CMS Publishes Additional (but Limited) Guidance on the Coverage with Evidence Development Process

by Robert Wanerman

December 2014

On November 20, 2014, the Centers for Medicare and Medicaid Services ("CMS") published its latest round of guidance on its Coverage with Evidence Development ("CED") policy for selected items and services under the Medicare program ("Guidance").[1] Although the Guidance is final, it is not a regulation and is not binding; nevertheless, it does provide useful information for manufacturers, providers, suppliers, and other stakeholders seeking more information on how CMS makes Medicare coverage determinations. Although CMS still retains broad discretion over the coverage process, the Guidance can help stakeholders evaluate the type of evidence that will be required to obtain a favorable coverage determination.

For many health care manufacturers, obtaining a Medicare National Coverage Determination ("NCD") is a considerable achievement: It is a binding determination that an item or service will be covered throughout the country. It provides certainty to manufacturers, providers, and suppliers, and avoids inconsistent local coverage determinations and the unpredictability of case-by-case determinations by Medicare contractors. However, obtaining a NCD is a rigorous process, and CMS typically demands a high level of clinical evidence and professional consensus before publishing a favorable decision. In addition, due to the wide discretion that CMS has under the "reasonable and necessary" standard in Section 1862(a)(1)(A) of the Social Security Act, it can be impossible to know in advance what quantity and quality of clinical evidence is needed to obtain a positive result.

Since 2006, CMS has carved out a middle ground for covering items and services when it judges the clinical data insufficient to issue a traditional NCD but believes that the item or service shows the potential for improving outcomes for the Medicare-

[1] "Guidance for the Public, Industry, and CMS Staff: Coverage with Evidence Development," Document Issued on November 20, 2014, available at: http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27

eligible population. In these cases, it has relied on the authority in Section 1862(a)(1)(E) of the Social Security Act to approve Coverage with Evidence Development ("CED") as part of the NCD process for selected items and services.[2] Under CED, an applicant must submit a NCD request, and if CMS agrees that CED is an available alternate, the item or service will be covered for Medicare beneficiaries provided that (1) those beneficiaries are enrolled in a clinical trial approved by CMS, and (2) the trial results are reported to CMS to allow it to make a final decision in the future regarding Medicare coverage. Recent examples of items and services that have obtained CED coverage include amyloid positron emission tomography imaging procedures using radiopharmaceuticals, and transcatheter mitral valve repair procedures.

If the applicant and CMS agree that CED is an option, the Guidance discusses threshold criteria to be used in making coverage decisions. These criteria largely mirror the factors that CMS has used on an *ad hoc* basis in recent favorable CED decisions; as such, the criteria published by CMS in the Guidance should be addressed in any future application where CED is sought as an alternative to a full NCD:

1. the principal purpose of the study must test whether the item or service meaningfully improves health outcomes of affected Medicare beneficiaries;

2. the rationale for the study is well supported by available scientific and medical evidence;

3. the study results are not expected to unjustifiably duplicate existing knowledge;

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

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

6. the research protocol complies with all relevant federal human subject protection regulations, including 42 C.F.R. Part 46 and 21 C.F.R. Parts 50 and 56, and must include notice to prospective subjects of the use and eventual disposition of the collected data;

7. the study will be conducted in accord with accepted scientific integrity standards;

[2] "National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development," available at: http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html

8. the study has a written protocol that plainly incorporates the CED approval criteria;

9. the study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals[3];

10. the studies or registries are registered on www.ClinicalTrials.gov by the principal sponsor or investigator prior to the enrollment of the first study subject—and registries must also be listed in the Agency for Healthcare Research & Quality (AHRQ) Registry of Patient Registries (RoPR);

11. the research study protocol specifies the method and timing of public release in either a peer-reviewed journal or in a publicly-available registry of all identified outcomes to be measured, including release of outcomes if outcomes are negative or the study is terminated early—this release of outcomes must be made within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint (even if the trial does not achieve its primary aim);

12. the study protocol must explicitly discuss beneficiary 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 the subpopulations; and

13. the study protocol must explicitly discuss how the results are or are not expected to be generalizable to affected beneficiary subpopulations.

The Guidance introduces two new elements into the CED process. First, it strongly suggests that in order to approve a CED protocol, there must be a comparator in a control group in order to minimize potential biases and evaluate the effectiveness of the new item or service. The Guidance states that there may be some flexibility in designating either a placebo or standard of care treatment as the control group. Although CMS does refer to blinding as a technique to minimize the placebo effect, the Guidance does not address evaluating (1) the risks to Medicare beneficiaries of sham procedures, such as a spine procedure to relieve back pain as discussed in the Guidance, or (2) how to offset the disincentives for a Medicare beneficiary to enroll in a clinical trial if there is a chance of receiving a sham procedure instead of treatment.

The second new element in the Guidance is CMS's suggestion that the CED study design include interim analyses that would be shared with CMS. Although this could potentially expedite a final NCD decision if the results are strongly positive, it may increase the burdens on the trial sponsor and could become problematic for the

[3] CMS may make an exception "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."

sponsor if the interim data is not promising and CMS in response changes its demands for data in order to make a final determination.

Finally, the Guidance clarifies two points limiting the scope of potential CED trials. Medicare contractors such as Medicare Durable Medical Equipment Contractors and Medicare Administrative Contractors, which process claims under Medicare Parts A and B, do not have the authority to approve CED trials within their respective jurisdictions. In addition, drugs and biologics that are self-administered are not eligible for CED trials, even though they may be covered under Medicare Part D.

Although the Guidance is something less than a roadmap for manufacturers and other stakeholders seeking Medicare coverage, it does provide a clearer idea of CMS's expectations when reviewing a request for a NCD when CED is an option. As in the past, interested parties are encouraged to meet with CMS's Coverage and Analysis Group and to maintain a dialogue with the agency throughout the process, to exchange ideas and to fine-tune the proposed clinical trial in order to reach a consensus with CMS.

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This Client Alert was authored by **Robert Wanerman**. *For additional information about the issues discussed in this Client Alert, please contact the author or the Epstein Becker Green attorney who regularly handles your legal matters.*

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