally considered the gold standard; however:

- In some clinical studies, it may be unnecessary or not feasible to use randomization, double-blind trials, placebos, or crossover.
- Non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.

**Case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.*

V. Dosage and Administration

Varies by drug product

VI. Product Availability

Varies by drug product

VII. References

1. Food and Drug Administration. Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices. January 2009. Available at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm. Accessed July 14, 2018.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 2018.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: Added criteria for labeled use without custom criteria; added initial approval criteria for off-label use to align with off-label use policy & procedures; allowed COC for listed disease states in continued approval; added references.	02.02.18	
2Q 2019 annual review: Clarified use of DrugDex I, IIa and IIb support for off-label use; added criteria for combinations products and alternative dosage forms or strengths of existing drugs; added redirection to PA.CP.PMN.16 for non-PDL agent under the pharmacy and medical benefit; for drugs without custom coverage criteria added requirement for trial and failure of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist; description section has been rewritten to clarify intent of policy; Added clarification to Labeled use without Coverage Criteria to indicate that combination HIV antiretrovirals products will not require use of individual components; references reviewed and updated.	04.17.19	