

Actosmet® 15 mg/850 mg Film-coated Tablets

Pioglitazone and Metformin hydrochloride

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.

The product is known by the name above but will be referred to as Actosmet throughout the rest of this leaflet.

In this leaflet:

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

1. What Actosmet is and what it is used for

Actosmet contains pioglitazone and metformin. It is an anti-diabetic medicine used in adults to treat type 2 (non-insulin dependent) diabetes mellitus when treatment with metformin alone is not sufficient. This type 2 diabetes usually develops in adulthood particularly as a result of the person being overweight and where the body either does not produce enough insulin (a hormone that controls blood sugar levels), or cannot effectively use the insulin it produces. Your doctor will check whether Actosmet is working 3 to 6 months after you start taking it.

Actosmet helps control the level of sugar in your blood when you have type 2 diabetes by helping your body make better use of the insulin it produces.

2. What you need to know before you take Actosmet

Do not take Actosmet

- If you are allergic to pioglitazone, metformin or any of the other ingredients of this medicine (listed in section 6).
- If you have heart failure or have had heart failure in the past.
- If you recently had a heart attack, have severe circulatory problems including shock, or breathing difficulties.
- If you have liver disease.
- If you drink alcohol excessively (either every day or only from time to time).
- If you have uncontrolled diabetes, with for example severe hyperglycaemia (high blood glucose), nausea, vomiting, diarrhoea, rapid weight loss, lactic acidosis (see section "Risk of lactic acidosis") or ketoacidosis. Ketoacidosis is a condition in which substances called 'ketone bodies' accumulate in the blood and which can lead to diabetic pre-coma. Symptoms include stomach pain, fast and deep breathing, sleepiness or your breath developing an unusual fruity smell.
- If you have or have ever had bladder cancer.
- If you have blood in your urine that your doctor has not checked.
- If you have severely reduced kidney function.
- If you have a severe infection or are dehydrated.
- If you are going to have a certain type of X-ray with an injectable dye, talk to your doctor as you must stop taking Actosmet for a certain period of time before and after the examination.
- If you are breast-feeding.

Warnings and precautions

Talk to your doctor or pharmacist before taking Actosmet (see also section 4):

- If you have a problem with your heart. Some patients with long-standing type 2 diabetes mellitus and heart disease or who were treated with pioglitazone and insulin together experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- If you retain water (fluid retention) or have heart failure problems in particular if you are over 75 years old. If you take anti-inflammatory medicines which can also cause fluid retention and swelling, you must also tell your doctor.
- If you have a special type of diabetic eye disease called macular oedema (swelling of the back of the eye), talk to your doctor if you notice any change to your vision.
- If you have cysts on your ovaries (polycystic ovary syndrome). There may be an increased possibility of becoming pregnant because you may ovulate again when you take Actosmet. If this applies to you, use appropriate contraception to avoid the possibility of an unplanned pregnancy.
- If you have a problem with your liver. Some patients who will have a blood sample taken to check your liver function. This check should be repeated at intervals. Inform your doctor as soon as possible if you develop symptoms suggesting a problem with your liver (like feeling sick without explanations, vomiting, stomach ache, tiredness, loss of appetite and/or dark urine) as your liver function should be checked. You may also experience a reduction in blood count (anaemia).

Risk of lactic acidosis

Actosmet may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious heart disease, prolonged intake of alcohol and dehydration (see further information below), liver problems and any medical conditions in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease).

If any of the above apply to you, talk to your doctor for further instructions.

Stop taking pioglitazone/metformin for a short time if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhoea, fever, exposure to heat or if you drink less fluid than normal. Talk to your doctor for further instructions.

Stop taking pioglitazone/metformin and contact a doctor or the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, as this condition may lead to coma.

Symptoms of lactic acidosis include:

- Vomiting
- Stomach ache (abdominal pain)
- Muscle cramps
- A general feeling of not being well with severe tiredness
- Difficulty in breathing
- Reduced body temperature and heartbeat

Lactic acidosis is a medical emergency and must be treated in a hospital.

During treatment with Actosmet, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

If you need to have major surgery you must stop taking Actosmet during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Actosmet.

Hypoglycaemia

If you take Actosmet with other medicines for diabetes, it is more likely that your blood sugar could fall below the normal level (hypoglycaemia). If you experience symptoms of hypoglycaemia such as weakness, dizziness, increased sweating, fast heart-beating, vision disorders or difficulty in concentration, you should take some sugar to increase your blood sugar level again. Ask your doctor or pharmacist for more information if you are not sure how to recognise this. It is recommended that you carry some sugar lumps, sweets, biscuits or sugary fruit juice.

Broken bones

A higher number of bone fractures was seen in patients, particularly women taking pioglitazone. Your doctor will take this into account when treating your diabetes.

Children and adolescents

Use in children and adolescents under 18 years is not recommended.

Other medicines and Actosmet

If you need to have an injection of a contrast medium that contains iodine into your bloodstream, for example in the context of an X-ray or scan, you must stop taking Actosmet before or at the time of the injection. Your doctor will decide when you must stop and when to restart your treatment with Actosmet.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. You may need more frequent blood glucose and kidney function tests, or your doctor may need to adjust the dose of Actosmet. It is especially important to mention the following:

- Gemfibrozil (used to lower cholesterol)
- Rifampicin (used to treat tuberculosis and other infections)
- Cimetidine (used to reduce stomach acid)
- Glucocorticoids (used to treat inflammation)
- Beta-2-agonists (used to treat asthma)
- Medicines which increase urine production (diuretics)
- Medicines used to treat pain and inflammation (NSAID and COX-2-inhibitors, such as ibuprofen and celecoxib)
- Certain medicines for the treatment of high blood pressure (angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists)

Actosmet with alcohol

Avoid excessive alcohol intake while taking Actosmet since this may increase the risk of lactic acidosis (see section "Risk of lactic acidosis").

Pregnancy and breast-feeding

You must tell your doctor if you are pregnant, think you may be pregnant or are planning to have a baby. Actosmet is not recommended in pregnancy. If you wish to become pregnant, your doctor will advise you to discontinue this medicine.

Do not use Actosmet if you are breastfeeding or are planning to breast-feed (see section "Do not take Actosmet").

Driving and using machines

This medicine will not affect your ability to drive or use machines but take care if you experience abnormal vision.

Actosmet contains sodium

Actosmet contains sodium. Each film-coated tablet of Actosmet 15 mg/850 mg Film-coated Tablets contains approximately 9.5 mg sodium which is less than 1 mmol (23 mg), that is to say essentially 'sodium-free'.

3. How to take Actosmet

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

The recommended dose is one tablet taken twice daily. If necessary your doctor may tell you to take a different dose. If you have reduced kidney function, your doctor may prescribe a lower dose, which may need to be given as separate tablets of pioglitazone and metformin. You should swallow the tablets with a glass of water. You may take your tablets with or just after food to reduce

the chance of an upset stomach.

If you are following a special diet for diabetes, you should continue with this while you are taking Actosmet. Your weight should be checked at regular intervals. If your weight increases, inform your doctor. Your doctor will ask you to have blood tests periodically during treatment with Actosmet. This is to check that your liver is working normally. At least once a year (more often if you are elderly or have kidney problems) your doctor will check that your kidneys are working normally.

If you take more Actosmet than you should

If you accidentally take too many tablets, or if someone else or a child takes your medicine, talk to a doctor or pharmacist immediately. Your blood sugar could fall below the normal level and can be increased by taking sugar. It is recommended that you carry some sugar lumps, sweets, biscuits or sugary fruit juice. If you have taken more Actosmet than you should have, you may experience lactic acidosis (see section "Risk of lactic acidosis").

If you forget to take Actosmet

Take Actosmet daily as prescribed. However if you miss a dose, skip the missed dose and just carry on with the next dose as normal. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Actosmet

Actosmet should be used every day to work properly. If you stop using Actosmet, your blood sugar may go up. Talk to your doctor before stopping this treatment.

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.

Pioglitazone/metformin may cause a very rare (may affect up to 1 in 10,000), but very serious side effect called lactic acidosis (see section "Risk of lactic acidosis"). If this happens you must stop taking pioglitazone/metformin and contact a doctor or the nearest hospital immediately, as lactic acidosis may lead to coma.

Bladder cancer has been experienced uncommonly (may affect up to 1 in 100 people) in patients taking pioglitazone/metformin. Signs and symptoms include blood in your urine, pain when urinating or a sudden need to urinate. If you experience any of these, talk to your doctor as soon as possible.

Allergic reactions have been reported commonly (may affect up to 1 in 10 people) in female patients taking pioglitazone/metformin and have also been reported in male patients (frequency cannot be estimated from the available data) taking pioglitazone/metformin. If you experience this side effect, talk to your doctor as soon as possible.

Blurred vision due to swelling (or fluid) at the back of the eye (macular oedema) has been reported (frequency cannot be estimated from available data). If you experience these symptoms for the first time talk to your doctor as soon as possible. Also, if you already have blurred vision and the symptoms get worse, talk to your doctor as soon as possible.

Allergic reactions have been reported with frequency not known (cannot be estimated from available data) in patients taking pioglitazone/metformin. If you have a serious allergic reaction, including hives and swelling of the face, lips, tongue, or throat that may cause difficulty in breathing or swallowing, stop taking this medicine and talk to your doctor immediately.

The following side effects have been experienced by some patients taking pioglitazone/metformin:

Very common (may affect more than 1 in 10 people)

- Stomach ache
- Feeling sick (nausea)
- Vomiting
- Diarrhoea
- Loss of appetite

Common (may affect up to 1 in 10 people)

- Localised swelling (oedema)
- Weight gain
- Headache
- Respiratory infection
- Abnormal vision
- Joint pain
- Impotence
- Blood in urine
- Reduction in blood count (anaemia)
- Numbness
- Taste disturbance

Uncommon (may affect up to 1 in 100 people)

- Inflammation of the sinuses (sinusitis)
- Gas
- Difficulty sleeping (insomnia)

Very rare (may affect up to 1 in 10,000)

- Decrease in amount of vitamin B₁₂ in the blood
- Redness of the skin
- Itchy skin
- Raised and itchy rash (hives)
- Not known (frequency cannot be estimated from the available data)
- Inflammation of the liver (hepatitis)
- Liver does not work as well as it should (changes in liver enzymes)

5. How to store Actosmet

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

Store below 30°C.

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

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

Do not use this medicine if you notice any 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 Actosmet contains

The active substances are pioglitazone hydrochloride and metformin hydrochloride. Each film-coated tablet of Actosmet 15 mg/850 mg Film-coated Tablets contains pioglitazone hydrochloride equivalent to 15 mg pioglitazone and 850 mg metformin hydrochloride.

The other ingredients are: Tablet core: Microcrystalline cellulose, povidone, croscarmellose sodium and magnesium stearate. Tablet coat: Hypromellose, macrogol, talc and titanium dioxide.

What Actosmet looks like and contents of the pack
Actosmet 15 mg/850 mg Film-coated Tablets are white to off-white oblong convex film-coated tablets, embossed with "15/850" on one side and "4633M" on the other in aluminium-aluminum blisters.

Pack size: 56 Film-coated Tablets.

Marketing Authorization Holder

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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. You can also report side effects directly (see details below). By reporting side effects, you can also help provide more information on the safety of this medicine.

• Jordan

Food and Drug Administration- Rational Drug Use and Pharmacovigilance Department

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Council of Arab Health Ministers, Union of Arab Pharmacists

This is a Medicament

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not put yourself in danger by interrupting the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.



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