

# TREATMENT-NAÏVE PEDIATRIC PATIENT WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (ATYPICAL-HUS): A CASE STUDY

**ULTOMIRIS**<sup>®</sup>  
(ravulizumab-cwvz)  
injection for intravenous use  
300 mg/3 mL vial

TO PROTECT THE PRIVACY OF PATIENTS,  
PHOTOS ARE FOR ILLUSTRATION ONLY

## SELECT IMPORTANT SAFETY INFORMATION

### WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

**ULTOMIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [see Warnings and Precautions (5.1)] Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.**

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. See Warnings and Precautions (5.1) for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving ULTOMIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

**Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [see Warnings and Precautions (5.2)].**

### INDICATION

ULTOMIRIS is indicated for the treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

#### Limitation of Use:

ULTOMIRIS is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information ([UltomirisHCP.com/PI](http://UltomirisHCP.com/PI)) for ULTOMIRIS, including **Boxed WARNING** regarding serious and life-threatening or fatal meningococcal infections.**



This is Patrick. He is 4 years old and was just diagnosed with atypical-HUS.

“WHEN PATRICK GOT SICK, I DIDN’T KNOW WHAT TO DO.”

— Patrick’s dad



Case presented by:

**Teri Mauch, MD, PhD**

Dr. Mauch is a paid consultant of Alexion Pharmaceuticals, Inc., and was compensated for her time.



Based on an actual patient in the 312 study<sup>1</sup>

**Patrick**

**Age:** 4 years old

**Height:** 104.5 cm (3 ft 5 in)

**Weight:** 17.5 kg (38.6 lbs)

**Diagnosed with atypical-HUS**

**Family history**

- Family history of diabetes, kidney disease, and anatomical defects of kidneys

**Select signs and symptoms at presentation**

- Vital signs: BP: 123/81, Temp: 37°C (98.6°F), HR: 120, RR: 26
- Seizures, cough, and emesis
- Patient had a single functioning kidney
- Patient had evidence of cerebellar lesions (possibly pre-existing)
- Patient did not present with fever or diarrhea

ADAMTS13=a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13; BP=blood pressure; eGFR=estimated glomerular filtration rate; HR=heart rate; HUS=hemolytic uremic syndrome; LDH=lactate dehydrogenase; RR=respiratory rate; TTP=thrombotic thrombocytopenic purpura.

**LAB VALUES AT DAY 1<sup>1,a</sup>**

<b>Hemoglobin (g/L)</b> (reference range: 107-139 g/L)	<b>79</b>
<b>LDH (U/L)</b> (reference range: 155-345 U/L)	<b>2228</b>
<b>Platelet count (x 10<sup>9</sup>/L)</b> (reference range: 217-497 x 10 <sup>9</sup> /L)	<b>41</b>
<b>Creatinine (ranges μmol/L)</b> (reference range: 18-62 μmol/L)	<b>256</b>
<b>eGFR (mL/min/1.73 m<sup>2</sup>)</b>	<b>15</b>
<b>Urine protein/creatinine (mg/mmol)</b> (reference range: <20 mg/mmol) <sup>2</sup>	<b>1252</b>
<b>ADAMTS13 activity (%)<sup>3,b</sup></b>	<b>76</b>
<b>Albumin (g/L)</b> (reference range: 32-47 g/L)	<b>27</b>

<sup>a</sup>Day 1 is relative to first dose of ULTOMIRIS administered intravenously.

<sup>b</sup>>5% ADAMTS activity=atypical-HUS. ≤5% ADAMTS13 activity=TTP (range found in published data is 5%-10%).

**SELECT IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS**

- Initiation in patients with unresolved serious *Neisseria meningitidis* infection.

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## Diagnosing atypical-HUS requires excluding other conditions<sup>1,3-5</sup>

- Patient showed evidence of TMA, including
  - Thrombocytopenia
  - Elevated LDH levels
  - Decreased hemoglobin levels
  - Evidence of microangiopathic hemolysis
  - Other symptoms:
    - Acute kidney injury, seizures, emesis, and new hypertension
- Patient had a negative stool test for Shiga toxin-producing *E coli* and a negative Coombs test<sup>1</sup>
- Patient had a negative Shiga toxin panel and ADAMTS13 activity of 76%, which ruled out TTP and STEC-HUS, indicating

atypical-HUS: a rare, life-threatening disease caused by dysregulation of the alternative pathway of the complement system<sup>1,3,5</sup>

- While not required for diagnosis, genetic analysis was performed, with the following results<sup>3</sup>
  - Het missense (c.359A>G, p.Asp120Gly) in exon 3 of *MASP*. This variant is associated with impairment of the Mannan-binding lectin pathway of the complement system. Its contribution to atypical-HUS is unknown<sup>6</sup>
  - Het, silent variant (c.417A>G, p.Leu139Leu) in exon 4 of *MCP*<sup>7</sup>



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## Differential diagnosis of TMA, including atypical-HUS<sup>3,5,8,9</sup>

Thrombocytopenia  
Platelet count  $<150 \times 10^9/L$   
or  $>25\%$  decrease from baseline

AND

Microangiopathic hemolysis  
Schistocytes and/or elevated LDH  
and/or decreased haptoglobin  
and/or decreased hemoglobin

## Plus 1 or more of the following

### Common symptoms

#### Neurological symptoms

Confusion and/or seizures  
and/or stroke and/or other cerebral  
abnormalities

#### Renal impairment

Elevated creatinine level and/or  
decreased eGFR and/or elevated  
blood pressure and/or abnormal  
urinalysis results

#### GI symptoms

Diarrhea  $\pm$  blood and/or nausea/  
vomiting and/or abdominal pain  
and/or gastroenteritis/pancreatitis

### Other symptoms

#### CV symptoms

MI and/or hypertension and/or arterial  
stenosis and/or peripheral gangrene

#### Pulmonary symptoms

Dyspnea and/or pulmonary hemorrhage  
and/or pulmonary edema

#### Visual symptoms

Pain and blurred vision and/or  
retinal vessel occlusion and/or  
ocular hemorrhage

## Evaluate ADAMTS13 activity and Shiga toxin/EHEC test<sup>a</sup>

While ADAMTS13 results are awaited, a platelet count  $>30 \times 10^9/L$  and/or sCr  $>1.7$  to  $2.3 \text{ mg/dL}$ <sup>b</sup> almost eliminates a diagnosis of severe ADAMTS13 deficiency (TTP)

$\leq 5\%$ <sup>c</sup> ADAMTS13 activity

TTP

$>5\%$  ADAMTS13 activity

Atypical-HUS

Shiga toxin/EHEC positive

STEC-HUS<sup>a</sup>

<sup>a</sup>Shiga toxin/EHEC test is warranted with history/presence of gastrointestinal symptoms.

<sup>b</sup>This is from a compilation of adult and pediatric studies.

<sup>c</sup>Range found in published data is 5%-10%.

CV=cardiovascular; EHEC=enterohemorrhagic *Escherichia coli*; GI=gastrointestinal; MI=myocardial infarction; sCr=serum creatinine; STEC=Shiga toxin-producing *Escherichia coli*; TMA=thrombotic microangiopathy; TTP=thrombotic thrombocytopenic purpura.





## Pediatric study design

- The pediatric study was a 26-week, ongoing, multicenter, open-label, single-arm study of 16 pediatric patients, of which 14 ecuzumab-naïve patients with documented diagnosis of atypical-HUS were enrolled and included in this interim analysis<sup>10</sup>
- Primary endpoint: complete TMA response, defined as normalization of hematological parameters (platelet count and LDH normalization)<sup>c</sup> and ≥25% improvement in serum creatinine from baseline during the 26-week initial evaluation period. Patients had to meet all complete TMA response criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and any measurement in between<sup>10</sup>
- Select secondary endpoints: time to complete TMA response and complete TMA response status over time, dialysis requirement and CKD stage as evaluated by eGFR, hemoglobin response, and change from baseline in quality of life<sup>1,10</sup>

## Pediatric study results

- Complete TMA response during the initial evaluation period was achieved at a median time of 30 days (range: 15 to 88 days). The median duration of complete TMA response was 5.08 months (range: 3.08 to 5.54 months). All responses were maintained through all available follow-up<sup>10</sup>
- An increase in mean platelet count was observed after commencement of ULTOMIRIS, increasing from 60.50 x 10<sup>9</sup>/L at baseline to 296.67 x 10<sup>9</sup>/L at Day 8, and remained above 296 x 10<sup>9</sup>/L at all subsequent visits in the initial evaluation period (26 weeks). The mean eGFR (+/- SD) increased from 28.4 (23.11) at baseline to 108.0 (63.21) by 26 weeks<sup>10</sup>
- The most frequent adverse reactions reported in ≥20% of pediatric patients treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, constipation, vomiting, headache, hypertension, and pyrexia. Clinically relevant adverse reactions in <10% of pediatric patients included viral infection<sup>10</sup>

## Efficacy results in aHUS during the 26-week initial evaluation period (ALXN1210-aHUS-312)

	TOTAL	RESPONDER	
		n	PROPORTION (95% CI) <sup>d</sup>
<b>Complete TMA response</b>	14	10	71% (42%-92%)
<b>Components of complete TMA response</b>			
Platelet count normalization	14	13	93% (66%-99%)
LDH normalization	14	12	86% (57%-98%)
≥25% improvement in serum creatinine from baseline	14	11	79% (49%-95%)
<b>Hematologic normalization (platelet count and LDH normalization)</b>	14	12	86% (57%-98%)

<sup>a</sup>The mean (%CV) terminal elimination half-life and clearance of ULTOMIRIS in patients with atypical-HUS are 51.8 (31.3) days and 0.08 (53.3) L/day, respectively. Half-life of ecuzumab is 11.25 to 17.25 days.<sup>10,11</sup>

<sup>b</sup>Targeted engineering to incorporate 4 amino acid substitutions designed to reduce TMDD and enhance FcRn-mediated recycling into ecuzumab has led to the generation of ULTOMIRIS, which exhibited an extended duration of action in preclinical models relative to ecuzumab.<sup>12</sup>

<sup>c</sup>Includes ≥150 x 10<sup>9</sup>/L for platelet count and a value less than the upper limit of normal for LDH.<sup>1</sup>

<sup>d</sup>95% CIs for the proportion were based on exact confidence limits using the Clopper-Pearson method.

CI=confidence interval; CKD=chronic kidney disease; FcRn=human neonatal Fc receptor; LDH=lactate dehydrogenase; TMA=thrombotic microangiopathy; TMDD=target-mediated drug disposition.

## Treatment discussion

- Discussed treatment options, including ULTOMIRIS risks and benefits. Parents felt ULTOMIRIS was the preferred option due to its long half-life, weight-based dosing for pediatric patients, safety profile and benefits, and every 4-week dosing interval<sup>10</sup>
- Because of the high morbidity of atypical-HUS, parents were willing to start treatment immediately<sup>2</sup>

## What is ULTOMIRIS?

- ULTOMIRIS, built on the foundation of ecuzumab, is a C5 inhibitor that has an ~4X longer half-life and a dosing schedule of maintenance doses every 4 or 8 weeks for pediatric patients (depending on body weight), starting 2 weeks after an initial loading dose<sup>10-12,a,b</sup>

## SELECT IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

#### Serious Meningococcal Infections

ULTOMIRIS, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Revaccinate patients in accordance with ACIP recommendations considering the duration of ULTOMIRIS therapy. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according

to ACIP recommendations, provide antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, as well as those associated with antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis*.

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**







**Patrick's parents were concerned about his diagnosis. Yet they were happy that ULTOMIRIS provided a path forward in managing his atypical-HUS.**

## ULTOMIRIS treatment

- Based on patient's weight of 17.5 kg, he was placed on a 600-mg initial loading dose of ULTOMIRIS within 12 hours post-diagnosis of atypical-HUS<sup>1,10</sup>
  - Within a day of receiving the first dose of ULTOMIRIS, patient was vaccinated with pneumococcal vaccine, meningococcal vaccine B, and meningococcal vaccine A/C/Y/W according to current Advisory Committee on Immunization Practices (ACIP) guidelines to reduce the risk of serious infection<sup>1,10</sup>
  - Patient was also prescribed 2 weeks of antibacterial drug prophylaxis, since ULTOMIRIS was initiated immediately and vaccines were administered less than 2 weeks before starting ULTOMIRIS<sup>1,10</sup>
- Starting 2 weeks after the initial loading dose, 600-mg maintenance doses were administered once every 4 weeks<sup>1,10</sup>
- Patient remained hospitalized for several weeks and required 3 packed red blood cell transfusions during the first week of treatment<sup>1</sup>
  - Patient exhibited complete TMA response<sup>a</sup> by Day 22 and maintained it through Day 351
  - His kidney function also showed improvement<sup>b</sup>

- Parents were advised that patient's ULTOMIRIS dose would be adjusted and dosing schedule increased to every 8 weeks as his weight increased to 20 kg and over<sup>10</sup>
- No adverse events were reported
  - The most frequent adverse reactions reported in ≥20% of adult and pediatric patients treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension and pyrexia<sup>10</sup>
- No signs or symptoms of infusion-related reactions were reported
  - Monitor the patient for at least one hour following completion of the infusion for signs or symptoms of an infusion-related reaction<sup>10</sup>
  - Administration of ULTOMIRIS may result in infusion-related reactions. In clinical trials, 5 out of 296 patients treated with ULTOMIRIS experienced infusion-related reactions (lower back pain, drop in blood pressure, infusion-related pain, elevation in blood pressure and limbs discomfort) during ULTOMIRIS administration which did not require discontinuation. Interrupt infusion and institute supportive measures if signs of cardiovascular instability or respiratory compromise occur<sup>10</sup>

## SELECT IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection depending on the risks of interrupting treatment in the disease being treated.

### ULTOMIRIS and SOLIRIS REMS

Due to the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program called ULTOMIRIS and SOLIRIS REMS.

Prescribers must enroll in the REMS, counsel patients about the risk of serious meningococcal infection, provide patients with the REMS educational materials, assess patient vaccination status for meningococcal vaccines (against serogroups A, C, W, Y, and B) and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of ULTOMIRIS. Antibacterial drug prophylaxis must be prescribed if treatment must be started urgently, and the patient is not up to date with both meningococcal vaccines according to current ACIP recommendations at least two weeks prior to the first dose of ULTOMIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card at all times during and for 8 months following ULTOMIRIS treatment.

Further information is available at [www.UltSolREMS.com](http://www.UltSolREMS.com) or [1-888-765-4747](tel:1-888-765-4747).

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information (UltomirisHCP.com/PI) for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.**

LAB VALUES	WEEK 1	WEEK 2	WEEK 4	WEEK 12	WEEK 26	WEEK 52
<b>Hemoglobin (g/L)</b> (reference range: 107-139 g/L)	83	87	117	121	115	128
<b>LDH (U/L)</b> (reference range: 155-345 U/L)	2480	808	310	302	244	271
<b>Platelet count (x 10<sup>9</sup>/L)</b> (reference range: 217-497 x 10 <sup>9</sup> /L)	N/A	243	395	350	344	246
<b>Creatinine (μmol/L)</b> (reference range: 18-62 μmol/L)	62	53	35	27	35	35
<b>eGFR (mL/min/1.73 m<sup>2</sup>)</b>	62	72	106	141	108	111
<b>Urine protein/creatinine (mg/mmol)</b> (reference range: <20 mg/mmol) <sup>2</sup>	N/A	269	15	11	8	9
<b>Albumin (g/L)</b> (reference range: 32-47 g/L)	28	35	41	42	39	40

<sup>a</sup>Complete TMA response was defined as normalization of hematological parameters (platelet count and LDH) and ≥25% improvement in serum creatinine from baseline during the 26-week initial evaluation period. Patients had to meet all criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart and any measurement in between.

<sup>b</sup>Secondary endpoint.

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### WARNINGS AND PRECAUTIONS (continued)

#### Other Infections

Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Children treated with ULTOMIRIS may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) infections according to ACIP recommendations. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

#### Monitoring Disease Manifestations after ULTOMIRIS Discontinuation

ULTOMIRIS treatment of aHUS should be a minimum duration of 6 months. Due to heterogeneous nature of aHUS events and patient-specific risk factors, treatment duration beyond the initial 6 months should be individualized. There are no specific data on ULTOMIRIS discontinuation. After discontinuing treatment with ULTOMIRIS, patients should be monitored for clinical symptoms and laboratory signs of TMA complications for at least 12 months. TMA complications post-discontinuation can be identified if any of the following is observed: Clinical symptoms of TMA include changes in mental status, seizures, angina, dyspnea, thrombosis or increasing blood pressure. In addition, at least two of the following laboratory signs observed concurrently and results should be confirmed by a second measurement 28 days apart with no interruption: a decrease in platelet count of 25% or more as compared to either baseline or to nadir during ULTOMIRIS treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during ULTOMIRIS treatment. If TMA complications occur after discontinuation, consider reinitiation of ULTOMIRIS treatment or appropriate organ-specific supportive measures.

#### Thromboembolic Event Management

The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

#### Infusion-Related Reactions

Administration of ULTOMIRIS may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients, including lower back pain, abdominal pain, muscle spasms, drop or elevation in blood pressure, rigors, limb discomfort, drug hypersensitivity (allergic reaction), and dysgeusia (bad taste). These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS and institute appropriate supportive measures.

#### ADVERSE REACTIONS

Most common adverse reactions in patients with aHUS (incidence  $\geq 20\%$ ) were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension and pyrexia. Serious adverse reactions were reported in 42 (57%) patients with aHUS receiving ULTOMIRIS. The most frequent serious adverse reactions reported in more than 2 patients (2.7%) treated with ULTOMIRIS were hypertension, pneumonia and abdominal pain.

Adverse reactions reported in  $\geq 20\%$  of pediatric patients treated with ULTOMIRIS were diarrhea, constipation, vomiting, pyrexia, upper respiratory tract infection, decreased vitamin D, headache, cough, rash, and hypertension.

#### DRUG INTERACTIONS

##### Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins

Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

##### Neonatal Fc Receptor Blockers

Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

#### USE IN SPECIFIC POPULATIONS

##### Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ULTOMIRIS during pregnancy. Healthcare providers and patients may call [1-833-793-0563](tel:1-833-793-0563) or go to [www.UltomirisPregnancyStudy.com](http://www.UltomirisPregnancyStudy.com) to enroll in or to obtain information about the registry.

**To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at [1-844-259-6783](tel:1-844-259-6783) or FDA at [1-800-FDA-1088](tel:1-800-FDA-1088) or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

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