Important Safety Information regarding PrBENLYSTA (belimumab) – Increased Risk of Serious Depression, Suicidal Ideation or Behaviour, or Self-Injury

2019/04/04

Audience
Healthcare professionals including rheumatologists, dermatologists, immunologists, internists, cardiologists, nephrologists, pulmonologists, neurologists, family physicians, nurses at clinics contracted to administer BENLYSTA, psychiatrists, psychologists, and pharmacists.

Key messages

- **In a recent post-marketing study (BEL115467), depression, suicidal ideation or behaviour, and self-injury were reported more frequently in patients receiving BENLYSTA plus standard therapy, when compared to patients taking placebo plus standard therapy**
- **Healthcare professionals are advised to:**
  - **Evaluate the risk of depression, suicidal ideation or behaviour, and self-injury before starting and during treatment with BENLYSTA.**
  - **Advise patients and their caregivers to contact a healthcare provider if patients experience new or worsening depression, suicidal ideation or behaviour, or self-injury.**
  - **Evaluate and refer patients experiencing new or worsening depression, suicidal ideation or behaviour, or self-injury to a mental health professional, as needed.**
- **Health Canada is currently working with the manufacturer to update the BENLYSTA Canadian Product Monograph regarding this risk, including data from the post-marketing study (BEL115467).**

What is the issue?
Serious adverse events of depression, suicidal ideation or behaviour, or self-injury were reported more frequently in patients with systemic lupus erythematosus (SLE) receiving BENLYSTA than in patients receiving placebo during a post-marketing study (BEL115467).

Products affected
BENLYSTA (belimumab), lyophilized powder for intravenous infusion, 120 mg and 400 mg vials, and solution for subcutaneous injection, 200 mg/mL.

Background information
BENLYSTA is a human IgG1λ monoclonal antibody specific for soluble human B Lymphocyte Stimulator indicated for use in addition to standard therapy for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE).

Recently, a one-year post-marketing study (BEL115467) was conducted to evaluate all-cause mortality and some adverse events including selected serious psychiatric events. This study was a randomized, double-blind, placebo-controlled post-marketing study of 4,003 subjects with SLE. The study did not exclude subjects who had a previous history of psychiatric/mood disorders.

An increase in serious adverse events of depression and suicidal ideation or behaviour or self-injury compared to placebo was observed. Suicidal ideation or behaviour or self-injury was reported in 0.7% (n= 15) of subjects receiving belimumab intravenously (IV) 10mg/kg vs. 0.2% (n=5) of subjects taking placebo. Serious depression was reported in 0.3% (n=7) of subjects receiving belimumab 10mg/kg IV vs. <0.1% (n=1) taking placebo. No suicide-related deaths were reported in BEL115467.

Reports of depression, suicidal thoughts and suicide attempts in the pivotal trial programme (including 2 completed suicides) in patients receiving BENLYSTA have previously been included in the Warnings and Precautions and Adverse Drug Reactions sections of the BENLYSTA Canadian Product Monograph.

Information for consumers
BENLYSTA is used in combination with other medicines to treat adults with lupus (systemic lupus erythematosus).

An increased risk of signs or symptoms of mental illness such as depression, thoughts of suicide and suicidal behaviour and mood changes have been observed in patients taking BENLYSTA.

Before taking the drug, patients should discuss with their healthcare professional if they have or have had signs or symptoms of mental illness such as depression, self-harm, and/or thoughts of suicide.

Patients receiving BENLYSTA should inform their healthcare professional if they experience signs or symptoms of mental illness such as thoughts of suicide or dying, thoughts of hurting themselves or others, attempting to commit suicide or acting on other dangerous impulses, trouble sleeping (insomnia), new or worse anxiety or depression, or other unexpected changes in their behaviour or mood. Patients receiving BENLYSTA should also inform their healthcare professional if they experience any other side effects or if they require additional information.

Information for healthcare professionals
Healthcare providers are advised to:

- Evaluate the risk of depression, suicidal ideation or behaviour, and self-injury, before starting and during treatment with BENLYSTA.
- Advise patients and/or their caregivers to contact a healthcare provider if patients experience new or worsening depression, suicidal ideation or behaviour, or self-injury.
- Evaluate and refer patients experiencing new or worsening depression, suicidal ideation or behaviour, or self-injury to a mental health professional, as needed.

Action taken by Health Canada
Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication update will be further distributed through the MedEffect™ e-Notice email notification system. Health Canada is currently working with the manufacturer to update the BENLYSTA Canadian Product Monograph.

Report health or safety concerns
Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of serious depression, suicidal ideation or behaviour, self-injury, or other serious or unexpected side effects in patients receiving BENLYSTA should be reported to GlaxoSmithKline Inc. or Health Canada.

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4
Tel: 1-800-387-7374

To correct your mailing address or fax number, contact GlaxoSmithKline Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: mhpd_dpsc.public@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

For more information, please contact GlaxoSmithKline Inc. Medical Information at 1-800-387-7374.

Sincerely,

Original Signed By

Dr. Alex Romanovschi
Country Medical Director
GSK Canada