Health Canada Endorsed Important Safety Information on PrBENLYSTA™

May 3, 2012

Dear Health Care Professional:

Subject: Association of BENLYSTA™ (belimumab) with hypersensitivity and infusion reactions

GlaxoSmithKline Inc., in consultation with Health Canada, would like to inform you of important new safety information related to hypersensitivity and infusion reactions associated with BENLYSTA™ (belimumab) treatment.

BENLYSTA™ is indicated, in addition to standard therapy, for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE). At the time of authorization, the Product Monograph included information and warnings related to a reported higher incidence of hypersensitivity reactions in treated patients compared to placebo.

After the review of post-marketing reports, the Product Monograph for BENLYSTA™ has been updated with new safety information that you need to be aware of. Other countries have made similar labeling changes.

- Administration of BENLYSTA™ may result in infusion and hypersensitivity reactions, which can be severe, and can be fatal.
- Patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk.
- Healthcare professionals should monitor patients during and for an appropriate amount of time after administration of BENLYSTA™, because a delay in the onset of acute hypersensitivity reactions has been observed. Patients should be informed of the potential risks.

Important information for healthcare professionals:

- In the event of a severe reaction, BENLYSTA™ administration must be interrupted and appropriate medical therapy administered.
- Patients treated with belimumab should be informed of the symptoms of hypersensitivity reactions, and the importance of immediately seeking medical attention.

Healthcare professionals are reminded that:

- Infusion reactions occurred more frequently with the first two infusions and tended to decrease with subsequent infusions.
- BENLYSTA™ treatment should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of SLE.
- BENLYSTA™ should be administered by qualified healthcare providers trained to give infusion therapy and prepared to manage anaphylaxis.
- In clinical trials, severe and/or serious infusion or hypersensitivity reactions were reported in 1.2% and 0.6% of subjects receiving BENLYSTA™10 mg/kg and placebo, respectively.

Recently, a number of post-marketing reports concerning serious acute hypersensitivity reactions have been received globally. Some of these appear to have been delayed beyond what had been observed in previous clinical trials where most events happened during or very shortly after completion of the infusion. Development of acute symptoms several hours after the infusion (i.e. in the evening on the day the drug was administered), has been reported. One patient, with a history of multiple drug allergies, died after developing dyspnea, respiratory distress, hypoxia and angioedema following the second infusion of belimumab. The onset of symptoms was suspected to have begun approximately 4 hours after the end of belimumab infusion.

The updated Product Monograph for BENLYSTA™ is available at www.gsk.ca. Any questions from healthcare professionals may be directed to our Medical Information department via GSK Customer Service at 1-800-387-7374.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious hypersensitivity and infusion reactions, or other serious or unexpected adverse reactions 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

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at: 1-866-234-2345
- Complete a Reporting Form and:
  - Fax toll- free to 1-866-678 6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator: 0701E
    Ottawa, Ontario, K1A 0K9

The Reporting Form, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php). The Reporting Form is also in the *Canadian Compendium of Pharmaceuticals and Specialties*.

For other health product inquiries related to this communication, please contact Health Canada at:
Marketed Heath Products Directorate
E-mail: mhpd dpsc@hc-sc.gc.ca
Tel: 613-954-6522
Fax: 613-952-7738

To change your mailing address or fax number, contact the Market Authorization Holder (GlaxoSmithKline Inc.)

Sincerely,

originally signed by

Dr. Glenn Crater,
Vice-President, Medical and Chief Medical Officer