CLINICAL UPDATE

Brand Name	Ultomiris®
Generic Name	ravulizumab-cwvz
Drug Manufacturer	Alexion Pharmaceuticals, Inc

Clinical Update

TYPE OF CLINICAL PDATE

Clinical Update - New strength (100mg/mL)

FDA APPROVAL DATE

October 09, 2020

LAUNCH DATE

October 16, 2020

REVIEW DESIGNATION

Orphan

TYPE OF REVIEW

Not available

DISPENSING RESTRICTIONS

Limited - REMS Program

Overview

INDICATION(S) FOR USE

Ultomiris® is a complement inhibitor indicated for:

- The treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).
- The treatment of adults and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

MECHANISMS OF ACTION

Ravulizumab-cwvz is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a (the proinflammatory anaphylatoxin) and C5b (the initiating subunit of the terminal complement complex [C5b-9]) and preventing the generation of the terminal complement complex C5b9. Ultomiris® inhibits terminal complement-mediated intravascular hemolysis in patients with PNH and complement-mediated thrombotic microangiopathy (TMA) in patients with aHUS.

DOSAGE FORM(S) AND STRENGTH(S)

Injection:

- 300 mg/30 mL (10 mg/mL) in a single-dose vial
- 300 mg/3 mL (100 mg/mL) in a single-dose vial
- 1,100 mg/11 mL (100 mg/mL) in a single-dose vial

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DOSE & ADMINISTRATION

The recommended dosing regimen in adult patients with PNH weighing 40 kg or greater, consists of a loading dose followed by maintenance dosing, administered by intravenous infusion. Administer the doses based on the patient's body weight, as shown in Table 1. Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 8-week interval.

Table 1: ULTOMIRIS Weight-Based Dosing Regimen - PNH

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Dosing Interval	
40 to less than 60	2,400	3,000	Every 8 weeks
60 to less than 100	2,700	3,300	
100 or greater	3,000	3,600	

The recommended dosing regimen in adult and pediatric patients one month of age and older with aHUS weighing 5 kg or greater, consists of a loading dose followed by maintenance dosing, administered by intravenous infusion. Administer the doses based on the patient's body weight, as shown in Table 2. Starting 2 weeks after the loading dose administration, begin maintenance doses once every 8 weeks or every 4 weeks (depending on body weight).

Table 2: ULTOMIRIS Weight-Based Dosing Regimen - aHUS

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Dosing Interval	
5 to less than 10	600	300	Every 4 weeks
10 to less than 20	600	600	
20 to less than 30	900	2,100	Every 8 weeks
30 to less than 40	1,200	2,700	
40 to less than 60	2,400	3,000	
to less than 100	2,700	3,300	
100 or greater	3,000	3,600	

Only administer as an intravenous infusion. Dilute Ultomiris® in an infusion bag using 0.9% Sodium Chloride Injection, USP to a final concentration of:

- 50 mg/mL for the 3 mL and 11 mL vial sizes or
- 5 mg/mL for the 30 mL vial size.

Administer Ultomiris® only through a 0.2 or 0.22 micron filter.

EFFICACY

The approval was based on a comprehensive chemistry, manufacturing and control submission and supplementary clinical data that showed comparable safety and efficacy data between Ultomiris® 10mg/mL and

100mg/mL. Findings showed that the 100mg/mL formulation required an infusion time of 0.4 to 1.3 hours depending on body weight compared with 1.3 to 3.3 hours for the 10mg/mL formulation. Ultomiris® 100mg/mL reduced the average annual infusion times by approximately 60% compared with the 10mg/mL formulation.