

Coverage with Evidence Development (CED): CED allows coverage of certain items or services where additional data gathered in the context of clinical care would further clarify the impact of these items and services on the health of Medicare beneficiaries. Medicare coverage may be extended to patients enrolled in a clinical research study. In this case, the research is conducted under section 1862(a)(1)(E) of the Social Security Act, which authorizes Medicare coverage for certain studies supported by AHRQ. CED allows us to provide coverage for an item or service because it is provided within a research setting where there are added safety, patient protections, monitoring, and clinical expertise.

CED projects provide the necessary new evidence to influence clinical practice and help Medicare beneficiaries and providers make more informed diagnostic and therapeutic decisions. CMS may use the evidence in a National Coverage Determination (NCD) reconsideration to determine if a change in Medicare coverage is appropriate under section 1862(a)(1)(A).

INSTRUCTIONS FOR SUBMISSION OF APPLICATIONS

Please complete the “Required Information” and “NCD/CED Coverage Requirements” sections listed below and submit to CMS for review (see email and mailing addresses below). Electronic submissions are preferable.

After preliminary review of the application (and any attached documentation) CMS will electronically notify the principal investigator (or the designated contact person) that we have received the application with all required information. Alternatively, we will request further information about an application with incomplete items.

The information provided in the sections on the following pages pertains to clinical research studies which intend to qualify for CED as specified in the NCD on Autologous Blood-Derived Products for Chronic Non-Healing Wounds, CAG-00190R3, issued in final form on August 2, 2013, by CMS, and available at <http://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=260>.

If the information provided fulfills these NCD requirements as judged by CMS, then Autologous Blood-Derived Products for Chronic Non-Healing Wounds required by the study may be reimbursable for study participants who are Medicare beneficiaries, pursuant to §1862(a)(1)(E) of the Social Security Act. If CMS approves the study, we will provide billing instructions for Medicare reimbursement of Autologous Blood-Derived Products for Chronic Non-Healing Wounds under CED.

Within 90 days of receipt of a completed application, we will send the results of CMS’ review of the application. There are three possible outcomes of the review process: accept, revise, and reject. If we request a revision, the applicant must submit the revision within 30 days of notification. CMS will review the revised application and notify the applicant of our final decision within 30 days of receipt of the revised application.

REQUIRED INFORMATION

1. Date of submission

2. Descriptive title

3. Contact information:

- Name and title of principal investigator (PI)
- Name and title of contact person if other than the PI
- PI's (or contact person's) mailing address, telephone number, fax, and email address
- Institutional or organizational affiliation

4. Study sponsor(s) **Quarterly Interim reports to CMS**

Please send study status updates electronically to Cheryl.Gilbreath@cms.hhs.gov that contain the following information:

- Number screened
- Number enrolled
- Reason for non-enrollment
- Number of dropouts
- Reason for dropout
- Number with completed data collection
- Progress of data analysis
- Analysis file constructed (y/n)
- Descriptive analysis completed
- Analyses to address each hypothesis completed (y/n)
- Manuscript completed (y/n)
- Manuscript sent to journal (date)

NCD/CED COVERAGE REQUIREMENTS

CMS will review and evaluate the protocol to ensure that the proposed study protocol meets the following requirements.

1. Study population: qualifications for study

The protocol should describe the criteria for Medicare beneficiaries to be included and excluded from the study.

2. Evaluation of outcomes

The protocol should define each outcome to be studied and explain method(s) and timing(s) of outcome assessment(s). The description should include expected length of follow up for

participants. The study sample size and duration should allow for reliable estimate(s) of all outcome endpoints.

At minimum, the outcomes to be studied must include the following for the study to be eligible for coverage:

- a. complete wound healing;
- b. ability to return to previous function and resumption of normal activities; or
- c. reduction of wound size or healing trajectory, which results in the patient's ability to return to previous function and resumption of normal activities?

3. Standards of scientific integrity and relevance to the Medicare population

Note: Please include a specific reference to the page or pages in your application with your response to the following.

- a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.

▲ *Describe how you will measure the outcomes listed in the NCD.*

- b. The research study 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.

▲ *Provide a brief review of pertinent published research that support your study hypotheses and methods.*

- c. The research study does not unjustifiably duplicate existing studies.

▲ *Justify that your study adds to existing evidence.*

- d. The research study design is appropriate to answer the research question being asked in the study.

The response to this Standard should contain the following:

- ▲ *Introduction*
- ▲ *Hypotheses to be tested*
- ▲ *Specific aims*
- ▲ *Background and significance*
- ▲ *Trial design*
- ▲ *Target population and recruitment target*

- ▲ *Inclusion/exclusion criteria*
 - ▲ *Power calculations*
- e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
- ▲ *Provide CVs of investigators with a description of their contribution to the project.*
 - ▲ *Describe the capabilities of the study sites.*
- f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it also must be in compliance with 21 CFR Parts 50 and 56.
- ▲ *Provide IRB approval letters from an IRB that is in compliance with 21 CFR Parts 50 and 56 for each site. Approvals should be updated before study initiation at each site. (Studies will be listed on the CMS website.)*
- g. All aspects of the research study are conducted according to the appropriate standards of scientific integrity.
- ▲ *Describe data safety monitoring procedures.*
 - ▲ *Describe stopping rules.*
- h. The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards.
- ▲ *Required of all CED projects*
- i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
- ▲ *Note: this standard is not relevant to this NCD. No answer required.*
- j. The clinical research study is registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
- *Plans to register the study if approved by CMS should be stated. (The ClinicalTrials.gov identifier is required for payment for platelet-rich-plasma for the treatment of chronic non-healing diabetic, pressure, and/or venous wounds.)*
- k. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of

Medical Journal Editors. However, a full report of the outcomes must be made public no later than three (3) years after the end of data collection.

▲ *Describe your approach to dissemination of the study results.*

- I. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary. Address the following:

▲ *Inclusion and exclusion criteria and how they will affect enrollment.*

▲ *Inclusion of women and minorities.*

▲ *Inclusion of Medicare enrollees.*

- m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

▲ *Discuss how the methodology addresses the above issues.*

Submit the "Required Information," "NCD/CED Coverage Requirements," and study protocol electronically to: Cheryl.Gilbreath@cms.hhs.gov

or hard-copy to: Dr. Louis Jacques, Director, Coverage and Analysis Group
Re: Autologous Platelet-Rich Plasma CED
Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850