

Corporate Medical Policy

Clinical Trial Services

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Origination:	3/2002
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Description of Procedure or Service

Clinical trials 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 clinicians' knowledge about a treatment and to improve clinical outcomes for future patients.

Clinical trials generally proceed through four phases:

Phase I clinical trials - the study drug or treatment 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 drug or treatment is given to a large group of people to see if it is effective and to further evaluate its safety;

Phase III clinical trials - the study drug or treatment 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 - studies performed after the drug or treatment has been marketed to collect information about its effects in various populations and any side effects associated with long-term use.

An Investigational Device Exemption (IDE) is an unphased trial in which an investigational device is used in a clinical study in order to collect safety and effectiveness data required to support submission for approval to the FDA. This classification is divided into two sub-categories:

- Category A (experimental/investigational) device, refers to a device for which the risk of the device has not been established and the FDA is unsure whether the device type can be safe and effective.
- Category B (nonexperimental/non-investigational) device, refers to a device for which the incremental risk is the primary risk in question and 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 premarket approval (PMA) or clearance for that device type.

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

North Carolina Statute

Based on North Carolina General Statutes § 58-3-255, **covered clinical trials** are defined as phase II, phase III, and phase IV patient research studies designed to evaluate new treatments, including

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prescription drugs, that 1) involve the treatment of life-threatening medical conditions, 2) are medically indicated and preferable for that patient compared to available noninvestigational treatment alternatives, and 3) have clinical and preclinical data demonstrating that the trial will likely be more effective for that patient than available noninvestigational alternatives.

Covered clinical trials under the North Carolina General Statutes must also meet the following requirements: 1) involve determinations by treating physicians, relevant scientific data, and opinions of experts in relevant medical specialties; 2) be approved by centers or cooperative groups that are funded by the National Institutes of Health, the Food and Drug Administration, the Centers for Disease Control, the Agency for Health Care Research and Quality, the Department of Defense or the Department of Veterans Affairs; 3) be conducted in a setting and by personnel that maintain a high level of expertise because of their training, experience and volume of patients.

Federal Statute

Section 10103(c) of PPACA (Patient Protection and Affordable Care Act of 2010) added a new provision to the federal Public Health Service Act which requires group health plans and health insurance issuers offering individual or group health insurance products to provide for coverage of routine patient costs associated with approved clinical trials. The term “approved clinical trial” under PPACA is defined in the statute as a phase I, phase II, phase III, or phase IV clinical trial that is conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening disease or condition and is one of the following:

1. A federally funded or approved trial. The study or investigation is approved or funded (which may include funding through in-kind contributions) by one or more of the following:
 - i. The National Institutes of Health.
 - ii. The Centers for Disease Control and Prevention.
 - iii. The Agency for Health Care Research
 - iv. The Centers for Medicare & Medicaid Services.
 - v. Cooperative group or center of any of the entities described in clauses (i) through (iv) or the Department of Defense or the Department of Veterans Affairs.
 - vi. A qualified non-governmental research entity identified in the guidelines issued by the National Institutes of Health for center support grants.
 - vii. Any of the following, if the conditions described for studies conducted by a Department are met:
 - I. The Department of Veterans Affairs
 - II. The Department of Defense
 - III. The Department of Energy

Studies or investigations conducted by a Department must be approved through a system of federal peer review to be comparable to the system of peer review of studies and investigations used by the National Institutes of Health, and that assure unbiased review of the highest scientific standards by qualified individuals who have no interest in the outcome of the review.

2. A clinical trial conducted under an FDA investigational new drug application.
3. A drug trial that is exempt from the requirement of an FDA investigational drug application.

Covered clinical trial services are exempt from the medical policy criteria outlined under the BCBSNC Investigational (Experimental) Services medical policy.

Policy

BCBSNC will provide coverage for Clinical Trial Services when benefits are available and criteria shown below are met.

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Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Clinical Trial Services are covered

BCBSNC may provide coverage for clinical trial services when **all** of the following criteria are met:

- A) The member, who is a potential clinical trial enrollee, has a "life-threatening condition" (see DEFINITIONS):
 - 1) even if treated with currently accepted treatment options; **and/or**
 - 2) standard therapies have not been effective in significantly improving the condition of the member or would not be medically appropriate;
(NOTE: Benefit plans covered under Section 10103(c) of PPACA (Patient Protection and Affordable Care Act of 2010) also include coverage of clinical trials related to the prevention, detection, or treatment of cancer, whether life threatening or not.)
- B) The clinical trial is a Phase II, III, or IV research study. (NOTE: Benefit plans covered under Section 10103(c) of PPACA (Patient Protection and Affordable Care Act of 2010) also include coverage of Phase I clinical trials); **and**
- C) The member is to be treated as part of a clinical trial satisfying **all** of the following criteria:
 - 1) The clinical trial has passed independent scientific review in a manner that is unbiased and comparable to the system of peer review of studies and investigation by the National Institutes of Health (NIH); **and**
 - 2) The clinical trial must be conducted in a setting and by personnel who maintain a high level of expertise because of their training, experience, and volume of patients; **and**
 - 3) The clinical trial been approved by an Institutional Review Board (IRB) that will oversee the investigation; **and**
 - 4) The research study has been approved by centers or cooperative groups that are funded by the National Institutes of Health, the Food and Drug Administration, the Centers for Disease Control, the Agency for Health Care Research and Quality, the Department of Defense, or the Department of Veterans Affairs.

NOTE: Benefit plans covered under Section 10103(c) of PPACA (Patient Protection and Affordable Care Act of 2010) also include coverage of clinical trials funded or approved by Centers for Medicare and Medicaid Services; the Department of Energy; drug trials conducted under an FDA investigational new drug application, or that are exempt from the requirement of an FDA investigational drug application; or a qualified non-governmental research entity identified in the guidelines issued by the National Institutes of Health (NIH) for center support grants. For further information regarding NIH grant eligibility, please see: http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_ch2.htm#determining_applicant_eligibility

- D) The member must:
 - a. Meet all protocol requirements; **and**
 - b. Be enrolled in the trial; **and**
 - c. Provide informed consent; **and**
 - d. Be treated according to protocol.

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When Clinical Trial Services are not covered

Clinical trial services are not covered according to the member benefit certificate when the criteria above are not met.

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.

Coverage is **not** allowed for any clinical trial services for which the costs have been or are funded by governmental/national agencies, foundations, commercial manufacturers, distributors, charitable grants or other such research sponsors of participants' individual trials. If the service provided includes a transplant, coverage is **not** provided for organs sold rather than donated to a recipient.

In addition, the following clinical trial costs are not covered:

- services that are not health care services;
- services provided solely to satisfy data collection and analysis needs;
- investigational drug costs for drugs that do not have unrestricted market approval from the U.S. Food and Drug Administration (FDA) for any diagnosis or treatment;
- services not provided for the direct clinical management of the patient.

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.

Policy Guidelines

Determinations of coverage are made by the Plan in accordance with North Carolina General Statutes § 58-3-255 and, for non-grandfathered plans, Section 10103(c) of PPACA (Patient Protection and Affordable Care Act of 2010) after BCBSNC's 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.

For clinical trials not meeting benefit coverage criteria, associated services are also non-covered. Associated services include treatments and services required solely for the provision of the item or study under investigation, the clinical monitoring of the effects of the investigational item or service, and the diagnosis and treatment of its complications.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: S9988, S9990, S9991, S9992, S9994, S9996.

Claims submitted for patient care in clinical research studies should include modifiers for routine and investigational clinical services.

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

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NOTE: Q1 modifier must be used with diagnosis code Z00.6 (encounter for examination for normal comparison and control in clinical research program). Z00.6 may not be used as the principal/first-listed diagnosis.

See procedure code for specific procedure or service.

For authorization and billing clinical trial claims associated with an IDE/Medical Device trial, utilize the CPT codes related to the surgical procedure being performed to implant the device.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Definitions

Informed Consent is the process of learning the key facts about a clinical trial before deciding whether or not to participate. The following facts must be included:

- Why the research is being done.
- What the researchers want to accomplish.
- What will be done during the trial and for how long.
- What risks are involved in the trial.
- What benefits can be expected from the trial.
- What other treatments are available.
- The right of the patient to ask questions or to leave the trial at any time.
- Informed consent must be documented in written form, in the language of the enrollee's choice.

Medical and Scientific Evidence is defined by BCBSNC as one of the following:

1. Peer-reviewed scientific studies published in or accepted for publication by medical journals that meet nationally recognized requirements for scientific manuscripts and that submit most of their published articles for review by experts who are not part of the editorial staff.
2. Peer-reviewed literature or biomedical compendia from such sources as the National Institute of Health's National Library of Medicine or The Cochrane Library.
3. An accepted indication for treatment in one of the following standard reference compendia:
 - The American Hospital Formulary Service-Drug Information,
 - The American Medical Association Drug Evaluations,
 - The American Dental Association Accepted Dental Therapeutics, and
 - The United States Pharmacopoeia Drug Information.
4. Findings, studies, or research conducted by or under the auspices of federal government agencies and nationally recognized federal research institutes including the:
 - U.S. Department of Health and Human Services,
 - Federal Agency for Healthcare Research and Quality,
 - National Institutes of Health,
 - National Cancer Institute,
 - National Academy of Sciences,
 - Center for Medicare and Medicaid Services, and
 - Any national board recognized by the National Institutes of Health for the purpose of evaluating the medical value of health services

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Life-Threatening Condition The term ‘life-threatening condition’ means any disease or condition from which the likelihood of death is probable unless the course of the disease or condition is interrupted.

Scientific Background and Reference Sources

General Assembly of N. C., Session 2001; Session Law 2001-446; Senate Bill 199; Part III. Mandated Benefits; Subpart A. Clinical Trials; Section 3.1; Article 3 of Chapter 58 of the General Statutes § 58-3-255. *Coverage of clinical trials.*

Medical Policy Advisory Group - 2/2002

Medical Policy Advisory Group - 3/2002

Medical Policy Advisory Group - 10/2003

Medical Policy Advisory Group - 9/2005

Specialty Matched Consultant Advisory Panel- 2/2013

<http://www.hhs.gov/healthcare/rights/law/title/i-amendments.pdf> Sec. 2709, page 26. Retrieved 1/6/14.

Medical Director review 1/2014

Specialty Matched Consultant Advisory Panel- 2/2014

National Institutes of Health (NIH).

http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_ch2.htm#determining_applicant_org_eligibility. Retrieved 8/12/14.

Medical Director review 9/2014.

Specialty Matched Consultant Advisory Panel- 2/2015

<https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R1418cp.pdf>

Medical Director review 2/2016

Specialty Matched Consultant Advisory Panel- 2/2016

Centers for Medicare & Medicaid Services (CMS). Medicare Benefit Policy Manual. Medical devices. Available at: <https://www.cms.gov>. Published January 1, 2015

Specialty Matched Consultant Advisory Panel review 2/2020

Specialty Matched Consultant Advisory Panel review 2/2021

Policy Implementation/Update Information

For Policy Named: Clinical Trial Services for Life Threatening Conditions

3/02 Original Policy issued.

4/02 Medical Policy Advisory Group meeting 2/02 and 3/02. Policy revised based on medical consultant recommendations. Revised the definition for Medical and Scientific Evidence to include review from The Cochrane Library. Policy name changed from "Clinical Trial

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- Services". Format changes. Codes added to Billing and Coding Section. Codes added to System Application Guidelines.
- 05/02 Processing instructions for codes S9992, S9994 and S9996 added to System Application Guidelines.
- 10/03 Medical Policy Advisory Group review. Information added to Billing and Coding section and Benefit Application section. No change to criteria.
- 11/03 Benefit Application Section corrected.
- 3/04 Policy Number changed from ADM9027 to MED1093.
- 7/29/04 Code S9988 added to Billing/Coding section of policy.
- 10/8/05 Specialty Matched Consultant Advisory Panel [MPAG] review on 09/08/2005. No changes to policy coverage criteria.
- 10/22/07 Updated Description of procedure for consistency with current NC Statute. Deleted following statement from Description, "Improvement of health outcomes for patients enrolled in clinical trials is a desirable but secondary consideration." References updated. Specialty Matched Consultant Advisory Panel review meeting 9/20/07. No changes to coverage criteria. (adn)
- 10/26/09 Specialty Matched Consultant Advisory Panel review 9/28/09. No change to policy statement.
- 6/22/10 Policy Number(s) removed (amw)
- 2/1/11 Policy status changed to "Active policy, no longer scheduled for routine literature review." Approved by medical director in 2010. (lpr)
- 3/12/13 Specialty Matched Consultant Advisory panel review meeting 2/20/2013. No change to policy statement. References updated. Converted policy to active status from active archive status. Medical director review 2013.(lpr)
- 1/14/14 Updated coverage criteria, description and benefits section for consistency with Patient Protection and Affordable Care Act of 2010. Medical director review 1/2014. (lpr)

For Policy Re-named: Clinical Trial Services

- 3/11/14 Policy renamed from "Clinical Trial Services for Life Threatening Conditions" to "Clinical Trial Services." No change to policy statement. Specialty Matched Consultant Advisory Panel review meeting 2/25/2014. Medical Director review 2/2014. (lpr)
- 8/26/14 Updated Policy Guidelines and Benefits Application sections. Reference added. No change to policy statement. Senior Medical Director review 8/2014. (lpr)
- 10/14/ 14 Under When Covered section, C.4. Note: added "a clinical trial conducted under an FDA investigational new drug application; and a drug trial that is exempt from the requirement of an FDA investigational drug application" for consistency with state statute language. Senior medical director review 9/2014. (lpr)
- 3/10/15 Specialty matched consultant advisory panel review meeting 2/25/2015. No change to policy statement. (lpr)
- 4/1/16 Specialty Matched Consultant Advisory Panel review 2/24/2016. Information added to Billing/Coding section. *Claims submitted for patient care in clinical research studies should include modifiers for routine and investigational clinical services. Q0 –*

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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. NOTE: Q1 modifier must be used with diagnosis code Z00.6 (encounter for examination for normal comparison and control in clinical research program). Z00.6 may not be used as the principal/first-listed diagnosis.
(adn)

- 3/31/17 Specialty Matched Consultant Advisory Panel review 2/22/2017. No change to policy statement. (an)
- 3/29/18 Specialty Matched Consultant Advisory Panel review 2/28/2018. No change to policy. (an)
- 9/7/18 Added definition of Investigational Device Exemption (IDE) to Description section. The following statement added to Billing/Coding section: For authorization and billing clinical trial claims associated with an IDE/Medical Device trial, utilize the CPT codes related to the surgical procedure being performed to implant the device. Reference added. (an)
- 3/12/19 Specialty Matched Consultant Advisory Panel review 2/20/2019. No change to policy. (an)
- 3/10/20 Specialty Matched Consultant Advisory Panel review 2/19/2020. No change to policy. (eel)
- 3/23/21 Specialty Matched Consultant Advisory Panel review 2/17/2021. No change to policy. (bb)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.