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

ULTOMIRIS Frequently Asked Questions (FAQ) for Patients With Atypical-HUS (aHUS)

Answers to your questions about ULTOMIRIS and how to make the transition

INDICATION

What is ULTOMIRIS?

ULTOMIRIS is a prescription medicine used to treat:

- adults and children 1 month of age and older with a disease called atypical Hemolytic Uremic Syndrome (aHUS). ULTOMIRIS is not used in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).
- adults with aHUS when administered subcutaneously (under your skin).

It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age. Subcutaneous administration of ULTOMIRIS has not been evaluated and is not approved for use in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ULTOMIRIS?

ULTOMIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections.

- ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections that may quickly become life-threatening and cause death if not recognized and treated early.

1. You must receive meningococcal vaccines at least 2 weeks before your first dose of ULTOMIRIS if you are not vaccinated.
2. If your healthcare provider decided that urgent treatment with ULTOMIRIS is needed, you should receive meningococcal vaccination as soon as possible.
3. If you have not been vaccinated and ULTOMIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations.
4. If you had a meningococcal vaccine in the past, you might need additional vaccination. Your healthcare provider will decide if you need additional vaccination.
5. Meningococcal vaccines reduce but do not prevent all meningococcal infections. Call your healthcare provider or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection: headache with nausea or vomiting, headache and fever, headache with a stiff neck or stiff back, fever, fever and a rash, confusion, muscle aches with flu-like symptoms and eyes sensitive to light.

Remember to speak with your doctor about your symptoms and how to manage atypical-HUS

Please see full Prescribing Information and Medication Guide for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis. Please see Indication and Important Safety Information throughout and on page 8.

HOW DOES ULTOMIRIS WORK?

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1. How does ULTOMIRIS work?

- Part of your immune system called complement protein 5 (C5) plays an important role in helping your body destroy foreign or damaged cells. Normally, control mechanisms in your body keep C5 and other complement proteins from attacking healthy cells.[1]
- In atypical-HUS, these control mechanisms fail, and uncontrolled C5 activity ultimately results in thrombotic microangiopathy (TMA), or blood clots in your small blood vessels. This TMA is what ultimately causes organ failure in atypical-HUS.[2]
- ULTOMIRIS works by binding to C5 and inhibiting its activity to prevent TMA events from occurring.[3,4]

ULTOMIRIS works by binding to C5 and inhibiting its activity to prevent TMA events

2. What is the difference between SOLIRIS® (eculizumab) and ULTOMIRIS?

- ULTOMIRIS was built on the foundation of SOLIRIS, but with modifications that allow it to last longer in the body.[4,5] This allows ULTOMIRIS to keep working longer between infusions–so that after your starting dose, you only need to be infused every 4 or 8 weeks (depending on body weight), compared to every 2 weeks with SOLIRIS.[3]

After your starting dose, you only need to be infused every 4 or 8 weeks (depending on body weight), instead of every 2 weeks

3. Does ULTOMIRIS block C5 immediately after the first infusion, or is there a delay before C5 is controlled?

- ULTOMIRIS controls C5 immediately. 100% (70 out of 70) of clinical trial patients (adult and pediatric) on ULTOMIRIS had complete C5 control by the end of their first infusion.[6,7]

ULTOMIRIS controls C5 immediately

4. If ULTOMIRIS is dosed up to every 8 weeks, does it "wear off" near the end of the treatment cycle?

- ULTOMIRIS is administered as a starting dose followed by maintenance doses every 4 or 8 weeks (depending on body weight) starting 2 weeks after the starting dose.[3]
- With ULTOMIRIS, C5 control is sustained, meaning it lasts the full 8 weeks between infusions for adult patients. Depending on body weight, pediatric patients receive infusions every 4 or 8 weeks in order to experience the same sustained C5 control.[3]
- You can feel confident in complete and sustained C5 control with ULTOMIRIS.[3]

With ULTOMIRIS, C5 control is sustained for up to 8 weeks

IMPORTANT SAFETY INFORMATION (CONT'D)

Your healthcare provider will give you a Patient Safety Card about the risk of meningococcal infection. Carry it with you at all times during treatment and for 8 months after your last ULTOMIRIS dose. It is important to show this card to any healthcare provider or nurse to help them diagnose and treat you quickly.

ULTOMIRIS is only available through a program called the ULTOMIRIS REMS. Before you can receive ULTOMIRIS, your healthcare provider must: enroll in the ULTOMIRIS REMS program; counsel you about the risk of meningococcal infection; give you information and a **Patient Safety Card** about the symptoms and your risk of meningococcal infection (as discussed above); and make sure that you are vaccinated with a meningococcal vaccine, and if needed, get revaccinated with the meningococcal vaccine. Ask your healthcare provider if you are not sure if you need to be revaccinated.

ULTOMIRIS may also increase the risk of other types of serious infections. Make sure your child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) if treated with ULTOMIRIS. Call your healthcare provider right away if you have any new signs or symptoms of infection.

WHAT RESULTS WERE SEEN IN ATYPICAL-HUS PATIENTS WHO TOOK ULTOMIRIS?

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5. What results were seen in atypical-HUS patients who took ULTOMIRIS?

- Study designs[3]:
  - 26-week study of adult patients (N=56) with no prior treatment for atypical-HUS; other causes of TMA were ruled out
  - 26-week ongoing study of pediatric patients (N=14) with no prior treatment for atypical-HUS; other causes of TMA were ruled out
- Our trials focused on "Complete TMA Response" as a measure of success. Complete TMA Response is made up of three parts: Platelet normalization, lactate dehydrogenase (LDH) normalization, and ≥25% improvement in serum creatinine levels, a measure of kidney function.[3]
- Patients had to meet all three criteria in order to count as a Complete TMA Response. For example, if a patient had improvements in 1 or 2 measurements, these improvements were not counted as a Complete TMA Response.[3]

In Two Separate Trials[3]

SAW THEIR PLATELET LEVELS RETURN TO NORMAL	SAW THEIR LDH LEVELS RETURN TO NORMAL	SAW ≥25% IMPROVEMENT IN THEIR SERUM CREATININE LEVELS (KIDNEY FUNCTION)
84% (47 out of 56) of adult patients	77% (43 out of 56) of adult patients	59% (33 out of 56) of adult patients
93% (13 out of 14) of pediatric patients	86% (12 out of 14) of pediatric patients	79% (11 out of 14) of pediatric patients

54% (30 out of 56) of adult patients | 71% (10 out of 14) of pediatric patients

HAD A COMPLETE TMA RESPONSE

Of the adult and pediatric patients who achieved Complete TMA Response, 100% (50 out of 50) of them maintained their response throughout the 26-week study period.[3]

73% (41 out of 56) of adult patients | 86% (12 out of 14) of pediatric patients

HAD HEMATOLOGIC NORMALIZATION[a]

[a]Hematologic normalization is a combination of platelet count normalization and LDH normalization.

6. How extensively has ULTOMIRIS been studied?

- ULTOMIRIS has been studied in 4 Phase 3 clinical trials, with over 500 patients across 2 diseases, including atypical-HUS.[3]

4 Phase 3 clinical trials over 500 patients across 2 diseases, including atypical-HUS

- The Phase 3 study of ULTOMIRIS in adults was the largest clinical trial of a long-acting treatment ever conducted in atypical-HUS.[8]

IMPORTANT SAFETY INFORMATION (CONT'D)

Who should not receive ULTOMIRIS?
Do not receive ULTOMIRIS if you have a meningococcal infection or have not been vaccinated against meningococcal infection unless your healthcare provider decides that urgent treatment with ULTOMIRIS is needed.

Before you receive ULTOMIRIS, tell your healthcare provider about all of your medical conditions, including if you: have an infection or fever, are pregnant or plan to become pregnant, and are breastfeeding or plan to breastfeed. It is not known if ULTOMIRIS will harm your unborn baby or if it passes into your breast milk. You should not breastfeed during treatment and for 8 months after your final dose of ULTOMIRIS.

Tell your healthcare provider about all the vaccines you receive and medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

7. How safe is ULTOMIRIS in atypical-HUS patients?

- ULTOMIRIS has an established safety profile based on 4 Phase 3 clinical trials across 2 diseases, including atypical-HUS.[3] The safety profile of ULTOMIRIS in adult patients is based on results from the largest clinical trial of a long-acting treatment ever conducted in atypical-HUS.[8]
- The most frequently reported side effects in people with atypical-HUS treated with ULTOMIRIS were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, high blood pressure, and fever.[3]
  - The majority of side effects with ULTOMIRIS were mild or moderate in intensity.[3]
- ULTOMIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections. ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections that may quickly become life-threatening and cause death if not recognized and treated early. Your doctor will ensure you receive meningococcal vaccinations prior to treatment.[3]
- ULTOMIRIS can cause serious side effects, including infusion-related reactions (lower back pain, feeling faint or discomfort in your arms or legs). Tell your doctor or nurse right away if you develop these symptoms or any other symptoms during your ULTOMIRIS infusion. These reactions do not require discontinuation, but your doctor may slow or interrupt the infusion.[3]

ULTOMIRIS has an established safety profile based on 4 Phase 3 clinical trials across 2 diseases, including atypical-HUS

8. What are the vaccination requirements for ULTOMIRIS?

- With ULTOMIRIS, you should receive meningococcal vaccines at least 2 weeks prior to your first dose of ULTOMIRIS if you have not already had this vaccine.[3]
- Your doctor will ensure you are properly vaccinated before beginning treatment.

You will receive meningococcal vaccines 2 weeks before your first dose of ULTOMIRIS

9. Is ULTOMIRIS safe for atypical-HUS patients who are pregnant or breastfeeding?

- ULTOMIRIS has not been studied in atypical-HUS patients who are pregnant or breastfeeding. Talk to your doctor about how to best manage your condition during and after pregnancy.[3]

Talk to your doctor about how to best manage your condition during and after pregnancy

HOW DOES ULTOMIRIS RELATE IN TERMS OF COST AND INFUSION LOGISTICS?

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10. Is ULTOMIRIS more expensive than SOLIRIS?

- ULTOMIRIS is priced to be less expensive than SOLIRIS for an average patient.[9]
- The exact amount you will pay depends upon your insurance provider and coverage plan.
- Your OneSource™ Case Manager can help you determine your exact out-of-pocket costs and whether copay assistance may be available.

ULTOMIRIS is priced to be less expensive than SOLIRIS for an average patient

11. How long are ULTOMIRIS infusions?

- Infusion time with ULTOMIRIS depends on patient body weight.[3]
- Annually, the average patient will spend about 60% less time being infused with ULTOMIRIS compared to SOLIRIS.[3,4]
- ULTOMIRIS also offers a reduced infusion volume compared with SOLIRIS, which may ease concerns if you have trouble with large infusions.[3,4]

The average annual infusion time for ULTOMIRIS is about 60% less than with SOLIRIS[3,4]

12. Why is ULTOMIRIS dosage based on weight?

- Weight-based dosing allows for individualized control of C5. ULTOMIRIS is dosed based on body weight in order to provide sustained control of C5 for the full 4- or 8-week treatment cycle.[3]

ULTOMIRIS is dosed based on body weight in order to provide sustained control of C5

13. Can I continue home infusions on ULTOMIRIS?

- Availability of home infusion services may depend on your insurance coverage. Your OneSource Case Manager can help you determine if your insurance will cover home infusions with ULTOMIRIS.

Talk to your OneSource Case Manager about home infusions

IMPORTANT SAFETY INFORMATION (CONT'D)

If you have aHUS, your healthcare provider will need to monitor you closely for at least 12 months after stopping treatment for signs of worsening aHUS or problems related to a type of abnormal clotting and breakdown of your red blood cells called thrombotic microangiopathy (TMA). Symptoms or problems that can happen with TMA may include: confusion or loss of consciousness, seizures, chest pain (angina), difficulty breathing and blood clots or stroke.

ULTOMIRIS can cause serious side effects including allergic reactions to acrylic adhesive. Allergic reactions to the acrylic adhesive may happen with your subcutaneous ULTOMIRIS treatment. If you have an allergic reaction during the delivery of subcutaneous ULTOMIRIS, remove the on-body injector and get medical help right away. Your healthcare provider may treat you with medicines to help prevent or treat allergic reaction symptoms as needed.

What are the possible side effects of ULTOMIRIS?
ULTOMIRIS can cause serious side effects including infusion-related reactions. Symptoms of an infusion-related reaction with ULTOMIRIS may include lower back pain, tiredness, feeling faint, discomfort in your arms or legs, bad taste, or drowsiness. Stop treatment of ULTOMIRIS and tell your healthcare provider or nurse right away if you develop these symptoms, or any other symptoms during your ULTOMIRIS infusion that may mean you are having a serious infusion reaction, including: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out.

14. If I want to make the transition to ULTOMIRIS, what should I do next?

- Talk to your doctor about making the transition to ULTOMIRIS. The decision to transition should be at the discretion of your treating physician, who will use his/her clinical judgment in deciding the appropriate timing for transitioning from SOLIRIS to ULTOMIRIS.
- When it's time to make the transition, your OneSource Case Manager can assist you with insurance-related matters. Once you have authorization from your insurance company, your OneSource Case Manager can also help you find an infusion center.

The decision to transition should be at the discretion of your treating physician

Your OneSource Case Manager can assist you with insurance-related matters

15. What is the process for making the transition to ULTOMIRIS?

- If you are transitioning from SOLIRIS to ULTOMIRIS, you will receive a "starting dose" of ULTOMIRIS 2 weeks after your final SOLIRIS infusion.[3]
- After that, you will be given ULTOMIRIS once every 4 or 8 weeks (depending on body weight), beginning 2 weeks after the ULTOMIRIS starting dose.[3]

2 weeks after a starting dose, you will be given ULTOMIRIS once every 4 or 8 weeks (depending on body weight)

IMPORTANT SAFETY INFORMATION (CONT'D)

The most common side effects of ULTOMIRIS in people treated for aHUS are upper respiratory tract infection, diarrhea, nausea, vomiting, headache, high blood pressure and fever.

The most common side effects of subcutaneous administration of ULTOMIRIS in adults treated for aHUS are local injection site reactions.

Tell your healthcare provider about any side effect that bothers you or that does not go away. These are not all the possible side effects of ULTOMIRIS. For more information, ask your healthcare provider or pharmacist. Call your healthcare provider right away if you miss an ULTOMIRIS infusion or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Read the Instructions for Use that comes with subcutaneous ULTOMIRIS for instructions about the right way to prepare and give your subcutaneous ULTOMIRIS injections through an on-body injector.

WHERE CAN I FIND OUT MORE?

16. Is there a way for me to connect with other patients who have made the transition to ULTOMIRIS?

- Every year, Alexion hosts webinars and events for patients to hear from leading physicians and patients like them. To learn more, and to sign up for upcoming events, please visit www.alexionahusevents.com.

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17. Where can I go to find out more about ULTOMIRIS?

- Ask your OneSource Case Manager to tell you more about ULTOMIRIS. OneSource has lots of additional educational resources that can help you prepare to make the transition. If you're not already enrolled in OneSource, you can sign up in 5 minutes or less by visiting www.AlexionOneSource.com and clicking "Get Started".

- In addition, you can visit the following websites:
  - **ULTOMIRIS aHUS Patient Website** (www.ULTOMIRIS.com/aHUS)
  - **ULTOMIRIS REMS Website** (www.ULTOMIRISrems.com)
  - **Alexion aHUS Webinars** (www.alexionahusevents.com)
  - **aHUS Foundation** (www.ahus.org)
  - **National Organization for Rare Disorders** (www.rarediseases.org)
  - **Global Genes Project** (www.globalgenes.org)
- Remember to speak with your doctor about how to manage atypical-HUS and ULTOMIRIS

ONESOURCE®
Personalized Patient Support from Alexion

1.888.765.4747

OneSource@Alexion.com

OneSource has many additional educational resources that can help you prepare to make the transition

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Read the Instructions for Use that comes with subcutaneous ULTOMIRIS for instructions about the right way to prepare and give your subcutaneous ULTOMIRIS injections through an on-body injector.

Please see the full Prescribing Information and Medication Guide for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis. Please see the accompanying Instructions for Use for the ULTOMIRIS On Body Delivery System.

References

1. Noris M, et al. *Nat Rev Nephrol*. 2012;8:622-633. **2.** Azoulay E, et al. *CHEST*. 2017;152:424-434. **3.** ULTOMIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **4.** SOLIRIS. Prescribing information. Alexion Pharmaceuticals, Inc. **5.** Sheridan D, et al. *PLoS One*. 2018;13(4):e0195909. **6.** Data on file [ALXN1210-aHUS-311 CSR]. **7.** Data on file [ALXN1210-aHUS-312 CSR]. **8.** Clinicaltrials.gov. Search results for Atypical hemolytic uremic syndrome. Accessed June 1, 2020. https://clinicaltrials.gov/ct2/results?cond=Atypical+hemolytic+uremic+syndrome&recrs=a&recrs=f&recrs=d&recrs=e&recrs=m&age_v=&gndr=&type=&rslt=&Search=Apply# **9.** Data on file. Alexion Pharmaceuticals, Inc.; 2019.