

Subject: Clinical Trials and Rare Disease Policy		Original Effective Date: 6/25/2014
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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. 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 (i.e., 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 Molina Clinical Policy (MCP) document and provide the directive for all Medicare members.

PURPOSE:

To define the process by which Molina Health Care will review requests for a transplant, medical and behavioral healthcare procedures, pharmaceuticals and devices in the management of a rare disease.

POLICY STATEMENT:

Coverage of Phase III or IV Clinical Trials or Rare Disease treatment may be mandated by applicable legal requirements of the State, Federal government or CMS for Medicare and Medicaid members. Additionally, some benefit plans may exclude coverage. 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 are met:

- The member has a life-threatening, chronic or severely debilitating condition, medical disease or illness (e.g., cancer, kidney failure, AIDS, and serious rare diseases with an incidence of less than 1:200,000). 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**
- No other treatment options are available; other available conventional treatment options have been exhausted without benefit; **and**

- ❑ A new treatment option will be considered if two (2) independent scientific or medical documents with relevant clinical evidence support the assertion that the requested treatment would likely provide a clinical advantage over its competitors. Reliable evidence may be obtained from good quality randomized-control trials or minimally biased cohort/comparison studies. Case reports, retrospective studies, opinion statements and abstracts are not sufficient. A treatment that is considered an established standard of medical practice with published data may be considered. (e.g., transplantation registry data supporting increased patient survival rates); **and**
- ❑ The new treatment option must also demonstrate a clinical advantage over current existing treatment options; **and**
- ❑ There is a reasonable expectation that the treatment could prolong the life of the member or restore physical and/or social functioning significantly enough to improve the member's ability to perform relevant daily activities.

DEFINITIONS:

1. 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.

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

- ❑ 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.

3. **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. Additionally, the disease is listed on the office of Rare Diseases Research of the NIH. Available at: <http://rarediseases.info.nih.gov/>

PROCEDURE:

- ❑ The requesting physician must be a board-certified or board-eligible qualified physician in the area of practice that is associated with the requested technology. The requesting physician must submit the following:
 - 1) A statement from the member's physician certifying that the Member has a life-threatening or debilitating condition as defined above and that standard treatment options are not available or have been ineffective; a description of the treatment options given with outcome(s), and the risks and benefits of the proposed treatment the benefits outweigh the potential harmful effects of the treatment.
 - 2) Copies of two (2) documents from the available scientific or medical literature as supporting evidence that the requested treatment or procedure would provide benefit to

- the Member; the physician's written statement/summary of how the technology will be utilized or will provide a positive effect on the member's condition or illness.
- 3) A written description of the proposed treatment plan or Clinical Protocol that is being followed, if applicable.

- The Molina Health Plan may notify/request that the Medical Policy Department assist with locating literature related to the requested Clinical Trial or Treatment for Rare Disease and assist with the determination if the proposed Clinical Trial is an open trial, or if the member's diagnosis is considered a Rare Disease.
- Sr. Medical Director of Medical Policy will notify Health Plan Medical Director if an external review is required for the request.
- After all pertinent required information has been received, the Plan's Medical Director, Plan's CMO, Senior Medical Director of Medical Policy, and if required, the V. P. of Clinical Programs and Molina CMO will discuss the case to determine if the criteria have been met.
- After a determination has been rendered by the above individuals, the Plan's Medical Director will document the decision in QNXT.

Review/Revision History:

6/25/14: Policy created

12/16/15, 6/15/16, 6/22/17, 7/10/18,

6/19/19: Policy reviewed, changed the word technology to treatment for clarification on page 2, policy statement.