

**THERE IS NO CLINICAL OR POLICY RATIONALE FOR CONGRESS TO LEGISLATE HOW PHYSICIANS PRACTICE MEDICINE – THE MAJORITY OF ERYTHROPOIESIS-STIMULATING AGENT (ESA) UTILIZATION IN ESRD IS APPROPRIATE**

***EPOGEN® (Epoetin alfa) has revolutionized End Stage Renal Disease (ESRD) care and has proven to be a good value, with Medicare spending almost 7% less per unit of EPOGEN® now than in 2005.***

- Nearly every patient with ESRD does not produce adequate amounts of erythropoietin, and consequently suffer from anemia. ESRD patients with anemia can suffer from fatigue and weakness, resulting in significantly diminished functional ability and activity level.
- Anemia, defined as a hemoglobin concentration below 11 g/dL, is associated with increased risk of hospitalization and death. Studies also have shown Medicare beneficiaries with hemoglobin concentrations less than 11 g/dL incur higher healthcare utilization and costs.
- Before the advent of EPOGEN® physicians had few options for treating anemia in dialysis patients, and had to rely on blood transfusions. Unfortunately, chronically administered blood transfusions put patients at risk for complications such as blood-borne infections and antibody responses that limit the chances for a successful kidney transplant.
- EPOGEN® has been shown to increase hemoglobin levels and reduce the need for red blood cell transfusion.
- Medicare per unit expenditures for EPOGEN® have *decreased* over time, from \$10 per 1,000 units in 1994 - 2004 to \$9.10 per 1,000 units in July 2007. Since the reimbursement method for EPOGEN® switched to average sales price (ASP)+6% in 2006, per unit Medicare payments for EPOGEN® have decreased by almost 7%.
- The higher average dose of Epoetin reported in the U.S. versus Europe is a consequence of more U.S. patients achieving the Medicare quality goal of hemoglobin of greater than 11g/dL, and the higher Epoetin dose requirements for diabetic and minority patients in the U.S.

***EPOGEN® is used appropriately in the vast majority of ESRD patients, and the current CMS Erythropoietin Monitoring Policy (EMP), with financial penalties for inappropriate EPOGEN® dosing, coupled with the revised FDA-approved prescribing information, has resulted in more nephrologists reducing EPOGEN® dose when hemoglobin levels exceed 12 g/dL.***

- The nephrology community consensus, as stated in the draft 2007 National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI™) guidelines, is that a hemoglobin target range of 11 to 12 g/dL minimizes risk and maximizes benefit in ESRD patients. It is further recognized that because of the general poor health status of a typical dialysis patient and the natural variability in patient hemoglobin levels, it is difficult to consistently maintain hemoglobin within a narrow band such as between 11 and 12 g/dL.
- Studies have demonstrated that patients with hemoglobin concentrations below 11 g/dL have the greatest risk for adverse clinical outcomes, and even transiently low hemoglobin concentrations are associated with worse outcomes than transiently high or persistently high hemoglobin concentrations above 12.5 g/dL.
- Studies have demonstrated that most physicians are not maintaining patients above 12g/dL. When looked at as a snapshot in time, 50% of patients may have hemoglobin levels above 12g/dL, however when individual patients' hemoglobin levels are followed over time, it is clear that hemoglobin levels are not being maintained above 12 g/dL.
  - Prior to the EMP, data demonstrated that 83% of hemoglobin excursions above 12 g/dL return back below 12g/dL within 3 months.
- New data analyses show that more physicians are promptly reducing doses in response to hemoglobins above 12 and 13 g/dL since the EMP and the March 2007 ESA label changes were announced.

- As of April 2007, 81% of hemoglobin excursions above 13 g/dL are followed by a dose reduction within 30 days compared to 72% in November 2005 when the EMP was announced. Data also demonstrate more dose reductions following hemoglobin excursions between 12 g/dL and 13 g/dL since the ESA label change in March 2007. In April 2007, 49% of hemoglobin excursions between 12 g/dL and 13 g/dL are followed by an ESA dose reduction within 30 days as compared with 37% in January of 2007. In addition, in some instances physicians are implementing a dose reduction in the subsequent 30 day window.

***There is extensive experience with Erythropoiesis-Stimulating Agents (ESAs) in Medicare beneficiaries with ESRD in routine clinical practice with a reassuring safety profile.***

- While not proof of causality, long-term surveillance of nearly 100% of the U.S. ESRD population shows that mortality rates have declined since the introduction of EPOGEN<sup>®</sup>, coincident with the rise in population hemoglobin levels. These data do not suggest evidence of increased mortality as ESAs have become a routine component of care for dialysis patients.
- Although recent studies evaluated ESAs in kidney disease have raised important safety questions, these studies targeted hemoglobin levels that are significantly higher than those recommended in the FDA-approved product labels. Amgen has promptly and regularly communicated new information, including recent ESA label changes, to prescribing physicians.
- Some retrospective analyses have linked ESA dose to mortality. However, analyses that carefully account for factors such as cardiac disease, infections, and hospitalizations demonstrate that ESA dose is not associated with mortality. Achieved hemoglobin is a much stronger predictor of better or worse clinical outcomes than is ESA dose, and transiently low hemoglobin values are associated with worse outcomes than transiently high hemoglobin levels.
- We are working with the FDA and the renal community to better understand patient management for those that are hyporesponsive to ESAs.

***There is no need for precipitous Medicare ESA payment reform using untested mechanisms that could potentially harm vulnerable dialysis patients and small providers.***

- Amgen believes that any change to the ESRD payment system should have a strong policy or clinical rationale, and any new system should maintain patient quality of care, ensure patient access, and be financially viable for dialysis providers, patients, and taxpayers.
- There does not appear to be a compelling policy or clinical rationale to make fundamental changes to the ESRD payment system based on the best available scientific evidence and utilization data.
- Congress must carefully consider the potential for negative patient outcomes as an unintended consequence of payment changes that are not carefully designed and implemented.
- As yet untested methods, such as bundling dialysis and drug payments or changing the ASP+6% ESRD drug reimbursement, could lead to unintended consequences including:
  - Poorer quality of care, as dialysis providers may need to make compromises to offset lower overall reimbursement.
  - Higher overall Medicare costs as a result of poor quality dialysis care.
  - Threats to access to quality care for patients treated in small dialysis facilities in both rural and underserved urban areas. Small clinics may begin to avoid more ill/costlier patients in order to control costs, or even close as a result of financial burden.
- Amgen supports that the Medicare Prescription Drug, Modernization, and Improvement Act (MMA) mandated demonstration project be completed prior to full implementation of a bundled payment system.