

PRESS RELEASE



Issued: 26 April 2019, London UK, Philadelphia USA.

GSK receives US approval of Benlysta for intravenous use in children with lupus aged five years and above

- **FDA approval marks the first medicine in the US approved for children with systemic lupus erythematosus (SLE)**

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GSK today announced that the US Food and Drug Administration (FDA) has approved, under priority review, the use of the intravenous (IV) formulation of Benlysta (belimumab), a B-lymphocyte stimulator (BLyS)-specific inhibitor, in children with lupus from as young as five years of age.

Dr Hal Barron, Chief Scientific Officer and President, R&D, GSK commented, "Children with lupus have had limited options available to help treat their condition. This accelerated decision means children in the US now have an innovative, FDA-approved medicine available to help manage the impact of living with this challenging autoimmune disease."

Stevan W Gibson, President and CEO, Lupus Foundation of America commented, "Lupus is a potential life-threatening disease that can be more aggressive and severe in children than it is in adults. For the first time, children with lupus will now have a lupus-specific treatment option for their disease. As a research community we all share in the excitement of this historic milestone as it underscores our dedication to bringing new treatments to people living with lupus."

Kenneth M Farber, President and CEO, Lupus Research Alliance, commented, "The go-ahead from the FDA for belimumab to be used to treat children with lupus is terrific news for a community desperate for more treatment options. As the only biologic approved for the disease, belimumab has been helping many adults with lupus, and now physicians will have another, much-needed tool for treating their pediatric patients."

The approval extends the current indication in the US for the IV formulation of Benlysta in adults, to patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy. Benlysta was approved in the US in March 2011 for adults, and is currently the only medicine specifically approved in the US for both adults and children with SLE. The IV formulation of Benlysta is currently not approved for use in children anywhere else in the world although regulatory submissions are ongoing in other parts of the world.

The supplemental Biologics License Application (sBLA), which received FDA priority review, to support today's approval was based on data from a post-approval commitment study (the 'PLUTO' study), assessing the efficacy, safety and pharmacokinetics of 10 mg/kg intravenous belimumab plus standard therapy compared with placebo plus standard therapy for one-year in children aged 5 – 11 years (n=13,) and 12 – 17 years (n=80) with SLE. As paediatric lupus is an uncommon disease, a fully powered study was not feasible.

The proportion of children achieving a clinically meaningful improvement in disease activity, as assessed by the SLE responder index (SRI) response rate, was numerically higher in patients receiving belimumab plus standard therapy (52.8%) compared with placebo plus standard therapy (43.6%) at Week 52.¹



The proportion of patients experiencing more than one adverse event (AE) and a serious AE was 79.2% and 17.0% for the belimumab group compared to 82.5% and 35.0% for the placebo group, respectively. AEs that led to discontinuation were lupus nephritis, hepatitis A, hypertransaminasemia, acute pancreatitis, post herpetic neuralgia, retinal vasculitis and pancreatitis. Refer to 'Important Safety Information for belimumab' below for further information on the safety of belimumab.

About the study

'PLUTO' (Pediatric Lupus Trial of Belimumab Plus Background Standard Therapy) is a multicentre, randomised, double-blind study (BEL114055) in 93 children with active SLE. The study comprises three phases: Part A (randomised double-blind 52-week treatment phase), Part B (long-term open-label safety phase) and Part C (long-term safety follow-up phase). The long-term follow-up phases of the study (Parts B and C) are planned for a total of up to 10 years.

The study results were first presented at the 2018 American College of Rheumatology (ACR). Abstract [2867](#).

About systemic lupus erythematosus (SLE)

SLE is a chronic, incurable, autoimmune disease associated with a range of symptoms that can fluctuate over time including painful or swollen joints, extreme fatigue, unexplained fever, skin rashes and organ damage. SLE is the most common form of lupus, affecting approximately 70 percent of an estimated 5 million people with lupus worldwide.²

Compared with adult SLE, children with SLE often have more active disease both at the time of diagnosis and over time. SLE in children is associated with more rapid accrual of damage, and has a higher degree of morbidity compared with SLE in adult populations.^{3,4} It has been calculated that there are between 5,000 and 10,000 children with SLE in the United States.⁵

About Benlysta (belimumab)

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

Benlysta is currently the only medicine specifically developed and approved for SLE. It is registered as both an IV and SC formulation in the US. In the US, the IV formulation of Benlysta is approved for use in adults and children, and the subcutaneous formulation of Benlysta is only approved for use in adults. The indication of the IV formulation of Benlysta is for the treatment of patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy.

Limitations of Use: The efficacy of Benlysta has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations.

Full US prescribing information including Medication Guide reflecting this recent approval will be available in the near future at: gsksource.com. In the meantime, you may request a copy through GSK Communications.

Benlysta is not licensed in the European Union or other countries for use in children.

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



paediatric 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.

Important Safety Information for belimumab

The following safety information is based on the US Prescribing Information. Please consult the full prescribing information in your country for all the labelled safety information for Benlysta (belimumab).

CONTRAINDICATION

Previous anaphylaxis with BENLYSTA.

WARNINGS AND PRECAUTIONS

MORTALITY

In controlled clinical trials in adults, death occurred in 0.8% (11/1,458) of patients treated with BENLYSTA IV and in 0.4% (3/675) of patients receiving placebo. Etiologies included infection, cardiovascular disease, and suicide.

In the controlled trial (N=836) in adults, death occurred in 0.5% (3/556) of patients receiving BENLYSTA SC and 0.7% (2/280) of patients receiving placebo. Infection was the most common cause of death.

SERIOUS INFECTIONS

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including BENLYSTA. The most frequent serious infections in adults were pneumonia, including bacterial pneumonia, urinary tract infection, cellulitis, herpes zoster, and bronchitis. Use caution in patients with severe or chronic infections. Consider interrupting therapy with BENLYSTA in patients who develop a new infection.

Progressive Multifocal Leukoencephalopathy (PML): Cases of JC virus-associated PML resulting in neurological deficits, including fatal cases, have been reported in patients with SLE receiving immunosuppressants, including BENLYSTA. If PML is confirmed, consider stopping immunosuppressant therapy, including BENLYSTA.

HYPERSENSITIVITY REACTIONS (INCLUDING ANAPHYLAXIS) AND INFUSION REACTIONS

Acute hypersensitivity reactions, including anaphylaxis and death, have been reported in association with infusions and injections of BENLYSTA, including in patients who have previously tolerated BENLYSTA. These events generally occurred within hours of the infusion; however, they may occur later. Non-acute hypersensitivity reactions including rash, nausea, fatigue, myalgia, headache, and facial edema, have been reported and typically occurred up to a week following the most recent infusion. Patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk. Premedication may mitigate or mask an infusion reaction or hypersensitivity response. In the controlled trial of BENLYSTA SC in adults, systemic hypersensitivity reactions were similar to those observed in the IV clinical trials. Anaphylaxis was observed in 0.6% and 0.4% of patients receiving BENLYSTA and placebo, respectively. Manifestations included hypotension, angioedema, urticaria or other rash, pruritus, and dyspnea.

Serious infusion reactions in adults (excluding hypersensitivity reactions) were reported in 0.5% and 0.4% of patients receiving BENLYSTA and placebo, respectively and included bradycardia, myalgia, headache, rash, urticaria, and hypotension. BENLYSTA IV should be administered by healthcare providers prepared to manage infusion reactions and anaphylaxis. The infusion rate may be slowed or interrupted if the patient develops an infusion reaction. In the event of a serious reaction, administration of BENLYSTA must be discontinued immediately and appropriate medical therapy administered. Patients should be closely monitored during and for an appropriate period of time after IV administration of BENLYSTA. Patients receiving BENLYSTA should be informed of the signs and symptoms of hypersensitivity reactions and seek immediate medical care should a reaction occur.



DEPRESSION

In the controlled clinical trials of BENLYSTA IV in adults, psychiatric events were reported more frequently with BENLYSTA than with placebo, related primarily to depression-related events, insomnia and anxiety. Serious psychiatric events were reported in trials with BENLYSTA. Serious depression and suicidality (including two completed suicides) were reported in trials with BENLYSTA IV. There were no serious depression-related events or suicides reported in the BENLYSTA SC trial in adults. Instruct patients to contact their healthcare provider if they experience new or worsening depression, suicidal thoughts, or other mood changes.

MALIGNANCY

The impact of treatment with BENLYSTA on the development of malignancies is not known. The mechanism of action of BENLYSTA could increase the risk for the development of malignancies.

IMMUNIZATION

Live vaccines should not be given for 30 days before or concurrently with BENLYSTA. BENLYSTA may interfere with the response to immunizations.

USE WITH BIOLOGIC THERAPIES OR IV CYCLOPHOSPHAMIDE

BENLYSTA has not been studied in combination with other biologic therapies, including B-cell targeted therapies, or IV cyclophosphamide. Therefore, use of BENLYSTA is not recommended in combination with these therapies.

ADVERSE REACTIONS

The most common serious adverse reactions were serious infections (6.0% and 5.2% in adult patients receiving BENLYSTA IV and placebo, respectively), some of which were fatal. Adverse reactions, regardless of causality, occurring in at least 3% of adult patients with SLE who received BENLYSTA 10 mg/kg and placebo respectively and, at an incidence at least 1% greater than that observed with placebo in the 3 controlled studies, were: nausea 15% and 12%; diarrhea 12% and 9%; pyrexia 10% and 8%; nasopharyngitis 9% and 7%; bronchitis 9% and 5%; insomnia 7% and 5%; pain in extremity 6% and 4%; depression 5% and 4%; migraine 5% and 4%; pharyngitis 5% and 3%; cystitis 4% and 3%; leukopenia 4% and 2%; viral gastroenteritis 3% and 1%.

Adverse reactions in pediatric patients aged 5 years and older receiving BENLYSTA IV were consistent with those observed in adults.

The safety profile observed for BENLYSTA SC plus standard therapy in adults was consistent with the known safety profile of BENLYSTA IV plus standard therapy, with the exception of local injection site reactions.

OTHER IMPORTANT INFORMATION FOR BENLYSTA

USE IN SPECIFIC POPULATIONS

Pregnancy: There are insufficient data on use of BENLYSTA in pregnant women to establish whether there is drug-associated risk for major birth defects or miscarriage. Following an assessment of benefit versus risk, if prevention is warranted, women of childbearing potential should use effective contraception during treatment and for at least 4 months after the final treatment.

Pregnancy Registry: Healthcare professionals are encouraged to register patients and pregnant women are encouraged to enroll themselves by calling 1-877-681-6296.

Lactation: There is no information available on the presence of belimumab in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BENLYSTA and any potential adverse effects on the breastfed child from BENLYSTA or from the underlying maternal condition.



Black/African American Patients: In clinical studies there have been mixed results regarding how well BENLYSTA works in black/African American patients. Consider the risks and benefits when prescribing BENLYSTA in black/African American patients

Pediatric Use: Intravenous dosing of BENLYSTA is indicated in children aged 5 years and older. Adverse reactions in pediatric patients aged 5 years and older receiving BENLYSTA IV were consistent with those observed in adults.

The safety and effectiveness of subcutaneous administration of BENLYSTA have not been established in pediatric patients younger than 18 years of age.

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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 under Item 3.D 'Principal risks and uncertainties' in the company's Annual Report on Form 20-F for 2018.

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