Efficacy and Tolerability of Glimepiride in Daily Practice
A Non-Interventional Observational Cohort Study

Gerhard H. Scholz, Kerstin Schneider, Wolfgang Knirsch and Gerhard Becker

1 Medizinische Klinik und Poliklinik III, Universität Leipzig, Leipzig, Germany
2 Aventis Pharma Deutschland GmbH, BU Diabetologie, Bad Soden am Taunus, Germany

Abstract

Objective: The aim of the present study was to monitor the efficacy and tolerability of glimepiride in daily practice.

Design: An 8-week non-interventional cohort study investigating glimepiride in daily practice.

Setting and Data Collection: 4810 general practitioners and hospital physicians were asked to report on demographics and medical history, glimepiride dose, glycated haemoglobin (HbA1c) levels, adverse events and causes of discontinuation of therapy.

Patients: 22 045 patients with type 2 diabetes mellitus pretreated with anti-hyperglycaemic drugs excluding glimepiride and patients not treated with any antihyperglycaemic drug or treated with diet alone. Most patients were either overweight (42.2%) or obese (26.1%).

Results: A total of 29.3% of patients were treated with glimepiride as a first-time antihyperglycaemic drug, whereas in 70.7% of patients pre-existing oral antihyperglycaemic medication was changed to glimepiride monotherapy (69.6%) or continued as combination therapy with glimepiride (30.4%). The initial and final doses were lower in patients who commenced oral antihyperglycaemic therapy (initial 1.3mg, final 1.8mg) compared with patients whose therapy was changed (initial 1.7mg, final 2.4mg). The mean reduction of HbA1c was more pronounced in newly treated patients (1.8%) compared with patients changed to glimepiride therapy (1.3%). The most marked reduction in HbA1c levels (1.9%) was achieved in obese patients (body mass index ≥ 30 kg/m²), treated for the first time with an antihyperglycaemic drug using glimepiride. Bodyweight was reduced on therapy with glimepiride in all patients (1.4kg). With a bodyweight reduction of 2.2kg, this effect was particularly outstanding in obese patients. Adverse events and discontinuation of therapy were observed in 2.3 and 4.9% of patients, respectively, including a hypoglycaemia rate of 0.3%.

Conclusion: This non-interventional study carried out under daily practice conditions confirmed the good efficacy and tolerability of glimepiride in a large number of patients, as documented in previous clinical trials.
Glimepiride is a sulphonylurea that is used as an antihyperglycaemic agent for the oral therapy of type 2 diabetes mellitus. Its main action is the release of insulin from pancreatic β-cells. Glimepiride specifically binds to a certain membrane protein close to the potassium channel of the β-cell membrane and reduces the opening probability of this channel. The resulting depolarisation opens voltage-dependent calcium channels and leads to calcium influx into the cell. In the presence of glucose, the elevated intracellular calcium levels trigger insulin secretion.

Extrapancreatic actions have also been demonstrated for glimepiride. The drug improves the insulin sensitivity of peripheral tissue. Glimepiride also increases the number of glucose transporter molecules in the plasma membrane of peripheral muscle and adipose tissue and enhances their glucose uptake. This agent activates insulin-mediated glycogen synthesis and lipogenesis, and it inhibits hepatic gluconeogenesis. Both the increase in insulin secretion (the main mechanism of action), and the improvement of glucose utilisation (an additional beneficial effect), are responsible for the glucose-lowering properties of this agent.

Following oral administration, glimepiride is rapidly and completely absorbed. Maximum plasma concentrations are achieved at approximately 2.5 hours. With continuous administration the half-life is 5 to 8 hours. The physiological response to physical exertion, including a reduction of insulin secretion, is maintained on therapy with glimepiride.

The initial dose of glimepiride when commencing therapy is 1mg daily. Depending on the metabolic situation, the daily dose can be increased stepwise in intervals of 1 to 2 weeks, to glimepiride 2 or 3mg (up to 6mg). The action of glimepiride is reproducibly dose-dependent.

The aim of the present non-interventional study was to monitor the efficacy and tolerability of glimepiride in daily practice. As the main parameter of efficacy, glycated haemoglobin (HbA1c), was recorded to assess tolerability, adverse events and discontinuation of therapy were also evaluated.

Methods

Collection of Data

During an 8-week non-interventional study 4810 general practitioners and hospital physicians collected data from 22 050 patients with type 2 diabetes mellitus. Inclusion and exclusion criteria adhered to the indications and contraindications documented in the Product Information Sheet (Bundesverband der Pharmazeutischen Industrie e.V., Aulendorf, Germany), according to the requirements of non-interventional observational studies. Consequently, treatment was at the discretion of the attending clinician and was individually adjusted to the patient’s glycaemic control. The switch from previous therapy (diet, antihyperglycaemic drug therapy without glimepiride) to glimepiride monotherapy or the addition of glimepiride to existing therapy was independent of recruitment into the study.

Physicians were asked to document their experiences in a provided case report form. Demographic data of the patient, history, concomitant illnesses and medication, prior antihyperglycaemic drug therapy, blood glucose levels, HbA1c levels, urinary glucose, blood pressure, changes in body-weight and the daily glimepiride dose were documented, as far as possible. Data were collected in 2-weekly intervals. In addition, adverse events and reasons for possible therapy discontinuation were recorded.

Data Analysis

For continuous variables, the mean and standard deviation were calculated; non-continuous variables were characterised by absolute and relative frequencies. The analysis of data was performed with the statistical software package SAS 6.11. Patients were assigned to different categories according to their initial body mass index (BMI). In accordance with the drug history, these were divided into the subgroups ‘initiation of therapy’