**Emerging Drug List**

**GLIMEPIRIDE**

**Generic (Trade Name):** Glimepiride (Amaryl™)

**Manufacturer:** Aventis Pharma

**Indication:** For the management of type II diabetes either as monotherapy or in combination with either metformin or insulin.

**Current Regulatory Status:** Glimepiride was launched onto the Canadian market at the end of January 2002. The FDA approved Glimepiride in February 1999.

**Description:** Similar to other sulphonylureas, glimepiride promotes insulin release. It acts via ATP-regulated potassium channels to depolarize the membranes of pancreatic β-cells resulting in insulin secretion.

**Current Treatments:** There are several other oral agents on the Canadian market for the treatment of type II diabetes. These include four other sulfonylureas (i.e. chlorpropamide, gliclazide, glyburide, tolbutamide), metformin, acarbose, the thiazolidinediones (i.e. pioglitazone and rosiglitazone), and the carbamoyl benzoic acid derivatives (i.e. repaglinide and nateglinide).

**Cost:** The cost for glimepiride is similar to micronized gliclazide (i.e. 1-8 mg of glimepiride daily is $21.00-42.00 and the cost for gliclazide MR 30-120 mg daily is $11.18-44.70). This is significantly higher than the cost for glyburide (i.e. 2.5-20 mg daily is $1.18-8.20) or metformin (i.e. 500-850 mg tid = $10.94-25.20).

**Evidence:** The clinical effects of glimepiride have been evaluated in several studies and summarizing them all is beyond the scope of this review. The majority of these studies are included in the references. Two comparative clinical trials are discussed in detail below.

Glimepiride was compared to glyburide in a randomized, double-blind, multicentre trial. Type 2 diabetic patients (n=1,044) who had been taking glyburide for at least two months and had a fasting plasma glucose (FPG) of ≤ 13.9 mmol/L were randomized to treatment with either glimepiride or glyburide. In the initial two-month phase, patients commenced therapy with either 1 mg of glimepiride or 2.5 mg of glyburide and were titrated to a target FPG of ≤ 8.3 mmol/L. Maximum daily doses were 8 mg and 20 mg of glimepiride and glyburide, respectively. At the end of the 10 month maintenance phase, HbA1c values had risen slightly from baseline and this increase tended to be higher in the glimepiride group (0.38 vs. 0.31%, p=0.25). Also, FPG values in both groups were slightly higher at endpoint. Although not clinically relevant, the mean change in FPG was higher in the glimepiride group (+0.9 vs. +0.5, p=0.005). At the end of the study, 457 patients continued in the follow-up phase and were followed for a mean of 251 days. At no time were there any significant differences in terms of FPG or HbA1c values between groups. A total of 74 glyburide and 60 glimepiride patients reported a hypoglycemia episode. Severe hypoglycemia, however, only occurred in three glyburide and one glimepiride subjects.

Patients (n=372) with type 2 diabetes who were poorly controlled with metformin monotherapy (FPG of 7.8-13.9 mmol/L) participated in a double-blind, multicentre trial. They were randomized to one of three treatment arms: glimepiride (1-6 mg) alone, metformin (constant dose of 850 mg tid) alone, or a combination of the two. Doses of
glimepiride were targeted to obtain a FPG of 3.9 to 7.8 mmol/L. Following an eight-week titration period, patients entered a twelve-week maintenance phase. The combination group was associated with a greater reduction in HbA1c (primary endpoint) than either monotherapy group (-0.74% with combination therapy vs. +0.07% and +0.27% with metformin and glimepiride, respectively, p<0.001). Combination therapy was also superior in reducing both fasting and post-prandial blood glucose compared to either glimepiride or metformin alone (p<0.001). Hypoglycemia was reported in 11, 13, and 22 patients taking metformin, glimepiride and the combination, respectively.

As compared to glyburide, it appears to have the advantage of causing fewer hypoglycemic episodes. In type 2 diabetic patients, glimepiride has demonstrated efficacy for controlling blood glucose when used alone or in combination with metformin or insulin. Although glimeperide has been shown to improve these surrogate outcomes, long-term trials are required to know whether this class of drugs reduces morbidity and mortality outcomes.

**References:**


This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.