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June 29, 2011

Louis B. Jacques, M.D.
Director, Coverage & Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop S3-02-01
Baltimore, MD 21244

RE: Proposed Decision Memo for Erythropoiesis Stimulating Agents (ESAs) for Treatment of Anemia in Adults with Chronic Kidney Disease (CKD) Including Patients on Dialysis and Patients not on Dialysis (CAG-00413N)

Dear Dr. Jacques:

This correspondence is to follow up on the Public Citizen Health Research Group's April 15 letter regarding the Centers for Medicare & Medicaid Services' (CMS) March 16, 2011 proposed decision memo referenced above. In our letter, we strongly opposed the proposal that CMS not issue a national coverage determination at this time for ESAs for treatment of anemia in adults with chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis. Furthermore, given that ESAs pose significant risks of cardiovascular morbidity and death, we urged CMS to issue, instead, a national coverage decision that incorporates the following elements:

(1) For patients on dialysis, a coverage decision for ESAs should be issued that promotes maintenance of hemoglobin levels within a target range of 10-12 grams/deciliter (g/dL), as recommended by the Food and Drug Administration (FDA), and preferably within a range of 10-11 g/dL.

(2) For CKD patients not on dialysis, a coverage decision for ESAs should be issued that limits ESA treatment to patients with hemoglobin levels less than 10 g/dL. The target hemoglobin level of ESA treatment in these patients should be 10 g/dL but no higher.

As you may be aware, on June 24, the FDA issued a safety announcement informing healthcare professionals and patients with CKD of the following modified recommendations for **more conservative dosing** of ESAs in patients with CKD to improve the safe use of these drugs:[1]

(1) For CKD patients on dialysis:

(a) Initiate ESA treatment when the hemoglobin level is less than 10 g/dL.

(b) If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of ESA.

(2) For CKD patients not on dialysis:

(a) Consider initiating ESA treatment only when the hemoglobin level is less than 10 g/dL and the following considerations apply:

- The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell transfusion; and
- Reducing the risk of alloimmunization and/or other red blood cell transfusion-related risks is a goal.

(b) If the hemoglobin level exceeds 10 g/dL, reduce or interrupt the dose of ESA and use the lowest dose of ESA sufficient to reduce the need for red blood cell transfusions.

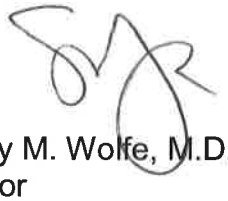
The FDA issued these new recommendations because the agency's analysis of data from clinical trials with CKD patients showed an increased risk of death, serious adverse cardiovascular reactions, and stroke when hemoglobin levels were targeted to greater than 11 g/dL.[1,2,3,4] The FDA's safety announcement also noted that no clinical trial to date has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase the cardiovascular risks in patients with CKD.[1] The FDA has required that the labels for ESAs be revised to reflect these new recommendations.

We endorse the FDA's recommendations and note that they are consistent with the proposals presented in our April 15, 2011 letter to CMS. It is imperative that CMS follow the FDA's lead and issue a national coverage decision for ESAs that fully aligns with FDA's new, more conservative recommendations regarding the dosing of ESAs and the upper limit of target hemoglobin levels in patients with CKD. CMS should take such action immediately because many Medicare beneficiaries with CKD currently being treated with ESAs have hemoglobin levels that exceed the new upper-limit targets recommended by the FDA and thus are at increased risk of serious adverse cardiovascular events and death. Unless CMS promptly implements such a national coverage decision, patients with CKD will continue to be needlessly harmed, and tens — if not hundreds — of millions of Medicare dollars will be wasted annually.

Thank you for considering these additional comments on the proposed national coverage decision memo.

Sincerely,

Michael A. Carome, M.D.
Deputy Director
Public Citizen Health Research Group



Sidney M. Wolfe, M.D.
Director
Public Citizen Health Research Group

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[1] Food and Drug Administration. FDA drug safety communication: modified dosing recommendations to improve the safe use of erythropoiesis-stimulating agents (ESAs) in chronic kidney disease. June 24, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm259639.htm#hcp. Accessed June 28, 2011.
[2] Besarab A, Bolton WK, Browne JK, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med. 1998;339:584-590.
[3] Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006;355:2085-2098.
[4] Pfeffer MA, Burdmann EA, Chen C, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. N Engl J Med. 2009;361:2019-2032.