# Alexion Receives Marketing Authorization from European Commission for New Formulation of ULTOMIRIS® (ravulizumab) with Significantly Reduced Infusion Time

November 20, 2020

*– The new 100 mg/mL formulation will reduce infusion time by approximately 60%, lessening the burden on patients –*

*– ULTOMIRIS is approved for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) –*

BOSTON--(BUSINESS WIRE)--Nov. 20, 2020-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that the European Commission (EC) has approved the new 100 mg/mL intravenous (IV) formulation of ULTOMIRIS® (ravulizumab) for the treatment of two ultra-rare diseases – paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). ULTOMIRIS is the first and only long-acting C5 inhibitor administered to patients every eight weeks or every four weeks for pediatric patients less than 20 kg. ULTOMIRIS 100 mg/mL is an advancement in the treatment experience for patients with aHUS and PNH by reducing average annual infusion times by approximately 60 percent compared to ULTOMIRIS 10 mg/mL, while delivering comparable safety and efficacy. With ULTOMIRIS 100 mg/mL, most patients will spend six hours or less a year receiving treatment.

"ULTOMIRIS has already provided patients with greater flexibility and this new formulation is another step forward in reducing the overall treatment burden," said Professor Alexander Röth, Department of Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany. "With this new formulation, patients will experience comparable safety and efficacy to the original formulation while spending significantly less time per year receiving treatment, which has the potential to make a meaningful difference in their lives."

PNH is a blood disorder characterized by complement-mediated destruction of the red blood cells that can cause a wide range of debilitating symptoms and complications, including thrombosis, which can occur throughout the body, and result in organ damage and premature death.[1] Atypical HUS can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots.[2] Affecting both adults and children, aHUS patients can present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of both aHUS and PNH can be poor in many cases, so a timely and accurate diagnosis—in addition to appropriate treatment—is critical to improving patient outcomes.

"The European Commission's approval of ULTOMIRIS in this new formulation will provide a meaningful benefit to patients' quality of life," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "This new formulation demonstrates Alexion's continued commitment to innovating for patients and their families. In addition, it lessens the overall burden on healthcare systems and practitioners with reduced infusion times, and on patients, who will only spend six hours or less a year receiving their treatment."

The European Commission approval is based on a comprehensive chemistry, manufacturing and control submission and a supplementary clinical data set showing that the safety, pharmacokinetics and immunogenicity following administration of ULTOMIRIS 10 mg/mL and ULTOMIRIS 100 mg/mL were comparable. Similarly, the data set showed no relevant changes in the efficacy measure of mean lactate dehydrogenase (LDH) levels across the two formulations. The new proposed formulation requires an infusion time of 0.4 to 1.3 hours (25 to 75 minutes) depending on body weight, reducing the infusion time by approximately 60 percent compared with the currently available 10 mg/mL IV formulation, which ranges from 1.3 to 3.3 hours (77 to 194 minutes) depending on body weight.

ULTOMIRIS 100 mg/mL was approved by the U.S. Food and Drug Administration (FDA) in October 2020, and a regulatory filing is under review in Japan.

Alexion continues to innovate with ULTOMIRIS, with the goal of improving the patient experience. We plan to submit regulatory filings in the U.S. and EU in the third quarter of 2021 for an ULTOMIRIS subcutaneous formulation and device combination for PNH and aHUS that can be self-administered at home, pending completion of the ongoing Phase 3 study and collection of 12-month safety data. In addition, the collective ULTOMIRIS clinical development programs present an opportunity to expand treatment for rare diseases across hematology, nephrology, neurology, and for the treatment of severe COVID-19, with seven Phase 3 programs that are ongoing or have planned clinical trial initiations in 2020.

**About Paroxysmal Nocturnal Hemoglobinuria (PNH)**
PNH is a serious ultra-rare blood disorder with devastating consequences. It is characterized by the destruction of red blood cells, which is also referred to as hemolysis. PNH occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own red blood cells. PNH often goes unrecognized, with delays in diagnosis from one to more than five years. Patients with PNH may experience a range of symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine and anemia. The most devastating consequence of chronic hemolysis is the formation of blood clots, which can occur in blood vessels throughout the body, damage vital organs, and potentially lead to premature death. PNH can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.

**About Atypical Hemolytic Uremic Syndrome (aHUS)**
aHUS is an ultra-rare disease that can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots. aHUS occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own healthy cells. aHUS can cause sudden organ failure or a slow loss of function over time—potentially resulting in the need for a transplant, and in some cases, death. aHUS affects both adults and children, and many patients present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, so a timely and accurate diagnosis—in addition to treatment—is critical to improving patient outcomes. Available tests can help distinguish aHUS from other hemolytic diseases with similar symptoms.

**About ULTOMIRIS®**

ULTOMIRIS® (ravulizumab) is the first and only long-acting 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 complement cascade over-responds, leading the body to attack its own healthy cells. ULTOMIRIS is administered intravenously every eight weeks or, for pediatric patients less than 20 kg, every four weeks, following a loading dose. ULTOMIRIS is approved in the United States (U.S.), European Union (EU) and Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (PNH). It is also approved in the U.S. and Japan for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA) in adult and pediatric (one month of age and older) patients, as well as in the EU for the treatment of adults and children with a body weight of at least 10 kg with aHUS. In the U.S., ULTOMIRIS is available in two formulations with the same mechanism of action and consistent safety and efficacy. The ULTOMIRIS 100 mg/mL formulation reduces average annual infusion time for patients with aHUS and PNH by approximately 60 percent (to approximately 45 minutes for adults in the average weight cohort) compared to the ULTOMIRIS 10 mg/mL formulation. To learn more about the regulatory status of ULTOMIRIS in the countries that we serve, please visit www.alexion.com.

**About Alexion**

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed and commercializes two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), as well as the first and only approved complement inhibitor to treat anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG) and 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) as well as the first and only approved Factor Xa inhibitor reversal agent. In addition, the company is developing several mid-to-late-stage therapies, including a copper-binding agent for Wilson disease, an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases and an oral Factor D inhibitor as well as several early-stage therapies, including one for light chain (AL) amyloidosis, a second oral Factor D inhibitor and a third complement inhibitor. 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, ophthalmology and acute care. Headquartered in Boston, Massachusetts, Alexion 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 that involve risks and uncertainties relating to future events and the future performance of Alexion, including statements related to: the safety, efficacy and benefits of the 100 mg/mL ULTOMIRIS formulation as a treatment for PNH and aHUS; that ULTOMIRIS 100 mg/mL formulation reduces infusion time as compared to the 10 mg/mL formulation of ULTOMIRIS by approximately 60% with comparable safety and efficacy; with ULTOMIRIS 100 mg/mL, most patients will spend six hours or less a year receiving treatment; this new formulation is another step forward in reducing the overall treatment burden; patients will experience comparable safety and efficacy to the original formulation while spending significantly less time per year receiving treatment; that shorter infusion times will make a meaningful difference in patient lives; that this new formulation demonstrates Alexion's continued commitment to innovating for patients and their families; that 100 mg/mL ULTOMIRIS lessens the overall burden on healthcare systems and practitioners with reduced infusion times, and on patients, who will only spend six hours or less a year receiving their treatment; Alexion plans to submit regulatory filings in the U.S. and EU in the third quarter of 2021 for an ULTOMIRIS subcutaneous formulation and device combination for PNH and aHUS that can be self-administered at home; the collective ULTOMIRIS clinical development programs present an opportunity to expand treatment for rare diseases across hematology, nephrology, neurology, and for the treatment of severe COVID-19; and that Alexion has seven Phase 3 programs that are ongoing or have planned clinical trial initiations in 2020. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those expected by these forward looking statements, including for example: the anticipated safety profile and the benefits of the ULTOMIRIS 100 mg/ml formulation may not be realized (and the results of the clinical trials may not be indicative of future results); results of clinical trials may not be sufficient to satisfy regulatory authorities; results in clinical trials may not be indicative of results from later stage or larger clinical trials (or in broader patient populations); 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); the severity of the impact of the COVID-19 pandemic on Alexion's business, including on commercial and clinical development programs; 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 regulatory agencies regarding our 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); 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 or that tax liabilities exceed current expectations; 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; adverse impacts on our supply chain, clinical trials, manufacturing operations, financial results, liquidity, hospitals, pharmacies and health care systems from natural disasters and global pandemics, including COVID-19; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk

that estimates regarding the number of patients with PNH, aHUS, gMG, NMOSD, HPP and LAL-D and other indications we are pursuing (as well as patients requiring a Factor Xa inhibitor reversal agent) are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the acquisitions of Portola Pharmaceuticals, Achillion 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 period ended September 30, 2020 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.

**References**


1. Peacock-Young B, Macrae F, Newton J, et al. *Haematologica 2018*. Volume 103(1):9-1
2. Yan K, Desai K, Gullapalli L, et al. Epidemiology of Atypical Hemolytic Uremic Syndrome: A Systematic Literature Review. *Clin Epidemiol*. 2020;12:295-305


**Short ULTOMIRIS SmPC – June 2020**

**ULTOMIRIS (ravulizumab) Prescribing Information**

**Please refer to the SmPC for further information before prescribing.**

**ULTOMIRIS** 300 mg concentrate for solution for infusion

**Qualitative and quantitative composition:** One vial of 30 mL contains 30 0mg of ravulizumab, produced in Chinese hamster ovary (CHO) cell culture by recombinant DNA technology. After dilution, the final concentration of the solution to be infused is 5 mg/mL. Excipient(s) with known effect: Sodium (5 mmol per vial). Clear to translucent, slight whitish colour, pH 7.0 solution.

**Therapeutic indication:** Treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) in patients with haemolysis with clinical symptom(s) indicative of high disease activity and in patients who are clinically stable after having been treated with eculizumab for at least the past 6 months. Treatment of patients with a body weight of 10 kg or above with atypical haemolytic uremic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab.

**Posology and method of administration.** Posology: The recommended dosing regimen consists of a loading dose followed by maintenance dosing, administered by intravenous infusion. The doses to be administered are based on the patient's body weight. For adult patients (≥ 18 years of age), maintenance doses should be administered at a once every 8 week interval, starting 2 weeks after loading dose administration. Dosing schedule is allowed to occasionally vary by ± 7 days of the scheduled infusion day (except for the first maintenance dose of ravulizumab) but the subsequent dose should be administered according to the original schedule. For patients switching from eculizumab to ravulizumab, the loading dose of ravulizumab should be administered 2 weeks after the last eculizumab infusion, and then maintenance doses are administered once every 8 weeks, starting 2 weeks after loading dose administration. Ravulizumab has not been studied in patients with PNH who weigh less than 40 kg. There is no experience of concomitant PE/PI (plasmapheresis or plasma exchange, or fresh frozen plasma infusion) use with ravulizumab. Administration of PE/PI may reduce ravulizumab serum levels. In aHUS, ravulizumab treatment to resolve TMA manifestations should be for a minimum duration of 6 months, beyond which length of treatment needs to be considered for each patient individually. Patients who are at higher risk for TMA recurrence, as determined by the treating healthcare provider (or clinically indicated), may require chronic therapy. Special Populations: Paediatric patients with aHUS with body weight ≥ 40 kg are treated in accordance with the adult dosing recommendations. The weight-based doses and dosing intervals for paediatric patients ≥ 10 kg to 20 kg is once every 4 week interval, for paediatric patients ≥ 20 kg to 40 kg once every 8 weeks, starting 2 weeks after loading dose administration. Data to support safety and efficacy of ravulizumab for patients with body weight below 10 kg are limited. No recommendation on a posology can be made for patients below 10 kg body weight (please refer to the SmPC for currently available data). The safety and efficacy of ravulizumab in children with PNH aged 0 to < 18 years have not been established. No data are available. Method of administration: For intravenous infusion only. ULTOMIRIS must be diluted to a final concentration of 5 mg/mL. This medicinal product must be administered through a 0.2 µm filter and should not be administered as an intravenous push or bolus injection. ULTOMIRIS must be diluted prior to administration by intravenous infusion over a minimal period of 1.7 to 2.4 hours depending of body weight (please refer to the SmPC).

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients; in patients with unresolved Neisseria meningitidis infection at treatment initiation; in patients who are not currently vaccinated against Neisseria meningitidis unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination. **Special warnings and precautions for use.** Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Serious meningococcal infection: Due to its mechanism of action, the use of ravulizumab increases the patient's susceptibility to meningococcal infection/sepsis (Neisseria meningitidis). Meningococcal disease due to any serogroup may occur. To reduce this risk of infection, all patients must be vaccinated against meningococcal infections at least two weeks prior to initiating ravulizumab unless the risk of delaying ravulizumab therapy outweighs the risk of developing a meningococcal infection. Patients who initiate ravulizumab treatment less than 2 weeks after receiving a meningococcal vaccine, must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. Vaccines against serogroups A, C, Y, W135 and B where available, are recommended in preventing the commonly pathogenic meningococcal serogroups. Patients must be vaccinated or revaccinated according to current national guidelines for vaccination use. If the patient is being switched from eculizumab treatment, physicians should verify that meningococcal vaccination is current according to national guidelines for vaccination use. Vaccination may not be sufficient to prevent meningococcal infection. Consideration should be given to official guidance on the appropriate use of antibacterial agents. Cases of serious meningococcal infections/sepsis have been reported in patients treated with ravulizumab. Cases of serious or fatal meningococcal infections/sepsis have been reported in patients treated with other terminal complement inhibitors. All patients should be monitored for early signs of meningococcal infection and sepsis, evaluated immediately if infection is suspected, and treated with appropriate antibiotics. Patients should be informed of these signs and symptoms and steps should be taken to seek medical care immediately. Physicians should provide patients with a patient information brochure and a patient safety card. Immunization: Prior to initiating ravulizumab therapy, it is recommended that PNH and aHUS patients initiate immunizations according to current immunization guidelines. Vaccination may further activate complement. As a result, patients with complement-mediated diseases, including PNH and aHUS, may experience increased signs and symptoms of their underlying disease, such as haemolysis. Therefore, patients should be closely monitored for disease symptoms after recommended vaccination. Patients below the age of 18 years old must be vaccinated against Haemophilus influenzae and pneumococcal infections, and strictly need to adhere to the national vaccination recommendations for each age group.

Other systemic infections: Ravulizumab therapy should be administered with caution to patients with active systemic infections. Ravulizumab blocks terminal complement activation; therefore, patients may have increased susceptibility to infections caused by Neisseria species and encapsulated bacteria. Serious infections with Neisseria species (other than Neisseria meningitidis), including disseminated gonococcal infections, have been reported. Patients should be provided with information from the Package Leaflet to increase their awareness of potential serious infections and their signs and symptoms. Physicians should advise patients about gonorrhea prevention. Infusion reactions: Administration of ravulizumab may result in infusion reactions. In clinical trials, with PNH and aHUS [(4 out of 296 in patients with PNH) and (4 of 89 patients with aHUS)] patients experienced infusion reactions which were mild in severity and transient [e.g., lower back pain, drop in blood pressure, elevation in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), and dysgeusia(bad taste)]. In case of infusion reaction, infusion of ravulizumab should be interrupted and appropriate supportive measures should be instituted if signs of cardiovascular instability or respiratory compromise occur.

Treatment discontinuation for PNH: If patients with PNH discontinue treatment with ravulizumab, they should be closely monitored for signs and symptoms of serious intravascular haemolysis, identified by elevated LDH (lactate dehydrogenase) levels along with sudden decrease in PNH clone size or haemoglobin, or re-appearance of symptoms such as fatigue, haemoglobinuria, abdominal pain, shortness of breath (dyspnoea), major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction. Any patient who discontinues ravulizumab should be monitored for at least 16 weeks to detect haemolysis and other reactions. If signs and symptoms of haemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ravulizumab. Treatment discontinuation for aHUS: There are no specific data on ravulizumab discontinuation. In a long-term prospective observational study, discontinuation of complement C5 inhibitor treatment (eculizumab) resulted in a 13.5-fold higher rate of TMA recurrence and showed a trend toward reduced renal function compared to patients who continued treatment. If patients must discontinue treatment with ravulizumab, they should be monitored closely for signs and symptoms of TMA on an on-going basis. However, monitoring may be insufficient to predict or prevent severe TMA complications. TMA complications post-discontinuation can be identified if any of the following is observed: (i) At least two of the following laboratory results observed concurrently: a decrease in platelet count of 25% or more as compared to either baseline or to peak platelet count during ravulizumab treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during ravulizumab treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during ravulizumab treatment (results should be confirmed by a second measurement), or (ii) any one of the following symptoms of TMA: a change in mental status or seizures or other extra-renal TMA manifestations including cardiovascular abnormalities, pericarditis, gastrointestinal symptoms/diarrhoea; or thrombosis. If TMA complications occur after ravulizumab discontinuation, consider reinitiation of ravulizumab treatment beginning with the loading dose and maintenance dose. This medicinal product when diluted with sodium chloride 9 mg/mL (0.9 %) solution for injection contains 2.65 g sodium per 720 mL at the maximal dose, equivalent to 133 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. **Interaction with other medicinal products and other forms of interaction:** No interaction studies have been performed. Chronic intravenous human immunoglobulin (IVIg) treatment may interfere with the endosomal neonatal Fc receptor (FcRn) recycling mechanism of monoclonal antibodies such as ravulizumab and thereby decrease serum ravulizumab concentrations. **Fertility, pregnancy and lactation.** Women of childbearing potential: Women of childbearing potential should use effective contraception methods during treatment and up to 8 months after treatment. Pregnancy: There are no clinical data from the use of ravulizumab in pregnant women. Nonclinical reproductive toxicology studies were not conducted with ravulizumab. Reproductive toxicology studies were conducted in mice using the murine surrogate molecule BB5.1, which assessed effect of C5 blockade on the reproductive system. No specific test-article related reproductive toxicities were identified in these studies. Human IgG are known to cross the human placental barrier, and thus ravulizumab may potentially cause terminal complement inhibition in the foetal circulation. Animal studies are insufficient with respect to reproductive toxicity. In pregnant women the use of ravulizumab may be considered following an assessment of the risks and benefits. Breast-feeding: It is unknown whether ravulizumab is excreted into human milk. Nonclinical reproductive toxicology studies conducted in mice with the murine surrogate molecule BB5.1 identified no adverse effect to pups resulting from consuming milk from treated dams. A risk to infants cannot be excluded. Since many medicinal products and immunoglobulins are secreted into human milk, and because of the potential for serious adverse reactions in nursing infants, breast-feeding should be discontinued during treatment with ravulizumab and up to 8 months after treatment. Fertility: No specific non-clinical study on fertility has been conducted with ravulizumab. Nonclinical reproductive toxicology studies conducted in mice with a murine surrogate molecule (BB5.1) identified no adverse effect on fertility of the treated females or males.

**Undesirable effects.** Summary of the safety profile: The most common adverse drug reactions (very common frequency) are diarrhea, nausea, vomiting, nasopharyngitis and headache. The most serious adverse reactions in patients in clinical trials are meningococcal infection and meningococcal sepsis. Tabulated list of adverse reactions: Very common adverse reactions observed from PNH and aHUS clinical trials (≥1/10): Upper respiratory tract infection, Nasopharyngitis, Headache, Diarrhoea, Nausea, Pyrexia, Fatigue. Common adverse reactions (≥1/100 to <1/10): Dizziness, Abdominal pain, Vomiting, Dyspepsia, Rash, Pruritus, Arthralgia, Back pain, Myalgia, Muscle spasms, Influenza like illness, Asthenia. Uncommon adverse reactions (≥1/1,000 to <1/100): Meningococcal infection, Chills. In paediatric patients with evidence of aHUS (aged 10 months to less than 18 years) included in the clinical study, the safety profile of ravulizumab appeared similar to that observed in adult patients with evidence of aHUS. The safety profiles in the different paediatric subsets of age appear similar. The safety data for patient below 2 years of age is limited to four patients. The most common adverse reaction reported in paediatric patients was pyrexia. The safety of ravulizumab in children with PNH aged 0 to < 18 years have not been established. No data are available.

**Storage:** 2°C – 8°C. **Marketing Authorization Holder:** Alexion Europe SAS, 1-15, 103-105 rue Anatole France, 92300 Levallois-Perret, FRANCE.

Marketing Authorisation Number: EU/1/19/1371/001. **Date of First Authorisation:** {02 July 2019}. **Date of revision:** {25 June 2020}. Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu/.

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