



## VOYDEYA™ approved in the US as add-on therapy to ravulizumab or eculizumab for treatment of extravascular hemolysis in adults with the rare disease PNH

April 1, 2024

### *Approval of first-in-class, oral, Factor D inhibitor based on results from pivotal ALPHA Phase III trial*

VOYDEYA™ (danicopan) has been approved in the US as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH).<sup>1</sup> VOYDEYA is a first-in-class, oral, Factor D inhibitor developed as an add-on to standard-of-care ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) to address the needs of the approximately 10-20% of patients with PNH who experience clinically significant EVH while treated with a C5 inhibitor.<sup>2,3</sup>

The approval by the US Food and Drug Administration (FDA) was based on positive results from the pivotal [ALPHA Phase III trial](#). Results from the 12-week primary evaluation period of the trial were published in [The Lancet Haematology](#).<sup>2</sup>

Bart Scott, MD, Professor, Division of Hematology and Oncology at the University of Washington Medical Center, and Professor, Clinical Research Division at Fred Hutchinson Cancer Center, said: “The approval of VOYDEYA offers this small subset of PNH patients an add-on therapy designed to address EVH, while maintaining disease control with ULTOMIRIS or SOLIRIS. Terminal complement inhibition with ULTOMIRIS can address the life-threatening complications of PNH, building on the efficacy and safety of SOLIRIS established over nearly 20 years.”

Marc Dunoyer, Chief Executive Officer, Alexion, said: “The approval of first-in-class, Factor D inhibitor VOYDEYA marks an important advancement in the treatment of PNH and builds on our leadership and commitment to bring forward innovation in complement science. As the ALPHA trial suggests, dual complement pathway inhibition at Factor D and C5 may be an optimal treatment approach for this subset of patients with EVH, enabling them to continue with proven standard-of-care therapy.”

The ALPHA Phase III trial evaluated the efficacy and safety of VOYDEYA as add-on to ULTOMIRIS or SOLIRIS in patients with PNH who experienced clinically significant EVH. Results showed that VOYDEYA met the primary endpoint of change in hemoglobin from baseline to week 12 and all key secondary endpoints, including transfusion avoidance and change in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue) score.<sup>2</sup>

Results from the ALPHA Phase III trial showed VOYDEYA was generally well tolerated, and no new safety concerns were identified. In the trial, the most common treatment-emergent adverse events were headache, nausea, arthralgia and diarrhea.<sup>2</sup>

VOYDEYA has been granted Breakthrough Therapy designation by the US FDA and PRiority MEDicines (PRIME) status by the European Medicines Agency. VOYDEYA has also been granted Orphan Drug Designation in the US, European Union (EU) and Japan for the treatment of PNH. VOYDEYA has been [approved in Japan](#) and [recommended for approval in the EU](#). Regulatory reviews are ongoing in additional countries.

### **INDICATION & IMPORTANT SAFETY INFORMATION FOR VOYDEYA™ (danicopan)**

#### **INDICATION**

##### **What is VOYDEYA?**

VOYDEYA is a prescription medicine used along with ravulizumab or eculizumab to treat breakdown of red blood cells that takes place outside of blood vessels (extravascular hemolysis), in adults with paroxysmal nocturnal hemoglobinuria (PNH).

It is not known if VOYDEYA is safe and effective in children.

#### **IMPORTANT SAFETY INFORMATION**

##### **What is the most important information I should know about VOYDEYA?**

**VOYDEYA is a medicine that affects your immune system. VOYDEYA may lower the ability of your immune system to fight infections.**

- **VOYDEYA increases your chance of getting serious infections caused by encapsulated bacteria.** These serious infections may quickly become life-threatening and cause death if not recognized and treated early.

1. You must complete or update meningococcal vaccine(s) and streptococcus vaccine(s) at least 2 weeks before your first dose of VOYDEYA.
2. If you have not completed your vaccinations and VOYDEYA must be started right away, you should receive the required vaccinations as soon as possible.
3. If you have not been vaccinated at least 2 weeks before your first VOYDEYA dose and VOYDEYA must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.
4. If you have been vaccinated against these bacteria in the past, you might need additional vaccinations before starting VOYDEYA. Your healthcare provider will decide if you need additional vaccinations.
5. Vaccines do not prevent all infections caused by encapsulated bacteria. **Call your healthcare provider or get emergency**

**medical care right away if you have any of these signs and symptoms of a serious infection:** fever with or without chills, fever and a rash, fever with chest pain and cough, fever with breathlessness/fast breathing, fever with high heart rate, headache with nausea or vomiting, headache and a fever, headache with a stiff neck or stiff back, confusion, body aches with flu-like symptoms, clammy skin, eyes sensitive to light.

**Your healthcare provider will give you a Patient Safety Card about the risk of serious infections.** Carry it with you at all times during treatment and for 1 week after your last VOYDEYA dose. Your risk of serious infections may continue for a few days after your last dose of VOYDEYA. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

**VOYDEYA is only available through a program called the VOYDEYA Risk Evaluation and Mitigation Strategy (REMS).** Before you can take VOYDEYA, your healthcare provider must: enroll in the VOYDEYA REMS; counsel you about the risk of serious infections caused by certain bacteria; give you information about the symptoms of serious infections; make sure that you are vaccinated against serious infections caused by encapsulated bacteria and that you receive antibiotics if you need to start VOYDEYA right away and you are not up to date on your vaccinations; give you a **Patient Safety Card** about your risk of serious infections, as discussed above.

#### **Who should not receive VOYDEYA?**

**Do not take VOYDEYA** if you have a serious infection caused by encapsulated bacteria, including *Neisseria meningitidis*, *Streptococcus pneumoniae*, or *Haemophilus influenzae* type B infection.

**Before taking VOYDEYA, tell your healthcare provider about all of your medical conditions, including if you:** have an infection or fever, have liver problems, are pregnant or plan to become pregnant or are breastfeeding. It is not known if VOYDEYA will harm your unborn baby or if it passes into your breast milk. Do not breastfeed during treatment with VOYDEYA and for 3 days after the last dose.

**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. VOYDEYA may affect the way other medicines work.

**If you stop taking VOYDEYA,** your healthcare provider will need to monitor you closely for at least 2 weeks after your last dose. **Stopping treatment with VOYDEYA may cause a breakdown of red blood cells due to PNH. Symptoms or problems that can happen due to breakdown of red blood cells include:** decreased hemoglobin level in your blood and tiredness.

#### **What are the possible side effects of VOYDEYA?**

**VOYDEYA can cause serious side effects including increased liver enzyme levels and increased cholesterol.** Your healthcare provider will do blood tests to check your liver enzyme levels and cholesterol before and during treatment with VOYDEYA. Your healthcare provider may temporarily or permanently stop treatment with VOYDEYA if you develop increased liver enzyme levels.

**The most common side effect of VOYDEYA is headache.**

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

**Please see the accompanying full [Prescribing Information and Medication Guide](#) for VOYDEYA (danicipan), including **Boxed WARNING** regarding serious infections caused by encapsulated bacteria.**

### **INDICATION(S) & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS® (ravulizumab-cwvz)**

#### **INDICATION(S)**

##### **What is ULTOMIRIS?**

ULTOMIRIS is a prescription medicine used to treat:

- adults and children 1 month of age and older with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH).
- 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 a disease called generalized Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
- adults with a disease called Neuromyelitis Optica Spectrum Disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody positive.

It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age.

It is not known if ULTOMIRIS is safe and effective for the treatment of gMG or NMOSD 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 may lower the ability of your immune system to fight infections.**

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

1. You must complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of ULTOMIRIS.
2. If you have not completed your meningococcal vaccines and ULTOMIRIS must be started right away, you should receive the required vaccine(s) as soon as possible.
3. If you have not been vaccinated and ULTOMIRIS must be started right away, you should also receive antibiotics for as long as your healthcare provider tells you.
4. If you had a meningococcal vaccine in the past, you might need additional vaccines before starting ULTOMIRIS. Your healthcare provider will decide if you need additional meningococcal vaccines.
5. Meningococcal vaccines 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:** fever, fever with high heart rate, headache and fever, confusion, muscle aches with flu-like symptoms, fever and a rash, headache with nausea or vomiting, headache with a stiff neck or stiff back, or eyes sensitive to light.

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

**ULTOMIRIS is only available through a program called the ULTOMIRIS and SOLIRIS Risk Evaluation and Mitigation Strategy (REMS).** Before you can receive ULTOMIRIS, your healthcare provider must: enroll in the REMS program; counsel you about the risk of serious meningococcal infections; give you information about the signs and symptoms of serious meningococcal infection; make sure that you are vaccinated against serious infections caused by meningococcal bacteria, and that you receive antibiotics if you need to start ULTOMIRIS right away and are not up to date on your vaccines; give you a **Patient Safety Card** about your risk of meningococcal infection.

**ULTOMIRIS may also increase the risk of other types of serious infections,** including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria gonorrhoeae*. Your child should receive vaccines against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) if treated with ULTOMIRIS. Certain people may be at risk of serious infections with gonorrhea.

#### **Who should not receive ULTOMIRIS?**

Do not receive ULTOMIRIS if you have a serious meningococcal infection when you are starting ULTOMIRIS.

**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.

**If you have PNH and you stop receiving ULTOMIRIS, your healthcare provider will need to monitor you closely for at least 16 weeks after you stop ULTOMIRIS. Stopping ULTOMIRIS may cause breakdown of your red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include:** drop in your red blood cell count, tiredness, blood in your urine, stomach-area (abdomen) pain, shortness of breath, blood clots, trouble swallowing, and erectile dysfunction (ED) in males.

**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.

#### **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, abdominal pain, muscle spasms, changes in blood pressure, tiredness, feeling faint, shaking chills (rigors), discomfort in your arms or legs, bad taste, or drowsiness. Stop treatment of ULTOMIRIS and tell your healthcare provider right away if you develop these symptoms, or any other symptoms during your ULTOMIRIS infusion that may mean you are having a serious infusion-related reaction, including: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out.

**The most common side effects of ULTOMIRIS in people treated for PNH are upper respiratory tract infection and headache.**

**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 ULTOMIRIS in people with gMG are diarrhea and upper respiratory tract infections.**

**The most common side effects of ULTOMIRIS in people with NMOSD are COVID-19 infection, headache, back pain, urinary tract infection, and joint pain (arthralgia).**

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.

**Please see the accompanying full [Prescribing Information and Medication Guide](#) for ULTOMIRIS, including Boxed WARNING regarding serious meningococcal infections.**

#### **INDICATION(S) & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)**

## INDICATION(S)

### What is SOLIRIS?

SOLIRIS is a prescription medicine used to treat:

- people with paroxysmal nocturnal hemoglobinuria (PNH).
- people with atypical hemolytic uremic syndrome (aHUS). SOLIRIS is not for use in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).
- adults with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
- adults with a disease called neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

It is not known if SOLIRIS is safe and effective in children with PNH, gMG, or NMOSD.

## IMPORTANT SAFETY INFORMATION

### What is the most important information I should know about SOLIRIS?

**SOLIRIS is a medicine that affects your immune system and may lower the ability of your immune system to fight infections.**

- **SOLIRIS increases your chance of getting serious meningococcal infections that may quickly become life-threatening or cause death if not recognized and treated early.**
1. You must complete or update your meningococcal vaccine(s) at least 2 weeks before your first dose of SOLIRIS.
  2. If you have not been vaccinated and SOLIRIS must be started right away, you should receive the required vaccine(s) as soon as possible.
  3. If you have not been vaccinated and SOLIRIS must be started right away, you should also receive antibiotics for as long as your healthcare provider tells you.
  4. If you had a meningococcal vaccine in the past, you might need additional vaccines before starting SOLIRIS. Your healthcare provider will decide if you need additional meningococcal vaccines.
  5. Meningococcal vaccines 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 serious meningococcal infection:** fever, fever with high heart rate, headache and fever, confusion, muscle aches with flu-like symptoms, fever and rash, headache with nausea or vomiting, headache with a stiff neck or stiff back, or eyes sensitive to light.

**Your healthcare provider will give you a Patient Safety Card about the risk of serious meningococcal infection.** Carry it with you at all times during treatment and for 3 months after your last dose of SOLIRIS. Your risk of meningococcal infection may continue for several weeks after your last dose of SOLIRIS. It is important to show this card to any healthcare provider who treats you. This will help them diagnose and treat you quickly.

**SOLIRIS is only available through a program called the ULTOMIRIS and SOLIRIS Risk Evaluation and Mitigation Strategy (REMS).** Before you can receive SOLIRIS, your healthcare provider must: enroll in the REMS program; counsel you about the risk of serious meningococcal infections; give you information about the signs and symptoms of serious meningococcal infection; make sure that you are vaccinated against serious infections caused by meningococcal bacteria, and that you receive antibiotics if you need to start SOLIRIS right away and you are not up to date on your vaccines; give you a **Patient Safety Card** about your risk of meningococcal infection.

**SOLIRIS may also increase the risk of other types of serious infections,** including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria gonorrhoeae*. Your child should receive vaccines against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) if treated with SOLIRIS. Certain people may be at risk of serious infections with gonorrhea. Certain fungal infections (*Aspergillus*) may occur if you take SOLIRIS and have a weak immune system or a low white blood cell count.

### Who should not receive SOLIRIS?

Do not receive SOLIRIS if you have a serious meningococcal infection when you are starting SOLIRIS.

**Before you receive SOLIRIS, 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 SOLIRIS will harm your unborn baby or if it passes into your breast milk.

**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.

**If you have PNH, your healthcare provider will need to monitor you closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS may cause breakdown of your red blood cells due to PNH.** Symptoms or problems that can happen due to red blood cell breakdown include: drop in the number of your red blood cell count, drop in your platelet count, confusion, kidney problems, blood clots, difficulty breathing, and chest pain.

**If you have aHUS, your healthcare provider will need to monitor you closely during and for at least 12 weeks after stopping SOLIRIS for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy).** Symptoms or problems that can happen with abnormal clotting may include: stroke, confusion, seizure, chest pain (angina), difficulty breathing, kidney problems, swelling in arms or legs, and a drop in your platelet count.

## What are the possible side effects of SOLIRIS?

**SOLIRIS can cause serious side effects including serious infusion-related reactions.** Tell your healthcare provider or nurse right away if you get any of these symptoms during your SOLIRIS infusion: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out. If you have an infusion-related reaction to SOLIRIS, your healthcare provider may need to infuse SOLIRIS more slowly, or stop SOLIRIS.

**The most common side effects in people with aHUS treated with SOLIRIS include:** headache, diarrhea, high blood pressure (hypertension), common cold (upper respiratory infection), stomach-area (abdominal) pain, vomiting, pain or swelling of your nose or throat (nasopharyngitis), low red blood cell count (anemia), cough, swelling of legs or feet (peripheral edema), nausea, urinary tract infections, and fever.

**The most common side effects in people with gMG treated with SOLIRIS include:** muscle and joint (musculoskeletal) pain.

**The most common side effects in people with NMOSD treated with SOLIRIS include:** common cold (upper respiratory infection), pain or swelling of your nose or throat (nasopharyngitis), diarrhea, back pain, dizziness, flu like symptoms (influenza) including fever, headache, tiredness, cough, sore throat, and body aches, joint pain (arthralgia), throat irritation (pharyngitis), and bruising (contusion).

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 SOLIRIS. For more information, ask your healthcare provider or pharmacist. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**Please see the accompanying full [Prescribing Information](#) and [Medication Guide](#) for SOLIRIS, including Boxed WARNING regarding serious meningococcal infections.**

## Notes

### PNH

PNH is a rare, chronic, progressive and potentially life-threatening blood disorder. It is characterized by red blood cell destruction within blood vessels (also known as intravascular hemolysis) and white blood cell and platelet activation, which can result in thrombosis (blood clots).<sup>4-6</sup>

PNH is caused by an acquired genetic mutation that may happen any time after birth and results in the production of abnormal blood cells that are missing important protective blood cell surface proteins. These missing proteins enable the complement system, which is part of the immune system and is essential to the body's defense against infection, to 'attack' and destroy or activate these abnormal blood cells. <sup>4</sup> Living with PNH can be debilitating, and signs and symptoms may include blood clots, abdominal pain, difficulty swallowing, erectile dysfunction, shortness of breath, excessive fatigue, anemia and dark-colored urine.<sup>4,7,8</sup>

### Clinically Significant EVH

EVH, the removal of red blood cells outside of the blood vessels, can sometimes occur in PNH patients who are treated with C5 inhibitors.<sup>9,10</sup> Since C5 inhibition enables PNH red blood cells to survive and circulate, EVH may occur when these now surviving PNH red blood cells are marked by proteins in the complement system for removal by the spleen and liver.<sup>4,6,11</sup> PNH patients with EVH may continue to experience anemia, which can have various causes, and may require blood transfusions.<sup>9,10,12,13</sup> A small subset of people living with PNH who are treated with a C5 inhibitor experience clinically significant EVH, which results in continued symptoms of anemia and may require blood transfusions.<sup>4,7,14,15</sup>

### ALPHA

ALPHA is a pivotal, global Phase III trial designed as a superiority study to evaluate the efficacy and safety of VOYDEYA as an add-on to C5 inhibitor therapy SOLIRIS or ULTOMIRIS in patients with PNH who experience clinically significant EVH. In the double-blind, placebo-controlled, multiple-dose trial, patients were enrolled and randomized to receive VOYDEYA or placebo (2:1) in addition to their ongoing SOLIRIS or ULTOMIRIS therapy for 12 weeks. A prespecified interim analysis was performed once 63 randomized patients had completed 12 weeks of the primary evaluation period or discontinued treatment as of June 28, 2022. At 12 weeks, patients on placebo plus SOLIRIS or ULTOMIRIS were switched to VOYDEYA plus SOLIRIS or ULTOMIRIS, and patients on VOYDEYA plus SOLIRIS or ULTOMIRIS remained on this treatment for an additional 12 weeks. Patients who completed both treatment periods (24 weeks) had the option to participate in a two-year long-term extension period and continue to receive VOYDEYA in addition to SOLIRIS or ULTOMIRIS. The open-label period of the study is ongoing.<sup>2,16</sup>

### VOYDEYA™ (danicopan)

VOYDEYA™ (danicopan) is a first-in-class oral Factor D inhibitor. The medication works by selectively inhibiting Factor D, a complement system protein that plays a key role in the amplification of the complement system response. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. VOYDEYA has been granted Breakthrough Therapy designation by the US Food and Drug Administration and PRiority MEDicines (PRIME) status by the European Medicines Agency. VOYDEYA has also been granted Orphan Drug Designation in the US, EU and Japan for the treatment of PNH.

VOYDEYA is approved in the US as add-on therapy to ravulizumab or eculizumab for the treatment of EVH in adults with PNH.

VOYDEYA is also approved in Japan for certain adults with PNH in combination with C5 inhibitor therapy.

Alexion is also evaluating VOYDEYA as a potential monotherapy for geographic atrophy in a Phase II clinical trial.

### ULTOMIRIS® (ravulizumab-cwvz)

ULTOMIRIS® (ravulizumab-cwvz), the first and only long-acting C5 complement inhibitor, provides immediate, complete and sustained complement inhibition. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. ULTOMIRIS is administered intravenously every eight weeks in adult patients, following a loading dose.

ULTOMIRIS is approved in the US, EU, Japan and other countries for the treatment of certain adults with generalized myasthenia gravis (gMG).



ULTOMIRIS is also approved in the US, EU, Japan and other countries for the treatment of certain adults with PNH and for certain children with PNH in the US and EU.

Additionally, ULTOMIRIS is approved in the US, EU, Japan and other countries for certain adults and children with atypical hemolytic uremic syndrome to inhibit complement-mediated thrombotic microangiopathy (aHUS).

Further, ULTOMIRIS is approved in the US, EU and Japan for the treatment of certain adults with neuromyelitis optica spectrum disorder (NMOSD).

As part of a broad development program, ULTOMIRIS is being assessed for the treatment of additional hematology and neurology indications.

### **SOLIRIS® (eculizumab)**

SOLIRIS® (eculizumab) is a first-in-class C5 complement inhibitor. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the terminal complement cascade over-responds, leading the body to attack its own healthy cells. SOLIRIS is administered intravenously every two weeks, following an introductory dosing period.

SOLIRIS is approved in the US, EU, Japan, China and other countries for the treatment of patients with PNH and aHUS.

Additionally, SOLIRIS is approved in Japan and the EU for the treatment of certain adult and pediatric patients with gMG, and in the US, China and other countries for certain adults with gMG.

Further, SOLIRIS is approved in the US, EU, Japan, China and other countries for the treatment of certain adults with NMOSD.

SOLIRIS is not indicated for the treatment of patients with Shiga-toxin E. coli-related hemolytic uremic syndrome.

### **Alexion**

Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for more than 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on hematology, nephrology, neurology, metabolic disorders, cardiology and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in 70 countries. For more information, please visit [www.alexion.com](http://www.alexion.com).

### **AstraZeneca**

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialization of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit [astrazeneca-us.com](http://astrazeneca-us.com) and follow the Company on social media [@AstraZeneca](https://twitter.com/AstraZeneca).

### **Media Inquiries**

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### **References**

1. VOYDEYA (danicopan) US prescribing information; March 2024.
2. Lee JW, et al. Addition of danicopan to ravulizumab or eculizumab in patients with paroxysmal nocturnal haemoglobinuria and clinically significant extravascular haemolysis (ALPHA): a double-blind, randomised, phase 3 trial. *The Lancet Haematology*. 2023;10(12):E955-E965.
3. Kulasekararaj AG, et al. Prevalence of clinically significant extravascular hemolysis in stable C5 inhibitor-treated patients with PNH and its association with disease control, quality of life and treatment satisfaction. Presented at: European Hematology Association (EHA) Hybrid Congress. 8-11 June 2023; Frankfurt, Germany. Abs PB2056.
4. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804-2811.
5. Griffin M, et al. Significant hemolysis is not required for thrombosis in paroxysmal nocturnal hemoglobinuria. *Haematologica*. 2019;104(3):E94-E96.
6. Hillmen P, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2006;355(12):1233-1243.
7. Kulasekararaj AG, et al. Ravulizumab (ALXN1210) vs eculizumab in C5-inhibitor-experienced adult patients with PNH: the 302 study. *Blood*. 2019;133(6):540-549.
8. Hillmen P, et al. Effect of the complement inhibitor eculizumab on thromboembolism on patients with paroxysmal nocturnal hemoglobinuria. *Blood*. 2007;110(12):4123-4128.
9. Brodsky RA. A complementary new drug for PNH. *Blood*. 2020;135(12):884-885.
10. Risitano AM, et al. Anti-complement treatment for paroxysmal nocturnal hemoglobinuria: time for proximal complement inhibition? A position paper from the SAAWP of the EBMT. *Front Immunol*. 2019;10:1157.
11. Kulasekararaj AG, et al. Long-term safety and efficacy of ravulizumab in patients with paroxysmal nocturnal hemoglobinuria: 2-year results from two pivotal phase 3 studies. *Eur J Haematol*. 2022;109(3):205-214.
12. Berentsen S, et al. Novel insights into the treatment of complement-mediated hemolytic anemias. *Ther Adv Hematol*. 2019;10:2040620719873321.
13. Kulasekararaj AG, et al. Monitoring of patients with paroxysmal nocturnal hemoglobinuria on a complement inhibitor. *Am J Hematol*. 2021;96(7):E232-E235.
14. Lee JW, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: the 301

study. *Blood*. 2019;133(6):530-539.

15. Röth A, et al. Transfusion requirements in adult patients with paroxysmal nocturnal hemoglobinuria naive to complement inhibitors receiving ravulizumab and eculizumab: results from a phase 3 non-inferiority study [abstract]. ECTH 2019. Glasgow, UK ed. Glasgow, UK2019.
16. ClinicalTrials.gov. Danicopan as Add-on Therapy to a C5 Inhibitor in Paroxysmal Nocturnal Hemoglobinuria (PNH) Participants Who Have Clinically Evident Extravascular Hemolysis (EVH)(ALPHA). NCT Identifier: NCT04469465. Available [here](#). Accessed March 2024.