Clinical Trials

Policy REIMB-036

Origination Date: 01/25/2023

Reviewed/Revised Date: 01/24/2024

Next Review Date: 01/24/2025

Current Effective Date: 01/24/2024

Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Clinical trials are studies involving human volunteers (also called participants) that add to medical knowledge. Participants receive specific interventions according to a research protocol created by the trial investigators. These interventions may be medical devices, drugs, procedures, or changes to participant's behavior. Clinical trials may compare a new medical approach to one that is already available, to a placebo, or to no intervention. A clinical trial may also compare existing interventions to each other. Clinical trials aim to determine safety and efficacy of interventions.

Policy Statement and Criteria

1. Commercial Plans

U of U Health Plans covers medically necessary routine patient care costs in qualified clinical trials*, consistent with Centers for Medicare & Medicaid Services (CMS) policy and the Patient Protection and Affordable Care Act (PPACA) requirements. All of the following limitations apply to coverage:

A. All applicable plan limitations for coverage of out-of-network care will apply to routine patient care costs in clinical trials; and

B. All utilization management rules and coverage policies that apply to routine care for members not in clinical trials will also apply to routine patient care for members in clinical trials; and

C. Members must meet all applicable plan requirements for precertification, registration, and referrals; and

D. To qualify, a 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. Providers will not routinely be required to submit documentation about the trial, however, at any time, U of U Health Plans may request such documentation to confirm that the clinical trial meets current standards for scientific merit and has the relevant IRB approval(s).

**Approved Clinical Trials are defined as:*
An approved clinical trial, as defined in the statute, is a phase I, II, III, or IV clinical trial that relates to the prevention, detection or treatment of cancer or other life-threatening diseases that also satisfies one of three requirements:

1. *The trial is federally funded;*
2. *The trial is conducted under an investigational new drug (IND) application; or*
3. *The trial is exempt from such an investigational new drug application.*

To qualify under the "Federally funded" requirement, trial must be one of the following entities:

1. *The National Institutes of Health (NIH) – which includes the National Cancer Institute (NCI)*
2. *The Centers for Disease Control and Prevention (CDC);*
3. *The Agency for Healthcare Research and Quality (AHRQ);*
4. *The Centers for Medicare & Medicaid Services (CMS);*
5. *A cooperative group or a center of any of the following: NIH, CDC, AHRQ, CMS, Department of Defense (DOD) or Department of Veterans Affairs (VA);*
6. *A qualified non-governmental research entity identified in the guidelines issued by NIH for center support grants;*
7. *Clinical trials performed by the VA, DOD or Department of Energy (DOE) are covered if certain additional criteria are met.*

U of U Health Plans covers costs of medically necessary treatments for conditions that result as unexpected consequences (complications) of clinical trials.

U of U Health Plans does NOT cover ALL the following clinical trial costs:

A. Items and services provided by the trial sponsor without charge;

B. Costs of collecting data, record keeping or other services to clinical trial participants solely for the purpose of satisfying data collection needs of the clinical trial (i.e., "protocol-induced costs");

C. The experimental intervention itself (except medically necessary Category B investigational devices and promising experimental and investigational interventions for terminal illnesses in certain clinical trials);

D. Travel, lodging and meals.

2. Medicaid Plans

Healthy U (Medicaid) Plans covers medically necessary routine patient care costs for services associated with an enrollee's participation in qualified clinical trials*, consistent with Centers for Medicare & Medicaid Services (CMS) policy and the Patient Protection and Affordable Care Act (PPACA) requirements.

Coverage Requirements:

A. To qualify, a 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. Providers need to add the National Clinical Trial Number to the Medicaid Attestation form and include that form with any preauthorization (PA) request, if one is needed. Providers will not routinely be required to submit documentation about the trial, however, at any time, Healthy U may request such documentation to confirm that the clinical trial meets current standards for scientific merit and has the relevant IRB approval(s).

B. Routine costs, which include any item or service provided to an individual under the qualifying clinical trial, including any item or service provided to prevent, diagnose, monitor or treat complications resulting from participation in the clinical trial to the extent that the provision of such services would otherwise be covered outside the course of participating in the qualifying clinical trial including services delivered out of network.

C. A determination for coverage "shall be based solely on the attestation regarding the appropriateness of the qualifying clinical trial by the health care provider and principal investigator…which shall be made using a streamlined, uniform form developed for national use."

D. Travel, lodging and meals.

E. Determinations for coverage must be expedited and completed within 72 hours.

**Approved Clinical Trials are defined as:*

An approved clinical trial, as defined in the statute, is a phase I, II, III, or IV clinical trial that relates to the prevention, detection or treatment of cancer or other life-threatening diseases that also satisfies one of three requirements:

1. *The trial is federally funded;*
2. *The trial is conducted under an investigational new drug (IND) application; or*
3. *The trial is exempt from such an investigational new drug application.*

To qualify under the "Federally funded" requirement, trial must be one of the following entities:

1. *The National Institutes of Health (NIH) – which includes the National Cancer Institute (NCI);*
2. *The Centers for Disease Control and Prevention (CDC);*
3. *The Agency for Healthcare Research and Quality (AHRQ);*
4. *The Centers for Medicare & Medicaid Services (CMS);*
5. *A cooperative group or a center of any of the following: NIH, CDC, AHRQ, CMS, Department of Defense (DOD) or Department of Veterans Affairs (VA);*
6. *A qualified non-governmental research entity identified in the guidelines issued by NIH for center support grants;*
7. *Clinical trials performed by the VA, DOD or Department of Energy (DOE) are covered if certain additional criteria are met.*

Healthy U Plans covers costs of medically necessary treatments for conditions that result as unexpected consequences (complications) of clinical trials.

Healthy U Plans does not cover the following clinical trial costs:

A. The investigational item or service that is the subject of the qualifying clinical trial and is not otherwise covered as a Medicaid benefit;

B. Costs of collecting data, record keeping or other services to clinical trial participants solely for the purpose of satisfying data collection needs of the clinical trial (i.e., "protocol-induced costs");

C. Items and services provided by the trial sponsor without charge;

D. The experimental intervention itself (except medically necessary Category B investigational devices and promising experimental and investigational interventions for terminal illnesses in certain clinical trials).

Clinical Rationale

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:

1. The device must be used within the context of an FDA-approved clinical trial;
2. The device must be used according to the clinical trial's approved protocols;

3. Must fall under a covered benefit category and must not be excluded by law, regulation or current Medicare coverage guidelines;
4. The device is medically necessary for the member, and the amount, duration and frequency of use or application of the service is medically appropriate;
5. The device is furnished in a setting appropriate to the member's medical needs and condition.

In a case series with historical controls, Nipp et al. (2016) implemented a cancer care equity program (CCEP) to address financial burden associated with trial participation. Linear regression models compared trial enrollment before and after the CCEP. Patient characteristics were compared before and after the CCEP and between CCEP and non-CCEP participants. CCEP and non-CCEP participants were surveyed to compare pre-enrollment financial barriers. After accounting for increased trial availability and the trends in accrual for prior years, the authors found that enrollment increased after CCEP implementation (18.97 participants per month greater than expected; $p < .001$). A greater proportion of CCEP participants were younger, female, in phase I trials, lived farther away, had lower incomes, and had metastatic disease. Of 87 participants who completed the financial barriers survey, 49 CCEP and 38 matched, non-CCEP participants' responded (63% response rate). CCEP participants were more likely to report concerns regarding finances (56% vs. 11%), medical costs (47% vs. 14%), travel (69% vs. 11%), lodging (60% vs. 9%), and insurance coverage (43% vs. 14%) related to trial participation (all $p < .01$). Since there were several limitations to the study, the authors could not definitively conclude that the intervention was responsible for the increase in clinical trial enrollment. Changes in the patient population enrolling in trials (e.g., younger patients, those with metastatic disease, those seeking phase I studies) may have contributed to, rather than resulted from, the increase associated with CCEP. Other factors, including increased awareness about the importance of clinical trials, the emergence of novel drug targets, and improved infrastructure for pursuing clinical trials in the cancer center, likely also contributed to the increase. The authors could not explain the exact mechanism by which the CCEP might have produced an increase in clinical trial enrollment, nor could they determine if the program reduced financial distress. Limitations of the study included a single academic institution with a distinct patient population and may not apply to a more general cancer clinical trial population. In conclusion, the authors found that financial concerns represent a major barrier to patient participation in clinical trials and emphasize the importance of efforts to address these concerns.

In 2019, Nipp et al. further noted financial burdens as being a barrier to clinical trial enrollment. Patient populations with historically lower financial resources are often underrepresented in cancer clinical trials. Disparities in clinical trial enrollment can contribute to a lack of data about the impact of therapies and disparities in care. The authors concluded that few practical solutions have emerged to prevent and alleviate the financial burden to clinical trial participation. Also, evidence to support efforts to address financial concerns associated with clinical trial participation is lacking to enhance clinical trial enrollment and retention.

A 2021 cross-sectional study (Huey et al.) conducted a survey regarding economic burden and financial toxicity in patients with cancer enrolled in phase I clinical trials for > 1 month. Financial toxicity score was assessed using the COmprehensive Score for financial Toxicity (COST) survey. Patients also reported monthly out-of-pocket (OOP) costs. Two hundred and thirteen patients completed the survey (72% non-Hispanic White; 45% with annual income ≤ $60,000; 50% lived > 300 miles from the clinic; 37% required air travel). Forty-eight percent of patients had monthly OOP costs of at least $1,000. Fifty-five percent and 64% of patients reported unanticipated medical and nonmedical expenses, respectively. Worse financial toxicity was associated with yearly household income < $60,000 (odds ratio [OR]: 2.7; $p = .008$), having unanticipated medical costs (OR: 3.2; $p = .024$), and living > 100 miles away from the clinical trial

hospital (OR: 2.3; p = .043). Non-White or Hispanic patients (OR: 2.5; p = .011) and patients who were unemployed or not working outside the home (OR: 2.5; p = .016) were more likely to report high unanticipated medical costs. The authors concluded that among patients with cancer participating in clinical trials, economic burden is high, and most of patients' OOP costs were nonmedical costs. Financial toxicity was disproportionally higher in patients with lower income, further distance to travel, unexpected medical costs and more common among non-White or Hispanic patients. However, the study was limited by a single center setting and lack of assessment of patients who may have been deterred from clinical trial enrollment due to concerns about financial toxicity.

In a 2018 American Society of Clinical Oncology (ASCO) policy statement, the ASCO Health Disparities Committee prioritized the development of a set of recommendations to address the financial barriers to clinical trials participation in the cancer setting. These recommendations broadly address the following key areas:

1. Improving the policy environment for coverage of clinical trials;
2. Facilitating transparency among providers, patients, and payers for trial-related out-of-pocket costs;
3. Refuting the specter of inducement to enable targeted financial support for patients; and
4. Improving the available data on costs of cancer clinical trials.

For informational purposes only, the FDA approval alone is not a basis for coverage. The FDA does not conduct clinical trials; however, it does provide oversight for some human drug, biological product, and device trials. The FDA also requires certain clinical trials to be registered in the ClinicalTrials.gov database.

Applicable Coding

Modifiers

Not covered

Q0 Investigational clinical service provided in a clinical research study that is in an approved clinical research study

Possibly Covered

Q1 Routine clinical service provided in a clinical research study that is in an approved clinical research study

CPT Codes

No applicable codes

HCPCS Codes

No applicable codes

ICD-10 Codes

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

References:

1. Centers for Medicare and Medicaid Services (CMS). 2007. "Routine Costs in Clinical Trials". Publication #100-3; Manual Section #310.0; Version 2. Accessed: November 18, 2022. Available at: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=1&ncdver=2&fromdb=true
2. Code of Federal Regulations (CFR). Medical services coverage decisions that relate to health care technology, Title 42 CFR Last amended 11/07/2022. Up to date as of 11/16/2022. Accessed: November 18, 2022. Available at: https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-B/part-405/subpart-B
3. Huey RW, George GC, Phillips P, et al. Patient-reported out-of-pocket costs and financial toxicity during early-phase oncology clinical trials. Oncologist. 2021 Jul;26(7):588-596.
4. Medicare Benefit Policy Manual, Chapter 14 - Medical Devices. § 20.2 Category B; Accessed: November 18, 2022. Available at: http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs-Items/CMS012673.html .
5. National Academy of Sciences, Institute of Medicine (US) Committee on Routine Patient Care Costs in Clinical Trials for Medicare Beneficiaries. (2000) "Extending Medicare Reimbursement in Clinical Trials". H. J. Aaron and H. Gelband. Washington (DC). National Academies Press (US); Accessed: November 18, 2022. Available at: https://pubmed.ncbi.nlm.nih.gov/25077253/
6. Nipp RD, Hong K, Paskett ED. Overcoming barriers to clinical trial enrollment. Am Soc Clin Oncol Educ Book. 2019 Jan;39:105114.
7. Nipp RD, Lee H, Powell E, et al. Financial burden of cancer clinical trial participation and the impact of a cancer care equity program. Oncologist. 2016 Apr;21(4):467-74.
8. The White House, Office of the Press Secretary. "President Clinton takes new action to encourage participation in clinical trials. Medicare will reimburse for all routine patient care costs for those in clinical trials". White House Press Release. Washington, DC: Office of the Press Secretary, the White House; June 7, 2000. Accessed November 18, 2022. Available at: https://clintonwhitehouse5.archives.gov/WH/New/html/20000607.html
9. U.S, Food and Drug Administration (FDA). "Basics About Clinical Trials" Accessed November 18, 2022. Available at: https://www.fda.gov/patients/clinical-trials-what-patients-need-know/basics-about-clinical-trials
10. U.S, Food and Drug Administration (FDA). "Clinical Trials and Human Subject Protection" Accessed November 18, 2022. Available at: https://www.fda.gov/science-research/science-and-research-special-topics/clinical-trials-and-human-subject-protection
11. U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services (CMS). "Decision Memorandum for the Clinical Trials Policy (CAG-00071R)". Baltimore, MD: CMS; July 9, 2007. Accessed: November 18, 2022. Available at: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=186
12. U.S. Food and Drug Administration (FDA) (2017). "FDA Categorization of Investigational Device Exemption (IDE) Devices to Assist the Centers for Medicare and Medicaid Services (CMS) with Coverage Decisions". Guidance for Sponsors, Clinical Investigators, Industry, Institutional Review Boards, and Food and Drug Administration Staff. Accessed: November 18, 2022. Available at: https://www.fda.gov/media/98578/download
13. U.S. National Library of Medicine; 2022. ClinicalTrials.gov. Accessed: November 18, 2022. Available at: https://clinicaltrials.gov
14. US Department of Health and Human Services. Health Care Law information page. Accessed: November 18, 2022. Available at: https://www.hhs.gov/healthcare/index.html.
15. Winkfield KM, Phillips JK, Joffe S, et al. (2018) "Addressing financial barriers to patient participation in clinical trials: ASCO policy statement". J Clin Oncol. 2018 Sep 13:JCO1801132