Off-Label Use of Drugs and Biologic Agents

PRODUCTS AFFECTED

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
N/A

LIMITATIONS OF COVERAGE

1. If the requested off-labeled use does not meet ANY of the criteria in the below ‘Required Medical Information’ section, such as (including but not limited to the following):
   a. Determined to be not indicated by the Centers for Medicare and Medicaid Services (CMS),
   b. Contraindicated or unsupported by the Food and Drug Administration (FDA),
   c. If the use is identified as not indicated by one of the above listed compendiums, or
   d. If the use is determined not safe and effective based on peer-reviewed medical literature,
      Then the off-labeled use will be considered by Molina Healthcare as not meeting the reasonable and necessary threshold, and therefore will not be authorized for coverage.

2. Regardless of the supporting evidence for coverage for an off-labeled use of a drug, authorization for coverage is only authorized based upon the criteria stated in this policy by Molina Healthcare.

3. If member meets ALL of the criteria below for the requested off-label use, the following may be applicable with the authorization for coverage, as deemed appropriate by Medical Reviewer: [ANY]
Drug and Biologic Coverage Criteria

a. Recommendation of formulary alternative(s), unless contraindicated, which is: [ANY]
   i. FDA-approved for the requested use/indication,
   or
   ii. Recommended or accepted by treatment guidelines listed in any compendia, or
       considered standard of care, as a treatment option of equal or greater efficacy
       compared to the requested drug/regimen,
   or
   iii. Use of accepted non-pharmacologic interventions of equal or greater efficacy

b. Quantity limits: In accordance to member's plan benefits

POSITION STATEMENT

- Molina Clinical Policy (MCP) criteria or drug-specific approved policies take precedence over the
  criteria in this policy; hence these drug-specific policies must be reviewed prior to applying the
  criteria in this policy.
- This policy should only be applied when there is no MCP (or drug-specific policy) addressing the
  requested off-label use of an FDA-approved drug.
- This policy shall not be interpreted to require coverage for any drug or biological agent when the
  FDA has determined its use to be contraindicated. Molina Healthcare will evaluate each request for
  an unlabeled use of any drug on a case-by-case basis.
- The FDA approves drugs for specific indications that are included in the drug's labeling. When a
  drug is used for an indication, dose, age and/or duration other than those specifically included in the
  labeling, it is referred to as an off-label use.
- FDA indication alone does not establish the medical necessity of a particular drug for a particular
  patient. Molina Healthcare reserves the right to review all treatments for their clinical
  appropriateness.
- If there is a discrepancy between this policy and the plan of benefits, the provisions of the member’s
  benefits plan will govern.
- Accepted Standard of Medical Practice: Acceptance by individual health care practitioners, or even
  a limited group of health care practitioners, does not translate to general acceptance by the medical
  community. Testimonials, recommendations, and declarations indicating such limited acceptance
  and limited case studies are not sufficient evidence of general acceptance by the medical community
- Molina Healthcare reserves the right to update the content or any portion of this policy, as well as
  any Molina Clinical Policy (MCP) and coverage criteria, to include or omit any off-label condition(s)
  as necessary based on medical literature and clinical studies that may become available. Molina
  Healthcare will continue to review clinical evidence related to this policy and may revise this policy
  based upon the development of the published clinical evidence.

REQUIRED MEDICAL INFORMATION:

A. ALL INDICATIONS

In the absence of a Molina Clinical Policy or prior authorization criteria addressing the requested off-label
use of the drug or biologic, requests will be reviewed on a case-by-case basis. Molina Healthcare may
authorize coverage of the requested off-label use drug or biologic if ALL of the following criteria are met:
[ALL]

1. Requested drug has been approved by the U.S. Food and Drug Administration (FDA) for at least
   ONE indication

NOTE: Medications and vaccines that have not received final FDA marketing approval for any indication
are considered investigational. Orphan designation is not synonymous to FDA-approval and orphan drug
status has no significance in the evaluation of off-label treatments. An orphan drug is one that is used
for the treatment of a rare disease or condition that either occurs in fewer than 200,000 individuals in
the US or is more prevalent but for which there is no reasonable expectation that the cost of developing
and marketing the drug in the US for such disease or condition would be recovered from US sales. The
orphan drug designation is independent from marketing approval status and may apply to medications
that are approved or unapproved for marketing. For the purposes of this policy, orphan drug
Drug and Biologic Coverage Criteria

status has no significance in the evaluation of off-label treatments.

2. Prescribed for the treatment of a life-threatening, chronic, and seriously debilitating conditions as defined by ONE of the following: [ONE: 2a or 2b]
   a) Life-threatening is defined as either or both of the following: [AT LEAST ONE]
      i. Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted
      ii. Diseases or conditions with potentially fatal outcomes, where the end point of clinical intervention is survival
   OR
   b) Chronic and seriously debilitating is defined as diseases or conditions that require ongoing treatment to maintain remission or prevent deterioration and cause serious long-term morbidity

AND

3. Documentation of ONE (1) of the following: [ONE: 3a or 3b]
   a) No other treatment options are available for member’s condition/illness. Submission of clinical rationale demonstrating there are no established treatments or recommended alternatives [Documentation required]
   OR
   b) Member has contraindications or has failure to all established therapies and alternative treatments that are FDA-approved requested indication [Documentation required]

AND

4. Requested drug is not contraindicated by the FDA for the off-label use prescribed

AND

5. Requested drug meets ONE of the following: [ONE: 5a or 5b]
   a) Documented as appropriate for the stated usage by ONE of the following CMS-approved drug compendia: [ONE]
      i. FDA Orphan Drug Approval Website
         http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm
         Medications and vaccines that have not received final FDA market approval for any indication are considered investigational. Orphan designation is not synonymous to FDA-approval and orphan drug status has no significance in the evaluation of off-label treatments. An orphan drug is one that is used for the treatment of a rare disease or condition that either occurs in fewer than 200,000 individuals in the US or is more prevalent but for which there is no reasonable expectation that the cost of developing and marketing the drug in the US for such disease or condition would be recovered from US sales. The orphan drug designation is independent from marketing approval status and may apply to medications that are either approved or unapproved for marketing. For the purposes of this policy, orphan drug status has no significance in the evaluation of off-label treatments.
         OR
      ii. Elsevier Gold Standard’s Clinical Pharmacology. Molina page access URL: https://www.clinicalkey.com/pharmacology/. The narrative text is supportive of the requested off-label use and noted as a ‘Strong Recommendation.’ Recommendations noted as ‘Equivocal/Weak’ are not considered supportive of an off-label indication.
         OR
      iii. American Hospital Formulary Service-Drug Information (AHFS-DI): The narrative text in AHFS-DI is supportive of the requested off-label use. NOTE: The "dagger" symbol is used to indicate off-label drug use by the American Hospital Formulary Service Drug Information® (AHFS®, Bethesda, MD). If AHFS indicates an off-label use, but qualifies that statement with "but additional study is needed" or "further study is needed to evaluate safety and efficacy", the qualifying language does not support an off-label indication as medically necessary. -Refer to Appendix 3 for AHFS Levels of Evidence Rating System
         Molina page access URL: https://online.statref.com/Default.aspx?grpalias=MH3AHFS Drug Information:
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b) Prescriber submitted copies of relevant full-text articles from at least two (2) major peer-reviewed journals* providing evidence of both safety and efficacy for the off-label requested use and meets ALL of the following: [ALL]

i. Phase III randomized-placebo controlled studies with subject size sufficient to determine statistical validity [Published studies required] or An adequate number of well-designed studies with sufficient numbers of subjects in relation to the incidence or prevalence of the disease [MCP-000]

NOTE: *Peer-Review Medical Literature: Off-label uses that are supported by clinical research peer-reviewed medical literature that may appear in scientific, medical, and pharmaceutical publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication. Molina Healthcare considers any drug being studied in a phase I or phase II clinical trial or use that is based solely on evidence from a phase I or phase II clinical trial, investigational. All submitted studies must be published Phase III randomized-placebo controlled studies with subject size sufficient to determine statistical validity. Refer to Appendix 2: ‘Clinical Trial Phases for Investigational New Drugs’

AND

ii. Published in the regular editions of the journals that publish original manuscripts only after the manuscripts have been critically reviewed by unbiased independent experts for scientific accuracy, validity, and reliability. NOTE: If ANY of the below are met, evidence is considered insufficient. Articles submitted must not be in the form of: [EXCLUSION CRITERIA if ANY are met]

• A special supplement or publication and not to include publications privately funded by parties (i.e. manufacturers of the product) with a vested interest in the recommendations and provides full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization

• In-house publications by pharmaceutical manufacturing companies or abstracts (including meeting abstracts) are not considered peer review medical literature

• Retrospective studies, opinion statements, *case reports, letters to the editor, abstracts of a publication, reports of Phase I or Phase II trials are not sufficient. *In general, case reports are considered uncontrolled, are based on anecdotal information, and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

AND

iii. Disease improvements must be attainable in clinical practice outside of the investigational/research setting [MCP-000]

AND

iv. Drug or biologic has all of the following outcomes [MCP-000]: A substantial probability of clinical benefit; and Improve the net health outcome as much as, or more than, established alternatives (as demonstrated by reduction in mortality, morbidity, and signs and symptoms)

AND

6. Prescriber must submit member’s medical records and other relevant documentation as
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deed necessary by Molina Healthcare to determine if an off-label use is reasonable and necessary for treatment of a member's condition or disease.
NOTE: It is the responsibility of the prescribing physician to submit to Molina Healthcare documentation supporting the proposed off-label use or uses, as requested. Otherwise, the request may be denied due to inadequate or incomplete information.

Evidence-Based Review

Centers for Medicare & Medicaid Services (CMS)
The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP) document and provide the directive for all Medicare members. The directives from this MCP document may be followed if there are no available NCD or LCD documents available and outlined below.
For Molina Medicare members, refer to the Preferred Prior Authorization Criteria below and available at: http://www.cms.hhs.gov/center/coverage.asp

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.

The following are currently the authoritative compendia for CMS approved clinical decision support tools to determine medically-accepted indication of off-label use:
1. American Hospital Formulary Service-Drug Information (AHFS-DI)
2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
3. Truven Micromedex DrugDex Compendium (DrugDex) [Successor to USP-DI]
4. Elsevier Gold Standard’s Clinical Pharmacology Compendium (Clinical Pharmacology)
5. Wolters Kluwer Lexi-Drugs (Lexi-Drugs)

Standard Drug Reference Compendia

“Compendia (compendiums)” is defined by Medicare as “a comprehensive listing of FDA-approved drugs and biological or a comprehensive listing of a specific subset of drugs and biological in a specialty compendium, for example, a compendium of anti-cancer treatment.” In this revised definition, 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. Has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.

The following resources/references are considered acceptable and utilized by Molina Healthcare to determinemedical necessity criteria based on the best available clinical evidence to support safety and efficacy. The order of these resources as listed below represents the hierarchy of evidence.

A. Applicable Federal or State mandates and guidelines Medicare Hierarchy:
1. National Coverage Determinations
2. Local Coverage Determinations
   • Search for LCD developed in state where health plan is located
   • Follow hierarchy path below if state LCD is not available
   • NCD’s or LCD’s that are silent on medical necessity directives require the next level of hierarchy to obtain the medical necessity directive
B. Corporate policy documents addressing new or existing technology
C. Approved clinical decision support tools to determine medically-accepted indication of off-label use:
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1. American Hospital Formulary Service-Drug Information (AHFS-DI)
2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
3. Truven Micromedex DrugDex Compendium (DrugDex) [Successor to USP-DI]
   - Indications that DrugDex lists as “Class I, Class IIa or Class IIb” recommendations and/or efficacy will be considered medically accepted indications for the purposes of determining coverage policy.
   - Indications that DrugDex lists as “Class III” recommendations and/or efficacy will not be considered medically accepted indications for the purposes of determining coverage policy.
4. Elsevier Gold Standard's Clinical Pharmacology Compendium (Clinical Pharmacology)
5. Wolters Kluwer Lexi-Drugs (Lexi-Drugs)

Evaluation of Off-label Requests

Molina Medical Reviewers/Staff, in addition to utilizing the above references with the hierarchy of evidence listed in this ‘Evidence Based Review’ section to evaluate a request for an off-label use, also considers/weights the following factors based on the clinical literature [submitted by requesting Prescriber]:

- Submitted peer-reviewed literature* by requesting Prescriber
  *Peer-Review Medical Literature: Off-label uses that are supported by clinical research peer-reviewed medical literature that may appear in scientific, medical, and pharmaceutical publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication.
- Availability of published reports of well-designed and well-conducted investigations published in peer-review journals
- Assessment of the quality and level of evidence reflected in published reports and systematic reviews
- Opinions and evaluations by national medical associations, consensus panels, or other technology evaluation bodies are evaluated according to the scientific quality of the supporting evidence and rationale
- Absence of potential clinically important concerns about the drug/biologic such as increased toxicity with no substantial therapeutic gain
- Positive therapeutic perspective as reflected by clinical evidence, expert opinion, best practices, and/or authoritative guidelines
- Evidence of improved risk-to-benefit ratios (including compliance) relative to existing therapeutic alternatives
- The importance and severity of the disease
- Availability of alternative therapies and their relative toxicities, the number of patients affected by the disease, other patient population considerations (e.g., age, gender, pharmacogenomics), and other factors (e.g., cost and economic considerations) also are important considerations.

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:

1. For continuation of therapy of medications for off-label uses for new Molina member: initial criteria must be met
   AND
2. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
   AND
3. Documentation of no intolerable adverse effects or drug toxicity
   AND
4. Documentation of positive clinical response as demonstrated by low disease activity and/or...
DURATION OF APPROVAL:
Initial authorization: up to 6 months, Continuation of Therapy: up to 12 months; duration of therapy needs to be supported by evidence requested above

PRESCRIBER REQUIREMENTS:
N/A

AGE RESTRICTIONS:
Needs to be supported by evidence requested above

QUANTITY:
Needs to be supported by evidence requested above

Maximum Quantity Limits –
Needs to be supported by evidence requested above

PLACE OF ADMINISTRATION:
N/A

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
N/A

DRUG CLASS:
N/A

FDA-APPROVED USES:
N/A

COMPRENDIAL APPROVED OFF-LABELED USES:
N/A
APPENDIX: Hayes Technology Assessments Rating

Hayes Rating System reflects the strength of the evidence in terms of safety, efficacy, impact on health outcomes, indications for use, patient selection criteria and technology comparisons. Hayes Ratings are scaled A through D1 and D2 and are defined as follows and provides Molina staff guidance on making coverage decisions:

A: Established benefit. Published evidence shows conclusively that safety and impact on health outcomes are comparable to or better than standard treatment/testing. Long-term safety and impact on health outcomes have been established, and other important questions concerning application of the technology have been answered.
Coverage Recommendation: Approve for use under recommended guidelines unless it is a non-covered state plan benefit such as for cosmetic purposes or if an existing Molina Clinical Policy provides an alternative directive.

B: Some proven benefit. Published evidence indicates that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, there are outstanding questions regarding long-term safety and impact on health outcomes, clinical indications, contraindications, optimal treatment/testing parameters, and/or effects in different patient subpopulations.
Coverage Recommendation: Approve for use under recommended guidelines unless it is a non-covered state plan benefit such as for cosmetic purposes or if an existing Molina Clinical Policy provides an alternative directive.

C - Potential but unproven benefit. Some published evidence suggests that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, substantial uncertainty remains about safety and/or impact on health outcomes because of poor-quality studies, sparse data, conflicting study results, and/or other concerns.
Coverage Recommendation: Medical Director review is required with a peer to peer discussion between the Plan Medical Director and the requesting physician in order for coverage to be approved. Recommend consideration of alternative treatments. Coverage considerations for approving in this category are based upon available Policy documents approved by the Molina Clinical Policy Committee following a review of evidence from other sources in addition to Hayes. Coverage may also be provided when all other conventional treatment options have been exhausted and there is reasonable evidence to support the technology could prolong the life of the member, restore physical and/or social functioning or benefit the member significantly enough that the benefits outweigh any risks to the member. Unique circumstances approved by a plan should be accompanied by well controlled or prospective cohort/comparison studies published and referenced in medical or scientific literature with relevant clinical evidence supporting the assertion that the requested modality would provide benefit to the member and a clinical advantage over its competitors, two independent studies are preferred.

D1: No proven benefit and/or not safe. Published evidence shows that the technology does not improve health outcomes or patient management for the reviewed application(s) or is unsafe.

D2: Insufficient evidence. There is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management.
Coverage Recommendation: Consider and treat as an experimental and investigational procedure. Coverage may be provided in this category if the Molina Clinical Policy Committee has obtained and reviewed information from other sources and has approved for coverage. New studies provided should be reviewed in accordance with ‘MCP-000 Evaluation of New and Existing Technologies Including Experimental and Investigational Designations’ Experimental/Investigational guidelines.
APPENDIX 2: Clinical Trial Phases for Investigational New Drugs

Clinical trial phases for Investigational New Drugs are defined by the FDA as follows:

- **Phase 1** trials are concerned primarily with determining dosing, documenting how a drug is metabolized and excreted and identifying acute side effects. A small number of healthy volunteers (between 20 and 80) are evaluated in Phase 1 trials.

- **Phase 2** trials involve approximately 100 to 300 participants who have the disease or condition that the product could treat. Researchers seek to gather further safety data and preliminary evidence of the drug's efficacy, and they develop and refine research methods for future trials. Drugs showing effectiveness with little risks identified will move to Phase 3.

- **Phase 3** trials include a population of patients between 1,000 to 3,000 with a disease. This phase further tests the product's effectiveness, monitors side effects, and compares the product's effects to a standard treatment, when available.

- **Phase IV** trials are conducted after a product is already approved and on the market to identify potential long-term risks, benefits, and optimal use, or to test the product in different populations of people, such as children.

APPENDIX 3: AHFS Levels of Evidence Rating System

**Level 1: High strength/Quality**
- Evidence consists of at least one randomized, double-blind trial without important limitations (i.e., large treatment effect); intent-to-treat analysis used, confidence intervals reported. If one more than one trial is available, these trials have consistent results; or
  - A meta-analysis of such trials with consistent results (i.e., low heterogeneity); or
  - Evidence consisting of a non-blinded or single-blinded trial that meets study objective endpoints may be considered as Level 1 evidence in some cancer-related cases (i.e. NCI-sponsored cooperative group study or a multi-center trial)

**Level 2: Moderate Strength/Quality**
- Evidence consists of at least one non-blinded or single-blinded, randomized clinical trial; or
- Evidence consists of at least one non-blinded or single-blinded, non-randomized clinical trial; or
- A meta-analysis of randomized, controlled clinical trials with heterogeneous results if reasons for heterogeneity in individual trials are adequately discussed; or
- Evidence consists of at least one randomized, controlled clinical trial, but with methodological limitations (e.g. large number of patients lost to follow-up and no intent-to-treat analysis and/or important data not recorded); or
- Evidence is inconsistent (i.e., two or more randomized controlled trials with unexplained, widely varying estimates of treatment effects, even if results of individual trials would constitute a strong Level 1 evidence when considered alone); or
- Evidence consisting of a non-blinded, non-randomized trial (e.g., a phase II study) may be considered as Level 2 in some cancer-related cases (e.g., rare cancers or cancers with limited available treatment options)

**Level 3: Low Strength/Quality**
- Evidence consists of observational studies, case reports or case series; may also include randomized-clinical trials with multiple serious deficiencies or study limitations.

**Level 4: Opinion/Experience**
- Expert consensus panel reports or expert reviewer’s comments

AHFS Grades of Recommendation

**A: Recommended; Accepted**
The drug or biologic should be used, is recommended, is useful/effective/beneficial in most cases

**B: Reasonable Choice (Accepted, with Possible Conditions) (e.g., option)**
The drug or biologic is reasonable to use under certain conditions (e.g., in certain patient groups), can be
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useful/effective/beneficial or is probably recommended or indicated.
C: Not Fully Established (Unclear risk/benefit, equivocal evidence, inadequate data and/or experience)
Usefulness and/or effectiveness is unknown, unclear, or uncertain or is not well established relative to the standard of care.
D: Not Recommended (Unaccepted)
The drug or biologic is considered inappropriate, obsolete, or unproven; is not recommended, is not indicated, or is not useful/effective/beneficial; or may be harmful.

Available at: https://www.ahfsdruginformation.com/levels-of-evidence-rating-system/

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Off-Label (also referred to as unlabeled or non-FDA-approved) drug use refers to the prescription of licensed drugs for clinical indications or in a manner different from that approved by the FDA and thus not included in the official FDA-approved labeling for the agents. Off-label drug use takes many forms, and versions of it occur in countries outside of the United States as well. Use of drugs for a clinical indication, in a patient population, through a route of administration, or with a dose not specified in the FDA-approved labeling can all be considered off-label.

A. Requests for coverage of medications or devices that are non-FDA approved or “off-label” will be considered on a case-by-case basis.
B. Determinations of coverage for an off-label use of a drug may be considered under ANY of the following circumstances:
   • A single case exception to current coverage policies, due to unique circumstances
   • Until relevant coverage policies undergo full review, revision and approval by the Molina Clinical Policy Committee (MCPC) or Molina Healthcare National P&T Committee
   • In the absence of a coverage policy currently addressing the drug or the requested use of the drug

C. The Emergency Use Authorization (EUA) is a statutory authority which allows the FDA to help strengthen the public health protections against chemical, biologic, radiological, or nuclear (CBRN) threats by facilitating the availability and use of medical countermeasures (MCMs – i.e., drugs, biologics, vaccines, diagnostic tests, etc.) during public health emergencies. The EUA allows for the unapproved use (i.e., off label use) of an approved medical product (drug, biologic, vaccine, or device) or the use of an investigational/unapproved product in order to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when there are no adequate, approved, and available alternatives. Refer to the FDA’s website for the current list of products that the FDA has authorized for emergency use in response to the COVID-19 public health emergency, including: FDA_EUA
   • In Vitro Diagnostic Products
   • High Complexity Molecular-Based Laboratory Developed Tests
   • SARS-CoV-2 Antibody Tests
   • Personal Protective Equipment and Related Medical Devices
   • Ventilators and Other Medical Devices
   • Drug Products

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Coverage will not be authorized for Off-Label usage unless prior authorization request meets ALL criteria defined in the above section. Off-label drugs are not covered when the following circumstances are applicable:
1. This policy shall not be construed to require coverage for any drug when ANY of the following applies:
   - The FDA has determined its use to be contraindicated; or
   - The benefit plan excludes drug coverage; or
   - The benefit plan includes drug benefit limitations based on a formulary and the off-label drug is not part of the formulary

Molina Staff Verify:
   - Benefits and benefit exclusions. Excluded products or treatments are not covered under this document (e.g., agents for impotency or weight loss)
   - Appropriate state mandates for laws that will supersede this document when applicable, such as those governing off-label use of prescription drugs

2. Requested use, regardless of medical necessity, is specifically excluded from coverage in a member’s plan benefit. Molina Reviewer to verify:
   - Member’s benefits and benefit exclusions (excluded products or treatments are not covered under this policy, e.g., agents for impotency or weight loss); AND
   - State mandates and regulations that will supersede this policy when applicable, such as those governing off-label use of prescription drugs

3. Pharmaceutical agents (and vaccines) that have not received final FDA marketing approval for any indication or has not been fully licensed or approved by the FDA are considered investigational and coverage will not be authorized

4. Use is identified as not indicated by CMS (in the case of Medicare members) or the FDA; or
   Use is specifically identified as not indicated in at least one of the major compendia; or
   Use is determined (based on peer-reviewed literature) that the drug is not safe and effective

5. Use of a product with only an orphan drug designation and without FDA marketing approval
   NOTE: An "orphan drug" is a product that treats a rare disease (e.g., affecting fewer than 200,000 Americans). Products have FDA orphan drug approval when they meet the orphan drug designation and marketing criteria established by the FDA. Reference: U.S. Food and Drug Administration (FDA). Developing Orphan Products: FDA and Rare Disease Day. Last updated 09/26/2009. Available at: http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107293.htm.

6. Use of any drug when the FDA has determined that use to be contraindicated

7. Services related to non-covered services are not covered (e.g., administration services)

8. Pre-marketing notification (PMN) or a 510(k) application: A 510(K) is a premarket submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent, to a legally marketed device (section 513(i)(1)(A) FD&C Act) that is not subject to premarket approval.

9. Expanded Access Program (EAP) (also referred to as ‘Managed Access Program (MAP), Early Access Program, or Compassionate Use Program (CUP’): A pathway for physicians and patients with an immediately life-threatening condition or serious disease or condition to gain access to pre-approval, investigational product* outside of the clinical trial setting.
   - *Investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.
   - *Investigational drugs, biologics or medical devices have not yet been approved or cleared by FDA and FDA has not found these products to be safe and effective for their specific use.
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Furthermore, the investigational medical product may, or may not, be effective in the treatment of the condition, and use of the product may cause unexpected serious side effects.

- There must be an unmet clinical need. The provision of a investigational treatments through expanded access is granted by the drug manufacturer (sponsor); a regulatory body or third-party provider cannot facilitate access without sponsor approval. Access to investigational treatments requires the FDA's review and authorization and the active involvement of health care providers.
- Molina Healthcare may authorize coverage of FDA-approved drug products associated with a clinical trial through the Plan’s standard authorization process, as applicable (PA, quantity limits, etc.)
- The investigational drug, cost of the treatment(s) or procedure(s) the clinical trial is investigating, or procedure(s) required to collect data for the study will not be authorized.

OTHER SPECIAL CONSIDERATIONS:
Molina Healthcare clinical reviewers or staff submitting case reviews to an Independent Review Organization (IRO) [e.g., Advanced Medical Review (AMR)] shall review the reference materials provided for decision-making.

1. Independent review reference materials which do not meet the requirements shall be routed back to the independent review organization and the following should be requested: [MCP-000]
   a. An explanation of the clinical rational and relevant, current evidence used to support the decision shall be requested to be reviewed by both the independent review quality check process and the oversight physician at the organization
   b. Independent review organization to provide an assessment of the quality of evidence utilized by the Peer Reviewer to perform the review
   c. Reviews deemed of insufficient quality shall be requested to be re-reviewed at the expense of the independent review organization

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

<table>
<thead>
<tr>
<th>HCPCS CODE</th>
<th>DESCRIPTION</th>
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<tbody>
<tr>
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AVAILABLE DOSAGE FORMS:
# REFERENCES