**NOTICE TO HOSPITALS**

**Health Canada Endorsed Important Safety Information on**

**[Pr]VENTOLIN® I.M. injection and [Pr]VENTOLIN® I.V. infusion solution**

**FOR PREGNANT WOMEN & LABOUR AND DELIVERY**


2007/06/12

To: The Chief of Medical Staff and Chief of the Obstetrics Department

Please distribute this letter to **all relevant Hospital/Medical staff** including the Departments of Surgery, Emergency Medicine, Pharmacy, Anaesthesia, Internal Medicine, Gynaecology, Intensive Care, Nursing and/or any other involved Departments and/or professional staff, and **post this Notice** in an appropriate location in your institution.

**Subject: Incidence of myocardial ischemia in pregnant women who receive [Pr]VENTOLIN® I.M. injection or [Pr]VENTOLIN® I.V. infusion solution (salbutamol sulphate for injection) to delay premature labour.**

GlaxoSmithKline (GSK), in consultation with Health Canada, would like to inform you of important safety information concerning **[Pr]VENTOLIN® I.M injection and [Pr]VENTOLIN® I.V. infusion solution (salbutamol sulphate for injection)** when used in pregnant women. GSK recently conducted a review of safety data available through the published literature, spontaneous reports and clinical trials. Up to the end of April 2007 there have been 17 occurrences worldwide of events considered to provide evidence of myocardial ischaemia in association with salbutamol when used to delay premature labor. Eleven of these reports were considered serious, which included one fatality. Where reported, 12 patients have fully recovered without sequelae. There have been no Canadian cases reported to date.

- There have been 17 occurrences reported worldwide of myocardial ischemia occurring in pregnant women receiving salbutamol for premature labour. The vast majority of reports were observed with the use of parenteral formulations. None of these 17 reports involved the use of inhaled salbutamol formulations for the treatment of bronchospasm.
- Salbutamol is not indicated to stop or prevent premature labour in Canada
- If benefit is determined to outweigh risk in women in premature labour, careful attention should be paid to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary edema or myocardial ischaemia develop, discontinuation of treatment should be considered.

The observation of myocardial ischemia in pregnant women following the administration of either beta-agonist as a class or salbutamol more specifically is further supported by the literature (Ref. 1-6). Therefore caution should be used if women are receiving intravenous salbutamol during premature labour.

The current safety information has been integrated in the ***Warnings and Precautions*** section of the **PrVENTOLIN®** Product Monograph. The following information can be found under the ***Pregnant Women*** and ***Labour and Delivery*** subsections.

**Pregnant Women**

- Salbutamol, in common with other betamimetics, is not approved to stop or prevent premature labour.
- Due to the risk of pulmonary edema and myocardial ischaemia that has been observed during the use of betamimetics in the treatment of premature labour, before PrVENTOLIN® injections are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.

**Labour and Delivery**

- Cautious use of PrVENTOLIN® injections is required in pregnant patients when it is given for relief of bronchospasm so as to avoid interference with uterine contractibility. During I.V. infusion of salbutamol, the maternal pulse rate should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.
- As maternal pulmonary edema and myocardial ischaemia have been reported during or following premature labour in patients receiving $beta_2$-agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary edema or myocardial ischaemia develop, discontinuation of treatment should be considered.

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-market adverse reactions are generally presumed to underestimate the risks associated with health product treatments.

Any cases of serious myocardial ischaemia or other serious or unexpected adverse reactions in patients receiving **PrVENTOLIN® I.M injection and PrVENTOLIN® I.V. infusion solution** should be reported to GSK or Health Canada at the following addresses:

GlaxoSmithKline Inc.
7333 Mississauga Road,
Mississauga, ON
L5N 6L4
Tel: 1-800-387-7374
Fax: 905-814-2291

**Any suspected adverse reaction can also be reported to:**
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335

To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in the *Compendium of Pharmaceuticals and Specialties*.

http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/ar-ei_form-eng.pdf
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php

**For other inquiries related to this communication, please contact Health Canada at:**
Marketed Health Products Directorate
MHPD_DPSC@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

GSK continually reviews new safety data on its products**,** including postmarketing adverse event reports, and encourages healthcare professionals to report any suspected adverse drug reactions or overdose associated with the use of **[Pr]VENTOLIN®** in pregnant patients.

Should you have any questions or require additional information, please contact our Medical Information department via Customer Service at 1-800-387-7374.

***Original signed by***

Rav Kumar, Ph.D.
VP, Regulatory Affairs and Pharmaceutical Development
GlaxoSmithKline Inc.



***References:***

1) Pincus R. Salbutamol infusion for premature labour – The Australian Trials experience. Aust N Z J Obstet Gynaecol 1981; 21: 1-4.
2) French/Australian Atosiban Investigators Group. Treatment of preterm labor with the oxytocin antagonist atosiban: a double-blind, randomized, controlled comparison with salbutamol. Eur J Obstet Gynecol Reprod Biol 2001; 98: 177-185.
3) Mulders LGM, Boers GHJ, Prickartz-Wijdewald MMJF, et al. A study of maternal ECG characteristics before and during intravenous tocolysis with beta-sympathomimetics. Effects of i.v. tocolysis on maternal ECG characteristics. Acta Obstet Gynecol Scand 1987; 66: 417-420.
4) Hadi HA, Alabazzaz SJ. Cardiac isoenzymes and electrocardiographic changes during ritodrine tocolysis. Am J Obstet Gynecol 1989; 161: 318-321.
5) Arulkumaran S, Kitchener HC, Balasingham S, et al. Myocardial strain associated with intravenous salbutamol therapy for preterm labour - ? drug effect. Case Report. Singapore J Obstet Gynaecol 1986;17:54-58.
6) Vermes E, Leroy G, Halphen C, et al. Myocardial infarction in a pregnant woman during treatment with salbutamol therapy. Arch Mal Coeur Vaiss 1997; 90:1651-1654.