PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Actos® 15 mg Tablets

Actos® 30 mg Tablets

Actos® 45 mg Tablets

The active ingredient and its quantity:

Each tablet contains:	Each tablet contains:	Each tablet contains:
pioglitazone (as HCl) 15 mg	pioglitazone (as HCl) 30 mg	pioglitazone (as HCl) 45 mg

For information about inactive ingredients and allergens in the medicine, see section 2 "Important information about some of the ingredients of the medicine" and section 6 - "Additional information".
The medicine contains lactose, see section 2 **"Special warnings regarding use of the medicine"**.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

The medicine is not intended for children and adolescents under 18 years of age.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for the treatment of type 2 diabetes (non-insulin dependent) in patients whose blood sugar level cannot be controlled by treatment with metformin alone.

Actos is given as monotherapy in patients who are unable to take metformin and whose blood sugar level cannot be controlled by diet or exercise. Likewise, Actos is also given in combination with other medicines for treatment of diabetes (such as metformin, sulphonylurea or insulin) when adequate control of the blood sugar level has not been achieved.

Actos helps control blood sugar levels by improving the response of the body cells to insulin produced in the body.

Therapeutic group:
The medicine belongs to the group of thiazolidinediones for treatment of diabetes.

2. BEFORE USING THE MEDICINE

Do not use the preparation if:

- There is known sensitivity to pioglitazone or to any of the ingredients of the medicine listed in section 6.
- You suffer or have suffered in the past from heart failure.
- You suffer from liver disease.

- You suffer from diabetic ketoacidosis, a complication of diabetes leading to rapid weight loss, nausea or vomiting.
- You suffer or have suffered in the past from bladder cancer.
- You have blood in your urine that your doctor has not yet diagnosed.

Special warnings regarding use of the medicine
Before beginning treatment, inform the doctor if:
- You have a known sensitivity to lactose, since the preparation contains lactose.
- You suffer from fluid retention in the body or from heart failure, particularly in people above 75 years of age. If you are taking anti-inflammatory medicines that may also cause fluid retention and swelling, you should consult the doctor.
- You suffer from a diabetic eye disease, called macular edema (swelling of the back part of the eye).
- You suffer from polycystic ovary syndrome, as Actos may cause ovulation and increase the chances of becoming pregnant. It is recommended to use contraceptive preparations in order to avoid an unplanned pregnancy.
- You suffer from a liver or heart problem. Before starting treatment with Actos, you should perform blood tests to assess liver function. It may be necessary to repeat the tests during treatment. Certain people with long-standing diabetes, as well as heart disease or stroke, who took Actos and insulin, developed heart failure. Inform the doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or sharp increase in body weight or localized edema (swelling).

Warnings
- If you are taking additional medicines for diabetes, precautionary measures should be taken to avoid the development of low blood sugar levels (hypoglycemia).
- You should perform blood tests at a frequency that will be determined by your doctor, as there may be a reduction in blood count (anemia).
- A high number of bone fractures have been observed in patients treated with this medicine, particularly in women. Consult the doctor.

Children and adolescents
This medicine is not recommended for children and adolescents under the age of 18 years.

Tests and follow-up
- Routine blood tests should be performed while using Actos in order to monitor liver function.
- Your body weight should be monitored on a regular basis. If there is an increase in body weight, consult the doctor.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

In particular, inform the doctor if you are taking the following medicines:
- Gemfibrozil (to lower cholesterol)
- Rifampicin (to treat tuberculosis and other infections)

If you are taking any of these medicines, check your blood sugar levels, in order to estimate the appropriate Actos dosage.

Use of the medicine and food
Actos can be taken with or without food. Swallow with a glass of water.

Pregnancy, breastfeeding and fertility

If you are pregnant, think you are pregnant or planning a pregnancy, breastfeeding or planning to breastfeed, tell the doctor. They may recommend that you stop using the medicine.

Driving and operating machinery
The medicine does not impair your ability to drive or operate machinery, but take care if you experience vision impairment during treatment.

Important information about some of the ingredients of the medicine
This medicine contains lactose. If you are sensitive to lactose, consult the doctor before taking this medicine.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.
The dosage is according to doctor's instructions only.
Use this medicine at specific time intervals as determined by your doctor.

Dosage
The dosage and treatment regimen will be determined by the doctor only.
The usual recommended directions for use are as follows:
One tablet of Actos 15 mg or 30 mg once daily. If necessary, the doctor will increase the dosage to a maximum of 45 mg once daily.

- If Actos is taken in combination with other medicines for treatment of diabetes (such as insulin, chlorpropamide, glibenclamide, gliclazide, tolbutamide), the doctor will determine whether a lower dosage of your medicines is required.
- Your doctor will perform tests to assess the effectiveness of the treatment with Actos 3 to 6 months after commencement of treatment.
- If you are on a special diet for diabetes, continue with it while taking Actos.

Do not exceed the recommended dose.

How to take the medicine
The medicine should be swallowed with a glass of water.
Do not split the tablets since there is no score line. There is no information regarding crushing.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

Effects of overdose:
Blood sugar levels could fall excessively. Blood sugar level can be increased by eating sugar. The patients are recommended to carry with them some sugary food (such as: candies, sweets, cookies or sweetened juice).

If you forgot to take the medicine at the required time, take the next dose at the usual time. Do not take two doses together to make up for a forgotten dose.

Adhere to the treatment as recommended by the doctor, even if your health improves. Do not stop the treatment without consulting the doctor.

If you stop taking the medicine

Actos should be taken every day in order for it to work properly. If you stop taking Actos, your blood sugar level will increase. Consult your doctor before discontinuing this treatment.

Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take a medicine. Wear glasses if you need them.
If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. <u>SIDE EFFECTS</u>

As with any medicine, use of Actos may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

- Heart failure can occur frequently (occurs in 1-10 out of 100 users) in patients taking Actos in combination with insulin. Typical symptoms are unusual shortness of breath or sharp increase in weight or localized swelling (edema). If you experience any of these effects, especially if you are over 65 years of age, seek medical attention immediately.
- Bladder cancer may occur infrequently (occurs in 1-10 out of 1,000 users) in patients taking Actos. Signs and symptoms include blood in the urine, pain upon urinating or a sudden urge to urinate. If you experience any of these effects, consult the doctor as soon as possible.
- Localized swelling (edema) may occur very frequently (occurs in more than one out of 10 users) in patients taking Actos in combination with insulin. If you experience this effect, consult the doctor as soon as possible.
- Bone fractures have been reported frequently (occur in 1-10 out of 100 users) in women taking Actos, and at an unknown frequency in men taking Actos. Whenever this side effect occurs, consult the doctor as soon as possible.
- Blurred vision due to swelling (or fluids) at the back part of the eye (unknown frequency). If you experience this effect for the first time, consult the doctor as soon as possible. If you suffer from blurred vision and the symptoms worsen, refer to the doctor as soon as possible.
- Allergic reactions (unknown frequency): If you experience a serious allergic reaction, including skin allergy (hives) which can be accompanied by itching and swelling of the face, lips, tongue or throat that may cause difficulty in breathing or swallowing, stop taking the medicine and consult the doctor as soon as possible.

Additional side effects:

Common side effects (effects that occur in 1-10 out of 100 users):
- Respiratory tract infections
- Visual disturbances
- Weight gain
- Numbness

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- Inflammation of the sinuses (sinusitis)
- Insomnia

Side effects with unknown frequency (effects whose frequency has not yet been determined):
- Increase in liver enzymes
- Allergic reactions

Possible side effects when Actos is taken in combination with other medicines for treatment of diabetes:

Very common side effects (effects that occur in more than 1 out of 10 users):
- Hypoglycemia - decreased blood sugar levels

Common side effects (effects that occur in 1-10 out of 100 users):
- Headache
- Dizziness
- Joint pain
- Impotence
- Back pain
- Shortness of breath
- Slight decrease in red blood cell count
- Flatulence

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- Sugar or protein in the urine
- Increase in enzyme levels
- Loss of balance (vertigo)
- Sweating
- Tiredness
- Increased appetite

If a side effect occurs, if any of the side effects worsen, or if you are suffering from a side effect not mentioned in the leaflet, consult the doctor.

Reporting side effects
Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
Do not use the medicine after the expiry date (expiry date) that appears on the package. The expiry date refers to the last day of that month.
Store in a dry place, below 25°C.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:
lactose monohydrate, carmellose calcium, hydroxypropylcellulose, magnesium stearate

Each Actos 15 mg tablet contains: 93 mg lactose monohydrate
Each Actos 30 mg tablet contains: 76.3 mg lactose monohydrate
Each Actos 45 mg tablet contains: 114.5 mg lactose monohydrate

What the medicine looks like and contents of the package:
Actos 15 mg: white, round convex tablet. The number "15" appears on one side, and ACTOS appears on the other side. The package contains 14, 28, 30, 50, 56, 84, 90, 98, 112 or 196 tablets packed in blister trays.

Actos 30 mg: white, round tablet that is flat on both sides. The number “30” appears on one side, and ACTOS appears on the other side. The package contains 14, 28, 30, 50, 56, 84, 90, 98 or 112 tablets packed in blister trays.
Actos 45 mg: white, round tablet that is flat on both sides. The number “45” appears on one side, and ACTOS appears on the other side. The package contains 14, 28, 30, 50, 56, 84 or 90 tablets packed in blister trays.

Not all package sizes may be marketed.

Name and address of the marketing authorization holder:
Tzamal Bio-Pharma Ltd., 20 Hamagshimim St., Petach Tikva.

Name and address of the manufacturer:
Cheplapharm Arzneimittel GmbH, Greifswald, Germany.

The leaflet was revised in February 2023 in accordance with the Ministry of Health guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Actos 15 mg: 149 69 33828
Actos 30 mg: 149 70 33829
Actos 45 mg: 149 71 33830

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