# PRESS RELEASE ARCHIVE

## 2021

- NICE recommendation for ULTOMIRIS for aHUS (May 20th)
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- NICE recommendation for ULTOMIRIS for PNH (April 15th)
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For Trade Media Only

# NICE Accepts ULTOMIRIS® (ravulizumab) for Use in Patients with Atypical Haemolytic Uraemic Syndrome (aHUS)

*Ravulizumab is the first approved long-acting C5 complement inhibitor for aHUS – a life-threatening, ultra-rare disease*

UXBRIDGE – May 20, 2021 – Alexion Pharma UK has announced that the National Institute for Health and Care Excellence (NICE) has accepted ULTOMIRIS® (ravulizumab) [https://www.nice.org.uk/guidance/gid-ta10564/documents/final-appraisal-determination-document] for use by the NHS in England for the treatment of patients with a body weight of 10kg or above with atypical haemolytic uraemic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received SOLIRIS® (eculizumab) for at least 3 months and have evidence of response to eculizumab.[1] Ravulizumab is the first and only long-acting complement inhibitor that provides infusions every eight weeks (or every four weeks for patients 10-20kg). Ravulizumab provides immediate, complete, and sustained C5 inhibition, allowing the majority of patients to achieve a complete thrombotic microangiopathy (TMA) response and improvement in kidney function.

“This is great news for the aHUS community, as ravulizumab will reduce the number of infusions needed per year compared to eculizumab, significantly improving the quality of life for all those living with the condition,” said David Kavanagh, Professor of Complement Therapeutics at the National Renal Complement Therapeutics Centre (NRCTC). “Ravulizumab is a long-acting formula, thus increasing the time between infusions, providing similar efficacy with an acceptable safety profile. Having this choice is good news for all those living with aHUS and their families.”

The NICE approval of ravulizumab is based on a comprehensive clinical and health economic submission by Alexion, as well as evidence provided by patient advocacy organisations and clinical experts.

"The NICE decision is excellent news for aHUS patients and their families. Ravulizumab will make their lives much freer and easier whilst providing management of a life-threatening rare disease,” said Len Woodward, Director Trustee aHUS alliance Global Action.

“We are extremely pleased to see NICE also welcome ravulizumab for the treatment of patients with aHUS in England,” said Sean Richardson, Alexion General Manager, UK & Ireland. “We know how impactful these decisions are for the rare disease community, and each approval we receive advances the quality of life for patients. At Alexion, we are relentless in our ambition to innovate for patients and it brings great pleasure knowing that patients in England will benefit from the approval of this new therapeutic option.”



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## About atypical haemolytic 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 haemolytic 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, following a loading dose, to treat PNH in adults, and aHUS patients weighing >20kg (every four weeks for aHUS patients weighing 10-20kg). ULTOMIRIS is approved in the UK for the treatment of adults and children with a body weight of at least 10kg with atypical haemolytic uremic syndrome (aHUS). ULTOMIRIS is also approved in the UK for 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.

## 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 commercialisation of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed two approved complement inhibitors to treat patients with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic 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. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on the core therapeutic areas of haematology, 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. Further information about Alexion can be found at: www.alexion.com/worldwide/UK.



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[1] NICE. Final appraisal document. Ravulizumab for treating atypical haemolytic uraemic syndrome. Available at: https://www.nice.org.uk/guidance/gid-ta10564/documents/final-appraisal-determination-document. Last accessed: May 2021



Date of Preparation: May 2021
Document Number: UK/ULT-a/0042

For Trade Media Only

# SMC Accepts ULTOMIRIS® (ravulizumab) for Restricted Use for Atypical Haemolytic Uremic Syndrome (aHUS)

*– Ravulizumab is the first and only long-acting C5 complement inhibitor for aHUS –*

UXBRIDGE – May 10, 2021 – Alexion Pharma UK has announced that the Scottish Medicines Consortium (SMC) has accepted ULTOMIRIS® (ravulizumab) for restricted use by the NHS in Scotland for the treatment of patients with a body weight of 10kg or above with atypical haemolytic uremic syndrome (aHUS). Under the advice of the National Renal Complement Therapeutics Centre (NRCTC), patients who are complement inhibitor treatment-naïve or have received SOLIRIS® (eculizumab) for at least 3 months and have evidence of response to eculizumab would be eligible for this new treatment.[1] Ravulizumab is the first and only long-acting complement inhibitor that is infused every eight weeks (or every four weeks for patients 10-20kg). Ravulizumab provides immediate, complete and sustained C5 inhibition, allowing the majority of patients to achieve a complete thrombotic microangiopathy (TMA) response and improvement in kidney function.

“This is great news for the aHUS community in Scotland, as ravulizumab will reduce the number of infusions needed per year, significantly improving the quality of life for all those living with the condition,” said David Kavanagh, Professor of Complement Therapeutics at the National Renal Complement Therapeutics Centre (NRCTC). “Ravulizumab was built on the foundation of eculizumab with similar efficacy and an acceptable safety profile in both adult and paediatric patients with aHUS. However, the advanced formula means that ravulizumab lasts longer in the body, thus increasing the time between infusions. Having this choice is good news for all those living in Scotland with the condition and their families.”

The SMC approval of ravulizumab is based on a comprehensive clinical and health economic submission by Alexion, as well as evidence provided by patient advocacy organisations and clinical experts.

"The SMC decision is excellent news for aHUS patients and their families. Ravulizumab will make their lives much freer and easier whilst providing management of a life-threatening rare disease,” said Len Woodward, Director Trustee aHUS alliance Global Action.

“We welcome the SMC decision to recommend ravulizumab for use in aHUS patients in Scotland. This is a huge step forward for the aHUS community and will have such a large impact on the lives of the many patients who live day to day with this devastating condition,” said Sean Richardson, Alexion General Manager, UK & Ireland. “Our purpose at Alexion is to push the boundaries for the rare disease community and we are driven to bring innovative therapies to the patients we strive to serve.



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## 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, following a loading dose, to treat PNH in adults and in aHUS patients weighing >20kg (every four weeks for aHUS patients weighing 10-20kg). ULTOMIRIS is approved in the UK for 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. ULTOMIRIS is also approved in the UK for the treatment of adults and children with a body weight of at least 10kg with atypical haemolytic uremic syndrome (aHUS).

## 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 commercialisation of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed two approved complement inhibitors to treat patients with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic 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. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on the core therapeutic areas of haematology, 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. Further information about Alexion can be found at: www.alexion.com/worldwide/UK.

## References



Date of Preparation: May 2021
Document Number: UK/ULT-a/0038

[1] [Placeholder for SMC link]

For Trade and Medical Media Only

# NICE recommends ULTOMIRIS® (ravulizumab) for patients with Paroxysmal Nocturnal Haemoglobinuria (PNH)

*– Ravulizumab is the first approved, long-acting C5 complement inhibitor for PNH administered every other month –*

**UXBRIDGE – APRIL 15th, 2021** – Alexion Pharma UK has announced that the National Institute for Health and Care Excellence (NICE) has recommended ULTOMIRIS® (ravulizumab) for use in the National Health Service (NHS) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) in adult patients with haemolysis with clinical symptoms suggesting high disease activity, or whose disease is clinically stable after having SOLIRIS® (eculizumab) for at least 6 months.[1] As the first and only long-acting C5 complement inhibitor, ravulizumab represents a step forward in the treatment of PNH, delivering comparable safety and efficacy to eculizumab with infusions every eight weeks compared to every two weeks.

"The availability of ravulizumab will have a meaningful impact on the lives of patients with PNH," said Professor Peter Hillmen, Professor of Experimental Haematology at the University of Leeds and Honorary Consultant in Clinical Haematology at Leeds Teaching Hospitals NHS Trust. "Ravulizumab is as effective as the previous standard of care, eculizumab, with a similar safety profile, but with a longer-acting formulation. Patients with PNH will now only require infusions every 8 weeks rather than every 2 weeks which will have a major impact on their quality of life."

PNH is a debilitating ultra-rare blood disorder characterised by complement-mediated destruction of red blood cells (haemolysis) as well as risk of blood clots (thrombosis), which can occur throughout the body, and result in organ damage and premature death.[2] It impacts approximately 16 people per million in the United Kingdom.[3] It can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.[4,5] PNH often goes unrecognised, with delays in diagnosis ranging from one to more than five years.[6] The prognosis of PNH can be poor in many cases, so a timely and accurate diagnosis – in addition to appropriate treatment – is critical to improving patient outcomes.

"We are delighted at the recommendation from NICE, meaning we will be able to offer ravulizumab as a new treatment option to adult patients with PNH across the UK, helping to improve their overall quality of life," said Sean Richardson, Alexion General Manager, UK & Ireland. "We believe ravulizumab will become the new standard of care for patients with PNH by providing immediate and complete C5 inhibition, sustained throughout the eight-week dosing interval."



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Date of preparation: April 2021

The NICE recommendation of ravulizumab is based on the assessment of a comprehensive clinical and health economic submission by Alexion, as well as evidence provided by patient advocacy organisations and clinical experts.

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## About Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a serious ultra-rare blood disorder with devastating consequences. It is characterised by the destruction of red blood cells, which is also referred to as haemolysis. 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 unrecognised, 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-coloured urine and anaemia. The most devastating consequence of chronic haemolysis 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 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, following a loading dose, to treat PNH. ULTOMIRIS is approved in the UK for 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. ULTOMIRIS is also approved in the UK for the treatment of adults and children with a body weight of at least 10kg with atypical haemolytic uremic syndrome (aHUS). ULTOMIRIS was also accepted by the Scottish Medicines Consortium (SMC) for restricted use within NHS Scotland for the treatment of adult patients with 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.

## 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 commercialisation of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed two approved complement inhibitors to treat patients with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic 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. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its

development efforts on the core therapeutic areas of haematology, 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. Further information about Alexion can be found at: www.alexion.com/worldwide/UK.

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[1] NICE. Final. Final appraisal document. Ravulizumab for treating paroxysmal nocturnal haemoglobinuria. Available at: https://www.nice.org.uk/guidance/gid-ta10690/documents/final-appraisal-determination-document. Last accessed April 2021

[2] Peacock-Young B, Macrae F, Newton J, et al. *Haematologica 2018*. Volume 103(1):9-1

[3] PNH Support. What is PNH? Available at: https://pnhuk.org/what-is-pnh/. Last accessed March 2021.

[4] Hillmen P, Lewis SM, Bessler M, et al. N Engl J Med. 1995 Nov 9;333(19):1253-8.

[5] Socié G, Mary JY, de Gramont A, et al. Lancet. 1996;348:573-577.

[6] Shammo JM, Mitchell RL, Ogborn K et al. Blood. 2015;126:3264.

For Trade Media Only

# SMC Accepts ULTOMIRIS® (ravulizumab) for Restricted Use for Adults with Paroxysmal Nocturnal Haemoglobinuria (PNH)

*– Ravulizumab is the first approved, long-acting complement inhibitor for PNH administered every other month –*

**UXBRIDGE – FEBRUARY 9th, 2021** – Alexion Pharma UK announced that the Scottish Medicines Consortium (SMC) has accepted ULTOMIRIS® (ravulizumab) for restricted use by the NHS in Scotland for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH). Subject to the advice of the national PNH service, adult patients with haemolysis with clinical symptom(s) indicative of high disease activity, and adults patients who are clinically stable after having been treated with SOLIRIS® (eculizumab) for at least the past 6 months, would be eligible for this new treatment. Ravulizumab is an advanced formulation that represents a step forward in the treatment experience for patients with PNH with infusions every eight weeks compared to every two weeks with eculizumab, while delivering comparable safety and efficacy.

"Ravulizumab provides a major step forward in the treatment of PNH," said Dr Richard Kelly, Consultant in Clinical Haematology, Leeds Teaching Hospitals NHS Trust, and Joint Service Lead for the English National PNH Service. "The introduction of eculizumab more than 10 years ago transformed the lives of patients with PNH. Thanks to ravulizumab, PNH patients will now be able to experience significantly fewer infusions per year without any compromise on efficacy or safety. This reduced treatment burden has the potential to make a meaningful difference in their lives."

PNH is an ultra-rare blood disorder that impacts approximately 16 people per million in the United Kingdom.[1] It can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.[2,3] It is characterised 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.[4] PNH often goes unrecognised, with delays in diagnosis ranging from one to more than five years.[5] The prognosis of 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 availability of ravulizumab is wonderful news for patients and families living with PNH" said Lesley Loeliger, Founder and Chair, PNH Scotland. "Less frequent treatment sessions provide patients with hope and the opportunity to contribute fully to family and work life. We are pleased that the patient voice could play an important role in the evaluation process, helping to ensure this new therapeutic option reaches patients."

The SMC approval of ravulizumab is based on a comprehensive clinical and health economic submission by Alexion, as well as evidence provided by patient advocacy organisations and clinical experts.

“We are delighted that the SMC has recognized the significance of ravulizumab for patients with PNH,” said Sean Richardson, Alexion General Manager, UK & Ireland. “At Alexion, we are committed to advancing innovation in order to continue to improve the lives of patients. Helping to reduce the number of infusions per year, while also lessening the burden on healthcare systems, brings us all closer to achieving a better standard of care.”

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## About Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a serious ultra-rare blood disorder with devastating consequences. It is characterised by the destruction of red blood cells, which is also referred to as haemolysis. 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 unrecognised, 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-coloured urine and anaemia. The most devastating consequence of chronic haemolysis 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 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, following a loading dose, to treat PNH. ULTOMIRIS is approved in the European Union (EU) for 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. ULTOMIRIS is also approved in the EU for the treatment of adults and children with a body weight of at least 10kg with atypical haemolytic uremic syndrome (aHUS).

## 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 commercialisation of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed and commercialises two approved complement inhibitors to treat patients with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic 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. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on the core therapeutic areas of haematology, nephrology, neurology, metabolic disorders, cardiology and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. Further information about Alexion can be found at: www.alexion.com/worldwide/UK.

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[1] PNH Scotland. Who gets PNH? Available at: https://pnhscotland.org.uk/service/what-is-paroxysmal-nocturnal-haemoglobinuria/. Last accessed January 2021.

[2] Hillmen P, Lewis SM, Bessler M, et al. N Engl J Med. 1995 Nov 9;333(19):1253-8.

[3] Socié G, Mary JY, de Gramont A, et al. Lancet. 1996;348:573-577.

[4] Peacock-Young B, Macrae F, Newton J, et al. *Haematologica 2018*. Volume 103(1):9-1

[5] Shammo JM, Mitchell RL, Ogborn K et al. Blood. 2015;126:3264.

# Genetic Alliance UK and Alexion call for urgent reforms to improve patient care as new survey reveals shortcomings with UK Rare Disease Strategy

*New survey findings provide patient and community led recommendations for change ahead of new framework for rare diseases.*

**December 9, 2020** – Genetic Alliance UK and Alexion Pharma UK are calling on Government and the NHS to continue to take collaborative action to improve the quality of care for the 3.5 million people living with a rare disease in the UK.[i] This coincides with the launch of the survey findings, presented today at the All-Party Parliamentary Group (APPG) meeting on Rare, Genetic and Undiagnosed Conditions. The survey highlights perspectives on overall patient care from over 1,000 patients and representatives from the rare disease community and shares clear recommendations to support implementation of a new framework to drive improved health system prioritisation and accountability by healthcare providers and in Government.

The survey reveals that, despite a Rare Disease Strategy having been published in 2013, there are still major unmet needs in the care of patients living with a rare disease, across the entire patient pathway, from diagnosis through to treatment access and ongoing disease management and care. With 50% of patients believing that there has been no change in quality of care, over one third (37%) rating their overall experience of care as poor or very poor, and half (50%) of patients stating that their care has not been effectively coordinated. Research also found that 52% diagnosed within the last five years had to wait over two years for their diagnosis, with 41% waiting over five years, and almost half (49%) of patients having been misdiagnosed at least once. Additionally, almost two thirds of patients felt that their care has been further disrupted as a result of COVID-19.[ii]

*"While the UK's first Rare Disease Strategy has made some strides, it is unfortunate to see that it has had little impact on care for the majority of rare disease patients. The findings from our survey show why it is so important to listen and learn from patients and their experiences," said Jayne Spink, Chief Executive, Genetic Alliance UK. "The new Rare Disease Framework will offer an opportunity to remedy this and to ensure that faster diagnosis and better coordination of treatment and care are available to all those affected by rare diseases."*

With the implementation period of the 2013 UK Rare Disease Strategy coming to an end this year, a new rare disease framework is expected imminently. It is therefore vital that perspectives from across the patient and medical community are considered to improve the experience of care across the entire patient journey. The new Reforming Rare Diseases Report provides this insight by sharing the survey findings, as well as a series of key recommendations to help improve the quality of

life for people in the UK affected by rare diseases. These recommendations should be considered in the effective implementation of a new rare disease framework:

- As a first step, the Government and NHS should ensure that the implementation plans for the new Rare Disease Framework should be based on an evaluation as to why previous initiatives have failed to improve care in the last five years for all patients living with a rare disease.
- The NHS must ensure it has the infrastructure in place to ensure that all patients suspected of having a rare disease are identified and able to access all the necessary diagnostic capabilities that the Genomic Medicine Service can offer.
- The Government and the NHS should focus on improving whole person care for patients with more complex conditions.
- The NHS should provide every patient with a rare disease with (i) a dedicated care coordinator, (ii) access to a specialist centre if available and (iii) a care plan if desired by the patient.
- The NHS should put metrics and standards in place to ensure that decision making is shared with the patient, including improving access to relevant information about their condition.

Whilst acknowledging that the NHS now is very different to the NHS in 2013, COVID-19 has also exacerbated the longstanding issues rare disease patients face.[ii] Implementation of the new framework must recognise previous shortcomings, the changing landscape and consider how future care may be impacted by an ongoing pandemic.

"*This survey brings the patient voice on satisfaction of care to the forefront. The lack of health system prioritisation to address the challenges facing people with a rare disease over the last seven years shows that the original aim – "to ensure no one gets left behind because they have a rare disease" – has not yet delivered on this promise. With the expected new framework, the time is now to listen to the rare disease community and look across the whole patent journey, in order to urgently address these shortcomings, and implement fully against this to ensure positive change," Sean Richardson, VP & General Manager UK & Ireland, Alexion.*

You can access the survey findings and recommendations via the Reforming Rare Diseases report here.

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**About Rare Diseases**

A rare disease is defined by the European Union (EU) as a disease affecting 5 or fewer people in 10,000 of the general population.[iii] It is estimated that 3.5 million people have a rare disease in the UK.[i] 1 in 17 people, or seven percent of the population, will be affected by a rare condition at some point in their lives.[i] Currently, there are over 6,000 known rare diseases.[iv] These cover a broad range of health conditions that are typically disabling for patients due to the chronic, progressive,

degenerative, and frequently life-threatening aspects of the disease.[iii] Many rare diseases start in childhood and disproportionately affect children.[iii] Rare diseases can be difficult to diagnose and devastating to live with. The impact they have on patients, their families, and society is profound.

**About Genetic Alliance UK**

Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic, rare and undiagnosed conditions. They are a membership organisation made up of over 200 patient groups and aim to upskill its members, bringing together knowledge and advice, and unifying the voice of members around key policy issues that affect the patient community. Genetic Alliance UK are experts in health policy and have a team of in-house academics who conduct psychosocial and economic research into the effects of living with genetic, rare and undiagnosed conditions. They also actively support research and innovation across the field of genetic medicine and raise awareness within the wider public.

**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.

**References**


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# SMC Advises Alexion's ONDEXXYA®▼ (andexanet alfa) in Adults if a Life-Threatening or Uncontrolled Bleed Occurs When Taking Direct Factor Xa (FXa) Inhibitors Apixaban or Rivaroxaban

*– Andexanet alfa has been accepted for use within NHS Scotland on an interim basis subject to ongoing evaluation and future reassessment –*

*– Until now, there has been no licensed therapy to reverse direct FXa-associated major bleeds when treated with apixaban or rivaroxaban –*

**UXBRIDGE, UK – SEPTEMBER 7 2020** – Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that the Scottish Medicines Consortium (SMC) has accepted ONDEXXYA®▼ (andexanet alfa) for use within NHS Scotland in adults treated with the direct Factor Xa (FXa) inhibitors apixaban or rivaroxaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding, on an interim basis subject to ongoing evaluation and future reassessment.

"As the number of patients on direct Fxa inhibitors continues to increase, so does the need to ensure we can protect patients who may experience life-threatening or uncontrolled bleeds," said Professor Henry Watson, Consultant Haematologist, University of Aberdeen. "Andexanet alfa will give clinicians an approved therapy option and clinical strategy for the reversal of major bleeding in patients being treated with rivaroxaban and apixaban. This is a positive step forward for the safety of patients being treated with these important and widely used drugs."

Direct FXas inhibitors are increasingly used for the prevention and treatment of thrombotic events, such as deep vein thrombosis and pulmonary embolism, or if a patient is at high risk of a stroke due to an irregular heart rate (atrial fibrillation). These direct FXa inhibitors stop the blood from clotting normally in order to prevent unwanted clots from forming, but in doing so, can also increase the risk of major bleeding which can be life-threatening.[1,2] Until now, there has been no licensed therapy to reverse direct-FXa-activity in the patients who experience these life-threatening bleeds. Andexanet alfa can neutralise the anticoagulant effect of apixaban and rivaroxaban, thus stopping the life-threatening bleed.

"Andexanet alfa is now available to patients in Scotland to reverse life-threatening and uncontrolled bleeds as a result of treatment with the direct FXas inhibitors apixaban or rivaroxaban," said Sean Richardson, Vice President and General Manager for Alexion UK & Ireland. "We are pleased to serve all patients in Scotland who could benefit from andexanet alfa in this area of critical need."

Data was provided from two Phase 3 ANNEXA studies (ANNEXA-R and ANNEXA-A) that evaluated the safety and efficacy of andexanet alfa in reversing the anticoagulant activity of rivaroxaban or apixaban in older subjects, and data from the Phase 3b/4 ANNEXA-4 study that evaluated efficacy and safety in approximately 350 patients with life-threatening or uncontrolled major bleeding associated with the use of a direct Fxa inhibitors. In these patients, treatment with andexanet alfa markedly reduced the anti-factor Xa activity of apixaban and rivaroxaban, reversing the anticoagulant effect. 82 percent of

efficacy evaluable bleeding patients had good hemostatic efficacy (stopping of bleeding) at 12 hours when compared to baseline when adjudicated according to pre-specified criteria.[3]

The most frequently reported adverse reactions in subjects administered andexanet alfa were mild or moderate infusion-related reactions. Very common infusion related reactions included flushing and feeling hot. Commonly observed infusion related- reactions include cough, dysgeusia and dyspnoea. Transient elevations of pro-coagulant markers D-dimer and F1+2 fragments were also very commonly observed in subjects. Amongst bleeding patients administered andexanet alfa, commonly reported side effects were ischaemic stroke and pyrexia, with uncommonly reported side effects of cerebral infarction, cerebrovascular accident, transient ischaemic attack, acute myocardial infarction, cardiac arrest, myocardial infarction, deep vein thrombosis, iliac artery occlusion and pulmonary embolism.[4]

The European Commission (EC) granted conditional Marketing Authorisation for andexanet alfa in Europe in April 2019.[4] Marketed in the US as ANDEXXA® [coagulation factor Xa (recombinant), inactivated-zhzo], it was approved by the U.S. Food and Drug Administration (FDA) in May 2018 under the FDA's Accelerated Approval pathway.[5]

Andexanet alfa was developed and launched by Portola Pharmaceuticals. In July 2020, Portola Pharmaceutical was acquired by Alexion. Andexanet alfa is now owned and marketed by Alexion.[6]

## About ONDEXXYA®▼

ONDEXXYA®▼ (andexanet alfa) is a recombinant protein specifically designed to bind to direct Factor Xa (FXa) inhibitors and reverse their anticoagulant effect. Andexanet alfa is a modified form of the human FXa molecule, an enzyme that helps blood clot. It works by acting as a decoy for oral and injectable FXa inhibitors, which target and bind to FXa. When andexanet alfa is given to a patient with FXa inhibitor-related bleeding, it binds to the FXa inhibitor and prevents it from inhibiting the activity of FXa and reverses the anticoagulant effects of the inhibitor.

Treatment with andexanet alfa has been associated with serious and life-threatening adverse events, including:

- Arterial and venous thromboembolic events
- Ischemic events, including myocardial infarction and ischemic stroke
- Cardiac arrest
- Sudden deaths

Please refer to the full SmPC for further information on side effects reported with andexanet alfa.

### IMPORTANT INFORMATION FOR ANDEXANET ALFA

### BOXED WARNING: THROMBOEMBOLIC RISKS, ISCHEMIC RISKS, CARDIAC ARREST AND SUDDEN DEATHS

## About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare and devastating diseases through the discovery, development and commercialisation of life-changing medicines. As the global leader in complement biology and inhibition for more than 20 years, Alexion has developed and commercialised 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 generalised myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Alexion also has two 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. 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, metabolic disorders and cardiology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. Further information about Alexion can be found at: https://alexion.com/worldwide/UK.

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## Forward-Looking Statement

**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. 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: 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); the severity of the impact of the COVID-19 pandemic on Alexion's business, including on commercial and clinical trial 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 complement inhibitors; 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 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 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; 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; 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 coronavirus; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk that estimates regarding the number of patients in key therapeutic areas we are pursuing are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructurings; and a variety of other risks set forth from time to time in Alexion's international company filings. 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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