ROUTINE COSTS IN CLINICAL TRIALS (NCD 310.1)

Guideline Number: MPG268.02
Approval Date: December 14, 2016

Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSTRUCTIONS FOR USE</td>
<td>1</td>
</tr>
<tr>
<td>POLICY SUMMARY</td>
<td>1</td>
</tr>
<tr>
<td>APPLICABLE CODES</td>
<td>3</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>4</td>
</tr>
<tr>
<td>GUIDELINE HISTORY/REVISION INFORMATION</td>
<td>5</td>
</tr>
</tbody>
</table>

INSTRUCTIONS FOR USE

This Policy Guideline is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates for health care services submitted on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450), or their electronic comparative. The information presented in this Policy Guideline is believed to be accurate and current as of the date of publication.

This Policy Guideline provides assistance in administering health benefits. All reviewers must first identify member eligibility, any federal or state regulatory requirements, Centers for Medicare and Medicaid Services (CMS) policy, the member specific benefit plan coverage, and individual provider contracts prior to use of this Policy Guideline. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document may differ greatly from the standard benefit plan upon which this Policy Guideline is based. In the event of a conflict, the member specific benefit plan document supersedes this Policy Guideline. Other Policies and Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary.

UnitedHealthcare follows Medicare coverage guidelines and regularly updates its Medicare Advantage Policy Guidelines to comply with changes in CMS policy. UnitedHealthcare encourages physicians and other healthcare professionals to keep current with any CMS policy changes and/or billing requirements by referring to the CMS or your local carrier website regularly. Physicians and other healthcare professionals can sign up for regular distributions for policy or regulatory changes directly from CMS and/or your local carrier. This Policy Guideline is provided for informational purposes. It does not constitute medical advice.

POLICY SUMMARY

Overview
Medicare Advantage covers the routine costs of qualifying clinical trials, as such costs are defined below, as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. All other Medicare rules apply.

Medicare Advantage is responsible for payment of claims related to enrollees’ participation in both Category A and B IDE studies that are covered by the MAC with jurisdiction over the MA plan’s service area. The MAO is responsible for payment of routine care items and services in CMS-approved Category A and Category B IDE studies. The MAO is also responsible for CMS-approved Category B devices. CMS will not approve Category A devices because they are statutorily excluded from coverage.

Medicare Advantage is responsible for payment of items and services in CMS-approved CED studies unless CMS determines that the significant cost threshold is exceeded for that item or service.

Routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision) that are provided in either the experimental or the control arms of a clinical trial except:

- The investigational item or service, itself unless otherwise covered outside of the clinical trial;
- 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 (e.g., monthly CT scans for a condition usually requiring only a single scan); and
- Items and services customarily provided by the research sponsors free-of-charge for any enrollee in the trial.

See References.
Routine costs in clinical trials include:

- Items or services that are typically provided absent a clinical trial (e.g., conventional care);
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for the diagnosis or treatment of complications.

This policy does not withdraw Medicare coverage for items and services that may be covered according to Local Coverage Determinations (LCDs) or the regulations on category B investigational device exemptions found in 42 CFR 405.201-405.215, 411.15, and 411.406. For information about LMRPs, refer to www.lmrp.net, a searchable database of Medicare Administrative Contractor local policies.

For non-covered items and services, including items and services for which Medicare payment is statutorily prohibited; Medicare only covers the treatment of complications arising from the delivery of the non-covered item or service and unrelated reasonable and necessary care. However, if the item or service is not covered by virtue of a national non-coverage policy in Pub. 100-03, National Coverage Determination (NCD) Manual, and is the focus of a qualifying clinical trial, the routine costs of the clinical trial (as defined above) will be covered by Medicare but the noncovered item or service, itself, will not.

**Requirements for Medicare Coverage of Routine Costs**

Any clinical trial receiving Medicare coverage of routine costs must meet the following three requirements:

- The subject or purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).
- The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.
- Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers.

Trials of diagnostic interventions may enroll healthy patients in order to have a proper control group.

The requirements above are insufficient by themselves to qualify a clinical trial for Medicare coverage of routine costs. Clinical trials also should have the following desirable characteristics; however, some trials, as described below, are presumed to meet these characteristics and are automatically qualified to receive Medicare coverage:

- The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
- The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The trial does not unjustifiably duplicate existing studies;
- The trial design is appropriate to answer the research question being asked in the trial;
- The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
- The trial is in compliance with Federal regulations relating to the protection of human subjects; and
- All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

**Qualification Process for Clinical Trials**

Using the authority found in §1142 of the Social Security Act (the Act) (cross-referenced in §1862(a)(1)(E) of the Act), the Agency for Healthcare Research and Quality (AHRQ) will convene a multi-agency Federal panel (the "panel") composed of representatives of the Department of Health and Human Services research agencies (National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), AHRQ, and the Office of Human Research Protection), and the research arms of the Department of Defense (DOD) and the Department of Veterans Affairs (VA) to develop qualifying criteria that will indicate a strong probability that a trial exhibits the desirable characteristics listed above. These criteria will be easily verifiable, and where possible, dichotomous. Trials that meet these qualifying criteria will receive Medicare coverage of their associated routine costs. This panel is not reviewing or approving individual trials. The multi-agency panel will meet periodically to review and evaluate the program and recommend any necessary refinements to the Centers for Medicare & Medicaid Services (CMS).

Clinical trials that meet the qualifying criteria will receive Medicare coverage of routine costs after the trial's lead principal investigator certifies that the trial meets the criteria. This process will require the principal investigator to enroll the trial in a Medicare clinical trials registry, currently under development.

Some clinical trials are automatically qualified to receive Medicare coverage of their routine costs because they have been deemed by AHRQ, in consultation with the other agencies represented on the multi-agency panel to be highly likely to have the above-listed seven desirable characteristics of clinical trials. The principal investigators of these
automatically qualified trials do not need to certify that the trials meet the qualifying criteria, but must enroll the trials in the Medicare clinical trials registry for administrative purposes, once the registry is established.

Clinical trials that are deemed to be automatically qualified are:
- Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA;
- Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD, and VA;
- Trials conducted under an investigational new drug application (IND) reviewed by the FDA; and
- Drug trials that are exempt from having an IND under 21 CFR 312.2(b) (1) will be deemed automatically qualified until the qualifying criteria are developed and the certification process is in place. At that time the principal investigators of these trials must certify that the trials meet the qualifying criteria in order to maintain Medicare coverage of routine costs. This certification process will only affect the future status of the trial and will not be used to retroactively change the earlier deemed status.

The CMS, through the NCD process, through an individualized assessment of benefits, risks, and research potential, may determine that certain items and services for which there is some evidence of significant medical benefit, but for which there is insufficient evidence to support a "reasonable and necessary" determination, are only reasonable and necessary when provided in a clinical trial that meets the requirements defined in that NCD.

Guidelines
It is mandatory to report a clinical trial number on claims for items/services provided in clinical trials/studies/registries, or under coverage with evidence development (CED).

Medicare will cover the routine costs of qualifying trials that either have been deemed to be automatically qualified, have certified that they meet the qualifying criteria, or are required through the NCD process, unless CMS's Chief Clinical Officer subsequently finds that a clinical trial does not meet the qualifying criteria or jeopardizes the safety or welfare of Medicare beneficiaries.

Should CMS find that a trial's principal investigator misrepresented that the trial met the necessary qualifying criteria in order to gain Medicare coverage of routine costs, Medicare coverage of the routine costs would be denied under §1862(a)(1)(E) of the Act. In the case of such a denial, the Medicare beneficiaries enrolled in the trial would not be held liable (i.e., would be held harmless from collection) for the costs consistent with the provisions of §§1879, 1842(l), or 1834(j) (4) of the Act, as applicable. Where appropriate, the billing providers would be held liable for the costs and fraud investigations of the billing providers and the trial's principal investigator may be pursued.

Medicare regulations require Medicare+Choice (M+C) organizations to follow CMS NCDs. This NCD raises special issues that require some modification of most M+C organizations' rules governing provision of items and services in and out of network. The items and services covered under this NCD are inextricably linked to the clinical trials with which they are associated and cannot be covered outside of the context of those clinical trials. M+C organizations therefore must cover these services regardless of whether they are available through in-network providers. M+C organizations may have reporting requirements when enrollees participate in clinical trials, in order to track and coordinate their members' care, but cannot require prior authorization or approval.

To access the list of CMS approved clinical trials/clinical research studies, go to Medicare Approved Facilities/Trials/Registries. Select the applicable Facility/Trial/Registry from the list on the left column to view the current approved clinical trials/clinical research studies.

### APPLICABLE CODES

The following list(s) of 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.

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<th>HCPCS Code</th>
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<tr>
<td>S9988</td>
<td>Services provided as part of a phase I clinical trial (Not covered by Medicare)</td>
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<td>S9990</td>
<td>Services provided as part of a phase II clinical trial (Not covered by Medicare)</td>
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<tr>
<td>S9991</td>
<td>Services provided as part of a phase III clinical trial (Not covered by Medicare)</td>
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<td>S9992</td>
<td>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/compassion (Not covered by Medicare)</td>
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<td>HCPCS Code</td>
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<td>S9994</td>
<td>Lodging costs (e.g., hotel charges) for clinical trial participant and one caregiver/companion (Not covered by Medicare)</td>
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<td>S9996</td>
<td>Meals for clinical trial participant and one caregiver/companion (Not covered by Medicare)</td>
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<td>Q0</td>
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<td>Q1</td>
<td>Routine clinical service provided in a clinical research study that is in an approved clinical research study</td>
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<tr>
<td>Z00.6</td>
<td>Encounter for examination for normal comparison and control in clinical research program</td>
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**REFERENCES**

**CMS National Coverage Determinations (NCDs)**
**NCD 310.1 Routine Costs in Clinical Trials**

**CMS Articles**

<table>
<thead>
<tr>
<th>Article</th>
<th>Medicare Part A</th>
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</tr>
</thead>
<tbody>
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<td>A52840 (Clinical Trials – Medical Policy Article) NGS</td>
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<td>A53784 (The Routine Costs of Investigational Chemotherapy Drugs Studied In a Qualifying Clinical Trial) Palmetto</td>
<td>NC, SC, VA, WV</td>
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<td>A53395 (The Routine Costs of Investigational Chemotherapy Drugs Studied In a Qualifying Clinical Trial) Palmetto Retired 09/30/2015</td>
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<td>A49286 (Clinical Trials – Medical Policy Article) NGS Retired 09/30/2015</td>
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**CMS Benefit Policy Manual**
**Chapter 14 Medical Devices**

**CMS Claims Processing Manual**
**Chapter 32; § 68 Investigational Device Exemption (IDE) Studies, § 69 - 69.11 Qualifying Clinical Trials**

**MLN Matters**
**Article MM8401, Revised June 9, 2014: Mandatory Reporting of an 8-Digit Clinical Trial Number on Claims**
**Article MM8921, Medicare Coverage of Items and Services in Category A and B Investigational Device Exemption (IDE) Studies**
**Article MM8961, Implementation of New National Uniform Billing Committee (NUBC) Condition Code “53” - “Initial placement of a medical device provided as part of a clinical trial or a free sample”**
**Article SE1344, Further Information on Mandatory Reporting of an 8-Digit Clinical Trial Number on Claims**

**Related Medicare Advantage Policy Guidelines**
**Artificial Hearts and Related Devices (NCD 20.9)**
**Avastin® (Bevacizumab)**
**Blood-Derived Products for Chronic Non-Healing Wounds (NCD 270.3)**
**Cochlear Implantation (NCD 50.3)**
**Continuous Positive Airway Pressure (CPAP) Therapy For Obstructive Sleep Apnea (OSA) (NCD 240.4) and Other Respiratory Assist Devices (RAD)**
**Extracorporeal Photopheresis (NCD 110.4)**
**Home Oxygen Use to Treat Cluster Headache (CH) (NCD 240.2.2)**
**Home Use of Oxygen in Approved Clinical Trials (NCD 240.2.1)**
**Infusion Pumps (NCD 280.14)**
**Islet Cell Transplantation in the Context of a Clinical Trial (NCD 260.3.1)**
Magnetic Resonance Imaging (NCD 220.2)
Percutaneous Image-Guided Lumbar Decompression for Lumbar Spinal Stenosis (NCD 150.13)
Percutaneous Transluminal Angioplasty (PTA) (NCD 20.7)
Pharmacogenomic Testing for Warfarin Response (NCD 90.1)
Positron Emission Tomography (PET) Scan (Including NCDs 220.6-220.6.20)
Transcatheter Aortic Valve Replacement (TAVR) (NCD 20.32)
Transcatheter Mitral Valve Repair (TMVR) (NCD 20.33)
Transcutaneous Electrical Nerve Stimulation (TENS) for Chronic Low Back Pain (CLBP) (NCD 160.27)

Related Medicare Advantage Coverage Summaries
Cardiac Pacemakers and Defibrillators
Chemotherapy, and Associated Drugs and Treatments
Deep Brain Stimulation for Essential Tremor and Parkinson’s Disease
Experimental Procedures and Items, Investigational Devices and Clinical Trials
Extracorporeal Photopheresis
Hearing Aids, Auditory Implants and Related Procedures
Infusion Pump Therapy
Oxygen for Home Use
Pain Management and Pain Rehabilitation
Percutaneous Transluminal Angioplasty and Stenting
Positron Emission Tomography (PET)/Combined PET-CT (Computed Tomography)
Stimulators: Electrical and Spinal Cord Stimulators
Transcatheter Heart Valve Procedures
Transplants: Organ and Tissue Transplants
Ventricular Assist Device (VAD) and Artificial Heart

Others
Affordable Care Act Coverage for Individuals Participating in Approved Clinical Trials
Clinical Trials Registry and Database
CMS Instructions: Medicare Coverage Related to Investigational Device Exemption (IDE) Studies
CMS Mandatory Reporting of National Clinical Trial (NCT) Identifier
Medicare Clinical Trial Policies
Medicare Managed Care Manual Chapter 4 § 10.7 Clinical Trials

GUIDEline HISTORY/Revision INFORMATION

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<thead>
<tr>
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