



Medicare Part C Medical Coverage Policy

Clinical Trial Services

Origination: June 28, 1999
Review Date: September 21, 2023
Next Review: September 2024

******This policy applies to all Blue Medicare HMO, Blue Medicare PPO, Blue Medicare Rx members, and members of any third-party Medicare plans supported by Blue Cross NC through administrative or operational services. ******

DESCRIPTION OF PROCEDURE

Clinical trials (or clinical research studies) are scientific investigations of treatment alternatives designed to help compare the safety and efficacy of new, untested, or non-standard treatments to standard currently accepted treatments. Clinical trials are intended to improve the clinicians' knowledge about a treatment and clinical outcomes for future members. Improvement of health outcomes for members enrolled in clinical trials is a desirable but secondary consideration.

Clinical trials generally proceed through four (4) phases:

Phase I clinical trials - the study of a drug or treatment that is given to a small group of people for the first time to evaluate its safety, determine a safe dosage range and to identify side effects;

Phase II clinical trials - the study of a drug or treatment that is given to a large group of people that have certain diseases or conditions to see if it is effective and to further evaluate its safety;

Phase III clinical trials - the study of a drug or treatment that is given usually to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments and collect information that will allow the drug or treatment to be used safely;

Phase IV clinical trials - studies performed after the marketing of the drug or treatment to collect information about its effects in various populations and any side effects associated with long-term use.

Members enrolled in clinical trials must be informed (if applicable) that they may be receiving standard treatment, investigational treatment, placebo treatment, or no treatment.

Covered clinical trial services are exempt from the medical policy criteria outlined under the Plan Coverage of Experimental and/or Investigational Treatments, Devices, Drug or Procedures. (See Medicare C Medical Coverage Policy: “Investigational (Experimental) Services.”)

POLICY

There are certain requirements for Plan coverage of clinical trials. If the member participates in a qualified Medicare clinical trial that is listed at <http://www.clinicaltrials.gov/>, then Original Medicare covers the clinical trial doctors, other providers and “routine cost” for the covered services the member receives that related to the clinical trial. Original Medicare also covers reasonable and necessary services related to any complications that are a direct result of the clinical trial. The Plan cannot choose the clinical trial or clinical trial items and services. When a member is in a clinical trial, he/she may stay enrolled in Blue Medicare HMO/ Blue Medicare PPO and continue to get the rest of their healthcare services that is unrelated to the clinical trial through the Plan.

Refer to the Blue Medicare HMO/Blue Medicare PPO Evidence of Coverage (EOC) for specific language regarding clinical trials or research studies.

Services related to clinical trials do not require a referral or provided by a contracting provider. However, members are asked to have their physicians notify the Plan before enrolling the member in a clinical trial in order for the Care Management staff to assist the provider (if appropriate) with covered services unrelated to the clinical trial.

Medicare has a free booklet “Medicare and Clinical Trials” that may be obtained by calling 1-800-MEDICARE (1-800-633-4227) or visit <http://www.medicare.gov/> on the web.

DEFINITIONS:

A. Informed Consent:

Informed consent is the process of learning the key facts about a clinical trial before deciding whether to participate or not. Informed consent must be documented in written form, in the language of the enrollee's choice.

The following facts must be included:

1. Why the research is being done;
2. What the researchers want to accomplish;
3. What will be done during the trial and for how long;
4. What risks are involved in the trial;
5. What benefits can be expected from the trial;
6. What other treatments are available; and
7. The right of the member to ask questions or to leave the trial at any time.

B. Food and Drug Administration Definitions for types of device approval:

1. FDA 510(k) Device Clearance; Device manufactures notify the FDA within ninety (90) days of intent to market a device, allowing the FDA time to research the device and categorize it. This type of premarket submission demonstrates that a device is at least as safe and effective to another legally marketed device.
2. Premarket approval (PMA): involves a more stringent review of whether the device and the research contain sufficient scientific evidence that provides reasonable assurance that the device is safe and effective for the intended uses.
3. Humanitarian device exemptions: is a device intended to benefit members by treating or diagnosing a disease or condition that affects fewer than 8,000 individuals in the U.S. per year.

C. Investigational Device Exemptions (IDE): Medicare coverage was expanded to allow coverage for certain medical devices being studied as part of the FDA approved clinical trials. The FDA determines if a device is a Category A or B device.

1. Category A (Experimental) device: These devices are considered experimental and not covered. They are Class III devices and their safety and effectiveness has not yet been determined. Original Medicare may cover the routine cost of the clinical trial when involving these devices. See Benefit Application.
2. Category B (Non-experimental/investigational) device: These are newer generations and proven devices, covered in accordance with FDA-approved protocols governing clinical trials. The manufactures of these devices have obtained FDA approval with a 510k or PMA clearance to be used in a qualified clinical trial.

D. Placebo:

1. Is an inactive medication or treatment that has no intended therapeutic value.
2. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment.

E. Original Medicare: This is referring to Medicare which is a fee for service health plan that has two parts: Part A and Part B. It is not the Blue HMO/PPO Plan.

BENEFIT APPLICATION

This medical coverage policy is applicable to all members.

- A. Original Medicare covers the routine costs of qualifying clinical trials (such costs are defined below), as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. Claims

for all services related to the clinical trial should be submitted to Original Medicare by the provider.

1. Routine costs in clinical trials include:
 - a. Items or services that are typically provided absent a clinical trial, (e.g., conventional care);
 - b. Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
 - c. Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for diagnosis or treatment of complications.
2. Medicare Advantage Plans cover the difference between Original Medicare Cost-sharing incurred for qualified clinical trial items and services and what the Plan would cover in network for like items or services.- (See the Explanation of Benefits; EOC, Chapter 3, Section 5.)
3. CMS determines the device coverage based on which category the FDA assigns the device as:
 - a. Category A IDE (Experimental or Investigational Device Exemption) are non-covered by Original Medicare because they do not satisfy the statutory requirement that Medicare pay for devices that are reasonable and necessary.
 - b. Category B IDE (Non-experimental/investigational Device Exemption) studies may be covered by the Plan. The manufacturers of these devices must obtain a number for this device from the FDA.
 - c. If Category B IDE is determined to be Medically necessary by Medical Director, then authorization entry will be required: (Please see authorization entry guidelines for Category B IDE devices)
4. The Plan only covers the treatment of complications arising from the items or services that are unrelated to the clinical trial and are reasonable and necessary. However, if the item or service is not covered by virtue of a national non-coverage policy in the CMS Coverage Issues Manual and is the focus of a qualifying clinical trial, the routine cost of the clinical trial (as defined above) will be covered by Original Medicare but the non-covered item or service itself will not be covered.

Benefit payments are subject to contractual obligations of the Plan. If there is a conflict between the general policy guidelines contained in the Medical Coverage Policy Manual and the terms of the member's particular Evidence of Coverage (EOC), the EOC always governs the determination of benefits.

INDICATIONS FOR COVERAGE:

A. Qualified clinical trials meet the following guidelines:

1. In general, the following criteria are necessary for Original Medicare coverage of routine costs associated with a clinical trial; however, these services do not have to be prior approved by the Plan. Routine Cost in a qualified clinical trial are Original Medicare's accountability.
 - a. Trials of therapeutic interventions must enroll members with diagnosed disease rather than healthy volunteers. Trials of diagnostic interventions may enroll healthy members in order to have a proper control group; **and**
 - b. The purpose or subject of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physician's service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids); **and**
 - c. The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.
2. The requirements above are insufficient by themselves to qualify a clinical trial for coverage of routine costs. Clinical trials also should have the following desirable characteristics; however, some trials, as described below, are presumed to meet these characteristics and are automatically qualified to receive Medicare Coverage:
 - a. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
 - b. The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
 - c. The trial does not unjustifiably duplicate existing studies;
 - d. The trial design is appropriate to answer the research question being asked in the trial;
 - e. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
 - f. The trial is in compliance with federal regulations relating to the protection of human subjects; **and**
 - g. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.
3. The following clinical trials are deemed to be automatically qualified for coverage of routine costs by Original Medicare:
 - a. Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA;
 - b. Trials supported by center or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD, and VA;
 - c. Trials conducted under an investigational new drug (IND) application reviewed by the FDA; **and**

- d. Drug trials that are exempt from having an IND under 21 CFR 312.2(b) (1) will be deemed automatically qualified until the qualifying criteria are developed and the certification process is in place. At that time, the principal investigators of these trials must certify that the trials meet the qualifying criteria in order to maintain coverage of routine costs. This certification process will only affect the future status of the trial and will not be used to retroactively change the earlier deemed status.

4. The member must:

- a. Be enrolled in the trial; **and**
- b. Provide informed consent; **and**
- c. Be treated according to protocol.

B. Clinical Trials involving Category B Devices:

1. The requester must have obtained Category B status by the FDA and submit a FDA letter of approval for use of the device in a clinical trial; **and**
2. Must be in a qualified FDA Medicare approved clinical trial listed at www.clinicaltrials.gov; **and**
3. The provider must notify the Plan of inpatient status; **and**
4. The trial must meet criteria per the NCD if one is available; **and**
5. A clinical trial related to a device must be reviewed by the medical director who will note the following:
 - a. The device must be used according to the clinical trials approved patient protocols; **and**
 - b. Must meet the criteria per a national coverage determination if one exist; **or**
 - c. Must meet local jurisdiction policy if one is applicable; **or**
 - d. There must be policy or position papers or recommendations made by the pertinent national and local specialty societies; **and**
 - e. Medical necessity for the member will be considered and whether the amount, duration and frequency of use of the application of the service are medically appropriate; **and**
 - f. The trial is furnished in a setting appropriate to the member's medical needs and condition.
6. If Category B IDE is determined to be medically necessary by the Medical Director, then authorization entry will be required (Please see authorization entry guidelines for Category B IDE devices).

C. Clinical Trials with Coverage of Evidence Development (CED):

- a. The participating hospital must be in a qualified CMS registry for the collection of post service data and the registry will have an NCT number;
- b. The trial and registry should be available at the CMS website: <https://www.cms.gov/medicare/coverage/coverage-with-evidence-development/>
- c. Prior approval of inpatient status is required.

- d. Medical director review is required.

WHEN COVERAGE WILL NOT BE APPROVED

Clinical trial services are not covered when the criteria above are not met:

1. In the event the manufacturer loses its Category B status, or violates relevant IDE requirements necessitating FDA's withdrawal of IDE approval, all payment for the device should stop.
2. After the clinical trial ends, coverage is not provided for non-FDA approved drugs that were provided or made available to an enrollee during a covered clinical trial.
3. Non-covered items and services, including items and services that are statutorily prohibited.
4. Routine costs of a clinical trial include all items and services that are otherwise generally available to Plan beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision) that are provided in either the experimental or the control arms of a clinical trial **except**:
 - a. Items and services provided solely to satisfy data collection and analysis needs that are not used in the direct clinical management of the member, (e.g., monthly CT scans for a condition usually requiring only a single scan);
 - b. The investigational item or service, itself unless otherwise covered outside of the clinical trial;
 - c. Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial.

CMS, through the National Coverage Determination (NCD) process, an individualized assessment of benefits, risks, and research potential, may determine that certain items and services for which there is some evidence of significant medical benefit, but for which there is insufficient evidence to support a "reasonable and necessary" determination, are only reasonable and necessary when provided in a clinical trial that meets the requirements defined in that NCD. In the event a claim contains charges related to covered clinical trial services but those charges have not been or cannot be separated from costs related to non-covered services, benefits will not be provided.

The Plan does not cover devices that would otherwise not be covered by Original Medicare; e.g., statutorily excluded devices or items and services excluded from coverage through regulation or current manual instructions.

POLICY GUIDELINES

Determinations of coverage are made by the Plan in accordance with Medicare Coverage Policies, Plan review of available scientific data and literature, medical records, statements from attending physicians and members, and other pertinent information. Opinions of experts in a particular field and opinions and assessments of nationally recognized review organizations may also be considered by the Plan but are not determinative or conclusive.

BILLING/CODING/PHYSICIAN DOCUMENTATION INFORMATION

Applicable Codes: See procedure code(s) for specific procedure or service. List is located at <https://www.bluecrossnc.com/content/dam/bcbsnc/pdf/providers/policies-guidelines-codes/cpt-service-codes/cpt-codes-2023.pdf>

Providers and suppliers must include an IDE identification number that has 8 digits when submitting claims for the clinical trial or have an FDA assigned category B device number.

All routine services must have a modifier Q1, or “routine clinical services.” The ICD-9 code V70.7 (ICD-10 Z00.6) (examination of participation in clinical trial) as either the primary or secondary diagnosis code.

References:

1. Medicare National Coverage Determination for Routine Costs in Clinical Trials (ID #310.1); Effective date: 7/9/07; accessed via Internet site www.cms.gov; viewed on 08/31/2023.
2. Medicare Benefit Policy Manual; Chapter 14 section 20; Viewed online at <http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c14.pdf> on 08/31/2023.
3. Medicare Managed Care Manual; Chapter 4; Clinical Trials; Section 10.7 and 10.7.1; Viewed online at <http://www.cms.gov>; Viewed on 08/31/2023.
4. Medicare Claims Processing Manual 100-4, Chapter 32; Section 68 “Investigational Device Exemptions (IDE) and 69 (Qualifying Clinical Trials) Effective date: 5/1/08; Viewed online at www.cms.gov on 08/31/2023.
5. Blue Medicare “Evidence of Coverage”, 2023 Chp 3-Using the plan for your medical benefits, section 5-How are your medical services covered when you are in a “clinical research study” accessed via www.bluecrossnc.com on 08/31/2023.
4. Department of Health and Human Services; CMS; Medicare Learning Network; “Items and Services That Are Not Covered Under the Medicare Program”; Published January, 2015 viewed online at <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/Items-and-Services-Not-Covered-Under-Medicare-Booklet-ICN906765.pdf> on 08/31/2023.
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6. “Medicare and Clinical Research Studies,” CMS publication no. 02226, Revised September 2019. Accessed via <https://www.medicare.gov/sites/default/files/2019-09/02226-medicare-and-clinical-research-studies.pdf> on 08/31/2023.
7. U.S. National Institutes of Health; <https://www.nlm.nih.gov/services/ctphases.html>; Viewed online on 4/11/22—Old reference.
8. U.S. Food and Drug Administration (FDA); Medical Devices; viewed online at <http://www.fda.gov/medical-devices>; Section on medical devices viewed on 08/31/2023

Policy Implementation/Update Information:

Revision Date: 07/2002 Clinical Trial Services for Life Threatening Conditions Policy replaces PARTNERS Policy of June 28, 1999:
Titled: Clinical Trials for Treatment Studies on Cancer: Coverage of Patient Costs;
Revision Date: 09/2002 Reviewed at Physician Advisory Committee, No change;
Revision Date: 12/16/02 Policy changed to Clinical Trial Services – Medicare;
Revision Date: 2/23/2005
Revision Date: 11/30/06: Language changed under “Policy” section to match new Evidence of Coverage; No criteria changes made
Revision Date: 11/2009: No criteria changes made
Revision Date: 11/2010: No criteria changes made. New reference added to policy.
Revision Date 3/25/11: Language removed under Policy section that references reimbursement and claims which does not pertain to coverage criteria.

Revision date: 08/21/2013: Reformatted Definitions; removed the definitions not applicable to Medicare; Added definitions for IDE, Category A/B according to Medicare Claims Manual; Chapter 32; Section 68; ICD 10 code added.

Revision Date: 07/16/2014; Added edits to policy to enhance clarity; Added FDA definitions for device exemptions; Defined Original Medicare to differentiate from Plan coverage; Added two sections under "Indications for Coverage" Section B, *Category B Devices* and Section C, *Clinical Trials with Coverage of Evidence Development (CED)*; Added statement to when coverage will not be approved regarding Category B devices; Updated references.

Revision Date: 7/20/16 Annual Review. No CMS updates. No changes to policy, minor revisions only.

Revision Date: 4/18/18 Annual Review. No CMS Updates. Formatting revisions only.

Revision Date: 2/20/19: Staff Clarification: Removed Benefit Application-#3. A-"are not covered unless they are a part of a clinical trial. These devices" Added: Benefit Application- #3. "C. If Category B IDE is determined to be medically necessary by Medical Director, then authorization entry will be required: (Please see authorization entry guidelines for Category B IDE device). Under Indications for Coverage B. Added #6. If Category B IDE is determined to be medically necessary by Medical Director, then authorization entry will be required: (Please see authorization entry guidelines for Category B IDE device). Under Indications for Coverage: C. Updated hyperlink as it was no longer accurate.

Revision Date: 4/22/20- Annual Review; No CMS Updates. Minor Revisions Only.

Revision Date: 4/13/22-Annual Review; No CMS Updates. Minor Revisions Only.

Revision Date: September 21, 2023-Annual Review; No CMS Updates. Minor Revisions only. Added additional references.

Approval Dates:

Medical Coverage Policy Committee: September 21, 2023

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Medical Policy Coordinator