GLAXOSMITHKLINE SAFETY ADVISORY

GlaxoSmithKline
Scientific Office
Saudi Arabia
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License 04-01-0004
جلاكسوسميث كلاين
المكتب العلمي
المملكة العربية السعودية
س.ت. ١٠١٠٠٩٠٧٦١
ترخيص ٠٤-٠١-٠٠٠٤

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 Benlsysta (Belimumab).

Benlysta is a human IgG1λ 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

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	
Number of subjects with at least one on-study C-SSRS assessment	Placebo (N=1988)	Belimumab IV 10mg/kg (N=1974)
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@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

GlaxoSmithKline safety:

Email: *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*

Fadel Mohamed
Country Medical Director- KSA *Interim*

P.P

References

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