



Initial therapy with rosiglitazone delayed progressive loss of blood sugar control more effectively than metformin or glyburide using different blood sugar thresholds – from FPG >180 mg/dl (>10 mmol/l) to a lower blood sugar level more consistent with current therapeutic approaches, FPG >140 mg/dl (>7.8 mmol/l).<sup>1,6,7</sup> Long-term blood glucose control as measured by a mean HbA1c of < 7 percent was maintained for longer with rosiglitazone-- 60 months versus 45 months with metformin and 33 months with glyburide.<sup>1</sup> According to the Canadian Diabetes Association Clinical Practice Guidelines, patients should be targeted to achieve an A1c of less than 7 percent in order to reduce their risk of microvascular and macrovascular complications.<sup>8</sup>

“Type 2 diabetes is a progressive disease that needs to be managed effectively to help prevent serious complications, such as heart disease, kidney disease, adult blindness and lower limb amputations” said Donna Lillie, Vice President of Research and Professional Education at the Canadian Diabetes Association. “The ADOPT study measured the long-term sustainability of three therapies commonly used as the first stages of treatment for type 2 diabetes. The intent was to understand if one therapy worked for a longer period of time than another – this information will provide important evidence regarding clinical decision making in newly diagnosed people with type 2 diabetes.”

In ADOPT, rosiglitazone was reported to be generally well tolerated among the large cohort of people with type 2 diabetes who were followed for up to six years. There was no significant difference between the rosiglitazone and metformin groups in treatment discontinuation, but the rate was higher for the glyburide group (44 percent in the glyburide group; 38 percent in the metformin group; 37 percent in the rosiglitazone group).<sup>1</sup> The difference was driven largely by a higher level of withdrawals due to hypoglycaemia for people in the glyburide group.<sup>1</sup>

The same number of congestive heart failure (CHF) serious adverse events was reported with rosiglitazone (0.8 percent); as for metformin (0.8 percent); however, people given glyburide experienced a lower rate of CHF events (0.2 percent).<sup>1</sup>

After the five-year period of study, commonly reported adverse events across the treatment groups were edema (rosiglitazone 14.1 percent; glyburide 8.5 percent; metformin 7.2 percent); weight gain (rosiglitazone 6.9 percent; glyburide 3.3 percent; metformin 1.2 percent); gastrointestinal side effects (metformin 38.3 percent; rosiglitazone 23.0 percent; glyburide 21.9 percent); and hypoglycemia (glyburide 38.7 percent; metformin 11.6 percent; rosiglitazone 9.8 percent).<sup>1</sup>

Recent further analysis showed a lower rate of fractures reports as adverse events in women taking glyburide or metformin versus rosiglitazone (glyburide 3.5 percent; metformin 5.1 percent; rosiglitazone 9.3 percent), most commonly involving fractures of the foot and upper limb bones.<sup>1</sup> There was no observed difference among treatment groups in the number of fractures reported in men.<sup>1</sup> These observed fracture rates appear to be within the range seen in a literature-based review of observational studies in women with diabetes, and analysis of large managed care databases.<sup>9-12</sup> This evidence suggests that older women with type 2 diabetes are at an increased risk of fractures.<sup>9-12</sup>

### **About ADOPT**

ADOPT is an international, multi-centre, randomised, double-blind study involving 4,360 drug-naïve people who had been recently diagnosed with type 2 diabetes (≤ 3 years) at over 400 sites throughout North America and Europe. In Canada, 39 trial sites participated in the ADOPT study and enrolled over 618 patients from coast to coast. People included in the study were randomised to rosiglitazone, a sulfonylurea (glyburide), or metformin and titrated to the maximum daily effective doses (rosiglitazone 4 mg twice daily; metformin 1 g twice daily; glyburide 7.5 mg twice daily). These people were followed for four to six years to examine the long-term efficacy of each drug used as initial monotherapy on blood sugar control, insulin resistance and  $\beta$ -cell function. At the time of monotherapy failure, 99.3 percent, 98.6 percent and 99 percent of participants were receiving maximal doses of rosiglitazone, metformin and glyburide, respectively.<sup>1</sup>

When ADOPT was designed, HbA1c was not chosen as the primary outcome because the guidelines at the time focused largely on FPG.<sup>13</sup> Nevertheless, HbA1c data collected in the study as a secondary endpoint provided results, which are consistent with those for FPG and are applicable to current clinical practice.<sup>1</sup>

ADOPT was funded by GlaxoSmithKline.

### **About Rosiglitazone**

Rosiglitazone belongs to the thiazolidinedione (TZD) class of drugs and is an approved treatment for type 2 diabetes that improves blood sugar control, enabling people to reach recommended blood sugar levels.<sup>14</sup> The addition of rosiglitazone to metformin and/or a sulphonylurea has been shown to help people with type 2 diabetes reach and maintain treatment goal, and findings from ADOPT support the long-term durability of rosiglitazone monotherapy.<sup>14</sup>

### **About Type 2 Diabetes**

Type 2 diabetes is a chronic, progressive illness often linked to premature death, and affects approximately 230 million individuals worldwide, nearly six percent of the world's adult population. The IDF estimates that by 2025, more than 350 million people worldwide will suffer from this disease.<sup>15</sup> In Canada, almost two million people have type 2 diabetes.<sup>16</sup> As type 2 diabetes naturally progresses, the combined effects of core defects of the disease, namely insulin resistance and beta-cell dysfunction, can make it increasingly difficult for physicians to help patients control blood sugar levels.<sup>2</sup>

Type 2 diabetes occurs when the body does not respond properly to or produce enough insulin.<sup>17</sup> Overtime, the chronic, progressive nature of type 2 diabetes makes it more difficult to maintain blood sugar levels and therefore more than one medication may be required to reach recommended goals.<sup>18-19</sup> Keeping blood sugar levels in control is important in preventing diabetes-related conditions such as eye disease (blindness), kidney disease (kidney failure/dialysis), nerve damage, amputation, heart disease, stroke and peripheral vascular disease.<sup>18, 20-23</sup> Such complications can decrease a person's quality of life and result in increased health costs.<sup>24</sup> Untreated diabetes can lead to death. Every ten seconds, a person dies from diabetes-related causes.<sup>25</sup>

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### **Important Information regarding *Avandia*<sup>®</sup> (rosiglitazone maleate)**

Rosiglitazone maleate (*Avandia*<sup>®</sup>) is indicated for use alone, or in combination with metformin or a sulphonylurea, to reduce insulin resistance and lower elevated blood sugar in patients with type 2 diabetes. Rosiglitazone directly targets insulin resistance and improves  $\beta$ -cell function, underlying causes of type 2 diabetes. The most common side effects reported in clinical trials with rosiglitazone were upper respiratory tract infection, headache, and back pain. Rosiglitazone is not for everyone. Rosiglitazone should not be used in patients with severe heart problems or serious liver problems, or in patients who are pregnant.

### **About GlaxoSmithKline**

GlaxoSmithKline – one of the world's leading research-based pharmaceutical and health-care companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. In Canada, GlaxoSmithKline Inc. is among the top 15 investors in research and development, contributing more than \$135 million in 2005 alone. GSK is an Imagine Caring Company, and is consistently recognized as one of the 50 best companies to work for in Canada.

### **ATTENTION TELEVISION ASSIGNMENT/PRODUCERS**

B-roll will be distributed via satellite feed at 2:00 p.m. EST on Monday December 4, 2006.

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**GlaxoSmithKline Inc.**

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**References:**

1. Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill C, Zinman B, Viberti G for the ADOPT Study Group. Glycemic Durability of Rosiglitazone, Metformin or Glyburide Monotherapy. *N Eng J Med.* 2006;355:2427-2443. Published online on: December 4, 2006.
2. Gerich JE. Redefining the clinical management of type 2 diabetes: matching therapy to pathophysiology. *Eur J Clin Invest.* 2002;32:46-53.
3. UKPDS Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *The Lancet.* 1998;352:837-853.
4. UKPDS Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes. *The Lancet.* 1998;352:854-865.
5. American Diabetes Association. "Rapid Increase in the Use of Oral Antidiabetic Drugs in the United States 1990-2001." *Diabetes Care;* 26: 1852-1855, 2003.
6. Harris SB, Lank CN. Recommendations from the Canadian Diabetes Association. 2003 guidelines for prevention and management of diabetes and related cardiovascular risk factors. *Can Fam Physician* 2004; 50:425-433.
7. Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 2006; 29:1963-1972.
8. Canadian Diabetes Association. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2003; 27 (Supplement 2):S1-S152.
9. Schwartz AV, Sellmeyer DE, Ensrud KE, Cauley JA, Tabor HK, Schreiner PJ, Black DM, Cummings SR. Older women with diabetes have an increased risk of fractures: a prospective study. *J Clin Endocrinol Metabol.* 2001;86:32-38.
10. de Liefde II, van der Klift M, de Laet CE, van Daele PL, Hofman A, Pols HA. Bone mineral density and fracture risk in type 2 diabetes mellitus: the Rotterdam Study. *Osteoporos Int.* 2005;16:1713-1720.
11. Strotmeyer ES, Cauley JA, Schwartz AV, Nevitt MC, Resnick HE, Bauer DC, Tylavsky FA, de Rekeneire N, Harris TB, Newman AB. Nontraumatic fracture risk with diabetes mellitus and impaired fasting glucose in older white and black adults: the health, aging, and body composition study. *Arch Intern Med.* 2005;165:1612-1617.
12. Data on file.
13. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 1998; 21 (Suppl 1):S23-S31.
14. Avandia® Product Monograph, November 2006.
15. Unite for Diabetes (International Diabetes Federation). About diabetes. Available at: [http://www.unitefordiabetes.org/assets/files/About\\_diabetes.pdf](http://www.unitefordiabetes.org/assets/files/About_diabetes.pdf). Accessed on November 3, 2006.
16. Health Canada. "Diabetes Facts and Figures." Available at: <http://www.phac-aspc.gc.ca/ccdpc-cpcmc/diabetes-diabete/english/facts/index.html>. Accessed on May 23, 2006.
17. Groop LC. Insulin resistance: The fundamental trigger of type 2 diabetes. *Diabetes, Obesity & Metabolism* 1999; 1 (Supplement 1):S1-S7.

18. Stratton IM, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal* 2000; 321:405 – 412.
19. Nathan DM. Initial management of glycemia in type 2 diabetes mellitus. *N Eng J Med.* 2002;347/11342-1349.
20. International Diabetes Federation. Fact Sheet: Diabetes and eye disease. Available at: <http://www.idf.org/home/index.cfm?unode=C1CCADE9-4A03-4D17-A662-155B3ED59FDB>. Accessed on November 3, 2006.
21. International Diabetes Federation. Fact Sheet: Diabetes and kidney disease. Available at: <http://www.idf.org/home/index.cfm?unode=BB08E3D8-4036-4C06-B654-5DC24D158820>. Accessed on November 3, 2006.
22. International Diabetes Federation. Complications of diabetes. Available at: <http://www.idf.org/home/index.cfm?node=13>. Accessed on November 3, 2006.
23. International Diabetes Federation. Fact Sheet: Diabetes and cardiovascular disease (CVD). Available at: <http://www.idf.org/home/index.cfm?unode=FCC1DD60-2C39-4D3C-A3C0-85247F1678F3>. Accessed on November 3, 2006.
24. Unite for Diabetes (International Diabetes Federation). The economic impact of diabetes. Available at: [http://www.unitefordiabetes.org/assets/files/Diabetes\\_econ\\_impact.pdf](http://www.unitefordiabetes.org/assets/files/Diabetes_econ_impact.pdf). Accessed on November 3, 2006.
25. Unite for Diabetes (International Diabetes Federation). A United Nations Resolution on diabetes. Available at: [http://www.unitefordiabetes.org/assets/files/UNR\\_overview.pdf](http://www.unitefordiabetes.org/assets/files/UNR_overview.pdf). Accessed on November 3, 2006.

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