CLINICAL TRIALS

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INSTRUCTIONS FOR USE

This Coverage Determination Guideline provides assistance in interpreting certain standard UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificates of Coverage (COCs), Schedules of Benefits (SOBs), or Summary Plan Descriptions (SPDs), and Medicaid State Contracts) may differ greatly from the standard benefit plans upon which this guideline is based. In the event of a conflict, the enrollee's specific benefit document supersedes these guidelines. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this guideline. Other coverage determination guidelines and medical policies may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its coverage determination guidelines and medical policies as necessary. This Coverage Determination Guideline does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care 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.

COVERAGE RATIONALE

Plan Document Language

Before using this guideline, please check enrollee's specific plan document and any federal or state mandates, if applicable.

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.

I. APPROVED CLINICAL TRIAL

A. 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
- That meets the requirements under Section II below.

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.

B. Additional Clinical Trials

The following clinical trials are not currently required by PPACA. However, these clinical trials are covered under United Healthcare's clinical trial benefit.

- 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. Please refer to the enrollee's plan-specific SPD for coverage
- That meets the requirements under Section II below.

II. CRITERIA FOR APPROVED CLINICAL TRIALS

A. **The clinical trial must be described in paragraph 1, 2 or 3 below.**

1. **Federally funded trials**. 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 and 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.
2. The study or investigation is conducted under an investigational new drug application reviewed by the *U.S. Food and Drug Administration*.
3. The study or investigation is a drug trial that is exempt from having such an investigational new drug application.

B. **Additional Requirements**

1. The clinical trial must have a written protocol that describes a scientifically sound study and have 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.

2. The subject or purpose of the trial must be the evaluation of an item or service that meets the definition of a Covered Health Service and is not otherwise excluded under the Policy.

III. QUALIFIED INDIVIDUAL

A. To be a qualified individual an individual must be

1. Covered under the health plan, and

2 Eligible to participate in an approved clinical trial according to the trial protocol based upon:

- 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**
- The individual 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.

IV. ROUTINE PATIENT COSTS DURING CLINCIAL TRIALS INCLUDE:

A. Covered Health Services for which Benefits are typically provided absent a clinical trial.

B. Covered Health Services required solely for:

1. The provision of the Investigational item or service (e.g. the infusion administration services to deliver an investigational drug), **and/or**
2. The clinically appropriate monitoring of the effects of the item or service (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**
3. The prevention of complications.

C. Covered Health Services needed for reasonable and necessary care arising from the provision of an Investigational item or service.

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:

A. The Experimental or Investigational Service or item that is used in the clinical trial is not covered, except for the following:
    1. Certain *Category B* devices (see definition below)
    2. Certain promising interventions for patients with terminal illnesses.
    3. Other items and services that, in our determination, meet specified criteria in accordance with our medical and drug policies.

B. Items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient. 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.

C. A service that is clearly inconsistent with widely accepted and established standards of care for a particular diagnosis.

D. Items and services provided by the research sponsors free of charge for any person enrolled in the trial.

E. Travel and transportation expenses are excluded from coverage. These include, but are not limited to, the following examples:
    1. Fees for all types of transportation (examples include, but are not limited to: personal vehicle, taxi, medical van, ambulance, commercial airline, and train)
    2. Rental car expenses
    3. Mileage reimbursement for driving a personal vehicle
    4. Lodging
    5. Meals

F. Routine patient costs obtained out-of-network where non-network benefits do not exist under the plan.

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:

a) The device must be used within the context of an FDA-approved clinical trial

b) The device must be used according to the clinical trial's approved protocols.

c) Must fall under a covered benefit category and must not be excluded by law, regulation or current Medicare coverage guidelines.

d) The device is medically necessary for the member, and the amount, duration and frequency of use or application of the service is medically appropriate.

e) The device is furnished in a setting appropriate to the member's medical needs and condition.

Experimental or Investigational Service(s): Medical, surgical, diagnostic, psychiatric, mental health, substance use 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 considered to be 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.

Exceptions:

- Clinical trials for which Benefits are available as described under Clinical Trials in Section 1: Covered Health Services.
- If you are not a participant in a qualifying clinical trial, as described under Clinical Trials in Section 1: Covered Health Services, and have a Sickness or condition that is likely to cause death within one year of the request for treatment we may, in our discretion, consider an otherwise Experimental or Investigational Service to be a Covered Health 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.

Clinical Trials/Studies Involving Investigational New Drugs:

(National Institutes of Health http://clinicaltrials.gov/ct2/about-studies/glossary#P **)**

- **Phase 0:** Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals (for example, screening studies, microdose studies).

- **Phase 1:** Studies that are usually conducted with healthy volunteers and that emphasize safety. The goal is to find out what the drug's most frequent and serious adverse events are and, often, how the drug is metabolized and excreted.

- **Phase 2:** Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition). For example, participants receiving the drug may be compared with 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:** Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs.

- **Phase 4:** Studies occurring after the US Food and Drug Administration (FDA) has approved a drug for marketing. These include post-market requirement and commitment studies that are required of or agreed to by the sponsor. These studies gather additional information about a drug's safety, efficacy, or optimal use.

Investigational Device Exemption (IDE): An exemption determined by the FDA which allows an investigational device to be used in a clinical study in order to collect safety and effective

APPLICABLE CODES

The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this guideline are for reference purposes only. Listing of a service code in this guideline does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the enrollee specific benefit 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 claims payment. Other policies and coverage determination guidelines may apply.

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Limited to specific modifiers?	☐ YES ☒ NO **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	**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.

Limited to specific procedure codes?	☐ YES ☒ NO

HCPCS Procedure Code	**Description** ***THESE CODES MAY BE COVERED DEPENDING ON WHETHER CRITERIA IS MET:***
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
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

HCPCS Procedure Code	**Description** ***THESE CODES ARE NOT COVERED***
G9057	Oncology; practice guidelines; management differs from guidelines as a result of patient enrollment in an institutional review board approved clinical trial (for use in a medicare-approved demonstration project)
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

Limited to specific diagnosis codes?	☐ YES ☒ NO **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.**

ICD-9 Diagnosis Code	Description
V70.7	Examination of participant in clinical trial

ICD-10 Codes
In preparation for the transition from ICD-9 to ICD-10 medical coding on **October 1, 2015***, a sample listing of the ICD-10 CM and/or ICD-10 PCS codes associated with this policy has been provided below for your reference. This list of codes may not be all inclusive and will be updated to reflect any applicable revisions to the ICD-10 code set and/or clinical guidelines outlined in this policy. **The effective date for ICD-10 code set implementation is subject to change.*

ICD-10 Diagnosis Code (Effective 10/01/15)	Description
Z00.6	Encounter for examination for normal comparison and control in clinical research program.

Limited to place of service (POS)?	☐ YES ☒ NO

Limited to specific provider type?	☐ YES ☒ NO

Limited to specific revenue codes?	☐ YES ☒ NO

REFERENCES

1. US Department of Health and Human Services, Healthcare.gov Health Care Law information page: http://www.healthcare.gov/law/index.html
2. 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=AgAAAAAAAAAA%3d%3d&
3. Medicare Transmittal 126, September 19, 2000, new section 30-1: http://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R126CIM.pdf
4. US National Institutes of Health, Learn About Clinical Studies information page: http://clinicaltrials.gov/ct2/info/understand
5. 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

GUIDELINE HISTORY/REVISION INFORMATION

Date	Action/Description
07/01/2014	• Routine review; updated references (no change to coverage determination guidelines) • Archived previous version CDG.006.01