European Commission approves Benlysta for adult patients with active lupus nephritis

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First and only biologic approved for both systemic lupus erythematosus and lupus nephritis

For media and investors only

GlaxoSmithKline plc (GSK) today announced the European Commission has approved the expanded use of intravenous and subcutaneous BENLYSTA (belimumab) in combination with background immunosuppressive therapies for the treatment of adult patients with active lupus nephritis (LN) in Europe, in addition to systemic lupus erythematosus (SLE). The EU marketing authorisation follows the recent approval for the similar expanded LN indication in the U.S.

Dr. Hal Barron, Chief Scientific Officer and President R&D, GSK said:

> Active lupus nephritis, which causes inflammation in the kidneys, is one of the most serious consequences of systemic lupus erythematosus and occurs in more than 1 million patients worldwide. Benlysta is the first biologic approved to treat lupus and lupus nephritis, representing a significant new treatment option for patients and physicians across Europe dealing with this complex autoimmune disease.

The marketing authorisation application was based on data from the BLISS-LN (Efficacy and Safety of Belimumab in Adult Patients with Active Lupus Nephritis) study, which showed that, over two years, belimumab added to standard therapy increased renal response rates and helped to prevent worsening of kidney disease in patients with active lupus nephritis compared to standard therapy alone.

The BLISS-LN study is the largest and longest phase 3 study conducted in active LN, involving 448 adult patients. The study met its

primary endpoint demonstrating that a statistically significant greater number of patients achieved Primary Efficacy Renal Response (PERR) at two years (or 104 weeks) when treated with belimumab plus standard therapy compared to placebo plus standard therapy in adults with active LN (43% vs 32%, odds ratio (95% CI) 1.55 (1.04, 2.32), p=0.0311). Statistical significance compared to placebo across all four major secondary endpoints was achieved, including Complete Renal Response at Week 104 and Time to Renal-Related Event or Death. The adverse reactions observed in BLISS-LN were consistent with the known safety profile of belimumab administered intravenously plus standard therapy in patients with SLE.

Dr. Y.K.O. (Onno) Teng, MD, PhD, Nephrology clinician-scientist at the Department of Internal Medicine of the Leiden University Medical Center (LUMC), The Netherlands said:

> In the BLISS-LN study the addition of Benlysta to standard therapy resulted in a 49% decrease in risk to patients of experiencing a renal-related event as well as a significantly higher number of study participants reaching the PERR. I'm encouraged that progress is being made for people with lupus nephritis as we work toward the overarching goal to delay the need for kidney replacement therapies, such as dialysis and transplantation.

Dr. Richard Furie, Chief of the Division of Rheumatology and Professor at the Feinstein Institutes for Medical Research at Northwell Health, and Lead Investigator of the BLISS-LN study commented:

> This achievement is derived from decades of research. For years, we have not been able to achieve remission for more than one-third of patients with lupus nephritis and, despite all of our efforts, 10% to 30% of patients with lupus kidney disease still progress to end-stage kidney disease. The data from the BLISS-LN study show that Benlysta added to standard therapy in management of active lupus nephritis may lead to improved long-term outcomes for patients by both increasing response rates and delaying further kidney disease progression.

BLISS-LN is a phase 3, 104-week, randomised, double-blind, placebo-controlled, post-approval commitment study to evaluate the efficacy and safety of intravenous (IV) belimumab 10 mg/kg plus standard therapy (mycophenolate mofetil for induction and maintenance, or

cyclophosphamide for induction followed by azathioprine for maintenance, plus steroids) compared to placebo plus standard therapy in adult patients with active LN. Active LN was confirmed by renal biopsy during screening visit using the 2003 International Society of Nephrology/Renal Pathology Society criteria within the past 6 months, and clinically active kidney disease requiring induction therapy.

Systemic lupus erythematosus (SLE), the most common form of lupus, is a chronic, incurable, autoimmune disease. It is difficult to diagnose and even more challenging to treat. The condition is associated with a range of debilitating symptoms that can fluctuate over time, including painful or swollen joints, extreme fatigue, unexplained fever, and skin rashes. In lupus nephritis (LN), SLE causes inflammation (swelling or scarring) of the small blood vessels that filter wastes in the kidney (glomeruli) and sometimes the kidneys, by attacking them like they would attack a disease. LN can lead to end-stage kidney disease, which could require dialysis or a kidney transplant. Despite improvements in both diagnosis and treatment over the last few decades, LN remains an indicator of poor prognosis., Manifestations of LN include proteinuria, elevations in serum creatinine and the presence of urinary sediment. Approximately 20% of patients with LN progress to end-stage kidney disease within 10 years of diagnosis.

About Benlysta (belimumab)

Benlysta, a BLyS-specific inhibitor, is a human monoclonal antibody that binds to soluble BLyS. Belimumab does not bind to B cells directly or directly deplete B cell populations. By binding BLyS, belimumab inhibits the survival of B cells, including autoreactive B cells, and reduces the differentiation of B cells into immunoglobulin-producing plasma cells.

In the EU, belimumab was first approved for use as add-on therapy in adults with SLE as an IV formulation in July 2011, and as a subcutaneous (SC) formulation in November 2017. The SLE indication was extended for the use in children for the IV formulation in October 2019:

Benlysta IV is indicated as add-on therapy in patients aged 5 years and older with active, autoantibody-positive systemic lupus

erythematosus with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy.

Benlysta IV is indicated in combination with background immunosuppressive therapies for the treatment of adult patients with active lupus nephritis.

Benlysta SC is indicated in the EU as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus with a high degree of disease activity (e.g., positive anti dsDNA and low complement) despite standard therapy.

Benlysta SC is indicated in combination with background immunosuppressive therapies for the treatment of adult patients with active lupus nephritis.

For the EU Summary of Product Characteristics for Benlysta, please visit www.ema.europa.eu.

IMPORTANT SAFETY INFORMATION

The following Important Safety Information is based on a summary of the European Summary of Product Characteristics. Please consult the full Summary of Product Characteristics for all the labelled safety information for Benlysta (belimumab).

Hypersensitivity to belimumab or any excipients.

Not recommended in patients with severe active central nervous system lupus, hypogammaglobulinaemia (IgG

Caution: If Benlysta co-administered with other B cell targeted therapy

Infusion reactions and hypersensitivity: Administration may result in hypersensitivity reactions and infusion reactions which can be severe, and fatal. In the event of a severe reaction, administration must be interrupted and appropriate medical therapy administered. Risk of hypersensitivity reactions is greatest with the first two doses; however, the risk should be considered for every dose. Advise patients reactions are possible on day of, or several days after. Delayed-type, non-acute hypersensitivity reactions (e.g. rash, nausea, fatigue, myalgia, headache, facial oedema) possible.

Benlysta IV: Infusions should be administered by qualified healthcare

professional trained to give infusion therapy. Severe or life-threatening hypersensitivity reactions and infusion reactions can occur, possibly after several hours and can recur after initial treatment of symptoms. Administer in an environment where resources for managing reactions are available. Clinical supervision required for several hours after infusion, following at least first 2 infusions. Make patients aware of potential risk of hypersensitivity reactions (day of, or several days after infusion, including signs/symptoms and recurrence) and provide package leaflet each time Benlysta administered. Premedication: An antihistamine, with/without an antipyretic, may be administered.

Benlysta SC: First subcutaneous (SC) injection should be supervised by a healthcare professional in a setting qualified to manage hypersensitivity reactions. Provide patient education on signs/symptoms of hypersensitivity reactions (day of, or several days after administration) and possibility of recurrence and training in SC technique. Inform patients to seek medical attention if symptoms experienced.

Infections: Increased risk of infections, including opportunistic. Younger children may be at increased risk. Fatal infections (e.g. pneumonia and sepsis) occurred more frequently in patients receiving Benlysta; consider pneumococcal vaccination prior to initiation. Do not initiate with active serious infections (including serious chronic); exercise caution and assess risk/benefit in patients with history of recurrent infection. Carefully monitor new infections - consider interrupting immunosuppressants including Benlysta until infection resolved.

Depression and suicidality: Before treatment assess risk of depression and suicide in patient; closely monitor during treatment – consider discontinuation if new or worsening psychiatric symptoms.

Progressive multifocal leukoencephalopathy: Monitor for new or worsening signs/symptoms – refer to neurologist if suspected; suspend further dosing until excluded.

Immunisation: Do not give live vaccines 30 days before, or concurrently with Benlysta.

Malignancy: May be increased risk with immunomodulatory medicines including Benlysta.

Women of childbearing potential must use effective contraception during Benlysta treatment and for at least 4 months after the last treatment. Limited data on use in pregnant women. Should not to be used unless the potential benefit justifies the potential risk to the foetus. Not known whether Benlysta is excreted in human milk or absorbed systemically after ingestion. Maternal IgG is secreted in breast milk so recommended to either discontinue Benlysta or breast feeding depending on the risk/benefit to mother and child.

Very common (≥1/10): Bacterial infections (e.g. bronchitis, urinary tract infections), diarrhoea, nausea. Common (≥1/100 to

GSK's commitment to immunology

GSK is focused on the research and development of medicines for immune-mediated diseases, such as lupus and rheumatoid arthritis, that are responsible for a significant health burden to patients and society. Our world-leading scientists are focusing research on the biology of the immune system with the aim to develop immunological-based medicines that have the potential to alter the course of inflammatory disease. As the only company with a biological treatment approved for adult and pediatric lupus, GSK is leading the way to help patients and their families manage this chronic, inflammatory autoimmune disease. Our aim is to develop transformational medicines that can alter the course of inflammatory disease to help people live their best day, every day.

GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com/about-us.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the Company's Annual Report on Form 20-F for 2020 and any impacts of the COVID-19 pandemic.

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