

ANNEX IIIB

PACKAGE LEAFLET: INFORMATION FOR THE USER

Name of the medicinal product

Amarel 4 mg tablets

Glimepiride

Text box

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 signs of illness 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. See section 4.

What is in this leaflet

1. What **Amarel** 4 mg tablets are and what they are used for
2. What you need to know before you take **Amarel** 4 mg tablets
3. How to take **Amarel** 4 mg tablets
4. Possible side effects
5. How to store **Amarel** 4 mg tablets
6. Contents of the pack and other information

1. WHAT Amarel 4 mg tablets ARE AND WHAT THEY ARE USED FOR

Pharmacotherapeutic group - Blood glucose-lowering drugs, excluding insulins: Sulfonylureas - ATC code: A10B B12

Amarel is an orally active blood sugar-lowering drug. This drug belongs to a blood sugar-lowering group of medicines called sulfonylureas.

Amarel works by increasing the amount of insulin released from your pancreas. The insulin then lowers your blood sugar levels.

Amarel is used to treat type 2 diabetes mellitus when diet, physical exercise and weight reduction alone have not been able to control your blood sugar levels.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE Amarel 4 mg tablets

Do not take Amarel 4 mg tablets:

- 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).
- If you have insulin-dependent diabetes (type 1 diabetes mellitus).
- If you have diabetic ketoacidosis (a complication of diabetes when the acid level in your blood is raised and you may have some of the following signs: fatigue, feeling sick (nausea), frequent urination and muscle stiffness).
- If you are in a diabetic coma.
- If you have serious kidney disease.
- If you have serious liver disease.

If any of the situations above applies to you, do not take this medicine.

If you are unsure of anything, talk to your doctor or pharmacist before taking **Amarel**.

Warnings and precautions

Talk to your doctor or pharmacist before taking **Amarel** 4 mg tablets.

- If you are recovering from an injury, operation, infection with fever, or from any other form of stress, inform your doctor as temporary change of treatment may be necessary.
- If you have a serious liver or kidney problem.

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

Lowering of hemoglobin levels and breakdown of red blood cells (hemolytic anemia) can occur in patients missing the enzyme glucose-6-phosphate dehydrogenase (G6PD) (hereditary red blood cell disease).

Information available on the use of **Amarel** in patients under 18 years of age is limited. It should therefore not be used in these patients.

Important information about hypoglycemia (low blood sugar):

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

The following factors could increase your risk of getting hypoglycemia:

- Undernourishment, irregular meal time, a missed or delayed meal or period of fasting;
- Changes to your diet;
- Taking more **Amarel** than needed;
- Having kidneys that do not work properly;
- Having serious liver disease;
- If you have particular hormone-induced disorders (disorders of the thyroid gland, of the pituitary gland or adrenal glands);
- Drinking alcohol (especially when you skip a meal);
- Taking certain other medicines (See “Other medicines and **Amarel 4 mg tablets**” below);
- If you increase the amount of exercise you do and you do not eat enough food or eat food containing less carbohydrate than usual.

Signs of hypoglycemia include:

- Hunger pangs, headache, nausea, vomiting, sluggishness, drowsiness, problems sleeping, restlessness, aggression, problems with concentration, reduced alertness and reaction time, depression, confusion, problems with your speech and sight, slurred speech, shakiness, partial paralysis, sensory disturbances, dizziness, feeling of weakness.
- The following signs may also occur: sweating, clammy skin, anxiety, fast or increased heartbeat, high blood pressure, awareness of your heart beat, sudden strong pain in the breast that may radiate into neighboring areas (angina pectoris) and cardiac arrhythmias.

If blood sugar levels continue to drop, you may experience considerable confusion (delirium), have seizures, lose self-control, breathing may be shallow and your heart beat slowed down and you may faint. A severely reduced blood sugar level may resemble a stroke.

Treating hypoglycemia

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 or sweetened tea. You should therefore always take some form of sugar with you (e.g. sugar cubes). Remember that artificial sweeteners are not effective.

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

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

Other medicines and Amarel 4 mg tablets

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 **Amarel** if you are taking other medicines, as they may weaken or strengthen the effect of **Amarel** on the level of sugar in your blood.

The following medicines can increase the blood sugar lowering effect of **Amarel**. This can lead to a risk of hypoglycemia:

- Other medicines to treat diabetes mellitus (such as insulin or metformin);
- Medicines to treat pain and inflammation (phenylbutazone, azopropazone, oxyphenbutazone, aspirin);
- 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 (vitamin K antagonist-type 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, sulfapyrazone);
- 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 **Amarel**. This can lead to a risk of hyperglycemia (high blood sugar level):

- Medicines containing female sex hormones (estrogens, progestogens);
- Medicines that promote urine production (thiazide diuretics);
- Medicines used to stimulate the thyroid gland (such as levothyroxine);
- Medicines to treat allergies and inflammation (glucocorticosteroids);
- Medicines to treat severe mental disorders (chlorpromazine and other phenothiazine derivatives);
- Medicines 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);
- Medicines to treat high cholesterol (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 (acetazolamide);
- Medicines to treat high blood pressure or low blood sugar (diazoxide);
- Medicines to treat infections, tuberculosis (rifampicin);
- Medicines to treat severe low blood sugar levels (glucagon).

The following medicinal products can increase or decrease the blood sugar lowering effect of **Amarel**:

- 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 hypoglycemia, so special care is needed when taking these medicines.

Amarel may either increase or weaken the effects of the following medicines:

- Medicines inhibiting blood clotting (vitamin K antagonist-type coumarin derivatives such as warfarin);

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

Amarel 4 mg tablets with food, drink and alcohol

Alcohol intake may increase or decrease the blood sugar lowering action of **Amarel** in an unpredictable way.

Pregnancy and breast-feeding

Pregnancy

Amarel should not be used during pregnancy. Tell your doctor if you are, or are planning to become pregnant.

Breast-feeding

Amarel may pass into breast milk. **Amarel** should not be used 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 reduced if your blood sugar is lowered (hypoglycemia), or raised (hyperglycemia), particularly if you develop visual problems. In these situations, you could endanger yourself or others (e.g. when driving a car or using machines).

Ask your doctor whether you can drive a car if you:

- have frequent episodes of hypoglycemia,
- have few or no warning signals of hypoglycemia.

Amarel 4 mg tablets contain: Lactose

3. HOW TO TAKE AMAREL 4 mg TABLETS

Always take this medicine exactly as instructed by your doctor.

If you are unsure of anything, consult your doctor.

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 skip any meals when you are taking **Amarel**.
- Swallow the tablets with at least half a glass of water. Do not crush or chew the tablets.
- Each tablet can be divided into equal doses.

Dosage

The dosage of **Amarel** 4 mg tablets depends on your needs and is determined by your doctor based on the results of blood and urine sugar tests.

Do not take more tablets than your doctor has prescribed.

- The usual starting dose is one **Amarel** 1 mg tablet once a day.
- If necessary, your doctor may increase the dose after 1 - 2 weeks of treatment.
- The maximum recommended dose is 6 mg of **Amarel** per day.
- A combination therapy of glimepiride plus metformin or of glimepiride plus insulin may be started. In this case, your doctor will determine the individual doses of glimepiride, metformin or insulin that you require.
- Your dose of **Amarel** 4 mg tablets may need to be adjusted if you change weight, change your lifestyle, or if you are under a lot of stress. Speak to your doctor if any of these situations apply to you.
- If you feel the effect of your medicine is too weak or too strong, do not change the dosage yourself, but ask your doctor.

If you take more Amarel 4 g tablets than you should:

If you have taken too much **Amarel**, there is a risk of hypoglycemia (for signs of hypoglycemia, see section 2 "Warnings and precautions").

You should immediately consume enough sugar (e.g. small sugar cubes, sweet drink or sweetened tea) and inform a doctor straight away.

When treating hypoglycemia due to accidental intake in children, the amount of sugar given must be carefully controlled to avoid the possibility of producing hyperglycemia which can be serious. Persons in a state of unconsciousness must not be given food or drink.

Since the state of hypoglycemia may last for some time, it is very important that the patient is carefully monitored until there is no more danger. Hospital admission may be necessary, also as a precaution. Keep the package or remaining tablets and show them to the doctor.

Serious hypoglycemia can be accompanied by loss of consciousness and severe neurological deficiency. It is a medical emergency requiring immediate medical treatment and admission to the hospital. It may be helpful to tell your family and friends to call a doctor immediately if this happens to you.

If you forget to take Amarel 4 mg tablets:

Do not take a double dose to make up for a forgotten individual dose.

If you stop taking Amarel 4 mg tablets:

If you interrupt or stop the treatment, the desired blood sugar lowering effect is no longer achieved and your diabetes will get worse.

Keep taking **Amarel** until your doctor tells you to stop.

If you have any questions about using this medicine, ask your doctor or pharmacist for more information.

4. POSSIBLE SIDE EFFECTS

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

Tell your doctor immediately if you have any of the following symptoms:

- Allergic reactions (including inflammation of blood vessels, often with skin rash) which may develop into serious reactions with difficulty breathing, drop in blood pressure and even shock;
- Abnormal liver function including yellowing of the skin and eyes (jaundice), problems with bile flow (cholestasis), inflammation of the liver (hepatitis) or impaired liver function;
- Allergy (hypersensitivity) of the skin such as itching, redness, hives and increased sensitivity to sun. Some mild allergic reactions may develop into serious reactions;
- Severe hypoglycemia including loss of consciousness, seizures or coma.

Certain patients had the following side effects during treatment with **Amarel**:

Rare side effects (may affect up to 1 in 1000 people):

- Lower blood sugar than normal (hypoglycemia) (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 **Amarel**.

- Weight gain
- Hair loss
- Changes in taste

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 breathing, drop in blood pressure and even shock; if you experience any of these symptoms, **tell your doctor immediately**.
- Abnormal liver function including yellowing of the skin and eyes (jaundice), problems with bile flow (cholestasis), inflammation of the liver (hepatitis) or impaired liver function. If you experience any of these symptoms, **tell your doctor immediately**.
- Feeling or being sick, diarrhea, feeling full or bloated and abdominal pain.
- Decrease in the amount of sodium level in your blood (shown by blood tests).

Unknown frequency (cannot be estimated based on available data):

- Allergy (hypersensitivity) of the skin may occur such as itching, redness, 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 if one of these side effects occurs, **tell your doctor immediately**.
- Allergic reactions to sulfonamides, sulfonamides, or related drugs may occur.

- Problems with your sight may occur when beginning treatment with **Amarel**. 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 or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system, i.e. *Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM)* under “Réseau des Centres de Pharmacovigilance” (Network of Pharmacovigilance Centers) - Website: www.ansm.sante.fr.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE AMAREL 4 mg TABLETS

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

Do not store above 30°C.

Store in the original outer packaging protected 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 Amarel 4 mg tablets contain

- The active substance is:
Glimepiride 4 mg
- The other ingredients are:
Lactose monohydrate, sodium starch glycolate (type A), povidone 25 000, microcrystalline cellulose, magnesium stearate, indigo carmine-aluminum lake (E132).

What Amarel 4 mg tablets look like and contents of the pack

This medicine is supplied as tablets. It is a pale blue, oblong tablet with a score line on both sides. Each tablet can be divided into equal doses.

Boxes of 14, 20, 28, 30, 50, 60, 90, 112, 120, 280 or 300.

Not all pack sizes may be marketed.

Marketing Authorization holder

sanofi-aventis France
82, avenue Raspail
94250 Gentilly, France

Operator

sanofi-aventis France
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Manufacturer

Sanofi SPA
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or

Sanofi Winthrop Industrie
30-36, avenue Gustave Eiffel
37100 Tours, France

Names of the medicinal product in the Member States of the European Economic Area

This medicinal product is authorized in the Member States of the EEA under the following names: In compliance with current regulations.

This leaflet was last revised in:

[To be completed by the Marketing Authorization Holder]

Other

Detailed information on this medicine is available on the ANSM website (France).