Clinical Policy: Global Medical Necessity

Reference Number: ERX.PA.01
Effective Date: 07.01.16
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description
This policy applies to both existing and newly approved drug therapies where no coverage criteria are available, including requests for an indication, treatment regimen, or patient population not approved by the FDA. All medical necessity determinations must be considered on a case-by-case basis by a physician, pharmacist, or ad hoc committee.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that the requested drug therapy 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 formulary* drug without custom coverage criteria;
   **All requests for non-preferred drug list (PDL) drugs, under the pharmacy benefit, should be reviewed against ERX.PA.03 - Request for Medically Necessary Drug Not on the PDL*
2. Diagnosis of a condition for which the product is FDA-approved;
3. Failure of an adequate trial of at least two preferred* 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 clinically significant adverse effects are experienced or all are contraindicated;
   **Generic is preferred, if available generically*
4. For combination product or alternative dosage form or strength of existing drugs, 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*
5. Member has no contraindications to the prescribed agent per the prescribing information;
6. If applicable, prescriber has taken necessary measures to minimize any risk associated with a boxed warning in the product information label;
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 (must meet all)**:**

1. There are no pharmacy and therapeutics committee approved off-label use criteria for the diagnosis;
2. Use is supported by one of the following (a, b, or c):

a. The National Comprehensive Cancer Network (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 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*);

3. Treatment is not for a benefit-excluded use (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 clinically significant adverse effects are experienced or all are contraindicated;
6. 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 F*);

   **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*
7. Member has no contraindications to the prescribed agent per the prescribing information;
8. If applicable, prescriber has taken necessary measures to minimize any risk associated with a boxed warning in the product information label;
9. Dosing regimen and duration are 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, b, or c):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions;
   b. Member has previously met initial approval criteria;
   c. State or health plan continuity of care programs apply to the requested drug and indication (e.g., seizures, heart failure, human immunodeficiency virus infection, and psychotic disorders [e.g., schizophrenia, bipolar disorder], oncology) with documentation that supports that member has received this medication for at least 30 days AND, if off-label, use is supported by one of the following (i, ii, or iii):
      i. The NCCN Drug Information and Biologics Compendium level of evidence 1, 2A, or 2B (*see Appendix D);*
      ii. 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 (1-4):
         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 E for additional information*);
      iii. Micromedex DrugDex® with strength of recommendation Class I or IIa (*see Appendix D*);

2. Member is responding positively to therapy;
3. 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 F*);
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 the prescribing information 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
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

Table 1. Strength of Recommendation		
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 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.

Appendix F: 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.

State	Step Therapy Prohibited?	Notes
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.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial requests only** 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. 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 22, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 22, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: added criteria for combinations products and alternative dosage forms or strengths of existing drugs; removed criteria requirements for non-formulary drugs as ERX.PA.03 would apply; references reviewed and updated.	08.14.18	11.18
4Q 2019 annual review: labeled use without coverage criteria – generalized criterion 1 to all requests for labeled use without coverage criteria, added requirement for trial of 2 agents; off-label use: removed DrugDex IIb support; references reviewed and updated.	08.12.19	11.19
4Q 2020 annual review: off-label use – added NCCN 2B as an acceptable level of evidence for off-label use per Compliance, added redirection to generics/biosimilars; references reviewed and updated.	07.13.20	11.20
Added bypass to biosimilar redirection for states with regulations against redirections in stage IV or metastatic cancer; added redirection to preferred biosimilar products for continued therapy.	03.15.21	
4Q 2021 annual review: Section IA added diagnosis requirement; added Nevada to Appendix F; references reviewed and updated.	07.22.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.