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FDA Approves Conversion of Soliris® (eculizumab) Accelerated Approval in aHUS to Regular Approval for the Treatment of Patients with aHUS

Regular Approval Includes Data from Four Multi-National Prospective Clinical Trials in a Broad Population of Adult and Pediatric Patients with aHUS and Includes Long-term Data with Two-Year Treatment Outcomes

Longer-Term Clinical Benefit Including Prevention of Thrombotic Microangiopathy and Continued Improvement in Renal Function Associated with Chronic and Sustained Soliris Treatment Now Specified in Revised Label with Inclusion of Two-Year Treatment Outcomes

Use of Soliris in aHUS Prior to Supportive Care with Either Plasma Exchange or Plasma Infusion - Now Specifically Included in Package Insert with Additional Two Prospective Trials

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) today announced that the U.S. Food and Drug Administration (FDA) has approved the Company's supplemental Biologics License Application (sBLA) providing regular approval for Soliris® (eculizumab) for the treatment of adult and pediatric patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA). This update reflects Alexion's fulfillment of post-marketing requirements, including the submission of confirmatory data from two additional prospective clinical trials, including one in pediatric patients with aHUS. The revised label now specifies important longer-term clinical benefit associated with chronic and sustained Soliris treatment with inclusion of results with two years of ongoing treatment in aHUS patients. The updated label also includes data on the use of Soliris treatment prior to use of supportive care with either plasma exchange or plasma in prospective clinical trials.

aHUS is a genetic, chronic, ultra-rare disease defined by immediate and lifelong risk of thrombotic microangiopathy (TMA) resulting in vital organ failure and premature death. Soliris, a first-in-class terminal complement inhibitor, specifically targets uncontrolled complement activation, and is the first and only approved treatment for pediatric and adult patients with aHUS in the United States, European Union, Japan and other countries. Soliris previously received Accelerated Approval (Subpart E) for this indication from the FDA in September 2011. The FDA grants Accelerated Approval to drugs based on an effect on a surrogate or intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit. To achieve regular approval, a drug company must usually submit additional data to verify clinical benefit.¹

"We are pleased that, since 2011, the FDA's Accelerated Approval process has enabled us to provide Soliris to individuals whose lives have been at risk of the severe clinical manifestations of aHUS and who would otherwise have had no safe or effective treatment options," said Leonard Bell, Chief Executive Officer of Alexion. "The results obtained from the two additional prospective clinical trials further confirm the safety, efficacy and life-transforming benefit of chronic Soliris treatment in both adult and pediatric patients with aHUS. The updated label now includes data that specifically supports the longer-term benefit associated with chronic and sustained Soliris treatment. We continue to work with a sense of urgency to bring Soliris to more patients suffering from this life-threatening disease worldwide."

The Clinical Studies section (Section 14.2) of the revised Soliris prescribing information now includes results from a total of four prospective, single-arm studies in patients with aHUS, three in adult and adolescent patients and one in pediatric patients, as well as one retrospective pediatric study, which evaluated the safety and efficacy of Soliris for the treatment of aHUS. Longer-term data of original registration studies demonstrated that chronic and sustained Soliris treatment inhibited complement-mediated TMA and resulted in significant and continuous time-dependent improvements in renal function, and was well tolerated. Importantly, 5 out of 18 patients in the original registration studies who deviated from the approved Soliris dosing, including discontinuation, experienced severe TMA manifestations whereas patients who stayed on therapy had complete inhibition of complement activity, which was sustained through 2 years. Results from the two additional prospective trials conducted by Alexion - one in adult and the other in pediatric patients with aHUS - showed that Soliris inhibited systemic complement-mediated TMA (the formation of blood clots in small blood vessels throughout the body), improved renal function, decreased or eliminated the need for dialysis and was well-tolerated.^{2,3} Efficacy and safety results from the additional prospective clinical trials were consistent with those observed in the original Soliris registration trials.⁴⁻⁶

Two-Year Treatment Outcome Data Provided in Package Insert (C08-002A/B and C08-003A/B)

The updated U.S. Package Insert includes longer-term data in patients from the two initial prospective, multinational registration trials (referred to as Trial 1 and Trial 2). In both Trial 1 and Trial 2, chronic and sustained Soliris treatment inhibited complement-mediated TMA and resulted in significant and continuous time-dependent improvements in renal function through 2 years. In Trial 1, the proportion of patients that achieved hematologic normalization increased from 76% at 26 weeks to 88% at 2 years and the mean eGFR increase by 32 mL/min/1.73m² from baseline achieved at 26 weeks was maintained through 2 years. Four of the five patients (80%), who discontinued dialysis by 26 weeks remained off dialysis and no patient required new dialysis through 2 years. In Trial 2, the proportion of patients that achieved TMA event-free status increased from 80% at 26 weeks to 95% at 2 years. Also, in Trial 2, patients that had a median of 48 months from aHUS diagnosis to screening for the trial and had sustained longer-term renal damage were observed to have a time-dependent improvement in renal function as measured by eGFR \geq 15 mL/min/1.73 m², which increased from 5% of patients at 26 weeks to 40% of patients at 2 years. In both Trials, responses to Soliris were similar in patients with and without identified mutations in genes encoding complement regulatory factor proteins or auto-antibodies to factor H. The most common serious adverse events (SAEs) with Soliris treatment were accelerated hypertension, hypertension and influenza. There was no increase in SAEs with ongoing Soliris treatment, as rates of SAEs remained steady or declined from the initial 26-week study period to the subsequent treatment periods.⁷ There were no deaths from Trial 1 and 1 patient death from Trial 2 due to gastrointestinal bleed after 1.9 years of Soliris treatment that was deemed unrelated to drug.

About the New and Largest Adult aHUS Study (C10-004)

The largest prospective trial of Soliris in adults with aHUS treated 41 patients, representing a broad patient population. Six of 41 patients received Soliris as initial treatment intervention prior to supportive care with either plasma exchange or plasma infusion. The primary endpoint of the study was the proportion of patients with complete TMA response, as measured by platelet count normalization, LDH normalization and preservation of renal function (< 25% increase in serum creatinine from baseline), at 26 weeks. The study met its primary endpoint, with 30 of 41 patients (73%) achieving a complete TMA response at 26 weeks. Ninety eight percent of patients (40/41) achieved platelet count normalization ($\geq 150 \times 10^9/L$) by week 26, and the mean increase in platelet count from baseline was $135 \times 10^9/L$ ($P < 0.0001$), demonstrating inhibition of complement-mediated TMA. Soliris significantly improved renal function with a mean increase in eGFR from baseline of 29 mL/min/1.73m² ($P < 0.0001$). Most importantly, 83% of patients on dialysis at baseline (20/24) discontinued dialysis by week 26. Baseline characteristics of presenting patients pre-treatment and responses to Soliris were similar in patients with and without identified mutations in genes encoding complement regulatory factor proteins or auto-antibodies to factor H. The most common adverse events (AEs) were headache (37%), diarrhea (32%) and peripheral edema (22%). There were no deaths. Two meningococcal infections occurred; both patients recovered, with one patient continuing on Soliris therapy and one discontinuing therapy with subsequent deterioration of renal function that necessitated dialysis support.²

About the New and First Prospective Pediatric aHUS Study (C10-003)

The first prospective trial in pediatric patients with aHUS treated 22 pediatric patients with aHUS who were at least 1 month old and less than 18 years of age.³ Fifty five percent of treated patients (12/22) received Soliris as initial intervention prior to supportive care with either plasma exchange or plasma infusion. The primary endpoint of the study was the proportion of patients with a complete TMA response, defined as platelet count normalization, lactate dehydrogenase (LDH) normalization, and $\geq 25\%$ decrease in serum creatinine from baseline, during 26 weeks of treatment. Sixty four percent of patients (14/22) achieved the study's primary endpoint of complete TMA response at 26 weeks, which required significant improvement in renal function ($\geq 25\%$ decrease in creatinine). Platelet count normalization was achieved in 21 of the 22 patients (95%); the median time to platelet count normalization was seven days and the mean improvement in platelet count from baseline was $164 \times 10^9/L$ ($p < 0.0001$). Hematologic normalization was observed in 82% of patients (18/22). Soliris significantly improved renal function with a mean 64 mL/min/1.73m² ($P < 0.0001$) increase in eGFR from baseline. Importantly 82% of patients on dialysis at baseline (9/11) discontinued dialysis by week 26 with Soliris treatment. Baseline characteristics of presenting patients pre-treatment and responses to Soliris were similar in patients with and without identified mutations in genes encoding complement regulatory factor proteins or auto-antibodies to factor H. The most common AEs were fever (50%) and cough (36%). One patient had a human anti-human antibody response, and continued chronic Soliris treatment without apparent adverse effect. There were no meningococcal infections and no deaths during the 26-week study.³

About aHUS

aHUS is a chronic, ultra-rare, and life-threatening disease in which a genetic deficiency in one or more complement regulatory genes causes chronic uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body.^{8,9} Permanent, uncontrolled complement activation in aHUS causes a life-long risk for TMA, which leads to sudden, catastrophic, and life-threatening damage to the kidney, brain, heart, and other vital organs, and premature death.^{8,10} Sixty-five percent of all patients with aHUS die, require kidney dialysis, or have permanent kidney damage within the first year after diagnosis despite plasma exchange or plasma infusion (PE/PI).^{11,12} The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90% transplant failure rate in these TMA patients.¹³

aHUS affects both children and adults. Complement-mediated TMA also causes reduction in platelet count (thrombocytopenia) and red blood cell destruction (hemolysis). While mutations have been identified in at least ten different complement regulatory genes, mutations are not identified in 30-50% of patients with a confirmed diagnosis of aHUS.¹⁴

About Soliris

Soliris® (eculizumab) is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is approved in the U.S. (2007), European Union (2007), Japan (2010) and other countries as the first and only treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis (destruction of red blood cells). Soliris is indicated to reduce hemolysis. Soliris is also approved in the U.S. (2011), the European Union (2011), Japan (2013) and other countries as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS), a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated thrombotic microangiopathy, or TMA (blood clots in small vessels). Soliris is indicated to inhibit complement-mediated TMA. The effectiveness of Soliris in aHUS is based on the effects on TMA and renal function. Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

Alexion's breakthrough approach in terminal complement inhibition has received the pharmaceutical industry's highest honors: the 2008 Prix Galien USA Award for Best Biotechnology Product with broad implications for future biomedical research and the 2009 Prix Galien France Award in the category of Drugs for Rare Diseases. More information, including the full prescribing information on Soliris, is available at www.soliris.net.

Important Safety Information

The U.S. product label for Soliris includes a boxed warning: "Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early [see Warnings and Precautions (5.1)]. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal

vaccination in patients with complement deficiencies. Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection [See Warnings and Precautions (5.1) for additional guidance on the management of the risk of meningococcal infection]. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected. Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program [see Warnings and Precautions (5.2)]. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747)."

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis (runny nose), back pain and nausea. Soliris treatment of patients with PNH should not alter anticoagulant management because the effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established. In patients with aHUS, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia. Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS). Please see full prescribing information for Soliris, including boxed WARNING regarding risk of serious meningococcal infection.
http://soliris.net/sites/default/files/assets/soliris_pi.pdf

About Alexion

Alexion is a biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Alexion is the global leader in complement inhibition and has developed and markets Soliris® (eculizumab) as a treatment for patients with PNH and aHUS, two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in nearly 50 countries for the treatment of PNH, and in the United States, European Union, Japan and other countries for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris in additional severe and ultra-rare disorders beyond PNH and aHUS, and is developing other highly innovative biotechnology product candidates across multiple therapeutic areas. This press release and further information about Alexion can be found at: www.alexionpharma.com.

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Safe Harbor Statement

This news release contains forward-looking statements, including statements related to anticipated clinical development, regulatory and commercial milestones and potential health and medical benefits of Soliris® (eculizumab) for the potential treatment of patients with aHUS. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of Soliris for its current or potential new indications, and a variety of other risks set forth from time to time in Alexion's filings with the Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the period ended March 31, 2014, and in Alexion's other filings with the Securities and Exchange Commission. Alexion does not intend 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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