Supplementary Table 1. Complete List of Inclusion and Exclusion Criteria.

Inclusion Criteria	**Exclusion Criteria**
Patient was informed of the investigational nature of this study and had given written informed consent in accordance with institutional, local, and national guidelines	Prior treatment with any erythropoiesis-stimulating agent (ESA) in the 12 weeks prior to study drug administration
Males or females ≥18 and ≤85 years of age	Life expectancy <12 months
Premenopausal females (with the exception of those who were surgically sterile) must have had a negative pregnancy test at screening; those who were sexually active must have practiced a highly effective method of birth control for at least 4 weeks prior to study start and must have been willing to continue birth control for at least 4 weeks after the last dose of study drug. A highly effective method of birth control was defined as one which results in a low failure rate (ie, less than 1% per year) when used consistently and correctly, such as implants,	High likelihood of early withdrawal or interruption of the study (eg, myocardial infarction; severe or unstable coronary artery disease; stroke; severe or unstable respiratory disease including reactive airway disease; autoimmune disease; neuropsychiatric or neurological abnormalities; liver disease including active hepatitis B or C; active human immunodeficiency virus [HIV] disease; history of significant multiple drug allergies; or any other clinically significant medical diseases or conditions within the prior 6 months that may, in the investigator's opinion, interfere with safety,

injectables, combined oral contraceptives, some intrauterine devices, sexual abstinence, or vasectomized partner. For patients using a hormonal contraceptive method, information regarding the product under evaluation and its potential effect on the contraceptive should have been addressed	assessment or follow-up of the patient)
Chronic kidney disease stage 3 or 4 (estimated glomerular filtration rate of ≤60 mL/min/1.73m^2 within 28 days prior to study drug administration) and not expected to begin dialysis for at least 12 weeks	Anticipated elective surgery during the study period that may be expected to lead to significant blood loss, including vascular access surgery (such as an arteriovenous fistula or graft) expected within 12 weeks of first study drug administration
Two hemoglobin values of ≥9.0 and <11.0 g/dL within 4 weeks prior to study drug administration, including at least one of the values drawn within 7 days prior to study drug administration	Prior hemodialysis or peritoneal dialysis treatment
One serum ferritin level ≥100 ng/mL and transferrin saturation (TSAT) ≥20% within 4 weeks prior to study drug administration	Known intolerance to parenteral iron supplementation

One serum or red cell folate level above the lower limit of normal (LLN) within 4 weeks prior to study drug administration	Red blood cell transfusion within 12 weeks prior to study drug administration
One vitamin B12 level above the LLN within 4 weeks prior to study drug administration	Hemoglobinopathy (homozygous sickle cell disease [sickle cell trait did not exclude patient], thalassemia of all types, etc)
Weight ≥45 kg within 4 weeks prior to study drug administration	History of antibodies to any ESA or history of pure red cell aplasia
One white blood cell (WBC) count ≥3.0 x 10^9/L within 4 weeks prior to study drug administration	Uncontrolled or symptomatic inflammatory disease (rheumatoid arthritis, systemic lupus erythematosus, etc)
One platelet count ≥100 x 10^9/L within 4 weeks prior to study drug administration.	C-reactive protein level greater than 30 mg/L within the 4 weeks prior to study drug administration
	Febrile illness within 7 days prior to study drug administration
	Uncontrolled or symptomatic secondary hyperparathyroidism
	Poorly controlled hypertension within 4 weeks prior to study drug administration, per investigator's clinical judgment (eg, systolic

	blood pressure [SBP] ≥170 mm Hg, diastolic blood pressure [DBP] ≥100 mm Hg on repeat readings)
	Epileptic seizure in the 6 months prior to study drug administration
	Chronic congestive heart failure (New York Heart Association class IV)
	Evidence of malignancy within the past 5 years (except nonmelanoma skin cancer, which was not an exclusion criterion)
	Previous exposure to any investigational agent within 6 weeks prior to administration of study drug or planned receipt during the study period
	Any prior treatment with Eprex®
	Known hemolysis
	Known intolerance to any ESA

Supplementary Table 2. Guidelines for Dose Adjustments After Week 5.

Hemoglobin Parameter	**Action**
Increased by ≤0.5 g/dL from baseline[a]	Dose increase of 25%
Increased by >2.0 g/dL from baseline[a] within any 4-week period or to a concentration >12.5 g/dL	Dose decrease of 25%
Increased to a concentration >13.0 g/dL	The dose was delayed until the patient's hemoglobin was ≤12.5 g/dL, the dose was reduced by 25%, and the patient was phlebotomized at the discretion of the investigator

[a] Mean of the 3 hemoglobin values (2 screening values and 1 predose value) collected most recently before the first peginesatide dose.

Supplementary Table 3. Safety Narratives.

Type of Narrative	**Narrative**
Patient deaths	The first death was in an 83-year-old man. Twenty-seven days after his third dose of peginesatide, the patient was hospitalized for weakness, confusion, suspected infection, suspected digoxin toxicity, and suspected dehydration (final recorded hemoglobin concentration, 13.6 g/dL). The patient was treated with intravenous antibiotics, but his renal function deteriorated, resulting in death (investigator determined cause of death, chronic renal failure). The second death was in a 76-year-old man. Forty-three days after his third dose of peginesatide, the patient was hospitalized for fever, cough, and sputum production. After hospitalization, measurements of cardiac enzymes indicated new myocardial infarction. Eleven days after admission, the patient experienced a second myocardial infarction. Subsequently, the patient experienced sudden respiratory and circulatory arrest; attempts at resuscitation were unsuccessful (final recorded hemoglobin concentration, 11.3 g/dL). The investigator determined cause of death was bronchitis and acute myocardial infarction.
Embolic cerebral infarction	Confusion, loss of balance, and slurred speech were noted 13 days after this patient's third dose of peginesatide. The patient was admitted to the hospital with a diagnosis of transient ischemic attack.

	Although the investigator considered paroxysmal atrial fibrillation to likely have been the primary cause of the event, the investigator also believed that study-related increased hemoglobin concentration and blood pressure (14.0 g/dL and 205/117 mm Hg, respectively) on the day of onset of the event may have contributed to the embolic cerebral infarction. Following 9 days of hospitalization, the patient was discharged without sequelae.
Withdrawals because of nonserious AEs	One of these AEs (dizziness) was considered by the investigators to be possibly related to peginesatide. This patient began to experience dizziness 5 days after Dose 3. After Dose 6, the patient was terminated from the study because of the ongoing AEs of nausea and dizziness, both of which were assessed as grade 1. The AE of skin necrosis occurred in a patient who was receiving IV peginesatide.
Elevations of ALT	Overall, 4 patients had at least 1 elevation of ALT value that was greater than 3 times the ULN during the study. One patient had ALT values above the ULN at baseline and at all subsequent time points, another patient had a single ALT elevation above the ULN, while the remaining 2 patients had ALT values within the normal range at baseline but experienced several ALT elevations above the ULN during the trial. Three of these patients were receiving concomitant statin therapy, which has been associated with elevations in liver function test results. None of these ALT elevations were associated with a concurrent increase in total

	bilirubin ≥2x ULN. Nonserious AEs of abnormal liver function test results were reported in 2 of the patients. Nonserious AEs of increased blood lactate dehydrogenase and increased gammaglutamyl transferase were reported in 1 patient.

Abbreviations: AEs, adverse events; ALT, alanine aminotransferase; ULN, upper limit of normal; AEs, adverse events.