Long-Term Safety and Tolerability of Epoetin Zeta, Administered Intravenously, for Maintenance Treatment of Renal Anemia

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ABSTRACT

Introduction: The aim of this trial was to gather data on the long-term safety of a new erythropoietin preparation (epoetin zeta), focusing on the formation of anti-erythropoietin antibodies, when administered intravenously for maintenance of target hemoglobin concentration in anemic patients with end-stage renal failure receiving chronic hemodialysis. In addition, we aimed to provide information on the efficacy of epoetin zeta under open, noncontrolled conditions.

Methods: Patients received epoetin zeta intravenously, 1-3 times/week for 56 weeks (overall patient group, n=745) or 108 weeks (Bulgarian subgroup,
The aim of treatment was to maintain hemoglobin values between 10.5 and 12.5 g/dL with constant epoetin dosage. Primary (safety) endpoints were the occurrence of anti-erythropoietin antibodies and the evaluation of adverse events (AEs). Secondary (efficacy) endpoints included the mean weekly dose of epoetin per kg of body weight and mean hemoglobin concentrations.

**Results:** No patients developed neutralizing anti-erythropoietin antibodies. The most commonly reported AEs were infections and infestations (34.1%); followed by injury, poisoning, and procedural complications (25.8%); and gastrointestinal disorders (21.9%); 37.3% of patients reported serious AEs. The hemoglobin values remained stable, with mean values after 56 weeks of 11.3-11.6 g/dL for the overall group and 11.1-11.6 g/dL for the Bulgarian subgroup. The dosage of epoetin zeta was stable throughout the course of the trial. No cases of lack of (or loss of) efficacy were observed in the course of the trial.

**Conclusions:** The evaluation of the primary endpoints provided data supporting the intravenous administration of epoetin zeta in patients with chronic renal failure. Neutralizing antibodies against erythropoietin were not detected, and there were no reports of patients with increasing erythropoietin resistance. Our results suggest that intravenous administration of epoetin zeta is effective regarding its ability to maintain stabilized hemoglobin levels within the target range of 10.5-12.5 g/dL.

**Keywords:** efficacy; epoetin zeta; erythropoietin; long-term safety; maintenance treatment; renal anemia

**INTRODUCTION**

Erythropoietin is an essential growth factor required for the production of red blood cells. The stimulus for erythropoietin production is believed to be the oxygen content of blood delivered to the renal interstitial cells. When the peritubular renal cells are functioning correctly, individuals with low hemoglobin concentrations will produce increased quantities of erythropoietin, resulting in increased red blood cell production.

Chronic kidney disease is characterized by a progressive loss of kidney function most commonly resulting from inherited disorders or other diseases such as diabetes mellitus or hypertension. More than 80% of patients with chronic renal failure have anemia, which is primarily caused by a deficiency in erythropoietin production.