sRMP

DK/H/2399/001-002/DC Gliclazid Win Medica

VI.2. Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

According to the World Health Organisationi, 347 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of diabetes. Over 80% of diabetes deaths occur in low and middle-income countries. Type 2 diabetes (formerly called non-insulin-dependent or adult-onset) results from the body's ineffective use of insulin. Type 2 diabetes comprises 90% of people with diabetes worldwide, and is largely the result of excess body weight and physical inactivity.

VI. .2.2 Summary of treatment benefits

A study was performed to evaluate the efficacy and safety of 30 mg slow-release- gliclazide on type 2 diabetes patients with the level of blood glucose poorly controlled formerly. A total of 154 type 2 diabetes patients with the level of blood glucose poorly controlled formerly were enrolled and treated with slow-release-gliclazide for 16 weeks. The efficacy of slow-release-gliclazide was evaluated through blood tests after 16 weeks of treatment period. The safety was evaluated through the adverse events including low blood sugar episodes and the change ofvital signs and clinic laboratory parameters. After
16 weeks of treatment period the glycated haemoglobin (HbA lc), fasting plasma glucose (FPG) and 2h post prandial blood glucose (PBG) were decreased by 1.89%, 2.31mmol!L and 3.94mmoi/L respectively. Glucose metabolism could be significantly improved by taking slow-release-gliclazide once-daily. Slow-release gliclazide offers a good treatment alternative, in order to optimize type 2 diabetes mellitus management.

VI.2.3 Unknowns relating to treatment benefits

Based on the currently available data an important gap in knowledge was identified in relation to gliclazide efficacy in children and adolescents less than 18 years of age and it is evaluated that further efficacy studies are needed in order to elucidate this efficacy issue.

VI. 2.4. Summary of safety concerns

Important indentified risks

Risk	What is known	Preventability
Low blood sugar (as an individual reaction or as a consequence of drug interaction)	Various circumstances and factors expose patients to an increase risk of low blood sugar Severity of hypoglycaemia may vary, some cases may be severe and prolonged. Hospitalisation may be necessary Possible symptoms of low blood sugar may vary from headache, intense hunger, nausea, vomiting, weariness, sleep disorders, too high blood pressure, sudden strong pain in chest, that may radiate into nearby areas (angina pectoris), confusion (delirium), convulsions, lose self-control The blood sugar lowering effect of gliclazide may be strengthened and signs of low blood sugar levels may occur when other medicines are taken.	Yes, close medical monitoring of blood sugar levels and/or glycated haemoglobin(HbA1c) Careful selection of patients by the doctors, of the dose used, and patient education on trigger factors, signs and symptoms measures. Measure to handle such low blood sugar episodes may be to consume carbohydrates, some form of sugar (not artificial sweeteners). Knowing the medicines that might strengthen the blood sugar lowering effect of gliclazide
Liver disorders	Possible symptoms of hepato-biliary disorders may occur , such as raised hepatic enzyme levels (AST, ALT, alkaline phosphatas), hepatitis (isolated reported)	The treatment should be discontinued if cholestatic jaundice appears.
Allergic skin reactions, including bullous reactions	Skin and subcutaneous tissue disorders : rash, pruritus, urticaria, angioedema, erythem, maulopapular rashes, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis) have been rarely reported as undesirable effects	Not applicable

Risk	What is known	Preventability
Use in patients with type 1 diabetes	The use of gliclazide in patients with type 1 diabetes is contra-indicated	Yes, reassure that patients are not suffering from type 1 diabetes

Increase in blood glucose levels following concomitant use of danazol, chlorpromazine, glucocorticoids, ritodrine, salbutamol, terbutaline (iv)	**Danazol** seems to have diabitogenic	If the use of this substance cannot be avoided, the patient should be warned and emphasised for the importance of urine and blood monitoring. It might be necessary to adjust the dose of the gliclazide during and after treatment with danazol
	Chropromazin is a neuroleptic agent. High doses (>100mg per day of chlorpromazine) increase blood glucose levels (reduced insulin release)	Patients should be warned and emphasised for the importance of urine and blood monitoring. It might be necessary to adjust the dose of the gliclazide during and after treatment with the neuroleptic agent.
	Ritdrine, salbutamol, terbutaline (i.v.) may increase blood glucose levels due to beta-2 antagonist effects.	Emphasise to the patient the importance of monitoring blood glucose levels. If necessary, switch to insulin.
Use in sever renal or hepatic insufficiency	The use of gliclazide in patients with severe renal or hepatic insufficiency is contra-indicated	In these cases the use of insulin is recommended

Potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Lowering of the haemoglobin level and break-down of red blood (haemolytic anaemia) in patients treated with glucose-6-phosphate	In Patients with a family history of or patients that have the hereditary condition glucose-6 cells phosphate dehydrogenase anaemia in (G6PD) deficiency, treatment with sulphonylurea agents can lead to haemolytic anaemia. Since gliclazide belongs to the chemical class of sulphonylurea drugs, caution should be used in patients with G6PD-deficiency and an non –sulphonylurea alternative should be considered.

Concomitant treatment of gliclazide with anticoagulant agents, such as Warfarin, may lead to a potentiation of the anticoagulant effect of this agent.	Sulphonylureas may lead to potentiation of anticoagulation during concurrent treatment, therefore adjustment of the anticoagulant treatment may be necessary.

Missing information

Risk	**What is known**
Use in children and adolescent under 18 years of age	Gliclazide is not recommended for use in children and adolescents due to lack of data
Use of gliclazide in pregnancy	There is no experience with the use of gliclazide during pregnancy in humans. In fact, control of diabetes should be obtained before the time of conception, in order to reduce the risk of congenital abnormalities linked to uncontrolled diabetes. However, oral hypoglycaemic agents such as gliclazide are not suitable in this case. Insulin is the drug of first choice for treatment of diabetes during pregnancy. Therefore it is recommended that therapy with gliclazide is changed to insulin before a pregnancy is attempted, or as soon as pregnancy is discovered.
Use of gliclazide in lactation is contra-indicated	Gliclazide is contra-indicated in breast –feeding mother because of the risk of neonatal hypoglycaemia, since it is not known whether the drug or its metabolites are excreted in breast-milk.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation safety or efficacy studies are ongoing or are planned to be conducted for gliclazide.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable as this is the first version