



Date: 25-March-2019

Dear Health Care Professional

**Title: Benlysta (belimumab) and Risk of Serious Depression and/or Suicidal Ideation or Behavior or Self-Injury**

GlaxoSmithKline Saudi Arabia in collaboration with SFDA, National Pharmacovigilance and Drug Safety Centre, KSA, draws your attention to the following safety information associated with Benlysta (Belimumab).

Benlysta is a human IgG1 $\lambda$  monoclonal antibody specific for soluble human B Lymphocyte Stimulator indicated for reducing disease activity in adult patients with active autoantibody positive systemic lupus erythematosus (SLE) who are receiving standard therapy.

**Key Messages**

- GlaxoSmithKline would like to inform health care providers that in clinical trials, an imbalance in psychiatric events (depression, suicidal ideation or behavior [including completed suicides], or self-injury) has been observed in subjects with SLE receiving belimumab plus standard therapy.
- In a recent one-year, randomized, double-blind, placebo-controlled post marketing study (BEL115467) of 4,003 subjects with SLE (1:1 randomisation):
  - Serious adverse events (SAE) of suicidal ideation or behavior or self-injury were reported in 0.7% (n= 15) of subjects receiving belimumab intravenously 10mg/kg (IV) vs. 0.2% (n=5) of subjects taking placebo.
  - No suicide-related deaths were reported.
  - SAEs of depression were reported in 0.3% (n=7) of subjects receiving belimumab 10mg/kg IV vs. <0.1% (n=1) taking placebo.
  - On the Columbia-Suicide Severity Rating Scale (C-SSRS), 2.4% (n=48) subjects on belimumab 10mg/kg IV reported suicidal ideation or behavior and 2.0% (n=39) subjects on placebo reported suicidal ideation or behavior.

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- Physicians should advise patients / caregivers of patients to contact the health care provider in a timely manner, if the patient experiences new or worsening depression, suicidal ideation or behaviour, or self-injury.
- Physicians should carefully assess the risk of depression, suicidal ideation or behavior, or self-injury considering the patient's medical history, current psychiatric status and SLE disease activity before treatment with Benlysta, and continue to monitor patients during treatment.
- See Supporting Information below.

### Action Being Taken by GlaxoSmithKline

GlaxoSmithKline is proposing label updates to regulatory agencies for Benlysta.

### Action required by Health Care Providers

Health care providers should:

- Maintain a heightened awareness of the risk of depression, suicidal ideation or behavior, or self-injury.
- Advise patients / caregivers of patients to contact the health care provider in a timely manner if the patient experiences new or worsening depression, suicidal ideation or behavior, or self-injury.
- Carefully assess the risk of depression, suicidal ideation or behavior, or self-injury considering the patient's medical history, current psychiatric status and SLE disease activity before treatment with Benlysta, and continue to monitor patients during treatment.
- Consider seeking advice from psychiatric care professionals if necessary.
- Ensure timely reporting of adverse events to GSK and relevant health authorities as appropriate according to local regulations.

### Supporting Information

BEL115467: The main purpose of this study is to evaluate all-cause mortality and pre-specified adverse events of special interest including selected serious psychiatric events. The study did not exclude subjects who had previous history of psychiatric/mood disorders.

An imbalance in serious adverse events of depression and serious adverse events of suicidal ideation or behaviour or self-injury were reported as summarised above. In addition, the study included an assessment of suicidal ideation and behavior as reported on the Columbia-Suicide Severity Rating Scale (C-SSRS) which was completed approximately every 4 weeks for the duration of the study. The C-SSRS was designed to quantify the severity of suicidal ideation and behavior and is considered suitable for use in clinical and research settings. The

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table below summarizes subjects reporting depression or suicidality SAEs and key C-SSRS results.

### Summary of subjects reporting depression or suicidality SAEs\* (As Treated Population)

	Number (%) of Subjects	
	Placebo (N=2001)	Belimumab IV 10 mg/kg (N=2002)
Number of subjects reporting depression SAE	1 (<0.1%)	7 (0.3%)
Number of subjects reporting suicidal ideation or behavior or self-injury SAE	5 (0.2%)	15 (0.7%)

\*as per study investigator report

### Summary of Subjects with C-SSRS# Suicidal Ideation or Behavior during Study Period (As Treated Population)

	Number (%) of Subjects	
	Placebo (N=1988)	Belimumab IV 10mg/kg (N=1974)
Number of subjects with at least one on-study C-SSRS assessment		
Number of subjects reporting Any Suicidal Ideation or Behavior event	39 (2.0%)	48 (2.4%)

Note: Percentages are based on the number of subjects with at least one on-study C-SSRS assessment.  
# as per C-SSRS assessment

### Further Information

Reporting Adverse Events: If you become aware of an adverse event involving Benlysta please contact:

#### The National Pharmacovigilance and Drug Safety Centre(NPC)

Toll free number : 8002490000  
Fax: +966 11 2057662  
Email: [npc.drug@sfd.gov.sa](mailto:npc.drug@sfd.gov.sa)  
Website: <https://ade.sfd.gov.sa/>

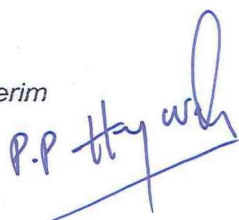
#### GlaxoSmithKline safety:

Email: [Saudi.safety@gsk.com](mailto:Saudi.safety@gsk.com)  
Mobile: +966 54 268 7301

### Contact for Questions

Should you have any questions or require additional information, please contact GSK Medical Information Department at [gcc.medinfo@gsk.com](mailto:gcc.medinfo@gsk.com)

Fadel Mohamed  
Country Medical Director- KSA Interim



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### References

Chi Chiu Mok, Kar Li Chan, Eric Fuk Chi Cheung, Paul Siu Fai Yip; Suicidal ideation in patients with systemic lupus erythematosus: incidence and risk factors, *Rheumatology*, Volume 53, Issue 4, 1 April 2014, Pages 714–721.

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Karassa, F. B., Magliano, M., & Isenberg, D. A. (2003). Suicide attempts in patients with systemic lupus erythematosus. *Annals of the rheumatic diseases*, 62(1), 58-60.

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