Treatment of Anemia in Zidovudine-treated HIV-infected Patients

For patients on CRF not requiring dialysis, a dose of 100,000 Units/kg/week was used in a non-randomized study in 1994. In this study, mean hemoglobin levels were maintained at approximately 13 g/dL in a group of 117 patients, with 60% of patients responding to EPOGEN® therapy. In a subsequent randomized study of two patient groups whose absolute neutrophil counts fell below 1000 cells/µL, mean hemoglobin levels of approximately 13 g/dL were maintained in 84% of patients in the EPOGEN® group compared to 38% of patients in the placebo group. In another study, a dose of 100,000 Units/kg/week was used in patients with end-stage renal disease (ESRD) who were not on regular dialysis. In this study, mean hemoglobin levels were maintained at approximately 13 g/dL in 76% of patients, with 60% of patients responding to EPOGEN® therapy. In a subsequent randomized study of two patient groups whose absolute neutrophil counts fell below 1000 cells/µL, mean hemoglobin levels of approximately 13 g/dL were maintained in 80% of patients in the EPOGEN® group compared to 38% of patients in the placebo group. In another study, a dose of 100,000 Units/kg/week was used in a non-randomized study in 1994. In this study, mean hemoglobin levels were maintained at approximately 13 g/dL in a group of 117 patients, with 60% of patients responding to EPOGEN® therapy. In a subsequent randomized study of two patient groups whose absolute neutrophil counts fell below 1000 cells/µL, mean hemoglobin levels of approximately 13 g/dL were maintained in 84% of patients in the EPOGEN® group compared to 38% of patients in the placebo group. In another study, a dose of 100,000 Units/kg/week was used in patients with end-stage renal disease (ESRD) who were not on regular dialysis. In this study, mean hemoglobin levels were maintained at approximately 13 g/dL in 76% of patients, with 60% of patients responding to EPOGEN® therapy. In a subsequent randomized study of two patient groups whose absolute neutrophil counts fell below 1000 cells/µL, mean hemoglobin levels of approximately 13 g/dL were maintained in 80% of patients in the EPOGEN® group compared to 38% of patients in the placebo group.

EPOGEN® is contraindicated in patients with:

- Pure red cell aplasia (PRCA), in association with neutralizing antibodies to native recombinant erythropoietin.
- Transferrin saturation ≤ 20%.
- Serum ferritin ≤ 100 ng/mL.
- Baseline hematocrit ≤ 30%.
- Baseline hemoglobin ≤ 10 g/dL.
- Baseline neutrophil count ≤ 1000 cells/µL.
- Baseline platelet count ≤ 100,000 cells/µL.
- Baseline creatinine ≥ 5 mg/dL.
- Baseline serum phosphorus ≥ 5.5 mg/dL.
- Baseline serum potassium ≥ 5.5 mEq/L.
- Baseline serum calcium ≥ 10.5 mg/dL.
- Baseline serum sodium ≤ 130 mEq/L.
- Baseline serum bicarbonate ≤ 16 mEq/L.
- Baseline serum aspartate transaminase ≥ 2.5 times the upper limit of normal.
- Baseline serum alanine transaminase ≥ 2.5 times the upper limit of normal.
- Baseline serum lactate dehydrogenase ≥ 1.5 times the upper limit of normal.
- Baseline serum bilirubin ≥ 1.5 times the upper limit of normal.
- Baseline serum creatinine phosphokinase ≥ 2.5 times the upper limit of normal.
- Baseline serum uric acid ≥ 7.0 mg/dL.
- Baseline serum cholesterol ≥ 6.5 mmol/L.
- Baseline serum triglycerides ≥ 2.5 mmol/L.
- Baseline serum total protein ≥ 6.5 g/dL.
- Baseline serum albumin ≤ 3.5 g/dL.
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In the US EPOGEN® studies in adult patients on dialysis (over 567 patients), hemoglobin of > 13 g/dL treated with 300 Units/kg of Epoetin alfa, the possibility is rare in patients treated with EPOGEN®. Nevertheless, blood pressure in patients treated with EPOGEN® (Epoetin alfa) 8 EPOGEN® (Epoetin alfa) 9 EPOGEN® (Epoetin alfa) 10 EPOGEN® (Epoetin alfa) 11 EPOGEN® (Epoetin alfa) 12 EPOGEN® (Epoetin alfa) 13 EPOGEN® (Epoetin alfa) 14 EPOGEN®. Therefore, blood pressure should be monitored carefully.

In perioperative clinical trials with orthopedic patients, the overall incidence of events due to EPOGEN® therapy was approximately 2.5% of patients) when compared to subsequent 90-day periods. The baseline incidence of events among patients treated with EPOGEN® includes a very rapid hematocrit response (eg, an increase of more than 10% in the first week following the first dose). Changes in hematocrit should be closely monitored to prevent development of hypertension or other hypertensive adverse effects.

Event (n = 200) (n = 135)

<table>
<thead>
<tr>
<th>Event</th>
<th>Percent of Patients Reporting Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>16%</td>
</tr>
<tr>
<td>Congestion</td>
<td>15%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>51%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>9%</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>10%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>21% a 7%</td>
</tr>
<tr>
<td>Headache</td>
<td>37%</td>
</tr>
<tr>
<td>Rash</td>
<td>8%</td>
</tr>
<tr>
<td>Constipation</td>
<td>12%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>9%</td>
</tr>
<tr>
<td>Dehydration</td>
<td>10%</td>
</tr>
<tr>
<td>Headache</td>
<td>9%</td>
</tr>
<tr>
<td>Weakness</td>
<td>9%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>9%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>6%</td>
</tr>
<tr>
<td>Convulsion</td>
<td>6%</td>
</tr>
<tr>
<td>Infection</td>
<td>9%</td>
</tr>
<tr>
<td>CVA/TIA</td>
<td>0.4% 0.6%</td>
</tr>
</tbody>
</table>

The hematocrit should be monitored on a weekly basis in patients receiving EPOGEN®. The hematocrit should be maintained within the suggested target range of 36% to 40% for most patients. If the hematocrit is increasing and approaching 36%, the dose should be decreased. If the hematocrit remains at or above the target range of 36% for 4 weeks, the dose may be increased. The dose should be increased at intervals of no less than 4 weeks and no greater than 12 weeks. The dose should be increased at intervals of no less than 4 weeks and no greater than 12 weeks. The dose should be increased at intervals of no less than 4 weeks and no greater than 12 weeks. The dose should be increased at intervals of no less than 4 weeks and no greater than 12 weeks.

The table below provides general therapeutic guidelines for the management of anemia in patients on EPOGEN® therapy. The table is intended to guide clinical decision-making and is not intended to be a comprehensive list of all possible dosing regimens. It is important that clinicians exercise caution when considering the use of EPOGEN® in the treatment of anemia in patients with a history of or recent history of cancer, particularly myeloid malignancies, neoplasms, or other hematopoietic disorders.

| Incidence of the above events. | 15. Geva P, Sherwood JB. Pharmacokinetics of recombinant human erythropoietin (r-HuEPO) with high flux dialysis (HFD) does not worsen azotemia compared to high-flux hemodialysis (HFD) with standard dialyzers. Kidney Int. 1989;33:239.