25 June 2026
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Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Benlysta

Belimumab

Procedure no: EMA/PAM/0000325282

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	30 March 2026	30 March 2026
☐	CHMP comments	13 April 2026	n/a
☐	Updated CHMP Rapporteur AR	16 April 2026	17 April 2026
☐	Request for supplementary information	23 April 2026	23 April 2026
☐	Re-start date	27 May 2026	27 May 2026
☐	CHMP Rapp AR	10 June 2026	10 June 2026
☐	CHMP Comments	15 June 2026	n/a
☐	Updated CHMP Rapp AR	18 June 2026	n/a
☒	CHMP outcome	25 June 2026	25 June 2026

[1] Tick the box corresponding to the applicable step – do not delete any of the steps. If not applicable, add n/a instead of the date.

[2] Criteria for CHMP plenary discussion: substantial disagreement between the Rapporteur and other CHMP members and/or at the request of the Rapporteur or the Chair

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1. Introduction

On 23 January 2026, the MAH submitted a completed paediatric study for Benlysta, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that the study is not a measure of any agreed Benlysta Paediatric Investigation Plan and therefore a line listing is not included in this submission.

2.2. Information on the pharmaceutical formulation used in the study

Both intravenous infusions and subcutaneous injections were used in the study, see table 2 in the safety section.

2.3. Clinical aspects

2.3.1. Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder characterized by autoantibody production and abnormal B lymphocyte function. Belimumab (also known as LymphoStat-B; BENLYSTA) is a B lymphocyte stimulator (BLyS)-specific inhibitor that blocks the binding of soluble BLyS, a B-cell survival factor, to its receptors on B cells. Belimumab IV use was approved in the USA in 2011 as an add-on treatment for adult patients with autoantibody positive SLE despite standard therapy. Belimumab IV has since been approved for adults with SLE in all European Economic Area (EEA) countries, the United Kingdom (UK) and Japan as well as over 25 further countries. Results from a global Phase 2 study (BEL110455) with belimumab IV in paediatric SLE patients have supported approval of belimumab for SLE pediatric indication in children 5-17 years of age in the USA (approval on 26 April 2019), the European Union (EU) (approval on 21 October 2019) and Japan (20 September 2019).

GSK received its first approval of belimumab solution for subcutaneous (SC) injection on 20 July 2017 in the US for adults with SLE at a recommended dosage of 200 mg once weekly in addition to standard therapy. Belimumab SC has since been approved for adults with SLE in all EEA countries, the UK and Japan as well as over 15 further countries.

2.3.2. Clinical study

Clinical study number and title

Study number: 207735

Study report title: BENLYSTA for Intravenous Injection / Subcutaneous Injection Special Drug Use Investigation.

Description

This was a multicenter, single arm, real-world study to assess the safety and efficacy of IV and SC belimumab administered to patients above 15 years of age in daily clinical practice in Japan.

This was an open-label study without randomization and blinding. The observation period was 52 weeks after the start of belimumab treatment, however patients were followed for adverse events (AEs) until they discontinued belimumab treatment and for up to 3 years after the start of belimumab treatment if they continued receiving belimumab.

Methods

Study participants

The investigation targets all patients receiving Benlysta (excluding those who are aged < 15 years who started Benlysta after approval of paediatric dosage*). In addition, this investigation also targets the patients who already started receiving Benlysta after the product launch and before the conclusion of the contract and those who already started Benlysta at diagnosis, before hospital transfer, etc.

*: To conduct another investigation in children in association with the approval of paediatric dosage

Treatments

Objective

The objective of this investigation was to collect and assess the information about the long-term safety and effectiveness of Benlysta for intravenous injection and Benlysta for subcutaneous injection in daily clinical practice.

Outcomes/endpoints

To collect information on the incidence of safety specifications and priority investigation items under the actual use conditions.

- Serious hypersensitivity
- Serious infections (including tuberculosis (TB), pneumonia, pneumocystis jiroveci pneumonia (PCP), sepsis, and opportunistic infection (OI))
- Reactivation of hepatitis B (HB) virus
- Progressive multifocal leukoencephalopathy (PML)
- Interstitial pneumonia
- Malignant tumour (MT)
- Depression, suicidal ideation, and suicide attempt

Results

Participant flow

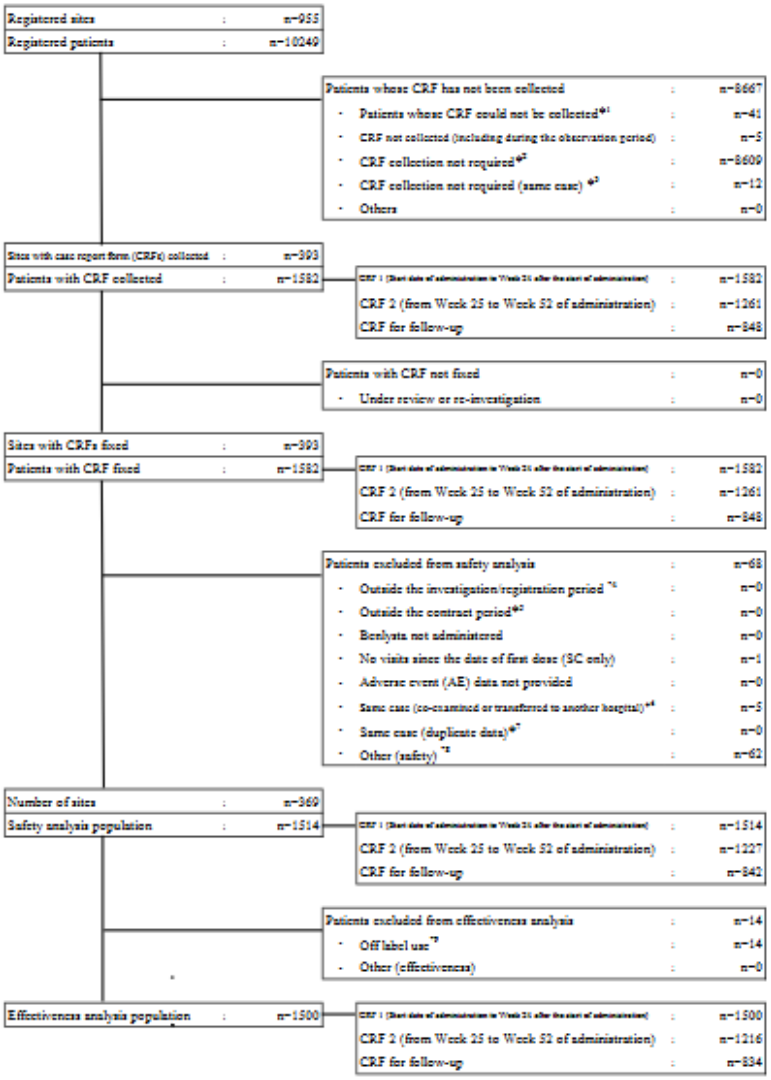

Fig. 2.1-1 Patient Composition

*1: Patients whose CRF could not be collected due to hospital or department closure, etc.
*2: Patients whose CRF collection was not required because they were not subject to CRF collection as agreed with PMDA
*3: Patients for whom collection of the CRF became unnecessary because the patient information was collectively entered at another site due to co-diagnosis, etc.
*4: Patients whose treatment with Benlysta /observation did not end within the study period or those who were registered outside the registration period
*5: Patients whose date of registration is outside the contract period.
*6: Patients who were co-examined or transferred to another hospital and determined to be the same patient
*7: Patients in which the same information was described redundantly and determined to be the same patients
*8: Of the patients whose CRF was NOT to be collected, 61 patients whose information was collected additionally in the spontaneously-reported CRFs due to an onset of AEs related to depression, suicidal ideation, and suicide attempt (the additional collection started on October 2023) in order to make the exploratory analysis of risk factors related to "depression, suicidal ideation, and suicide attempt," before final reporting; 1 patient whose investigator was an non-contract physician
*9: mixed connective tissue disease (7 patients), systemic lupus erythematosus (2 patients), immunoglobulin G4-related disease (1 patient), systemic scleroderma (1 patient), pediatric use (2 patients), the reason for the use of Benlysta not specified (1 patient)

Baseline data

Table 1 Summary of Patient Demographics (Age <18 years)

Patient Background		Safety Population	Efficacy Population
Total		29	27
Age [yrs]	n	29	27
	mean +- SD	15.8+-1.1	16.0+-0.9
	Max	17	17
	Q3	17.0	17.0
	Median	16.0	16.0
	Q1	15.0	15.0
	Min	13	15
Baseline Daily Corticosteroid Dose*1 [mg/day]	n	28	26
	mean +- SD	14.09+-9.27	13.83+-9.56
	Max	35.0	35.0
	Q3	20.00	20.00
	Median	11.75	10.50
	Q1	7.50	7.00
	Min	0.0	0.0
Disease duration, SLE [yrs]	n	29	27
	mean +- SD	3.86+-2.67	3.98+-2.68
	Max	9.0	9.0
	Q3	6.25	6.33
	Median	3.92	3.92
	Q1	1.67	1.67
	Min	0.4	0.5
Weight [kg]	n	28	26
	mean +- SD	51.14+-10.21	51.49+-10.47
	Max	83.0	83.0
	Q3	53.00	54.00
	Median	49.30	49.30
	Q1	44.15	44.80
	Min	40.0	40.0

*1: Prednisolone Equivalent

Number analysed

There were 1,514 patients in the safety analysis population of belimumab. Among these, 2 patients were less than 15 years of age and 29 subjects were less than 18 years of age.

Efficacy results

The applicant states that since a separate investigation in children was conducted in association with the approval of the paediatric dosage, the effectiveness in children (aged <15 years) was not investigated in this investigation.

Safety results

Table 2 Summary of Investigated Treatment (Age <18 years)

		Safety Population		Efficacy Population	
		n	(%)	n	(%)
Total		29	100.0	27	100.0
First Dose Route[*1]	IV	15	51.7	13	48.1
	SC	14	48.3	14	51.9
Dose Route	IV	12	41.4	11	40.7
	SC	11	37.9	11	40.7
	Change[*2]	6	20.7	5	18.5
	Unknown	0	0.0	0	0.0
Treatment Period [days]	< 28	1	3.4	1	3.7
	28 <= - < 168	4	13.8	3	11.1
	168 <= - < 364	7	24.1	7	25.9
	364 <=	17	58.6	16	59.3
Number of doses (IV)[*3]	< 6	3	16.7	3	18.8
-	6 <= - < 11	5	27.8	3	18.8
-	11 <= - < 15	6	33.3	6	37.5
-	15 <=	4	22.2	4	25.0
Number of doses (SC)[*4]	< 13	6	35.3	5	31.3
-	13 <= - < 25	1	5.9	1	6.3
-	25 <= - < 37	1	5.9	1	6.3
-	37 <= - < 52	3	17.6	3	18.8
-	52 <=	6	35.3	6	37.5
Cumulative Dosage (IV)[mg/kg][*3]	<= 50	4	22.2	4	25.0
-	50 < - <= 100	4	22.2	2	12.5
-	100 < - <= 140	6	33.3	6	37.5
-	140 <	4	22.2	4	25.0
Cumulative Dosage (SC)[mg][*4]	<= 2400	6	35.3	5	31.3
-	2400 < - <= 4800	1	5.9	1	6.3
-	4800 < - <= 7200	1	5.9	1	6.3
-	7200 < - <= 10200	3	17.6	3	18.8
-	10200 <	6	35.3	6	37.5
Once Dosage (IV)[mg/kg][*3]	< 10	2	11.1	2	12.5
-	10	16	88.9	14	87.5
-	10 <	0	0.0	0	0.0
Once Dosage (SC)[mg][*4]	< 200	0	0.0	0	0.0
-	200	17	100.0	16	100.0
-	200 <	0	0.0	0	0.0

*1 IV: Intravenous injection, SC: Subcutaneous injection

*2 Number of patients with IV or SC exclude patients with change

*3 Number of patients based on patients who dosed IV

*4 Number of patients based on patients who dosed SC

Table 3 Summary of Drug-Related Adverse Events (Age <18 years)

	Total		Serious	
Safety Population	29			
Number of Patient with Drug-Related Adverse Events (%)	6 (20.7)		1 (3.4)	
Drug-Related Adverse Events	n (%)			
Infections and infestations	4	(13.8)	1	(3.4)
Herpes zoster	2	(6.9)	1	(3.4)
Acute sinusitis	1	(3.4)	-	-
Chronic sinusitis	1	(3.4)	-	-
General disorders and administration site conditions	3	(10.3)	-	-
Condition aggravated	1	(3.4)	-	-
Injection site pain	1	(3.4)	-	-
Pain	1	(3.4)	-	-
Nervous system disorders	2	(6.9)	-	-
Dizziness	1	(3.4)	-	-
Post herpetic neuralgia	1	(3.4)	-	-
Psychiatric disorders	1	(3.4)	-	-
Depressive symptom	1	(3.4)	-	-

3. CHMP overall conclusion and recommendation

The MAH has, in accordance with the P46 regulation, submitted data from Study 207735, entitled "BENLYSTA for Intravenous Injection / Subcutaneous Injection Special Drug Use Investigation". This was a multicenter, single arm, real-world study to assess the safety and efficacy of IV and SC belimumab administered to patients above 15 years of age in daily clinical practice in Japan. A total of 1,514 patients was included in the study.

In the initial submission, the MAH stated that only 2 paediatric patients were included in the study and safety data for these patients were summarized. However, the age cutoff was below 15 years of age. Thus, the MAH was asked to provide information regarding demographics, posology used and safety results for all the patients below 18 years of age. Of the 29 persons aged <18 years of age, there were 6 patients reporting adverse drug reactions whereof one was serious (herpes zoster). Other reported events were sinusitis, injection site pain, condition aggravated, dizziness, post herpetic neuralgia and depressive symptoms.

The provided information does not evoke new safety concerns. The MAH has not suggested any update of the Summary of Product Characteristics, which is endorsed by the CHMP.

☒ **Fulfilled:**

No regulatory action required.

4. Request for supplementary information

Based on the data submitted, the MAH should address the following questions as part of this procedure:

1. provide information regarding demographics, posology used and safety results for the patients below **18** years of age

The timetable is a 30 day response timetable with clock stop.

MAH responses to Request for supplementary information

Question 1

provide information regarding demographics, posology used and safety results for the patients below **18** years of age

Summary of the MAHs response

The safety population for study 207735 included 29 subjects below 18 years of age. Data for these patients is shown in the tables including demographics (Table 1), posology (Tables 2), and safety results (Table 3).

Rapporteurs Assessment of the MAHs response:

The applicant has provided the requested information. The provided data does not evoke any further concerns. The AR has been updated with the new tables.