Health Canada Endorsed Important Safety Information on
PrFLOLAN® (eprostenol sodium)

April 19, 2013

Dear Healthcare Professional:

Subject: **Potential for Glass-related Particles in FLOLAN® (epoprostenol sodium) Sterile Diluent and the Essential Use of a Filter with the Administration of the Reconstituted Product**
(FLOLAN® 0.5 mg vial, DIN: 02230845; FLOLAN® 1.5 mg vial, DIN: 02230848; Sterile Diluent DIN: 02230857)

GlaxoSmithKline Inc., in consultation with Health Canada, would like to inform you that some vials of Sterile Diluent for FLOLAN® have been found to contain glass-related particles that may form because of an interaction between the surface of the glass vial container and the Sterile Diluent for FLOLAN®. Due to their size, these glass-related particles may not be easily visible under normal lighting. *In vitro* studies indicate filtration through a 0.22 or 0.2 micron pore size filter is an effective means to remove these glass-related particles.

FLOLAN® is supplied as a vial containing freeze-dried active drug (epoprostenol sodium) and a vial containing specialized diluent for reconstituting the active drug to produce the final solution for continuous intravenous infusion. FLOLAN® should only be reconstituted with Sterile Diluent supplied with FLOLAN®.

Based on this information, GlaxoSmithKline would like to advise you of the following:

- Some vials of Sterile Diluent for FLOLAN® have been found to contain glass-related particles
- In the hospital setting, ensure that reconstituted FLOLAN® is filtered with a 0.22 or 0.2 micron pore size filter
- In the ambulatory setting, patients should be instructed to administer FLOLAN® using only the supplies provided. In Canada, Pharmaprix/Shoppers Drug Mart Specialty Health Network Inc., the sole national wholesaler of FLOLAN®, supplies all patients who are prescribed FLOLAN® with intravenous extension tubing that includes an integrated in-line 0.2 micron filter.
- Ensure that your patients are using the tubing supplied to them with their medication kits, and reinforce the importance of using only the supplied infusion tubing that incorporates the 0.2 micron filter
- Remind patients that FLOLAN® should be inspected for visible particulate matter prior to use. Product containing visible particulate matter should not be used.

FLOLAN® is a prostacyclin vasodilator indicated for the long-term intravenous treatment of primary pulmonary hypertension (PPH) and secondary pulmonary hypertension (SPH) due to scleroderma spectrum of diseases (SSD) in NYHA functional Class III and Class IV patients who did not respond adequately to conventional therapy.

Due to the medical necessity and need for continued availability of this product for those patients who require FLOLAN®, a risk management strategy of designating the use of a 0.2 or 0.22 micron filter for the administration of the reconstituted product as essential is being implemented until GSK finds a permanent solution to the problem of glass-related particles in the sterile diluent.

There have been no reports of adverse events that could be definitively attributed to these glass-related particles in GlaxoSmithKline's safety database for FLOLAN® (i.e. injection site reactions, vascular reactions, or end-organ complications).

GlaxoSmithKline continues to search for improvements in the manufacturing process of the Sterile Diluent for FLOLAN® so that no vials will contain glass particles. In the interim, the use of a filter with the administration of the reconstituted product is essential in both the hospital setting and by patients in the ambulatory setting.

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 or other serious or unexpected adverse reactions in patients receiving FLOLAN® should be reported to GlaxoSmithKline or Health Canada.

GlaxoSmithKline Inc.
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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 Forms, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section. 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:
Health Products and Food Branch Inspectorate
E-mail: DCVIU_UVECM@hc-sc.gc.ca
Telephone: 1-800-267-9675
Fax: 1-613-946-5636

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

If you have any questions about this new information, please contact GlaxoSmithKline Medical Information Department at 1-800-387-7374.

Sincerely,

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