Clinical Trials

Guideline Number: IEX.CDG.006.03
Effective Date: January 1, 2022

Instructions for Use

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Related Policies
None

Applicable States

This Coverage Determination Guideline only applies to the states of Alabama, Arizona, Florida, Georgia, Illinois, Louisiana, Maryland, Michigan, North Carolina, Oklahoma, Tennessee, Texas, Virginia, and Washington.

Coverage Rationale

Indications for Coverage

Effective for plan years starting on or after January 1, 2014, the Patient Protection and Affordable Care Act ("PPACA") requires non-grandfathered health plans to cover "Routine Patient Costs" incurred by a "Qualifying Individual" who is participating in an "Approved Clinical Trial." Benefits include the reasonable and necessary items and services used to prevent, diagnose and treat complications arising from participation in a qualifying clinical trial. Benefits are available only when the Covered Person is clinically eligible for participation in the qualifying clinical trial as defined by the researcher.

Approved Clinical Trial

An "Approved Clinical Trial" is defined as:

- Phase I, Phase II, Phase III, or Phase IV clinical trial;
- Being conducted in relation to the prevention, detection or treatment for Cancer or other life threatening disease or condition; and
- Meets the requirements under Criteria for Approved Clinical Trials.

For purposes of this benefit, a "life-threatening disease or condition" is one from which the likelihood of death is probable unless the course of the disease or condition is interrupted.

Additional Clinical Trials

Coverage of Routine Patient Costs incurred by members participating in the following types of Clinical Trials is not currently mandated by PPACA. However, UnitedHealthcare's standard Clinical Trial benefit would also include coverage of the Routine Patient Costs when a member is participating in a:

- Phase I, Phase II or Phase III clinical trial
- Being conducted in relation to the detection or treatment of non-life threatening:
  - Cardiovascular disease (cardiac/stroke);
  - Surgical musculoskeletal disorders of the spine, hip and knees; and/or

- Other Clinical Trials: Certain plans may allow Clinical Trials relating to other diseases or disorders which are not life-threatening
- Meets the requirements under Criteria for Approved Clinical Trials.

Criteria for Approved Clinical Trials

The Clinical Trial must be described in one of the main bullets below.

- The study or investigation is approved or funded (which may include funding through in-kind contributions) by one or more of the following:
  - National Institutes of Health (NIH) [includes National Cancer Institute (NCI)]
  - Centers for Disease Control and Prevention (CDC)
  - Agency for Healthcare Research and Quality (AHRQ)
  - Centers for Medicare & Medicaid Services (CMS)
  - A cooperative group or center of any of the entities described above or the Department of Defense (DOD) or the Veterans Administration (VA)
  - A qualified non-governmental research entity identified in the guidelines issued by the National Institutes of Health for center support grants
  - The Department of Veterans Affairs, the Department of Defense or the Department of Energy as long as the study or investigation has been reviewed and approved through a system of peer review that is determined by the Secretary of Health and Human Services to meet both of the following criteria:
    - Comparable to the system of peer review of studies and investigations used by the National Institutes of Health
    - Ensures unbiased review of the highest scientific standards by qualified individuals who have no interest in the outcome of the review

  or
- The study or investigation is conducted under an investigational new drug application reviewed by the U.S. Food and Drug Administration; or
- The study or investigation is a drug trial that is exempt from having such an investigational new drug application.

In addition to the above, Louisiana, North Carolina and Virginia have the following requirements:

Louisiana:

- The clinical trial must have a written protocol that describes a scientifically sound study. It must have been approved by all relevant institutional review boards (IRBs) which operates in Louisiana and which has a multiple project assurance contracts approved by the Office of Protection from research risks before you are enrolled in the trial. We may, at any time, request documentation about the trial.
- Facility and personnel providing the protocol must provide the treatment within their scope of practice, experience, and training. They must be capable of doing so by virtue of their experience, training and volume of patients treated to maintain expertise.
- There must be no clearly superior, non-investigational approach.
- The available clinical or pre-clinical data provide a reasonable expectation that the treatment will be at least as efficacious as the non-investigational alternative.
- The Covered Person has signed an IRB approved consent form.

North Carolina:

- Covered Clinical Trials must be conducted in a setting and by personnel that maintain a high level of expertise because of their training, experience, and volume of patients.
- The drug, however, must be approved by the FDA and must have been proven effective and accepted for treatment of the specific type of cancer for which the drug has been prescribed in any one of the following established reference compendia:
- The National Comprehensive Cancer Network Drugs & Biologics Compendium;.
- The Thomson Micromedex DrugDex.
- The Elsevier Gold Standard's Clinical Pharmacology.
- Any other authoritative compendia as recognized periodically by the United States Secretary of Health and Human Services.

Virginia:

- An institutional review board of an institution in the Commonwealth of Virginia that has a multiple project assurance contract approved by the Office of Protection from Research Risks of the NCI.

Additional Requirements

- The clinical trial must have a written protocol that describes a scientifically sound study that has been approved by all relevant institutional review boards (IRBs) before participants are enrolled in the trial. We may, at any time, request documentation about the trial.
- The subject or purpose of the trial must be the evaluation of an item or service that meets the definition of a Covered Care Health Service and is not otherwise excluded under the policy.

Qualified Individual

A qualified individual must be:

- Covered under the health plan; and
- Eligible to participate in an approved clinical trial according to the trial protocol when the individual:
  - Was referred to the clinical trial by an in-network health care professional who has concluded that the individual's participation would be appropriate because the individual is eligible for the trial according to its protocol; or
  - Provides the plan with medical and scientific information that establishes that participation would be appropriate because the individual is eligible for the trial according to its protocol.

Routine Patient Costs During Clinical Trials Include Covered Health Care Services

- For which Benefits are typically provided absent a clinical trial.
- Required solely for:
  - The provision of the Experimental or Investigational Service(s) or item (e.g., the infusion administration services to deliver an investigational drug); and/or
  - The clinically appropriate monitoring of the effects of the service or item (e.g., lab tests and imaging done at a frequency consistent with signs and symptoms and other standards of care for that diagnosis or treatment type); and/or
  - The prevention of complications.
- Needed for reasonable and necessary care arising from the provision of an Experimental or Investigational Service(s) or item.

Network Plans

If one or more network providers are participating in a clinical trial, then UnitedHealthcare may require that the Qualified Individual participate in the clinical trial using a network provider, as long as the network provider will accept the qualifying individual as a participant in the trial. However, if an Approved Clinical Trial is conducted outside of the Qualified Individual's state of residence, then UnitedHealthcare may not deny or otherwise limit payment for Routine Patient Services solely on the basis that the trial is conducted out-of-state.

Coverage Limitations and Exclusions

Benefits for Clinical Trials do not include:

- The Experimental or Investigational Service(s) or item that is used in the clinical trial is not covered, except for the following:
  - Certain Category B Devices
  - Certain promising interventions for members with terminal illnesses
  - Other items and services that, in our determination, meet specified criteria in accordance with our medical and drug policies
- Items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the member. Examples include, but are not limited to:
  - Laboratory tests and imaging studies done at a frequency dictated by the study protocol and not consistent with signs and symptoms and other standards of care for that diagnosis or treatment type.
- A service that is clearly inconsistent with widely accepted and established standards of care for a particular diagnosis
- Items and services provided by the research sponsors free of charge for any person enrolled in the trial
- Travel and transportation expenses are excluded from coverage. These include, but are not limited to:

- Fees for all types of transportation (Examples include, but are not limited to: personal vehicle, taxi, medical van, ambulance, commercial airline, and train)
- Rental car expenses
- Mileage reimbursement for driving a personal vehicle
- Lodging
- Meals

- Routine patient costs obtained out-of-Network where non-network benefits do not exist under the plan.
- Clinical Trials that do not meet the requirements listed in the Indications for Coverage section above. An example includes, but is not limited to, Phase 0 drug Clinical Trials.

Definitions

The following definitions may not apply to all plans. Refer to the member specific benefit plan document for applicable definitions.

Category B Devices: As determined by the FDA, non-experimental and/or investigational devices where the incremental risk is the primary risk in question (i.e., underlying 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 approval for that device type. Only certain FDA-designated Category B Devices are covered. In order to be covered, all of the following criteria must be met:

- The device must be used within the context of an FDA-approved clinical trial.
- The device must be used according to the clinical trial's approved protocols.
- Must fall under a covered benefit category and must not be excluded by law, regulation or current Medicare coverage guidelines.
- The device is medically necessary for the member, and the amount, duration and frequency of use or application of the service is medically appropriate.
- The device is furnished in a setting appropriate to the member's medical needs and condition.

Clinical Trials/Studies Involving Investigational New Drugs: (National Institutes of Health) (https://clinicaltrials.gov/ct2/about-studies/home – About Clinical Studies > Glossary of Common Site Terms > P)

- Early Phase 1 (formerly listed as Phase 0): A phase of research used to describe exploratory trials conducted before traditional phase 1 trials to investigate how or whether a drug affects the body. They involve very limited human exposure to the drug and have no therapeutic or diagnostic goals (for example, screening studies, microdose studies).
- Phase 1: A phase of research to describe clinical trials that focus on the safety of a drug. They are usually conducted with healthy volunteers, and the goal is to determine the drug's most frequent and serious adverse events and, often, how the drug is broken down and excreted by the body. These trials usually involve a small number of participants.
- Phase 2: A phase of research to describe clinical trials that gather preliminary data on whether a drug works in people who have a certain condition/disease (that is, the drug's effectiveness). For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.
- Phase 3: A phase of research to describe clinical trials that gather more information about a drug's safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These studies typically involve more participants.
- Phase 4: A phase of research to describe clinical trials occurring after FDA has approved a drug for marketing. They include postmarket requirement and commitment studies that are required of or agreed to by the study sponsor. These trials gather additional information about a drug's safety, efficacy, or optimal use.

Covered Health Care Service(s): Health care services, including supplies or Pharmaceutical Products, which we determine to be all of the following:

- Provided for the purpose of preventing, evaluating, diagnosing or treating a Sickness, Injury, Mental Illness, substance-related and addictive disorders, condition, disease or its symptoms.
- Medically Necessary.

- Described as a Covered Health Care Service in the Certificate under Section 1: Covered Health Care Services and in the Schedule of Benefits.
- Not excluded in the Certificate under Section 2: Exclusions and Limitations.

Exceptions:
- Clinical Trials for which Benefits are available as described under Clinical Trials in Section 1: Covered Health Care Services.
- If you are not a participant in a qualifying clinical trial, as described under Clinical Trials in Section 1: Covered Health Care Services, and have a Sickness or condition that is likely to cause death within one year of the request for treatment we may, as we determine, consider an otherwise Experimental or Investigational Service to be a Covered Health Care Service for that Sickness or condition. Prior to such a consideration, we must first establish that there is sufficient evidence to conclude that, albeit unproven, the service has significant potential as an effective treatment for that Sickness or condition.

Experimental or Investigational Service(s): Medical, surgical, diagnostic, psychiatric, mental health, substance- related and addictive disorders or other health care services, technologies, supplies, treatments, procedures, drug therapies, medications or devices that, at the time we make a determination regarding coverage in a particular case, are determined to be any of the following:
- Not approved by the U.S. Food and Drug Administration (FDA) to be lawfully marketed for the proposed use and not identified in the American Hospital Formulary Service or the United States Pharmacopoeia Dispensing Information as appropriate for the proposed use.
- Subject to review and approval by any institutional review board for the proposed use. (Devices which are FDA approved under the Humanitarian Use Device exemption are not Experimental or Investigational.)
- The subject of an ongoing clinical trial that meets the definition of a Phase I, II or III clinical trial set forth in the FDA regulations, regardless of whether the trial is actually subject to FDA oversight.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Coding Clarification: Clinical Trials claims are not limited to these modifiers. However, if a claim has one of these modifiers it is considered to be a Clinical Trials claim.

Modifier Code	Description
Q0	Investigational clinical service provided in a clinical research study that is in an approved clinical research study
Q1	Routine clinical service provided in a clinical research study that is in an approved clinical research study

HCPCS Code	Description
Covered When Criteria Are Met	
G0276	Blinded procedure for lumbar stenosis, percutaneous image-guided lumbar decompression (PILD) or placebo-control, performed in an approved coverage with evidence development (CED) clinical trial
G0293	Noncovered surgical procedure(s) using conscious sedation, regional, general, or spinal anesthesia in a Medicare qualifying clinical trial, per day
G0294	Noncovered procedure(s) using either no anesthesia or local anesthesia only, in a Medicare qualifying clinical trial, per day
G2000	Blinded administration of convulsive therapy procedure, either electroconvulsive therapy (ECT, current covered gold standard) or magnetic seizure therapy (MST, noncovered experimental therapy), performed in an approved IDE-based clinical trial, per treatment session
S9988	Services provided as part of a Phase I clinical trial

HCPCS Code	Description
Covered When Criteria Are Met	
S9990	Services provided as part of a Phase II clinical trial
S9991	Services provided as part of a Phase III clinical trial
Not Covered	
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 Clarification: Clinical Trials claims are not limited to this diagnosis code. However, if a claim has this code it is considered to be a Clinical Trials claim.

Diagnosis Code	Description
Z00.6	Encounter for examination for normal comparison and control in clinical research program

References

Medicare Benefit Policy Manual, Chapter 14 - Medical Devices. § 20.2 Category B; available at: http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs-Items/CMS012673.html. Accessed March 16, 2021.

Medicare Transmittal 126, September 19, 2000, new section 30-1https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/Downloads/R126CIM.pdf Accessed March 16, 2021.

NCD for Routine Costs in Clinical Trials, Section 310.1, Publication 100-3 @ http://www.cms.gov/medicare-coverage-database/indexes/ncd-alphabetical-index.aspx?bc=AgAAAAAAAAAAAA%3d%3d&. Accessed March 16, 2021.

US Department of Health and Human Services, Healthcare.gov Health Care Law information page: http://www.healthcare.gov/law/index.html, https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies. Accessed March 16, 2021.

Guideline History/Revision Information

Date	Summary of Changes
01/01/2022	**Template Update** • Updated policy header to reflect the most current product branding for UnitedHealthcare Individual Exchange Plans **Applicable States** • Revised list of applicable states to encompass new benefit plans effective Jan. 1, 2022; added language to indicate this policy applies to the states of Alabama, Florida, Georgia, Illinois, Louisiana, Michigan, and Texas **Coverage Rationale** ***Criteria for Approved Clinical Trials*** • Revised coverage criteria; added language to indicate: Louisiana ○ The clinical trial must have a written protocol that describes a scientifically sound study: ▪ [The clinical trial] must have been approved by all relevant institutional review boards (IRBs) which operates in Louisiana and which has a multiple project assurance contracts approved by the Office of Protection from research risks before you are enrolled in the trial ▪ [UnitedHealthcare] may, at any time, request documentation about the trial

Date	Summary of Changes
	○ Facility and personnel providing the protocol must provide the treatment within their scope of practice, experience, and training; they must be capable of doing so by virtue of their experience, training and volume of patients treated to maintain expertise ○ There must be no clearly superior, non-investigational approach ○ The available clinical or pre-clinical data provide a reasonable expectation that the treatment will be at least as efficacious as the non-investigational alternative ○ The covered person has signed an IRB approved consent form **North Carolina** ○ Covered Clinical Trials must be conducted in a setting and by personnel that maintain a high level of expertise because of their training, experience, and volume of patients ○ The drug, however, must be approved by the FDA and must have been proven effective and accepted for treatment of the specific type of cancer for which the drug has been prescribed in any one of the following established reference compendia: ▪ The National Comprehensive Cancer Network Drugs & Biologics Compendium ▪ The Thomson Micromedex DrugDex ▪ The Elsevier Gold Standard's Clinical Pharmacology ▪ Any other authoritative compendia as recognized periodically by the United States Secretary of Health and Human Services **Virginia** ○ An institutional review board of an institution in the Commonwealth of Virginia that has a multiple project assurance contract approved by the Office of Protection from Research Risks of the NCI **Supporting Information** • Archived previous policy version IEX.CDG.006.02

Instructions for Use

This Coverage Determination Guideline provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Coverage Determination Guideline is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Coverage Determination Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.