

PUBLIC COMMUNICATION

Health Canada Endorsed Important Safety Information on $^{Pr}AVANDIA^{\circledcirc}, ^{Pr}AVANDAMET^{\circledcirc}$ and $^{Pr}AVANDARYL^{^{IM}}$

February 28, 2007

Subject: Association between Long-Term Treatment with AVANDIA® (rosiglitazone maleate)
Tablets for Type 2 Diabetes Mellitus and Fractures in Women

Mississauga, Ontario (February 28, 2007) — AVANDIA® (rosiglitazone maleate) tablets, AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) tablets and AVANDARYL $^{\text{TM}}$ (rosiglitazone maleate/glimepiride) tablets are medications authorized for sale in Canada to control blood sugar levels in people with type 2 diabetes whose blood sugar levels have not been controlled by diet, exercise or other medications. GlaxoSmithKline Inc. (GSK), after discussions with Health Canada, would like to provide Canadians with new safety information regarding an increased number of bone fractures in women who participated in the recently completed ADOPT¹ study (\underline{A} \underline{D} iabetes \underline{O} utcome and \underline{P} rogression \underline{T} rial).

ADOPT was a clinical study conducted in patients with recently diagnosed type 2 diabetes mellitus whose progression of diabetes was followed for 4-6 years. The primary goal of the study was to compare the control of blood sugar levels by rosiglitazone, with other antidiabetic medications, namely, metformin and glyburide in 4,360 patients.

Findings from this study revealed that significantly more women who received rosiglitazone experienced fractures than did women who received either metformin or glyburide (9.3% vs. 5.1% and 3.5% respectively). The majority of fractures observed in these women who received rosiglitazone were in the upper arm, hand or foot. These fractures were in different sites from those associated with bone loss happening after menopause (e.g., fractures in the hip and spine). In the ADOPT study, the number of women with a hip or spine fracture was low and similar among the three treatment groups. The number of fractures for men in the ADOPT study was similar among the three treatment groups.

Patients, (especially women) using a rosiglitazone-containing product (Avandia[®], Avandamet[®] and Avandaryl[™] tablets) should:

- Speak with their doctor about the risk of fracture.
- Continue their medication until they have actually consulted with their doctor about their treatment options.

GSK has sent a letter to Canadian health-care professionals informing them of this new safety information. You may view this letter on the Health Canada website (www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/index_e.html). GSK will continue to review new safety data for Avandia[®], including post-marketing adverse event reports. GSK will be working with Health Canada to further integrate new safety information in the Canadian Product Monograph.

Managing marketed health product-related adverse reactions depends on health-care professionals and consumers reporting them. Any case of serious or unexpected adverse reactions in patients receiving a rosiglitazone-containing product should be reported to GlaxoSmithKline Inc. or Health Canada at the following addresses:

GlaxoSmithKline Inc. 7333 Mississauga Road Mississauga, Ontario L5N 6L4

Tel.: 1-800-387-7374

Any suspected adverse reaction can 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 <u>AR Reporting Form</u> and the <u>AR Guidelines</u> can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

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

Marketed Health Products Directorate (MHPD)

E-mail: mhpd_dpsc@hc-sc.gc.ca

Tel: (613) 954-6522 Fax: (613) 952-7738

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 $AVANDARYL^{^{\mathrm{TM}}}$ is a trademark, used under license by $GlaxoSmithKline\ Inc.$

For media inquiries, please contact GSK Corporate Communications, (905) 819-3363.

References:

1. Kahn SE, Haffner SM, Heise MA, et al. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. New Engl J Med. 2006;355:2427-2443.