JOHNS HOPKINS HEALTH PLANS	Johns Hopkins Health Plans **Medical Policy Manual** **Medical Policy**	*Policy Number*	CMS03.01
		Effective Date	08/01/2023
		Approval Date	05/16/2023
	Subject **Clinical Trials**	*Supersedes Date*	11/01/2022
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This document applies to the following Participating Organizations:

EHP	Johns Hopkins Advantage MD	Johns Hopkins Health Plan of Virginia Inc. (JHHPVA)	Priority Partners
US Family Health Plan			

Keywords: Clinical Trials, Investigational, Phase I, Phase II, Research

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I. ACTION

	New Policy	
x	Revising Policy Number	CMS03.01
	Superseding Policy Number	
	Archiving Policy Number	
	Retiring Policy Number	

II. POLICY DISCLAIMER

Johns Hopkins Health Plans (JHHP) provides a full spectrum of health care products and services for Advantage MD, Employer Health Programs, Johns Hopkins Health Plan of Virginia Inc., Priority Partners, and US Family Health Plan. Each line of business possesses its own unique contract, benefits, regulations, and regulators' clinical guidelines that supersede the information outlined in this policy.

III. POLICY

For Advantage MD refer to: Medicare Coverage Database

- National Coverage Determination (NCD) 310.1 Routine Costs in Clinical Trials
- Medicare Managed Care Manual Chapter 4 - Benefits and Beneficiary Protections 10.7 – Clinical Trials

For Employer Health Programs (EHP) refer to:

- Plan Specific Summary Plan Descriptions (SPD's)

For Johns Hopkins Health Plan of Virginia Inc. (JHHPVA) refer to: Medicare Coverage Database (Effective 1/1/2024)

- National Coverage Determination (NCD) 310.1 Routine Costs in Clinical Trials
- National Coverage Determination (NCD) 240.2.1 Home Use of Oxygen in Approved Clinical Trials
- Medicare Managed Care Manual Chapter 4 - Benefits and Beneficiary Protections 10.7 – Clinical Trials

For Priority Partners (PPMCO) refer to: Code of Maryland Regulations

- Code of Maryland Regulations(COMAR) 10.67.06.26-1 Clinical Trial Items and Services-Coverage for Routine Costs
- Code of Maryland Regulations (COMAR)10.67.06.27 Benefits - Limitations
- Maryland Department of Health (MDH) PT 52-23 MCO Transmittal No. 171 Coverage of Routine Costs Associated with a Qualifying Clinical Trial

For US Family Health Plan (USFHP) refer to: Tricare Policy Manuals

- TRICARE Policy Manual 6010.63-M, April 2021, Chapter 7, Section 24.1 Phase I, Phase II, and Phase II Cancer Clinical Trials
- TRICARE Policy Manual 6010.63-M, April 2021, Chapter 8, Section 5.1 Medical Devices
- TRICARE Policy Manual 6010.63-M, April 2021, Chapter 1, Section 3.1 Rare Diseases

IV. POLICY CRITERIA

A. When benefits are provided under the member's contract, JHHP considers routine patient care costs associated with the participation in a clinical trial (e.g. diagnostic procedures, medically necessary treatment, cost of *administration* of investigational drug, clinical monitoring) medically necessary when the following requirements are met:
   1. To the extent that routine non-investigational treatment (not for clinical trial) may require prior authorization in accordance with a member's health plan, the member or treating physician must request prior authorization for participation in clinical trial, including supporting documentation specified in A.4 below; AND,
   2. The clinical trial is a Phase I, Phase II, Phase III, or Phase IV interventional study with a therapeutic or diagnostic intent, aimed to address the following conditions:
      a. Prevention, early detection, and treatment of cancer; OR,
      b. Prevention, early detection, and treatment of life-threatening illness (any disease or condition from which there is a probable likelihood of death unless the course of the disease or condition is interrupted); OR,
      c. Treatment of unstable chronic condition; AND,
   3. The clinical trial meets the following regulatory requirements:
      a. Approved by an Institutional Review Board (IRB) of an institution conducting a clinical trial before participants are enrolled, AND;
      b. Approved or funded and monitored by one or more of the following entities:
         i. National Institutes of Health (NIH) (e.g. National Cancer Institute (NCI));
         ii. Centers for Disease Control and Prevention (CDC);
         iii. Agency for Health Care Research and Quality (AHRQ);
         iv. Centers for Medicare and Medicaid Services (CMS);
         v. A cooperative group or center of the entities described above (e.g. National Clinical Trials Network (NCTN), Imaging and Radiation Oncology Group (IROC), ECOG-ACRIN Cancer Research Group, AIDS Clinical Trials Group, Community Programs for Clinical Research in AIDS);
         vi. Department of Defense (DOD) or the Department of Veterans Affairs (VA);

vii. A qualified non-governmental research entity identified in NIH guidelines for center support grants (e.g. Patient-Centered Outcomes Research Institute (PCORl, American Association for Cancer Research (AACR), International Society for Infectious Diseases (ISID));
viii. Food and Drug Administration (FDA) when a clinical trial is intended to use a drug, biologic, or medical device regulated by the FDA or intended to study a new drug, biologic, or medical device in humans;
ix. Funded in part or completely by an individual investigator or/and a research institution and approved and monitored by the IRB overseeing the site where research is conducted; AND,

4. Documentation submitted for review includes but not limited to the following:
   a. Clinical note from the qualified provider describing patient's condition, prognosis, rationale for participation in clinical trial, and whether standard of care alternatives are available.
   b. Signed Informed Consent indicating that the patient has agreed to be a part of the clinical trial. Patient and provider should sign the consent prior to conducting any protocol related interventions (e.g. laboratory or imaging tests that are done uniquely for the purpose of the trial). Informed consent should include the following information:
      i. Title of the trial and name of the Primary Investigator (PI) conducting the trial;
      ii. IRB application number and approval date;
      iii. Clinical trial identification number (e.g. IRB#, NCT#, NCI#) for the applicable national database (e.g. NIH ClinicalTrials.gov database, National Cancer Institute (NCI) database, VA Cooperative Studies Program (CSP)) for verification or to obtain additional information if needed;
      iv. An explanation of the purposes of the research;
      v. A description of all the procedures that will be completed during enrollment in a clinical trial (e.g. screening procedures, treatment plan, schedule of visits, follow-up visits);
      vi. Information about sponsor/supporter/funding entity of the trial and regulatory agencies overseeing the trial;
   c. Information from the financial office of the institution conducting research specifying costs associated with the participation in a clinical trial (can be a part of the informed consent). Including a description of:
      i. The procedures, tests, drugs or devices that are part of the research and that will be paid for by the clinical trial (no cost to the member).
      ii. The procedures, tests, drugs or devices that will be billed to the health plan and, therefore, may be subject to any co-pays or deductibles not covered by a member's plan.
5. The clinical trial is conducted at one of the designated academic research medical centers or affiliated facilities (e.g. NCI-designated cancer centers, NCCN member institutions).

B. Unless benefits are provided under the member's contract, JHHP considers the following patient care costs associated with the participation in a clinical trial not medically necessary:
1. Experimental, investigational or unproven treatment, drugs or devices that the trial is testing.
2. Items and services provided or covered by the clinical trial sponsor free of charge for any person enrolled in the trial.
3. Services that are inconsistent with accepted standards of care or provided primarily to meet the needs of the trial, including services that are typically covered but are being provided at a greater frequency, duration, or intensity than is medically necessary.
4. Services or items that would not be covered if a member was not enrolled in a clinical trial.
5. Non-health care items and services (e.g., food products, personal care services, transportation, and lodging) are required as a result of the member's enrollment in the clinical trial.

V. DEFINITIONS

Clinical Trial: Clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related

biomedical or behavioral outcomes. The term “prospectively assigned” refers to a pre-defined process (e.g., randomization) specified in an approved protocol that requires the assignment of research subjects (individually or in clusters) to one or more arms/cohorts (e.g., intervention, placebo or other control) of the clinical trial. When used in relation to a clinical trial, an intervention is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related processes and/or endpoints (e.g. drugs or biologics administration, procedures, strategies to change health-related behavior, prevention or diagnostic strategies). A health-related biomedical or behavioral outcome of the clinical trial is defined as the pre-specified effect of an intervention on the study subjects (NIH, 2022c).

Phases of Clinical Trial: Biomedical clinical trials of an experimental drug, treatment, device, or behavioral intervention may proceed through four phases:

- Phase I: Tests a new biomedical intervention in a small group of people (e.g. 20-80) for the first time to determine efficacy and evaluate safety (e.g., determine a safe dosage range and identify side effects).
- Phase II: Study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and further evaluate safety.
- Phase III: Study to determine the efficacy of the biomedical or behavioral intervention in large groups of people (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the interventions to be used safely.
- Phase IV: Studies conducted after the intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use (NIH, 2022c).

Informed Consent: Informed consent is the process in which a health care provider educates a patient about the risks, benefits, and alternatives of a given procedure or intervention. The patient must be competent to make a voluntary decision about whether to undergo the procedure or intervention. Informed consent is both an ethical and legal obligation of medical practitioners in the US and originates from the patient's right to direct what happens to their body. Implicit in providing informed consent is an assessment of the patient's understanding, rendering an actual recommendation, and documentation of the process. The Joint Commission requires documentation of all the elements of informed consent "in a form, progress notes or elsewhere in the record." The following are the required elements for documentation of the informed consent discussion: (1) the nature of the procedure, (2) the risks and benefits and the procedure, (3) reasonable alternatives, (4) risks and benefits of alternatives, and (5) assessment of the patient's understanding of elements 1 through 4. (Shah et al., 2020).

Institutional Review Board (IRB): The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the organization with which it is affiliated. The IRB has the authority to approve, require modifications to, or disapprove all research activities that fall within its jurisdiction. All human subjects research projects should be evaluated and continually monitored by the IRB (NIH, 2022c).

VI. BACKGROUND

According to the National Institutes of Health (NIH), clinical research can be divided into three categories. The first category is patient-oriented research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or designee) directly interacts with human subjects. This type of research includes studying mechanisms of human disease; conducting therapeutic interventions, clinical trials, or developing new technologies. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. The second category is epidemiological and behavioral studies. The third category is outcomes research and health services research (NIH, 2022c).

The FDA has an authority over clinical trials for drug, biologic, and medical device products that are regulated by the FDA. This authority includes studies that are funded by the U.S. Department of Health and Human Services (with joint oversight by FDA and the Office for Human Research Protections), as well as studies that are solely funded by industry or by private parties. To help protect the rights and welfare of volunteers and verify the quality and integrity of data submitted for review, FDA performs inspections of clinical trial study sites and anyone involved in the research (FDA, 2018c).

The Institutional Review Board (IRB) has the authority to approve, require modifications to, or disapprove all research activities that fall within its jurisdiction. As part of the review process, the IRB reviews the adequacy of the informed consent document to ensure that it includes all the elements required by law. For the process of informed consent to be effective, FDA recommends including sufficient time for participants to consider the information and providing time and opportunity for the participant to ask questions and have those questions answered (FDA, 2018c; NIH, 2022c).

Every clinical study is led by a Principal Investigator (PI), who is often a medical doctor. Clinical studies also have a research team that may include doctors, nurses, social workers, and other health care professionals. Clinical studies can be sponsored, or funded, by pharmaceutical companies, academic medical centers, voluntary groups, and other organizations, in addition to Federal agencies such as the National Institutes of Health, the U.S. Department of Defense, and the U.S. Department of Veterans Affairs. Doctors, other health care providers, and other individuals can also sponsor clinical research (e.g. investigator initiated research) (NIH, 2019a).

It is customary that participants in clinical trials continue to see their usual health care providers while enrolled in a clinical study. While most clinical studies provide participants with medical products or interventions related to the illness or condition being studied, they do not provide extended or complete health care. By having his or her usual health care provider and health plan to work with the research team, a participant can make sure that the study protocol will not conflict with other medications or treatments that he or she receives (NIH, 2019a).

VII. CODING DISCLAIMER

Note: The following CPT/HCPCS codes are included below for informational purposes and may not be all inclusive. Inclusion or exclusion of a CPT/HCPCS code(s) below does not signify or 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's 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 of payment. Other policies and coverage determination guidelines may apply.

Note: All inpatient admissions require preauthorization.

Adherence to the provisions in this policy may be monitored and addressed through post payment data analysis and/or medical review audits
Advantage MD: Regulatory guidance supersedes JHHP Medical Policies. If there are no statutes, regulations, NCDs, LCDs, or LCAs, or other CMS guidelines, apply the Medical Policy criteria.
Employer Health Programs (EHP): Specific Summary Plan Descriptions (SPDs) supersedes JHHP Medical Policy. If there are no criteria in the SPD, apply the Medical Policy criteria.
Johns Hopkins Health Plan of Virginia, Inc. (JHHPVA): Regulatory guidance supersedes JHHP Medical Policies. If there are no statutes, regulations, NCDs, LCDs, or LCAs, or other CMS guidelines, apply the Medical Policy criteria.

Priority Partners (PPMCO): Regulatory guidance supersedes JHHP Medical Policy. If there are no criteria in COMAR regulations, or other State guidelines, apply the Medical Policy criteria.
US Family Health Plan (USFHP): Regulatory guidance supersedes JHHP Medical Policy. If there are no TRICARE policies, or other regulatory guidelines, apply the Medical Policy criteria.

VIII. CODING INFORMATION

HCPCS CODES ARE FOR INFORMATIONAL PURPOSES	
HCPCS CODE	**DESCRIPTION**
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
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
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

IX. REFERENCE STATEMENT

Analyses of the scientific and clinical references cited below were conducted and utilized by the Johns Hopkins Health Plans (JHHP) Medical Policy Team during the development and implementation of this medical policy. The Medical Policy Team will continue to monitor and review any newly published clinical evidence and revise the policy and adjust the references below accordingly if deemed necessary.

X. REFERENCES

Aetna. (2022, June 16). *Clinical Trials, Coverage of Routine Patient Care Costs.* Medical Clinical Policy Bulletin 0466. http://www.aetna.com

National Library of Congress. (2010, March 23). *H.R.3590 - Patient Protection and Affordable Care Act.* https://www.congress.gov

Cigna. (2022, November 1). *Clinical Trials.* Administrative Policy: A003. https://cignaforhcp.cigna.com

Harvard Pilgrim. (20221, April). *Clinical Trials.* Payment Policies. https://www.harvardpilgrim.org

Humana. (2022, September 22). *Clinical Trials.* Medical Coverage Policy: HCS-0410-023. http://apps.humana.com

Johns Hopkins Medicine. (2023). *Office of Human Subjects Research - Institutional Review Board.* https://www.hopkinsmedicine.org/institutional_review_board/

National Cancer Institute. (2023). *Clinical Trial Information for Patients and Caregivers.* https://www.cancer.gov/about-cancer/treatment/clinical-trials

National Comprehensive Cancer Network (NCCN). (2023). *NCCN Oncology Research Program (ORP).* https://www.nccn.org/education-research

National Institutes of Health (NIH). (2019a, March). *ClinicalTrials.gov. Learn About Clinical Studies.* http://clinicaltrials.gov

National Institutes of Health (NIH). (2021b, May) *ClinicalTrials.gov. Background.*https://clinicaltrials.gov/

National Institute of Health (NIH). (2022c, December). *NIH Grants Policy Statement: Definition of Terms.* https://grants.nih.gov/grants/policy

NIH Fogarty International Center. (2021). *Non-NIH Funding Opportunities - Grants and Fellowships.* https://www.fic.nih.gov

Patient-Centered Outcomes Research Institute (PCORI). (2017). *Clinical Effectiveness and Decision Science.* https://www.pcori.org

Shah, P., Thornton, I., Turrin, D., & Hipskind, J. E. (2022). Informed Consent. In *StatPearls.* StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK430827/

U.S. Department of Veteran Affairs (VA). (n.d.) *Active CSP Studies.* Office of Research & Development. Retrieved April 20, 2023 from: https://www.research.va.gov

U.S. Department of Veteran Affairs (VA). (n.d.) *Volunteering for a Clinical Trial.* Office of Research & Development. https://www.research.va.gov/programs/csp/participation.cfm

U.S. Food and Drug Administration (FDA). (2018a, January 4). *Step 3: Clinical Research.* https://www.fda.gov

U.S. Food and Drug Administration (FDA). (2023). *CFR - Code of Federal Regulations Title 21*. Retrieved April 20, 2023 from https://www.ecfr.gov/current/title-21

U.S. Food and Drug Administration (FDA). (2018b, January 4). *Clinical Trials: What Patient Needs to Know.* https://www.fda.gov

U.S. Food and Drug Administration (FDA). (2018c, January 26). What Patients Need to Know About Institutional Review Boards. https://www.fda.gov/

World Health Organization (WHO). (2018, January 10). *International Standards for Clinical Trial Registers* . https://www.who.int

XI. APPROVALS

Historic Effective Dates: 06/06/2003, 10/22/2003, 03/29/2004, 10/22/2004, 10/20/2005, 10/20/2006, 10/22/2007, 09/08/2008, 2010, 05/24/2011, 05/22/2012, 06/05/2015, 06/02/2017, 11/20/2018, 02/19/2019, 08/02/2021, 08/16/2022, 11/01/2022, 08/01/2023