

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Diabetes mellitus type 2 is a chronic condition (*i.e.* it develops slowly) that affects the way one's body metabolises sugar (glucose). With type 2 diabetes, one's body either resists the effects of insulin — a hormone that regulates the movement of sugar into cells — or doesn't produce enough insulin to maintain a normal glucose level.

Type 2 diabetes is more common in adults, but it increasingly affects children as childhood obesity increases. Symptoms may include: increased thirst and frequent urination, increased hunger, weight loss, fatigue, blurred vision, slow healing of sores or frequent infections and areas of darkened skin.

There's no cure for type 2 diabetes, but one may be able to manage the condition by eating well, exercising and maintaining a healthy weight. If diet and exercise aren't enough to manage one's blood sugar well, one also may need diabetes (hypoglycaemic) medications or insulin therapy.

VI.2.2 Summary of treatment benefits

Glimepiride is an orally active hypoglycaemic substance belonging to the sulfonylurea group. It is used to treat type 2 diabetes mellitus when diet, physical exercise and weight reduction alone have not been able to control the blood sugar levels. Glimepiride acts mainly by stimulating insulin release from pancreatic beta cells (these cells produce insulin in pancreas). It also improves the sensitivity of the peripheral cells for insulin and a decrease of the insulin uptake by the liver.

VI.2.3 Unknowns relating to treatment benefits

No experience has been gained concerning the use of glimepiride in patients with severe impairment of liver function or dialysis patients.

There are no data available on the use of glimepiride in patients under 8 years of age. For children aged 8 to 17 years, there are limited data on glimepiride as monotherapy.

There are no adequate data from the use of glimepiride in pregnant women. Animal studies have shown reproductive toxicity which likely was related to the pharmacologic action (hypoglycaemia) of glimepiride.

The excretion of glimepiride in human milk is unknown. As other sulfonylureas are excreted in human milk and because there is a risk of hypoglycaemia in nursing infants, breast-feeding is advised against during treatment with glimepiride.

VI.2.4 Summary of safety concerns

Important identified risk

Risk	What is known	Preventability
Decrease in blood sugar (glucose) levels either because of individual use of glimepiride or due to concomitant use with other drugs (Hypoglycaemia as an individual reaction or as a consequence of drug interaction)	A person taking glimepiride may get low blood sugar (hypoglycaemia). Factors that could increase the risk of getting hypoglycaemia may include: undernourishment, irregular meal time, missed or delayed meal or period of fasting;	The levels of sugar in one's blood or urine should be checked regularly. Glimepiride must be taken shortly before or during a meal. The patient should immediately take some form of sugar <i>e.g.</i> sugar cubes, sweet juice and

Risk	What is known	Preventability
	<p>changes in one's diet; taking more glimepiride than needed/prescribed; having kidneys that do not work properly; having severe liver disease; drinking alcohol (especially when one skip a meal); taking certain other medicines that can potentiate blood glucose lowering effect of glimepiride; if one increase the amount of exercise one does and don't eat enough food or eat food containing less carbohydrate than usual.</p> <p>Signs of hypoglycaemia may include: hunger pangs; headache; nausea; vomiting; sluggishness; sleepiness; problems sleeping; restlessness; aggression; problems with concentration; reduced alertness and reaction time; depression; confusion; shakiness; dizziness; sweating; clammy skin; anxiety; fast heartbeat; high blood pressure; awareness of one's heartbeat; strong pain in breast that may radiate into neighbouring area.</p> <p>If blood sugar levels continue to drop one may suffer from considerable confusion, develops fits, lose self-control, breathing may be shallow and heartbeat may slow down and one may fall into unconsciousness. The clinical picture of a severe reduced blood sugar level may resemble that of a stroke.</p> <p>The ability to concentrate or react may be impaired if one's blood sugar is lowered. One should bear this in mind that</p>	<p>sweetened tea if one feels any of the named signs and symptoms of low blood sugar (hypoglycaemia). Artificial sweeteners should be avoided as these are not at all effective.</p> <p>Doctor should be contacted immediately if taking sugar does not help or if the symptoms recur.</p> <p>Doctor should be informed if one is taking other medicines which may weaken or strengthen the effect of glimepiride on the level of sugar in one's blood.</p> <p>Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or operate machinery in these circumstances.</p>

Risk	What is known	Preventability
	<p>he/she can endanger himself or others (e.g. when driving a car or using machines).</p> <p>If a person happen to have taken too much Glimepirid Orion or an additional dose there is a danger of hypoglycaemia. The following medicines can increase the blood sugar lowering effect of Glimepirid Orion. This can lead to a risk of hypoglycaemia (low blood sugar):</p> <ul style="list-style-type: none"> - other medicinal products to treat diabetes mellitus (such as insulin or metformin) - medicinal products to treat pain and inflammation (phenylbutazone, azopropazone, oxyphenbutazone, aspirin-like medicines) - medicinal products to treat urinary infections (such as some long acting sulfonamides) - medicinal products to treat bacterial and fungal infections (tetracyclines, chloramphenicol, fluconazole, miconazole, quinolones, clarithromycin) - medicinal products to inhibit blood clotting (coumarin derivatives such as warfarin) - medicinal products supporting muscle build up (anabolics) - medicinal products used for male sex hormone replacement therapy 	

Risk	What is known	Preventability
	<ul style="list-style-type: none"> - medicinal products to treat depression (fluoxetine, MAO-inhibitors) - medicinal products lowering high cholesterol level (fibrates) - medicinal products lowering high blood pressure (ACE inhibitors) - medicinal products called anti-arrhythmic agents used to control abnormal heartbeat (disopyramide) - medicinal products to treat gout (allopurinol, probenecid, sulfinpyrazone) - medicinal products to treat cancer (cyclophosphamide, ifosfamide, trofosfamide) - medicinal products used to reduce weight (fenfluramine) - medicinal product to increase circulation when given in a high dose intravenous infusion (pentoxifylline) - medicinal products to treat nasal allergies such as hay fever (tritoqualine) - medicinal products called sympatholytics to treat high blood pressure, heart failure, or prostate symptoms. <p>The following medicinal products can increase or decrease the blood sugar</p>	

Risk	What is known	Preventability
	<p>lowering effect of Glimepirid Orion:</p> <ul style="list-style-type: none"> - medicinal products to treat stomach ulcers (called H₂ antagonists) - medicinal products to treat high blood pressure or heart failure such as beta-blockers, clonidine, guanethidine and reserpine. These can also hide the signs of hypoglycaemia, so special care is needed when taking these medicines. <p>Alcohol intake may increase or decrease the blood sugar lowering action of Glimepirid Orion in an unpredictable way.</p>	
Disturbance of liver functions (Liver disorders)	Use of glimepiride can lead to abnormal liver function including yellowing of the skin and eyes (jaundice), increased liver enzymes, problems with the bile flow (cholestasis), inflammation of the liver (hepatitis) or liver failure.	<p>Regular liver function monitoring is required during treatment with Glimepirid Orion.</p> <p>Doctor should be contacted immediately if a person experience any of these symptoms.</p>
Use in patients with insulin dependent/type I diabetes mellitus (Use in type I diabetes)	Glimepiride is not recommended for use in patients with insulin dependent diabetes, diabetic ketoacidosis (a complication of diabetes when acid level is raised in one's body and one may have some of the following signs: fatigue, feeling sick [nausea], frequent urination and muscular stiffness), and in diabetic coma, as it would not be effective and may worsen these conditions.	Glimepiride should not be used for the treatment of type 1 diabetes mellitus.
Interaction with drugs that may lead to increase in blood	The following medicines may decrease the blood sugar	Doctor should be informed if one is taking other medicines

Risk	What is known	Preventability
glucose levels (Drug-drug interactions/increase in blood glucose levels)	<p>lowering effect of Glimepirid Orion. This can lead to a risk of hyperglycaemia (high blood sugar level):</p> <ul style="list-style-type: none"> - medicinal products containing female sex hormones (oestrogens, progestogens) - medicines to treat high blood pressure called thiazide diuretics (water tablets) - medicinal products used to stimulate the thyroid gland (such as levothyroxine) - medicinal products to treat allergies and inflammation (glucocorticoids) - medicinal products to treat severe mental disorders (chlorpromazine and other phenothiazine derivatives) - medicinal products used to raise heartbeat, to treat asthma or nasal congestion, coughs and colds, used to reduce weight, or used in life-threatening emergencies (adrenaline and sympathomimetics) - medicinal products to treat high cholesterol level (nicotinic acid) - medicinal products to treat constipation when they are used long term (laxatives) - medicinal products to treat seizures (phenytoin) - medicinal products to treat nervousness and 	<p>which may weaken or strengthen the effect of glimepiride on the level of sugar in one's blood.</p> <p>One should be advised to take Glimepirid Orion at least 4 hours before colesevelam.</p>

Risk	What is known	Preventability
	<p>sleep problems (barbiturates)</p> <ul style="list-style-type: none"> - medicinal products to treat increased pressure in the eye (azetazolamide) - medicinal products to treat high blood pressure or lowering blood sugar (diazoxide) - medicinal products to treat infections, tuberculosis (rifampicine) - medicinal products to treat severe low blood sugar levels (glucagon) <p>The following medicinal products can increase or decrease the blood sugar lowering effect of Glimepirid Orion:</p> <ul style="list-style-type: none"> - medicinal products to treat stomach ulcers (called H₂ antagonists) - medicinal products to treat high blood pressure or heart failure such as beta-blockers, clonidine, guanethidine and reserpine. These can also hide the signs of hypoglycaemia, so special care is needed when taking these medicines. <p>Colesevelam, a medicine used to reduce cholesterol, has an effect on the absorption of Glimepirid Orion.</p> <p>Alcohol intake may increase or decrease the blood sugar lowering action of Glimepirid Orion in an unpredictable way.</p>	

Risk	What is known	Preventability
<p>Use in patients with severe impairment of kidney or liver functions (Use in severe renal or hepatic insufficiency)</p>	<p>No experience has been gained concerning the use of glimepiride in patients with severe impairment of liver function or dialysis patients.</p> <p>Use of glimepiride can lead to abnormal liver function including yellowing of the skin and eyes (jaundice), increased liver enzymes, problems with the bile flow (cholestasis), inflammation of the liver (hepatitis) or liver failure.</p>	<p>One should not take glimepiride if one is having severe kidney or liver disease.</p> <p>In patients with severe impairment of kidney or liver function change over to insulin is indicated.</p> <p>Regular liver function monitoring is required during treatment with Glimepirid Orion.</p> <p>Doctor should be contacted immediately if a person experience any of these symptoms.</p>
<p>Decrease in production of cells responsible for providing immunity (leukocytes), carrying oxygen (erythrocytes), and/or those responsible for normal blood clotting (thrombocytes) (Myelosuppression [not including haemolytic anaemia])</p>	<p>During treatment with glimepiride decrease in the number of blood cells can occur as follows:</p> <ul style="list-style-type: none"> - blood platelets (which increases risk of bleeding or bruising) - white blood cells (which makes infections more likely) - red blood cells (which can make the skin pale and cause weakness or breathlessness). <p>These problems generally get better after one stops taking Glimepirid Orion.</p>	<p>Regular haematological monitoring (especially white blood cells and blood platelets) are required during treatment with Glimepirid Orion.</p> <p>Doctor should be contacted immediately if a person experience any of these symptoms/signs.</p>

Important potential risk

Risk	What is known (Including reason why it is considered a potential risk)
Use of glimepiride along with drugs that prevent blood clotting (Concomitant use of glimepiride with anticoagulant therapy)	Glimepirid Orion may either increase or weaken the effects of the medicinal products inhibiting blood clotting (coumarin derivatives such as warfarin).
Decrease in haemoglobin (anaemia) due to destruction of red blood cells in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency (Haemolytic anaemia in patients with G6PD] deficiency)	Lowering of the haemoglobin level and breakdown of red blood cells (haemolytic anaemia) can occur in patients missing the enzyme glucose-6-phosphate dehydrogenase.

Missing information

Risk	What is known
Use in children (Paediatric use)	<p>There are no data available on the use of glimepiride in patients under 8 years of age. For children aged 8 to 17 years, there are limited data on glimepiride as monotherapy.</p> <p>The available data on safety and efficacy are insufficient in the paediatric population and therefore such use is not recommended.</p>
Use in pregnant and breastfeeding women (Use during pregnancy and lactation)	<p>There are no adequate data from the use of glimepiride in pregnant women. Animal studies have shown reproductive toxicity which likely was related to the pharmacologic action (hypoglycaemia) of glimepiride. Consequently, glimepiride should not be used during the whole pregnancy. In case of treatment by glimepiride, if the patient plans to become pregnant or if a pregnancy is discovered, the treatment should be switched as soon as possible to insulin therapy.</p> <p>The excretion in human milk is unknown. Glimepiride is excreted in rat milk. As other sulfonylureas are excreted in human milk and because there is a risk of hypoglycaemia in nursing infants, breast-feeding is advised against during treatment with glimepiride.</p>

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. The Summary of Product Characteristics and the Package leaflet for Glimepirid Orion can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable.

