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

Reference Number: CP.PMN.53
Effective Date: 09.12.17
Last Review Date: 05.18
Line of Business: Medicaid

Revision Log

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

Description
This policy is to be used to determine medical necessity of existing or newly approved drug therapy where there are no coverage criteria and for off-label requests for an indication, treatment regimen, or patient population not approved by the U.S. FDA (Food and Drug Administration).

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 drug therapy without Centene® coverage criteria or 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.

I. Initial Approval Criteria

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

1. The drug is prescribed for an FDA-approved indication, dose, and frequency;
2. Request meets one of the following:
   a. Request is for a new drug approved by the FDA within the last 12 months without a custom coverage criteria;
   b. Request is for an existing drug prescribed for new indication approved by the FDA within the last 12 months without a custom coverage criteria;
3. If request is for a non-formulary agent, failure of an adequate trial of at least two formulary agents that are FDA-approved for the same indication and/or drugs that are considered the standard of care for the indication, when such agents exist, at maximum indicated doses, unless member experiences clinically significant adverse effect or has contraindication(s);
4. Requested dosage regimen and duration is within dosing guidelines recommended for the specific indication according to the product information label of the drug;
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.

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

B. Off-label Use (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 (*see Appendix C*);
   b. The use is supported by 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. 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 C for additional information*);
   c. Safety and efficacy is supported by Micromedex DrugDex® with strength of recommendation Class I, IIa, or IIb (*see Appendix C*);
3. Treatment is not for a benefit-excluded purpose (e.g., cosmetic);
4. Prescribed by or in consultation with an appropriate specialist for the diagnosis;
5. 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 member experiences clinically significant adverse effect or has contraindication(s);
6. Member has no contraindications to prescribed agent per the product information label;
7. If applicable, prescriber have taken necessary measures to minimize any risk associated with a boxed warning in the product information label;
8. 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. All Requests from Section I (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or initial approval criteria are met;
   b. Documentation via pharmacy claims supports that member has received this medication for at least 30 days and is currently receiving the drug for one of the disease states that are granted continuity-of-care (i.e., heart failure, seizure, HIV, psychotic disorder, or oncology) AND, if off-label, request meets one of the following (i, ii, or iii):
      i. Use is supported by the National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1 & 2A (*see Appendix C);*

ii. The use is supported by 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:
    1) Adequate representation of the member's clinical characteristics, age, and diagnosis;
    2) Adequate representation of the prescribed drug regimen;
    3) Clinically meaningful outcomes as a result of the drug therapy in question;
    4) Appropriate experimental design and method to address research questions (*see Appendix C for additional information*);
iii. Safety and efficacy is supported by Micromedex DrugDex® with strength of recommendation Class I, IIa, or IIb (*see Appendix C*);

2. Documentation supports positive response to therapy (e.g., sign/symptom reduction, no disease progression, no significant toxicity);
3. 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 less)

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
HIV: human immunodeficiency virus
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: General Information

- These criteria are to be used only when specific prior authorization criteria do not exist.
- The U.S. Food and Drug Administration (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).
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 D: 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

Not applicable

VI. Product Availability

Not applicable

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, 2017.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 12, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Edited Description of Plan criteria. Added "labeling" to FDA labeled indications section. Edited Criteria for approval Section B. "Standard of care" recommendation moved to Section B. Added "current standard of care treatment" in Section E.	11.13	11.13
Reviewed.	12.14	12.14
Updated criteria E with (i.e. improved health outcomes, reduced adverse health event or reduced adverse drug event)"	05.15	05.15
Converted to new guideline template Guideline reviewed Modified initial approval duration to 3 months or the requested length of therapy, whichever is less	11.15	11.15
Converted to new template. 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.	09.12.17	11.17
2Q 2018 annual review: no significant changes; Section IA2a/b: added "approved within the last 12 months"; Section IB: Added the requirement that a P & T off-label use criteria must not be available as several criteria address off-label uses.	02.02.18	05.18

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.