Package leaflet: Information for the user

Amaryl® 1 mg, 2 mg, 3 mg and 4 mg tablets

glimepiride

SANOFI

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Amaryl is and what it is used for
2. What you need to know before you take Amaryl
3. How to take Amaryl
4. Possible side effects
5. How to store Amaryl
6. Contents of the pack and other information

Pharmacotherapeutic group

Amaryl is an orally active blood sugar lowering medicine. This medicine belongs to a blood sugar lowering group of medicines called sulfonylurea. Amaryl works by increasing the amount of insulin released from your pancreas. The insulin then lowers your blood sugar levels.

Therapeutic indications

What Amaryl is used for:
- Amaryl is used to treat a certain form of diabetes (type 2 diabetes mellitus) when diet, physical exercise and weight reduction alone have not been able to control your blood sugar levels

Contraindications

Do not take Amaryl and tell your doctor if:
- You are allergic to: glimepiride or other sulfonylureas (medicines used to lower your blood sugar such as glibenclamide) or sulfonamides (medicines for bacterial infections such as sulfamethoxazole) or any of the other ingredients of this medicine (listed in section 6)
- You have insulin dependent diabetes (type 1 diabetes mellitus)
- You have diabetic ketoacidosis (a complication of diabetes when your acid level is raised in your body and you may have some of the following signs: fatigue, feeling sick (nausea), frequent urination and muscular stiffness)
- You are in a diabetic coma
- You have severe kidney disease
- You have a severe liver disease

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Amaryl.

Appropriate precautions for use; special warnings

Warnings and precautions

Talk to your doctor or pharmacist before taking your medicine if:
- You are recovering from an injury, operation, infections with fever, or from other forms of stress, inform your doctor as temporary change of treatment may be necessary
- You have a severe liver or kidney disorder

If you are not sure if any of these apply to you, talk to your doctor or pharmacist before taking Amaryl.

Lowering of the haemoglobin level and breakdown of red blood cells (haemolytic anemia) can occur in patients missing the enzyme glucose-6-phosphate dehydrogenase.

The information available on the use of Amaryl in people under 18 years of age is limited. Therefore, its use in these patients is not recommended.

Important information about hypoglycaemia (low blood sugar)

When you take Amaryl, you may get hypoglycaemia (low blood sugar). Please see below for additional information about hypoglycaemia, its signs and treatment.

Following factors could increase the risk of you getting hypoglycaemia:
- Undernourishment, irregular meal time, missed or delayed meal or period of fasting
- Changes to your diet
- Taking more Amaryl than needed
- Having decreased kidney function
- Having severe liver disease
- If you suffer from particular hormone-induced disorders (disorders of the thyroid glands, of the pituitary gland or adrenal cortex)
- Drinking alcohol (especially when you skip a meal)
- Taking certain other medicines (see below "Other medicines and Amaryl")
- If you increase your body exercise and you do not eat enough or eat food containing less carbohydrate than normal

Signs of hypoglycaemia include:
- Hunger pangs, headache, nausea, vomiting, sluggishness, sleepiness, disordered sleep, restlessness, aggression, impaired concentration, reduced alertness and reaction time, depression, confusion, speech and visual disorders, slurred speech, shakiness, partial paralysis, sensory disturbances, dizziness, helplessness
- The following signs may also occur: sweating, clammy skin, anxiety, accelerated heart beat, high blood pressure, palpitations, sudden strong pain in the breast that may radiate into neighbouring areas (angina pectoris and cardiac arrhythmias)

If blood sugar levels continue to drop you may suffer from considerable confusion (delirium), develop convulsions, lose self control, breathing may be shallow and your heart beat slowed down, you may fall into unconsciousness. The clinical picture of a severe reduced blood sugar level may resemble that of a stroke.

Treating hypoglycaemia:

In most cases the signs of reduced blood sugar vanish very quickly when you consume some form of sugar, e.g. sugar cubes, sweet juice, sweetened tea.
You should therefore always take some form of sugar with you (e.g. sugar cubes). Remember that artificial sweeteners are not effective. Please contact your doctor or go to the hospital if taking sugar does not help or if the symptoms recur.

Laboratory tests

The level of sugar in your blood or urine should be checked regularly. Your doctor may also take blood tests to monitor your blood cell levels and liver function.

Children and adolescents

Amaryl is not recommended for use in children under 18 years of age.

Other medicines and Amaryl

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Your doctor may wish to change your dose of Amaryl if you are taking other medicines, which may weaken or strengthen the effect of Amaryl on the level of sugar in your blood.

The following medicines can increase the blood sugar lowering effect of Amaryl. This can lead to a risk of hypoglycaemia (low blood sugar):
- Other medicines to treat diabetes mellitus (such as insulin or metformin)
- Medicines to treat pain and inflammation (phenylbutazone, azopropazone, oxyphenbutazone, aspirin-like medicines)
- Medicines to treat urinary infections (such as some long acting sulfonamides)
- Medicines to treat bacterial and fungal infections (tetracyclines, chloramphenicol, fluconazole, miconazole, quinolones, clarithromycin)

- Medicines to inhibit blood clotting (coumarin derivatives such as warfarin)
- Medicines supporting muscle build up (anabolics)
- Medicines used for male sex hormone replacement therapy
- Medicines to treat depression (fluoxetine, MAO-inhibitors)
- Medicines lowering high cholesterol level (fibrates)
- Medicines lowering high blood pressure (ACE inhibitors)
- Medicines called anti-arrhythmic agents used to control abnormal heart beat (disopyramide)
- Medicines to treat gout (allopurinol, probenecid, sulfinpyrazone)
- Medicines to treat cancer (cyclophosphamide, ifosfamide, trofosfamide)
- Medicines used to reduce weight (fenfluramine)
- Medicines to increase circulation when given in a high dose intravenous infusion (pentoxifylline)
- Medicines to treat nasal allergies such as hay fever (tritoqualine)
- Medicines called sympatholytics to treat high blood pressure, heart failure, or prostate symptoms

The following medicines may decrease the blood sugar lowering effect of Amaryl. This can lead to a risk of hyperglycaemia (high blood sugar level):
- Medicines containing female sex hormones (oestrogens, progestogens)
- Medicines supporting urine production (thiazide diuretics)
- Medicines used to stimulate the thyroid gland (such as levothyroxine)
- Medicines to treat allergies and inflammation (glucocorticoids)
- Medicines to treat severe mental disorders (chlorpromazine and other phenothiazine derivatives)
- Medicines used to raise heart beat, to treat asthma or nasal congestion, coughs and colds, used to reduce weight, or used in life-threatening emergencies (adrenaline and sympathomimetics)
- Medicines to treat high cholesterol level (nicotinic acid)
- Medicines to treat constipation when they are used long term (laxatives)
- Medicines to treat seizures (phenytoin)
- Medicines to treat nervousness and sleep problems (barbiturates)
- Medicines to treat increased pressure in the eye (azetazolamide)
- Medicines to treat high blood pressure or low blood sugar (diazoxide)
- Medicines to treat infections, tuberculosis (rifampicine)
- Medicines to treat severe low blood sugar levels (glucagon)

The following medicines can increase or decrease the blood sugar lowering effect of Amaryl:
- Medicines to treat stomach ulcers (called H2 antagonists)
- Medicines 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

Amaryl may either increase or weaken the effects of the following medicines:
- Medicines inhibiting blood clotting (coumarin derivatives such as warfarin)

Colesevelam, a medicine used to reduce cholesterol, has an effect on the absorption of Amaryl. To avoid this effect, you should be advised to take Amaryl at least 4 hours before colesevelam.

Amaryl with food, drink and alcohol
Alcohol intake may increase or decrease the blood sugar lowering action of Amaryl in an unpredictable way.

Pregnancy and breast-feeding
Pregnancy
Amaryl should not be taken during pregnancy. Tell your doctor if you are, you think you might be or are planning to become pregnant.

Breast-feeding
Amaryl may pass into breast milk. Amaryl should not be taken during breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Your ability to concentrate or react may be impaired if your blood sugar is lowered (hypoglycaemia), or raised (hyperglycaemia) or if you develop visual problems as a result of such conditions. Bear in mind that you could endanger yourself or others (e.g. when driving a car or using machines). Please ask your doctor whether you can drive a car if you:
- have frequent episodes of hypoglycaemia
- have fewer or no warning signals of hypoglycaemia

Amaryl contains lactose
If you have been told by your doctor that you cannot tolerate some sugars, contact your doctor before taking this medicine.

3. How to take Amaryl

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Taking this medicine
- Take this medicine by mouth, just before or with the first main meal of the day (usually breakfast). If you do not have breakfast you should take the medicine on schedule as prescribed by your doctor. It is important not to leave out any meal when you are on Amaryl
- Swallow the tablets with at least half glass of water. Do not crush or chew the tablets

Dosage
The dose of Amaryl depends on your needs, condition and results of blood and urine sugar tests and is determined by your doctor. Do not take more tablets than your doctor has prescribed.
- The usual starting dose is one Amaryl 1 mg tablet once a day
- If necessary, your doctor may increase the dose after each 1 - 2 weeks of treatment
- The maximum recommended dose is 6 mg Amaryl per day
- A combination therapy of glimepiride plus metformin or of glimepiride plus insulin may be initiated. In such a case your doctor will determine the proper doses of glimepiride, metformin or insulin individually for you
- If your weight changes or if you change your lifestyle, or you are in a stress situation this may require changed Amaryl doses, therefore inform your doctor
- If you feel the effect of your medicine is too weak or too strong do not change the dose yourself, but ask your doctor

If you take more Amaryl than you should
If you happen to have taken too much Amaryl or an additional dose there is a danger of hypoglycaemia (signs of hypoglycaemia see section 2) and therefore you should instantly consume enough sugar (e.g. a small bar of sugar cubes, sweet juice, sweetened tea) and inform a doctor immediately. When treating hypoglycaemia due to accidental intake in children, the quantity of sugar given must be carefully controlled to avoid the possibility of producing dangerous hyperglycaemia. Persons in a state of unconsciousness must not be given food or drink.

Since the state of hypoglycaemia may last for some time it is very important that the patient is carefully monitored until there is no more danger. Admission into hospital may be necessary, also as a measure of precaution. Show the doctor the package or remaining tablets, so the doctor knows what has been taken.

Severe cases of hypoglycaemia accompanied by loss of consciousness and severe neurological failure are cases of medical emergency requiring immediate medical treatment and admission into hospital. It should be ensured that there is always a pre-informed person that can call a doctor in case of emergency.

If you forget to take Amaryl
If you forget to take a dose, do not take a double dose to make up for forgotten doses.

If you stop taking Amaryl
If you interrupt or stop the treatment you should be aware that the desired blood sugar lowering effect is not achieved or that the disease will deteriorate again. Keep taking Amaryl until your doctor tells you to stop.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately if you experience any of the following symptoms:
- Allergic reactions (including inflammation of blood vessels, often with skin rash) which may develop into serious reactions with difficulty in breathing, fall in blood pressure and sometimes progressing to shock
- Abnormal liver function including yellowing of the skin and eyes (jaundice), problems with the bile flow (cholestasis), inflammation of the liver (hepatitis) or liver failure
- Allergy (hypersensitivity) of the skin such as itching, rash, hives and increased sensitivity to sun. Some mild allergic reactions may develop into serious reactions
- Severe hypoglycaemia including loss of consciousness, seizures or coma

Some patients experienced the following side effects whilst taking Amaryl:

Rare side effects (may affect up to 1 in 1,000 people)
- Lower blood sugar than normal (hypoglycaemia) (see section 2)
- Decrease in the number of blood cells:
  - 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)

These problems generally get better after you stop taking Amaryl

Very rare side effects (may affect up to 1 in 10,000 people)
- Allergic reactions (including inflammation of blood vessels, often with skin rash) which may develop into serious reactions with difficulty in breathing, fall in blood pressure and sometimes progressing to shock. If you experience any of these symptoms, **tell your doctor immediately**
- Abnormal liver function including yellowing of the skin and eyes (jaundice), impairment of the bile flow (cholestasis), inflammation of the liver (hepatitis) or liver failure. If you experience any of these symptoms, **tell your doctor immediately**
- Feeling or being sick, diarrhoea, feeling full or bloated, and abdominal pain
- Decrease in the amount of sodium level in your blood (shown by blood tests)

Other side effects include:
- Allergy (hypersensitivity) of the skin may occur such as itching, rash, hives and increased sensitivity to sun. Some mild allergic reactions may develop into serious reactions with swallowing or breathing problems, swelling of your lips, throat or tongue. Therefore in the event of one of these side effects, **tell your doctor immediately**
- Allergic reactions with sulfonylureas, sulfonamides, or related medicines may occur
- Problems with your sight may occur when beginning treatment with Amaryl. This is due to changes in blood sugar levels and should soon improve
- Increased liver enzymes
- Severe unusual bleeding or bruising under the skin

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Amaryl

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use this medicine after the expiry date which is stated after 'EXP' on the blister and carton. The expiry date refers to the last day of that month.

Amaryl 1 mg, 2 mg, 3 mg, and 4 mg tablets: do not store above 30°C.

Store in the original package in order to protect from moisture.

Do not use this medicine if you notice visible signs of deterioration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Amaryl contains
- The active substance is glimepiride.
  Each tablet contains 1 mg, 2 mg, 3 mg or 4 mg of glimepiride depending on the strength indicated on the blister and carton.
- The other ingredients are: lactose monohydrate, sodium starch glycollate (type A), magnesium stearate, microcrystalline cellulose, povidone 25000.
- In addition the tablets contain colouring agents:
  - 1 mg tablets contain red iron oxide (E172)
  - 2 mg tablets contain yellow iron oxide (E172) and indigo-carmine aluminium lake (E132)
  - 3 mg tablets contain yellow iron oxide (E172)
  - 4 mg tablets contain indigo-carmine aluminium lake (E132)

What Amaryl looks like and contents of the pack
Each tablet of Amaryl is oblong and scored on both sides. Each tablet can be divided into equal doses. They are different in colour:
- 1 mg tablets are pink
- 2 mg tablets are green
- 3 mg tablets are pale yellow
- 4 mg tablets are light blue

Amaryl is supplied in blister packs of 30 and 120 tablets. Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
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