

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Competact 15 mg/850 mg Film-coated tablets

Active ingredients and quantities:

Each tablet contains:

pioglitazone (as hydrochloride) 15 mg

metformin hydrochloride 850 mg

For information about inactive ingredients and allergens in this medicine, see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. 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.

Use of this medicine in children and adolescents under 18 years of age is not recommended.

1. What is this medicine intended for?

This medicine is intended for treating type 2 diabetes mellitus (non-insulin dependent) in adults with blood sugar levels that cannot be controlled with metformin treatment alone.

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 Competact is working properly 3 to 6 months after you start taking it.

Competact helps control the level of sugar in your blood by helping your body make better use of the insulin it produces.

Therapeutic group:

Pioglitazone: a thiazolidinedione.

Metformin: a biguanide.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients (pioglitazone and metformin) or to any of the other ingredients in this medicine (see section 6).
- You have heart failure or have had heart failure in the past.
- You recently had a heart attack, have severe circulatory problems including shock, or breathing difficulties.
- You have liver disease.
- You drink alcohol excessively (either every day or only from time to time).
- You have uncontrolled diabetes, with for example severe hyperglycemia (high blood glucose), nausea, vomiting, diarrhea, rapid weight loss, lactic acidosis (see the 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 sweet smell.
- You have or have had in the past bladder cancer.
- You have blood in your urine that your doctor has not checked yet.
- You have severely reduced kidney function.

- You have a severe inflammation or are dehydrated.
- You are going to have a certain type of X-ray with an injectable dye: Talk to your doctor because you must stop taking Competact for a certain period of time before and after the examination.
- You are breastfeeding.

Special warnings about using this medicine

Before using Competact, tell your doctor if (see also section 4):

- You have a problem with your heart. Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone together with insulin, developed 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 localized swelling (edema).
- You have fluid retention or have heart failure problems, particularly 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.
- You have a certain type of eye disease that is typical for diabetics called macular edema (swelling of the back of the eye). Consult your doctor if you notice any change to your vision.
- 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 Competact. If this applies to you, use appropriate contraception to avoid the possibility of an unplanned pregnancy.
- You have a problem with your liver. Before you start taking Competact you will have a blood test to check your liver function. This blood test should be repeated at intervals. Inform your doctor as soon as possible if you develop symptoms suggesting a problem with your liver (like unexplained nausea, 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 (anemia).

Risk of lactic acidosis

Competact 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 the following conditions: uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, 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 and severe heart disease).

If any of these conditions apply to you, talk to your doctor for further instructions.

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

Stop taking Competact and contact a doctor or the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, because this condition may lead to coma. Symptoms of lactic acidosis include:

- vomiting
- stomach ache
- 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 Competact, 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 are about to have major surgery, you must stop taking Competact during and for some time after surgery. Your doctor will decide when you must stop and when to restart your treatment with Competact.

Hypoglycemia

If you take Competact with other medicines for diabetes, it is more likely that your blood sugar could fall below the normal level (hypoglycemia). If you experience symptoms of hypoglycemia such as weakness, dizziness, increased sweating, fast heartbeat, 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 recognize this condition. It is recommended that you carry some sugar lumps, sweets, biscuits or sweet 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 of this medicine in children and adolescents under 18 years of age is not recommended.

Tests and follow-up

- You should monitor your body weight at regular intervals. If your body weight increases, inform your doctor.
- The doctor will refer you for periodic blood tests during treatment with Competact, in order to check that your liver is functioning normally.
- At least once a year (more frequently if you are elderly or have kidney problems), the doctor will refer you to check whether your kidneys are functioning normally.

Drug interactions

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

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. You may need more frequent blood glucose and kidney function tests, or your doctor may need to adjust the dose of Competact.

It is especially important to tell your doctor if you are taking any of the following medicines:

- 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 (nonsteroidal anti-inflammatory drugs [NSAIDs] 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)

Using this medicine and food

Swallow the tablets with a glass of water. You may take your tablets with or just after a meal to reduce the chance of an upset stomach.

Using this medicine and alcohol consumption

Avoid excessive alcohol intake while taking Competact since this may increase the risk of lactic acidosis (see section 2 under 'Risk of lactic acidosis').

Pregnancy, breastfeeding and fertility

- You must tell your doctor if you are pregnant, think you may be pregnant or are planning to have a baby. Competact is not recommended in pregnancy. If you wish to become pregnant, your doctor will advise you to discontinue this medicine.
- Do not use Competact if you are breastfeeding or are planning to breastfeed (see section 2 under 'Do not use this medicine if:').

Driving and using machines

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

Important information about some of this medicine's ingredients

This medicine contains less than 23 mg of sodium per tablet, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.

Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Dosage

Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually:

one Competact tablet twice a day. If necessary, your doctor may decide to give you a different dose.

If you have poor kidney function, your doctor may prescribe a lower dose, which you may need to take as separate tablets of pioglitazone and metformin.

Do not exceed the recommended dose.

How to take the medicine

Swallow the tablets with a glass of water. You may take your tablets with or just after a meal to reduce the chance of an upset stomach.

Do not crush, split, or chew the tablets.

If you are following a special diet for diabetes, you should continue with this while you are taking Competact.

If you have taken a higher dose

Your blood sugar level 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 sweet fruit juice.

If you have taken an overdose of Competact, you may experience lactic acidosis (see section 2 under 'Risk of lactic acidosis').

If you have accidentally take an overdose or if another person or a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine

Take Competact every day as prescribed by your doctor. However, if you miss a dose, skip the missed dose and take your next dose as usual. Do not take a double dose to make up for a missed dose.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine

Competact should be used every day to work properly. If you stop taking Competact, your blood sugar level may go up. Consult your doctor before stopping this treatment.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. **Side effects**

Like with all medicines, using Competact may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

- Competact may cause a very rare (affects up to 1 in 10,000 users), but very serious side effect called lactic acidosis (see section 2 under 'Risk of lactic acidosis'). If this happens you must **stop taking Competact and contact a doctor or the nearest hospital immediately**, because lactic acidosis may lead to coma.
- Bladder cancer may occur uncommonly (affects up to 1 in 100 users) in patients taking Competact. 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.
- Broken bones have been reported commonly (affect up to 1 in 10 users) in women taking Competact and have also been reported in men taking Competact (frequency cannot be estimated from the available data). 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 edema) 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 unknown frequency (frequency cannot be estimated from available data) in patients taking Competact. 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 Competact:
Very common side effects (effects that occur in more than 1 out of 10 users):

- stomachache
- nausea
- vomiting
- diarrhea
- loss of appetite

Common side effects (effects that occur in 1-10 out of 100 users):

- localized swelling (edema)
- weight gain
- headache
- respiratory infection
- abnormal vision
- joint pain
- impotence
- blood in urine
- reduction in blood count (anemia)
- numbness
- taste disturbance

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

- inflammation of the sinuses (sinusitis)
- gas
- difficulty sleeping (insomnia)

Very rare side effects (effects that occur in less than 1 out of 10,000 users):

- reduced blood level of vitamin B₁₂ in the blood
- redness of the skin
- itchy skin
- raised and itchy rash (hives)

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- inflammation of the liver (hepatitis)
- impaired liver function (changes in levels of liver enzymes)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:

<https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions

Store in a dry place, below 25°C.

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

6. Additional information

In addition to the active ingredients, this medicine also contains:

microcrystalline cellulose, povidone, croscarmellose sodium, magnesium stearate, hypromellose, macrogol 8000, talc, titanium dioxide.

What the medicine looks like and contents of the pack:

A Competact 15 mg/850 mg film-coated tablet is white to off white, oblong, convex, embossed '15/850' on one side and '4833M' on the other.

Packs contain 14, 28, 30, 50, 56, 60, 90, 98, 112, 180 tablets or multipack of 196 tablets (2 packs of 98).

Not all pack sizes may be marketed.

Registration holder's name and address:

Tzamal Bio-Pharma Ltd., 20 Hamagshimim St., Petah-Tikva.

Manufacturer's name and address:

Cheplapharm Arzneimittel GmbH, Greifswald, Germany.

The leaflet was revised in February 2023 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry:

150-65-33826