

**New Drug Bulletin:**  
**Eculizumab (Soliris®) - Alexion Pharmaceuticals)**

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Eculizumab is a recombinant humanized IgG monoclonal antibody approved by the FDA on March 16, 2007 for the reduction of hemolysis in patients with paroxysmal nocturnal hemoglobinuria (PNH). Eculizumab binds to the complement protein C5 and prevents its cleavage as well as the formation of the terminal complement complex C5b-9. Inhibiting the terminal complement complex prevents erythrocyte lysis and prolongs the survival of erythrocytes which reduces signs of hemolysis in patients; however, this inhibition may also increase a patient's susceptibility to infections.

Eculizumab is administered as an intravenous infusion and has an average clearance of 22 mL/hour and an average volume of distribution of 7.7 liters. The mean half-life is 272 hours. Other pharmacokinetic parameters are not available. Pharmacokinetic parameters have not been evaluated in special patient populations.

The efficacy of eculizumab was assessed in 87 PNH patients with hemolysis in a randomized, double-blind, placebo-controlled, 26-week study. Eculizumab significantly reduced hemolysis ( $p < 0.001$ ), increased hemoglobin stabilization (eculizumab = 49%; placebo = 0%), and decreased the need for red blood cell transfusions (transfusion avoidance: eculizumab = 51%; placebo = 0%). Less fatigue and improved health-related quality of life were also reported by the patients receiving eculizumab compared to those receiving placebo. Efficacy was maintained with eculizumab therapy for up to 54 months in an extension study.

The most serious adverse reaction associated with eculizumab therapy is meningococcal infections. Eculizumab is contraindicated in patients who are not vaccinated against *Neisseria meningitidis* or who have *Neisseria meningitidis* infections. Other serious adverse reactions reported with eculizumab include anemia, headache, pyrexia, and viral infections. The most common adverse reactions with eculizumab include headache (44%), nasopharyngitis (23%), back pain (19%), and nausea (16%). Drug-drug interaction studies have not been conducted with eculizumab.

Administer eculizumab 600 mg every 7 days for the first 4 weeks, and follow with 900 mg for the fifth dose 7 days later, then 900 mg every 14 days thereafter. Administer doses within two days of these time points. Give eculizumab as a 5 mg/mL intravenous infusion over 35 minutes via gravity feed, a syringe pump, or an infusion pump. Do not administer eculizumab as an intravenous push or bolus injection. Allow the infusion solution mixture to adjust to room temperature (64 -77° F) before administering. Slow or stop eculizumab administration in patients experiencing infusion reactions and administer appropriate medical therapy as needed. Do not exceed two hours for the total infusion time. All patients must be monitored for signs and symptoms of infections. Monitor patients for signs of serious hemolysis for at least 8 weeks after eculizumab discontinuation.

Eculizumab is supplied as 10 mg/mL, 300 mg, single-use, preservative-free vials which must be stored in the original container, away from light, and in a refrigerator until use. Do not freeze or shake vials. The average wholesale price (AWP) for an eculizumab 300mg vial is \$5990. The wholesale acquisition cost (WAC) is \$4992.

In summary, eculizumab is a monoclonal antibody that inhibits terminal complement activation which reduces hemolysis and transfusion requirements in patients with PNH. It is the first product approved by the FDA specifically for the treatment of hemolysis in patients with PNH. Eculizumab provides another treatment option for patients limited by medication toxicity as well as inconsistent efficacy associated with other PNH therapies.

#### Reference

1. Soliris® (eculizumab) package insert. Cheshire, CT: Alexion Pharmaceuticals, Inc; March 2007.
2. Red Book UPDATE, June 2007. Montvale, NJ: Thompson PDR; 2007.

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