Molina Clinical Policy
Clinical Trials and Rare Disease: Policy No. 183

Last Approval: 6/8/2022
Next Review Due By: June 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy outlines recommendations for coverage of services and/or supplies for Molina Healthcare members enrolled in clinical trials.

RELATED POLICIES

Experimental and Investigational Services: Policy No. 184
Medically Necessary Services: Policy No. 332

COVERAGE POLICY

Coverage of Clinical Trials and/or related services and supplies may be mandated by applicable legal requirements of the State, Federal government or Centers for Medicare and Medicaid Services (CMS) for Medicare and Medicaid members. Additionally, some benefit plans may exclude coverage. **Please check State Health Plan regulations for all LOBs and local compliance and/or legal team before applying this policy.**

The requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

If there are no mandates or exclusions in the benefit plan, **coverage may be considered on a case-by-case basis** when **ALL** of the following criteria and supporting documentation are met:

1. Member has a current *life-threatening, chronic or **severely debilitating diagnosis (e.g., cancer, kidney failure, AIDS, and serious rare diseases with an incidence of less than 1:200,000).
   ** A life-threatening condition means any disease or condition from which the likelihood of death is probable unless the course of the disease or condition is interrupted.*
   *** A debilitating condition is defined as the member being unable to engage in substantial gainful activities due to the medically determinable mental or physical condition; the impairment is expected to result in death and has remained or expected to remain continuously for at least a twelve-month period*

AND

2. Other treatment options are not available or have been exhausted: Standard therapies have either not been effective in significantly improving the member's condition or are not medically appropriate; **AND**

3. The trial must have therapeutic intent and not solely designed to test toxicity or disease pathophysiology; **AND**

4. The clinical trial is approved by all relevant institutional review boards and defined as an ***approved clinical trial** under the under Section 10103(c) of Patient Protection and Affordable Care Act of 2010 as a Phase I, Phase II, Phase III, or Phase IV clinical trial that is conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening disease or condition and is **ONE** of the following:

    a. A federally funded or approved trial by **ONE** of the following agencies: National Institutes of Health; National Cancer Institute, Centers for Disease Control and Prevention, Agency for Healthcare Research and Quality, CMS; **OR**
    b. A cooperative group or center of any of the above listed entities or the Department of Defense (DoD) or Department of Veterans Affairs (VA); or
    c. A qualified nongovernmental research entity identified in the guidelines issued by the NIH for center support grants; or
    d. The Departments of VA, DoD, or Energy if the trial has been reviewed and approved through a system of peer review comparable to the system used by the NIH and that ensures unbiased review of the highest scientific standards by qualified individuals who have no interest in the outcome of the review; **OR**
    e. The study or investigation is conducted under an investigational new drug application reviewed by the Food and Drug Administration (FDA); **OR**
    f. The study or investigation is a drug trial that is exempt from having such an investigational new drug application.

AND

5. **ALL** of the following are met by Member with documentation:
    a. All clinical trial protocol requirements are met for enrollment as a participant in the clinical trial; and
    b. Provide informed consent; and
    c. Member must be treated according to clinical trial protocol.

AND

6. Requested treatment must demonstrate a likely clinical benefit over current existing treatment options; **AND**

7. There is a reasonable expectation that the treatment will extend the member's life or considerably improve the member's physical and/or social functioning, thereby improving the member's capacity to perform relevant daily activities.

Routine Costs during Clinical Trials

Covered routine patient care costs for an enrolled member in an approved clinical trial requested include:

1. Items or services that are typically provided absent a clinical trial (e.g., conventional care, laboratory services, radiologic services, office visits, hospital services, etc.);
2. Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
3. Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for the diagnosis or treatment of complications.

Reference: CMS NCD Routine Costs in Clinical Trials (310.1)

Limitations and Exclusions

The following limitations/exclusions apply to routine costs and services from participation in a qualifying clinical trial for Molina members that meet the clinical coverage criteria (as outlined above). Routine patient costs NOT eligible for coverage include:

1. Clinical trials that do not meet the criteria in the 'Coverage Policy' section above (e.g., Phase 0 drug Clinical Trials; a patient registry);
2. The experimental intervention itself (except medically necessary Category B investigational devices)
3. Items and services customarily provided by the research sponsors free-of-charge for any enrollee in the trial;

4. Items and services necessary solely to satisfy data collection needs of the clinical trial (e.g., "protocol-induced costs");
5. Routine patient costs obtained out-of-network where non-network benefits do not exist under the plan (NOTE: All applicable plan limitations for coverage of out-of-network care will apply to routine patient care costs in clinical trials);
6. Travel and transportation expenses, including but are not limited to:
   - Any transportation costs to and from trial location (e.g., personal vehicle mileage reimbursement, taxi, medical van, ambulance, commercial airline, train, rental car expenses)
   - Lodging and meals
7. Non-FDA authorized interventions or medications delivered or made available to a member during a covered clinical trial will not be covered after the trial is completed.

Medicare Members

- Coverage for items and services that may be covered or the regulations on Category B exemptions for investigational devices are found in 42 CFR 405.201-405.215, 411.15, and 411.406.
- The Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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.

SUMMARY OF MEDICAL EVIDENCE

There are no published guidelines or recommendations by national/professional societies and organizations.

SUPPLEMENTAL INFORMATION

Definitions

Category B (Non-experimental/investigational) device refers to a device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA premarket approval or clearance for that device type.

Clinical Trial/Studies involving **Investigational New Drugs** (FDA; Clinical Research)

- **Phase I** 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 I trials.
- **Phase II** 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 III.
- **Phase III** 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 pediatric populations.

Clinical trial phases for **cancer** are defined by the National Cancer Institute are as follows:

- **Phase I** studies are the initial clinical tests for new treatments to define a safe dose and schedule of agent or combination of agents or to evaluate the feasibility of combining treatment modalities in typically less than 100 patients. This phase develops as a result of promising pre-clinical data, such as in vitro cytotoxicity in tumor cell lines and safe administration with reproducible antitumor effect in animals if a stable and safe formulation of the agent is available.
- **Phase II** studies assess the antitumor efficacy of a new cancer agent, a new combination of agents, a new modality of therapy and further determination of toxicity. The new treatment is given to groups of patients with one type of cancer or related cancers using the dosage and scheduling found safe from Phase I trials. Unusual or chronic toxicities may appear during Phase II testing; this is considered when deciding whether the agent should be further evaluated in Phase III studies.
- **Phase III** studies are designed to compare one or more treatments. A new drug or drug combination may be tested against one of proven efficacy. Phase III studies often have multiple endpoints. Overall and disease-free survival is nearly always endpoints; differences in response rates, toxicity, patterns of recurrence, and quality of life might also be endpoints. The new drug or drug combination will be found to be inferior, equivalent, or superior to the standard treatment in respect to the major endpoints. The degree of difference will be known, and statistical significance will be estimated.
- **Phase IV** trials are conducted to further evaluate the long-term safety and effectiveness of a treatment. They usually take place after the treatment has been approved for standard use. Several hundred to several thousand people may take part in a phase IV study.

Rare Disease. A condition will be considered a rare disease when a review of the current published peer reviewed medical literature, the National Cancer Institute Physician Data Query (PDQ), the NCCN Clinical Practice Guidelines, and other appropriate sources indicates that there is no standard treatment available for the condition. See the list on the NIH Office of Rare Diseases Research website (http://rarediseases.info.nih.gov/).

CODING & BILLING INFORMATION

Modifier	Description
Coding Clarification: These modifiers are not required for Clinical Trial claims; nonetheless, if one of these modifiers is present, the claim is deemed a Clinical Trials claim.	
Modifier Q0	Investigational clinical service provided in a clinical research study that is in an approved clinical research study
Modifier Q1	Routine clinical service provided in a clinical research study that is in an approved clinical research study

HCPCS	Description
S9988	Services provided as part of a Phase I clinical trial
S9990	Services provided as part of a Phase II clinical trial
S9991	Services provided as part of a Phase III clinical trial

HCPCS codes not covered for indications listed (not all inclusive):	
S9992	Transportation costs to and from trial location and local transportation costs (e.g., fares for taxicab or bus) for clinical trial participant and one caregiver/companion
S9994	Lodging costs (e.g., hotel charges) for clinical trial participant and one caregiver/companion
S9996	Meals for clinical trial participant and one caregiver/companion

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/8/2022 Policy revised. Added 'Related Polices' section. Rewrote 'Coverage Policy' section. Notable revisions include:
- Clarified 'a life-threatening condition' in criterion #1.
- Removal criteria requiring two (2) independent scientific or medical documents.
- Removal of the procedure section for internal process (at the end of the coverage criteria section previously).
- Added criterion "The trial must have therapeutic intent and not solely designed to test toxicity or disease pathophysiology".
- Added a criterion defining a qualifying clinical trial.
- Added the 'Routine Cost during Clinical Trials' section and a 'Limitations/Exclusions' section.
- Added notation for Medicare members (at the end of the coverage criteria section).
- Added definition for Category B devices in supplemental information section.
- Updated coding section.

6/17/2020, 6/9/2021 Policy reviewed, no changes.
6/19/2019 Policy reviewed, changed the word technology to treatment for clarification on page 2, policy statement.
12/16/2015, 6/15/2016, 6/22/2017, 7/10/2018 Policy reviewed, no changes.
6/25/2014 New policy.

REFERENCES

1. Centers for Medicare and Medicaid (CMS). NCD for routine costs in clinical trials (section 310.1), publication 100-3. Available from CMS. Accessed June 2022.
2. United States Department of Health and Human Services (HHS). Medicare benefit policy manual – chapter 14, section 20. Guidance for Food and Drug Administration (FDA)-approved Investigational Device Exemption (IDE) studies. Available from HHS. Published January 1, 2020. Accessed June 2022.
3. United States Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act and Health-Related Portions of the Health Care and Education Reconciliation Act Of 2010. 42 U.S.C. § 18001 et seq. (2010). Available from HHS. Accessed June 2022.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*