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Client Alert

FDA & Life Sciences and Healthcare Practice Groups

July 25, 2013

CMS Proposes New Standards and Processes for Medicare Coverage of Investigational Devices and Related Clinical Studies and Trials

In its proposed update to the Physician Fee Schedule for calendar year 2014,[1] the Centers for Medicare & Medicaid Services (CMS) suggested major revisions to its regulations governing Medicare coverage of investigational devices and the routine items and services furnished to beneficiaries during the clinical studies or trials conducted under the Food and Drug Administration (FDA) Investigational Device Exemption (IDE) regulations. In its proposal, CMS sets forth new standards that would need to be met for the costs of certain investigational devices as well as the costs of routine items and services incurred by Medicare beneficiaries participating in FDA-approved IDE studies to be eligible for Medicare coverage. In addition, CMS proposes to consider and grant coverage of these investigational devices, as well as routine items and services otherwise available to Medicare beneficiaries, through a centralized review process rather than through local Medicare contractors, as it is currently performed. Revisions to this policy will be of particular interest to sponsors conducting clinical studies or trials of device technologies for which they seek Medicare coverage, as well as medical centers. Comments on the proposal may be submitted to CMS until September 6, 2013.

Background on Medicare Coverage of Investigational Devices and Associated Clinical Trial Costs

On September 8, 1995, the FDA and CMS entered into an interagency agreement in which FDA agreed to categorize IDEs for purposes of Medicare coverage. The process was codified in regulations at 42 C.F.R. § 405.201 *et seq.*, which describe two categories of investigational devices: (1) Category A devices and (2) Category B devices. Category A devices are "experimental" investigational devices where the "absolute risk" of the device type has not been established and FDA is unsure whether the device type can be safe and effective. This category typically encompasses only FDA Class III devices. Category B devices are "non-experimental" investigational devices where the "incremental risk" is the primary risk in question, *i.e.*, underlying questions of safety and effectiveness of the device type have been resolved. FDA Class I, II or III devices may fall within this category.

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The regulations created a path to Medicare coverage under certain circumstances for Category B investigational devices and the costs of routine items and services related to clinical trials for both Category A and Category B investigational devices. Category A investigational devices themselves are not eligible for Medicare coverage.[2] Coverage and payment decisions are currently made by local Medicare contractors consistent with general CMS coverage policies,[3] and are applicable only to the clinical trial items and services furnished to beneficiaries within the contractor's particular jurisdiction.

CMS's Proposal for Future Coverage Decisions

CMS proposes to modify the existing regulations because of its understanding that the current processes for determining coverage of IDE devices and clinical trials are inefficient, burdensome and create national variability that make it difficult for sponsors to obtain Medicare coverage for national IDE clinical studies. Local Medicare contractors apply various levels of scrutiny to IDE study protocols, use different review processes, and sometimes make coverage decisions on a claim-by-claim basis. According to CMS, this has led to inconsistent IDE coverage across Medicare contractors. Thus, CMS is proposing a transparent, centralized review process that it believes would be more efficient because it will reduce the burden for stakeholders interested in conducting nationwide trials. Once the IDE coverage process is centralized, a single entity at CMS would make IDE coverage decisions, which would eliminate the need for duplicate review by local Medicare contractors.

In addition, CMS proposes certain minimum standards to ensure that Medicare beneficiaries who volunteer to participate in studies are adequately protected and that the study design addresses questions of importance to Medicare and its beneficiaries. Although an item or service may be considered "reasonable and necessary" when used by a clinician for the benefit of an individual patient, CMS believes that it may not necessarily be reasonable and necessary when used in the context of an IDE clinical study or trial. Also, there are numerous studies and trials that may be considered "scientifically valid," but are of little benefit to Medicare beneficiaries. Thus, CMS proposes that clinical trials or studies evaluating Category A or Category B IDE devices meet the following standards in order for the costs of "routine care items and services"[4] in those trials (and the costs of Category B IDE devices themselves) to be eligible for Medicare coverage:

1. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of patients who are represented by the Medicare-enrolled subjects.

2. The rationale for the 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.

3. The study results are not anticipated to unjustifiably duplicate existing knowledge.

4. The study design is methodologically appropriate and the anticipated number of enrolled subjects is appropriate to answer the research question(s) being asked in the study.

5. The study is sponsored by an organization or individual capable of completing it successfully.

6. The study is in compliance with all applicable federal regulations concerning the protection of human subjects found at 45 C.F.R. Part 46.

7. All aspects of the study are conducted according to appropriate standards of scientific integrity set by the International Committee of Medical Journal Editors.

8. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.

9. Where appropriate, 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 may be exempt from this standard only if the disease or condition being studied is life threatening as defined in 21 C.F.R. § 312.81(a) and the patient has no other viable treatment options.

10. The study is registered on the ClinicalTrials.gov website and/or the Registry of Patient Registries by the principal sponsor/investigator prior to the enrollment of the first study subject.

11. The study protocol specifies the method and timing of public release of results on all pre-specified outcomes, including release of negative outcomes. The release should be hastened if the 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 3 years after the end of data collection.

12. The study protocol explicitly discusses subpopulations affected by the item or service 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 in the study. 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.

13. The study protocol explicitly discusses how the results are or are not expected to be generalizable to subsections of 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.

Further, if the Category A or Category B IDE clinical trial meets all of the above 13 criteria and is a pivotal study with a superiority study design, CMS will automatically cover the costs of routine care items and services in the clinical trial. CMS proposes to define "pivotal" studies or trials as clinical investigations designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. They may or may not be preceded by an early and/or a traditional feasibility study or trial. CMS proposes to define "superiority" studies as studies or trials intended to demonstrate at some pre-specified level of confidence that the effect of an investigational treatment is superior to that of an active control by more than a pre-specified margin. CMS believes that meeting pivotal study and superiority study design criteria assures that the study results will be informative

for beneficiary choices and medical decision-making in the non-trial settings where most care is actually furnished. These trial designs allow beneficiaries to compare their options and determine which one is superior for the beneficiary, whereas a non-inferiority trial design (evaluating whether the investigated device is no worse than the comparator treatment) supports more limited and less useful conclusions. If an IDE device is furnished in an FDA-approved IDE study that is not a pivotal study with a superiority study design, but has still met all of the above 13 criteria, CMS will consider whether Medicare coverage is appropriate, but coverage is not automatically guaranteed. The proposed regulations do not permit CMS to exercise discretion to consider coverage where most, but not all, of the 13 criteria are met.

The centralized review process proposed by CMS would require that any interested party who seeks coverage in an IDE study send to the Coverage and Analysis Group at CMS (the same group that issues National Coverage Determinations) a request letter that describes the scope and nature of the study and addresses each of the applicable standards for coverage. The request would also include: (1) the FDA approval letter; (2) the IDE study protocol; (3) the IRB approval letter; and (4) the ClinicalTrials.gov registry identifier. Other supporting materials may be submitted. CMS proposes that it would notify the public of IDE studies eligible for Medicare coverage by posting the IDE study title and ClinicalTrials.gov registry identifier on the CMS website and publishing a list in the Federal Register.

Considerations

Both medical device manufacturers and health care providers should carefully review these proposed changes and submit comments. As part of such review, the following potential issues, among others, should be evaluated and considered for potential comment and practical implementation:

1. The proposed amendments would result in centralized CMS decision-making regarding coverage of the cost of a Category B device as well as coverage of "routine care items and services" provided in connection with Category A and Category B IDE trials. Thus, distinct from coverage of the cost of the investigational device itself, Medicare beneficiaries who choose to participate in IDE trials approved by the FDA may be at risk for non-coverage of "routine care items and services," including even routine items and services for medical emergencies and injuries that would otherwise be available to and covered for all Medicare beneficiaries outside of a clinical trial.

2. The proposed centralized CMS review process of the request for coverage provides no definitive timeline for provision of the coverage decision; thus, the timing of actual initiation of a clinical trial and access of Medicare beneficiaries to investigational device therapies could be substantially delayed.

3. No criteria are proposed regarding the composition or expertise of the CMS group or panel that will review the IDE study protocol and make the coverage determination.

4. CMS proposes a novel and arguably ethically unjustified definition of a "superiority" trial, which is not consistent with current FDA guidance, including the International Conference on Harmonisation Guidance on Statistical Principles for Clinical Trials,[5] that would require the comparator group to be an "active control." If no "active control" therapy has ever been shown to be safe and effective for treatment of the condition, a placebo control is both ethical and scientifically sound.

5. Extensive and novel proposed requirements for publication of study results are specified. These proposed new requirements are duplicative of, and inconsistent with, the current statutory requirements under Title VIII of the FDA Amendments Act of 2007 (FDAAA) regarding the process and timing of public disclosure of study results of Applicable Device Clinical Trials on ClinicalTrials.gov. As an example, the proposed regulations would require results to be made public within 24 months of data collection, which is inconsistent with the one-year requirement after the earlier of the actual or anticipated study completion date specified by FDAAA. Further, public disclosure of the results of a clinical trial of a device or drug that is never approved or cleared for marketing in the United States for any use is currently not required under FDAAA but would be required under these proposed regulations.

6. There does not appear to be any method to appeal or challenge CMS decisions through the centralized review process. Thus, even after incurring potentially substantial delays to commence a clinical trial while undertaking this process, a manufacturer might still be without an ability to challenge a negative coverage determination.

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The proposal may be found in the Physician Fee Schedule Proposed Rule for calendar year 2014, located at: https://www.federalregister.gov/articles/2013/07/19/2013-16547/medicare-program-revisions-to-payment-policies-under-the-physician-fee-schedule-clinical-laboratory.

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[1] 78 Fed. Reg. 43282 (July 19, 2013).

[2] CMS has treated non-significant risk investigational devices, *i.e.*, investigational devices that are subject to the FDA's abbreviated requirements for IDE approval pursuant to 21 C.F.R. § 812.2(b), as similar to Category B investigational devices for Medicare coverage purposes. *See* Medicare Benefit Policy Manual, Chapt. 14, § 60. CMS's proposed regulations do not specifically address Medicare coverage of non-significant risk investigational devices, but it is expected that CMS will continue to apply its current policy and treat these devices as Category B IDE devices if the proposed regulations are finalized.

[3] These coverage policies include a National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1). The new standards for coverage proposed by CMS would presumably eliminate the need to consult this NCD when determining Medicare coverage of the routine costs in clinical studies and trials related to investigational devices.

[4] CMS proposes to define "routine care items and services" as items and services that are otherwise generally available to Medicare beneficiaries (that is, there exists a benefit category, it is not statutorily excluded, and there is not a national noncoverage decision) that are furnished in either the experimental or the control arms of a clinical trial and that would be otherwise furnished even if the beneficiary were not enrolled in a clinical trial.

[5] 63 Fed. Reg. 49583 (Sept. 16, 1998).