



Alexion Receives FDA Approval of SOLIRIS® (eculizumab) for the Treatment of Adults with Neuromyelitis Optica Spectrum Disorder (NMOSD) who are Anti-Aquaporin-4 (AQP4) Antibody Positive

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- At 48 weeks, 98% of patients treated with SOLIRIS were relapse free compared to 63% of patients receiving placebo -

- SOLIRIS is the first and only FDA approved treatment for this rare, severe, condition that attacks the central nervous system without warning -

BOSTON--(BUSINESS WIRE)--Jun. 27, 2019-- [Alexion Pharmaceuticals, Inc.](https://www.businesswire.com/news/home/20190627005768/en/) (NASDAQ:ALXN) today announced that the U.S. Food and Drug Administration (FDA) approved SOLIRIS® (eculizumab) for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.¹ Approximately three quarters (73%) of all patients with NMOSD test positive for anti-AQP4 auto-antibodies.² The FDA approved SOLIRIS following an expedited six-month priority review. NMOSD is a rare, severe autoimmune disease that attacks the central nervous system without warning. These attacks, also referred to as relapses, can cause progressive and irreversible damage to the brain, optic nerve and spinal cord, which may lead to long-term disability.³⁻⁶ Complement activation due to anti-AQP4 antibodies is one of the primary underlying causes of the destruction in these patients.^{3,7} In the PREVENT trial, SOLIRIS, a first-in-class complement inhibitor, demonstrated safety and efficacy and met its primary endpoint of prolonging the time to first adjudicated relapse and reducing the risk of relapse.^{1,8}

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SOLIRIS® Product Photo (Photo: Business Wire)

“NMOSD is a serious disease with devastating consequences,” said Michael Levy, M.D., Ph.D., a consultant to the company and Associate Professor of Neurology at Massachusetts General Hospital in Boston. “Each attack can result in potentially irreversible consequences—causing blindness or losing the ability to walk—so preventing relapse is the primary goal of treatment. With the approval of SOLIRIS, there is now for the first time an FDA-approved treatment available to NMOSD patients to help reduce the risk of relapse.”

NMOSD disproportionately strikes young women in the prime of their lives, with the average age of first onset at just 39 years.³ Race is also a significant risk factor for disability and mortality in NMOSD.⁹⁻¹¹ In the U.S., African Americans are over-represented among patients diagnosed with NMOSD and more likely to suffer more frequent and more severe attacks.⁹⁻¹¹ Previously known as Devic’s Disease, NMOSD is often confused with other neurological illnesses such as

multiple sclerosis (MS), which can lead to delays in diagnosis and treatment with medicines that can worsen disease progression.^{3,12,13}

“Today’s approval represents an important milestone for the NMOSD community,” said Victoria Jackson, co-founder of the [Guthy-Jackson Charitable Foundation \(GJCF\)](https://www.guthy-jackson.org/), a non-profit organization dedicated to funding research and raising awareness about NMOSD. “We are thrilled to have partnered with industry to catalyze research and development of targeted therapies to treat NMOSD. The FDA approval of SOLIRIS is the beginning of a new era for these NMOSD patients as we continue on our mission to cure this life-threatening disease.”

This approval is based on comprehensive results from the Phase 3 randomized, double-blind placebo controlled PREVENT trial, which were recently published in [The New England Journal of Medicine](https://doi.org/10.1093/ajph/2019.09.1587). In the study, patients with NMOSD who were anti-AQP4 antibody positive were treated with SOLIRIS (n=96) or placebo (n=47). At 48 weeks, 98 percent of patients treated with SOLIRIS were relapse free compared to 63 percent of patients receiving placebo. This effect was observed through 144 weeks of treatment, with 96 percent of patients treated with SOLIRIS relapse free compared to 45 percent of patients in the placebo arm. SOLIRIS-treated patients experienced similar improvement in time to first adjudicated on-trial relapse with or without concomitant treatment. Of the patients treated solely with SOLIRIS, without receiving other immunosuppressive therapies (IST), (n=21), 100 percent were relapse free at 144 weeks compared to 20 percent in the placebo group (n=13).⁸

The safety profile of SOLIRIS was consistent with that seen for SOLIRIS in other clinical studies. The most common adverse events observed in the

PREVENT study were upper respiratory tract infection (29 percent of patients in the SOLIRIS group vs. 13 percent in the placebo group), nasopharyngitis (21 vs. 19 percent), diarrhea (16 vs. 15 percent), back pain (15 vs. 13 percent) and dizziness (15 vs. 13 percent). The serious adverse events that were reported for more than one patient in either group were pneumonia (three patients in the SOLIRIS group vs. one patient in the placebo group) and cellulitis, sepsis and urinary tract infection (two patients for each event in the SOLIRIS group vs. no patient in the placebo group). One patient receiving SOLIRIS and concomitant supportive IST died from infectious pleural effusion. The patient had an extensive history of pulmonary disease and was an active smoker. No cases of meningococcal infection were observed in the study.

"In NMOSD, disease progression is driven by attacks, and so preventing future relapses is the primary goal of treatment. Today, for the first time, adults living with anti-AQP4 antibody-positive NMOSD have an approved treatment to reduce the risk of an unpredictable relapse – or attack," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion.

The European Medicines Agency (EMA) and the Japanese Ministry of Health, Labour and Welfare (MHLW) are reviewing Alexion's applications to add the treatment of NMOSD to the marketing authorizations for SOLIRIS in the European Union (EU) and Japan, respectively. SOLIRIS has received Orphan Drug Designation (ODD) for the treatment of patients with NMOSD in the U.S., EU and Japan.

About NMOSD

NMOSD is a rare and devastating disorder that attacks the central nervous system (CNS), in which complement activation due to anti-aquaporin-4 (AQP4) antibodies plays a significant role in the disease process.^{3,7} Patients with NMOSD experience unpredictable attacks, also referred to as relapses, which can cause irreversible damage to the brain and spinal column— and can lead to long-term disability^{2–6} The most common symptoms of NMOSD are optic neuritis and transverse myelitis. Transverse myelitis can cause mobility problems including paralysis; optic neuritis can cause visual problems including blindness.^{14,15}

Race and gender are risk factors for NMOSD.^{9–11} The prevalence of NMOSD may be more common and more severe in non-Caucasian populations worldwide.^{9–11} People of African heritage, including African Americans, are disproportionately affected compared to the general NMOSD population.^{9,16} The disease primarily affects women, often in the prime of their lives, with an average age of onset of 39 years.³

Approximately three quarters (73%) of all patients with NMOSD have AQP4 auto-antibodies.² Anti-AQP4 auto-antibody testing is part of the diagnostic criteria for NMOSD.¹⁷ In patients with anti-AQP4 antibody-positive NMOSD, the body's own immune system can turn against itself to produce auto-antibodies against AQP4, a protein on certain cells in the eyes, brain and spinal cord that are critical for the survival of nerve cells. The binding of these anti-AQP4 auto-antibodies activates the complement cascade, another part of the immune system. Complement activation by anti-AQP4 auto-antibodies can cause destruction of vital cells in the CNS, leading to demyelination and to the death of neurons, predominantly in the spinal cord and optic nerve.^{13,18–20}

About SOLIRIS® (eculizumab)

SOLIRIS is a first-in-class complement inhibitor that works by inhibiting the C5 protein in the terminal part of the complement cascade, a part of the immune system. Activation of the complement cascade, plays a role in severe rare and ultra-rare disorders like paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG), and anti-aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD). SOLIRIS is approved in the U.S., EU, Japan and other countries as a treatment for adult patients with PNH and for adults and children with aHUS. SOLIRIS is not indicated for the treatment of patients with Shiga-toxin E. coli-related hemolytic uremic syndrome (STEC-HUS). In the U.S., SOLIRIS is also approved for the treatment of adult patients with generalized MG (gMG) who are anti-AchR antibody-positive, in the EU as the first and only approved treatment of refractory gMG in adults who are anti-AchR antibody-positive and in Japan for the treatment of patients with gMG who are AchR antibody-positive and whose symptoms are difficult to control with high-dose intravenous immunoglobulin (IVIg) therapy or plasmapheresis (PLEX).

SOLIRIS has received Orphan Drug Designation (ODD) for the treatment of patients with PNH in the U.S., EU, Japan and many other countries, for the treatment of patients with aHUS in the U.S., EU and many other countries, for the treatment of patients with gMG in the U.S. for the treatment of patients with refractory gMG in EU and Japan, and for the treatment of NMOSD in the U.S., EU and Japan. Alexion and SOLIRIS have received some of the pharmaceutical industry's highest honors for the medical innovation in complement inhibition: the Prix Galien USA (2008, Best Biotechnology Product) and France (2009, Rare Disease Treatment).

INDICATIONS & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

INDICATIONS

What is SOLIRIS?

SOLIRIS is a prescription medicine called a monoclonal antibody. SOLIRIS is used to treat patients with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). SOLIRIS is used to treat adults and children with a disease called atypical Hemolytic Uremic Syndrome (aHUS). SOLIRIS is not for use in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). SOLIRIS is used to treat adults with a disease called generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive. SOLIRIS is used to treat 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

SOLIRIS is a medicine that affects the immune system. SOLIRIS can lower the ability of the immune system to fight infections. SOLIRIS increases the chance of getting serious and life-threatening meningococcal infections. Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

Meningococcal vaccines must be received at least two weeks before the first dose of SOLIRIS if one has not already had this vaccine. If one's doctor decided that urgent treatment with SOLIRIS is needed, meningococcal vaccination should be administered as soon as possible. If one has not been vaccinated and SOLIRIS therapy must be initiated immediately, two weeks of antibiotics should also be administered with the vaccinations. If one had

a meningococcal vaccine in the past, additional vaccination might be needed before starting SOLIRIS. Patients should ask their doctor if an additional meningococcal vaccination is needed. Meningococcal vaccines reduce the risk of meningococcal infection but do not prevent all meningococcal infections. Call one's doctor or get emergency medical care right away if any of these signs and symptoms of a meningococcal infection occur: 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. One's doctor will provide a Patient Safety Card about the risk of meningococcal infection. Carry the card at all times during treatment and for 3 months after the last SOLIRIS dose.

SOLIRIS is only available through a program called the [SOLIRIS REMS](#).

SOLIRIS may also increase the risk of other types of serious infections. If one's child is treated with SOLIRIS, make sure that the child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Certain people may be at risk of serious infections with gonorrhea. Talk to the doctor about whether one is at risk for gonorrhea infection, about gonorrhea prevention, and regular testing. Certain fungal infections (*Aspergillus*) may also happen if one takes SOLIRIS and has a weak immune system or a low white blood cell count.

Do not receive SOLIRIS if one has a meningococcal infection, or has not been vaccinated against meningitis infection unless one's doctor decides that urgent treatment with SOLIRIS is needed.

Before one receives SOLIRIS, tell the doctor about all of the medical conditions, including if one: has an infection or fever, is pregnant or plans to become pregnant, and is breastfeeding or plans to breastfeed. It is not known if SOLIRIS will harm an unborn baby or if SOLIRIS passes into the breast milk.

Tell the doctor about all the medicines one takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SOLIRIS and other medicines can affect each other, causing side effects.

It is important that one: has all recommended vaccinations before starting SOLIRIS, receives 2 weeks of antibiotics if one immediately starts SOLIRIS, and stays up-to-date with all recommended vaccinations during treatment with SOLIRIS. Know the medications one takes and the vaccines one receives. Keep a list of them to show the doctor and pharmacist when one gets a new medicine.

If one has PNH, the doctor will need to monitor closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS may cause breakdown of the red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in the number of the red blood cell count, drop in the platelet counts, confusion, kidney problems, blood clots, difficulty breathing, and chest pain. If one has aHUS, the doctor will need to monitor closely during and for at least 12 weeks after stopping treatment 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, swellings in arms or legs, and a drop in the platelet count.

SOLIRIS can cause serious side effects including serious allergic reactions. Serious allergic reactions can happen during one's SOLIRIS infusion. Tell the doctor or nurse right away if one gets any of these symptoms during the SOLIRIS infusion: chest pain, trouble breathing or shortness of breath, swelling of the face, tongue, or throat, and feeling faint or pass out. If one has an allergic reaction to SOLIRIS, the doctor may need to infuse SOLIRIS more slowly, or stop SOLIRIS.

The most common side effects in people with PNH treated with SOLIRIS include: headache, pain or swelling of the nose or throat (nasopharyngitis), back pain, and nausea. 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 the 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 the 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).

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

About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases through the discovery, development and commercialization of life-changing therapies. As the global leader in complement biology and inhibition for more than 20 years, Alexion has developed and commercializes two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH), as well as the first and only approved complement inhibitor to treat atypical hemolytic uremic syndrome (aHUS), anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG) and anti-AQP4 antibody-positive neuromyelitis optica spectrum disorder (NMOSD). Alexion also has two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare metabolic disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). In addition, the company is developing several mid-to-late-stage therapies, including a second complement inhibitor, a copper-binding agent for Wilson disease and an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases as well as several early-stage therapies, including one for light chain (AL) amyloidosis and a second anti-FcRn therapy. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on the core therapeutic areas of hematology, nephrology, neurology and metabolic disorders. Alexion has been named to the *Forbes*' list of the World's Most Innovative Companies seven years in a row and is headquartered in Boston, Massachusetts' Innovation District. The company also has offices around the globe and serves patients in more than 50 countries. This press release and further information about Alexion can be found at: www.alexion.com.

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Forward-Looking Statement

This press release contains forward-looking statements, including statements related to: the consequences of NMOSD attacks and relapses; the primary goal of treatment for patients with NMOSD; and the potential benefits of SOLIRIS as a treatment for patients with NMOSD. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those forward-looking statements, including for

example: results in clinical trials may not be indicative of results from later stage or larger clinical trials (or in broader patient populations once the product is approved for use by regulatory agencies); the possibility that results of clinical trials are not predictive of safety and efficacy and potency of our products (or we fail to adequately operate or manage our clinical trials) which could cause us to discontinue sales of the product (or halt trials, delay or prevent us from making regulatory approval filings or result in denial of approval of our product candidates); unexpected delays in clinical trials; unexpected concerns regarding products and product candidates that may arise from additional data or analysis obtained during clinical trials or obtained once used by patients following product approval; future product improvements may not be realized due to expense or feasibility or other factors; delays (expected or unexpected) in the time it takes regulatory agencies to review and make determinations on applications for the marketing approval of our products; inability to timely submit (or failure to submit) future applications for regulatory approval for our products and product candidates; inability to timely initiate (or failure to initiate) and complete future clinical trials due to safety issues, IRB decisions, CMC-related issues, expense or unfavorable results from earlier trials (among other reasons); our dependence on sales from our principal product (Soliris); future competition from biosimilars and novel products; decisions of regulatory authorities regarding the adequacy of our research, marketing approval or material limitations on the marketing of our products; delays or failure of product candidates to obtain regulatory approval; delays or the inability to launch product candidates due to regulatory restrictions, anticipated expense or other matters; interruptions or failures in the manufacture and supply of our products and our product candidates; failure to satisfactorily address matters raised by the FDA and other regulatory agencies regarding products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; inability to complete acquisitions or grow the product pipeline through acquisitions (including due to failure to obtain antitrust approvals); the possibility that current rates of adoption of our products are not sustained; the adequacy of our pharmacovigilance and drug safety reporting processes; failure to protect and enforce our data, intellectual property and proprietary rights and the risks and uncertainties relating to intellectual property claims, lawsuits and challenges against us (including intellectual property lawsuits relating to Ultomiris brought by third parties and inter partes review petitions submitted by third parties); the risk that third party payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all; failure to realize the benefits and potential of investments, collaborations, licenses and acquisitions; the possibility that expected tax benefits will not be realized; potential declines in sovereign credit ratings or sovereign defaults in countries where we sell our products; delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement; uncertainties surrounding legal proceedings, company investigations and government investigations, including investigations of Alexion by the U.S. Securities and Exchange Commission (SEC) and U.S. Department of Justice; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, HPP and LAL-D and other indications we are pursuing are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the acquisition of Syntimmune and other companies and co-development efforts; and a variety of other risks set forth from time to time in Alexion's filings with the SEC, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 and in our other filings with the SEC. Alexion disclaims any obligation to update any of these forward-looking statements to reflect events or circumstances after the date hereof, except when a duty arises under law.

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