

MEDICATION GUIDE
ACTOPLUS MET[®] (ak-TÖ-plus-met)
(pioglitazone hydrochloride and metformin hydrochloride) tablets

Read this Medication Guide carefully before you start taking ACTOPLUS MET and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment. If you have any questions about ACTOPLUS MET, ask your doctor or pharmacist.

What is the most important information I should know about ACTOPLUS MET?

ACTOPLUS MET can cause serious side effects, including **new or worse heart failure**.

- Pioglitazone, one of the medicines in ACTOPLUS MET, can cause your body to keep extra fluid (fluid retention), which leads to swelling (edema) and weight gain. Extra body fluid can make some heart problems worse or lead to heart failure. Heart failure means your heart does not pump blood well enough.
- If you have severe heart failure, you cannot start ACTOPLUS MET.
- If you have heart failure with symptoms (such as shortness of breath or swelling), even if these symptoms are not severe, ACTOPLUS MET may not be right for you.

Call your doctor right away if you have any of the following:

- swelling or fluid retention, especially in the ankles or legs.
- shortness of breath or trouble breathing, especially when you lie down.
- an unusually fast increase in weight.
- unusual tiredness.

Metformin, one of the medicines in ACTOPLUS MET, can cause a rare but serious condition called lactic acidosis (a buildup of an acid in the blood) that can cause death. Lactic acidosis is a medical emergency and must be treated in the hospital.

Most people who have had lactic acidosis with metformin have other things that, combined with the metformin, led to the lactic acidosis. Tell your doctor if you have any of the following, because you have a higher chance for getting lactic acidosis with ACTOPLUS MET if you:

- have kidney problems or your kidneys are affected by certain x-ray tests that use injectable dye. People whose kidneys are not working properly should not take ACTOPLUS MET.
- have liver problems.
- drink alcohol very often, or drink a lot of alcohol in short-term "binge" drinking.
- get dehydrated (lose a large amount of body fluids). This can happen if you are sick with a fever, vomiting, or diarrhea. Dehydration can also happen when you sweat a lot with activity or exercise and -do not drink enough fluids.
- have surgery.
- have a heart attack, severe infection, or stroke.
- are 80 years of age or older, and your kidneys are not working properly.

The best way to keep from having a problem with lactic acidosis from metformin is to tell your doctor if you have any of the problems in the list above. Your doctor may decide to stop your ACTOPLUS MET for a while if you have any of these things.

Lactic acidosis can be hard to diagnose early, because the early symptoms could seem like the symptoms of many other health problems besides lactic acidosis. You should call your doctor right away if you get the following symptoms, which could be signs of lactic acidosis:

- You feel very weak or tired.
- You have unusual (not normal) muscle pain.
- You have stomach pains, nausea or vomiting.
- You have trouble breathing.
- You feel dizzy or lightheaded.
- You have a slow or irregular heartbeat.

ACTOPLUS MET can have other serious side effects. See "What are the possible side effects of ACTOPLUS MET?"

What is ACTOPLUS MET?

ACTOPLUS MET is a prescription medicine used with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes.

ACTOPLUS MET contains 2 prescription diabetes medicines called pioglitazone hydrochloride (ACTOS) and metformin hydrochloride (GLUCOPHAGE).

Your doctor will decide if you should take ACTOPLUS MET.

ACTOPLUS MET can be used for adults with type 2 diabetes who:

- are taking pioglitazone alone and do not have good enough blood sugar control,
- are taking metformin alone and do not have good enough blood sugar control, or
- are already taking both pioglitazone and metformin.

If you are taking pioglitazone or metformin, check with your healthcare provider and make sure you understand exactly how your healthcare provider wants you to switch over to ACTOPLUS MET.

It is important to eat the right foods, lose weight if needed, and exercise regularly in order to manage your type 2 diabetes. Diet, weight loss, and exercise are the main treatments for type 2 diabetes and they also help your diabetes medicines work better for you.

ACTOPLUS MET has not been studied in children and is not recommended for children under the age of 18. The risks of giving ACTOPLUS MET to a child are not known. See “What are some other possible side effects of ACTOPLUS MET?”

Who should not take ACTOPLUS MET?

Do not take ACTOPLUS MET if you:

- are allergic to any of the ingredients in ACTOPLUS MET. See the end of this Medication Guide for a complete list of ingredients in ACTOPLUS MET.
- have kidneys which are not working properly.
- have a condition called metabolic acidosis, including diabetic ketoacidosis. Diabetic ketoacidosis should be treated with insulin.
- are going to have an x-ray procedure with an injection of dyes (contrast agents) in your vein with a needle. Talk to your doctor about when to stop ACTOPLUS MET and when to start it again.

People with severe heart failure should not start taking ACTOPLUS MET. See “What is the most important information I should know about ACTOPLUS MET?”.

What should I tell my doctor before taking ACTOPLUS MET?

Before starting ACTOPLUS MET, ask your doctor about what the choices are for diabetes medicines and what the expected benefits and possible risks are for you in particular.

Tell your doctor about all of your medical conditions, especially if you:

- **have heart failure.**
- **have kidney problems.**
- **are going to have dye injected into a vein for an x-ray, CAT scan, heart study, or other type of scanning.**
- **drink a lot of alcohol** (all the time or short binge drinking).
- **have type 1 (“juvenile”) diabetes or had diabetic ketoacidosis.** These conditions should be treated with insulin.
- **are 80 years old or older.** People over 80 years should not take ACTOPLUS MET unless their kidney function is checked and it is normal.
- **have a type of diabetic eye disease called macular edema** (swelling of the back of the eye).
- **have liver problems.** Your doctor should do blood tests to check your liver before you start taking ACTOPLUS MET and during treatment as needed.
- **are pregnant or planning to become pregnant.** ACTOPLUS MET should not be used during pregnancy. It is not known if ACTOPLUS MET can harm your unborn baby. Talk to your doctor about the best way to control your blood glucose levels while pregnant.
- **are a premenopausal woman (before the “change of life”), who does not have periods regularly or at all.** ACTOPLUS MET may increase your chance of becoming pregnant. Talk to your doctor about

birth control choices while taking ACTOPLUS MET. Tell your doctor right away if you become pregnant while taking ACTOPLUS MET.

- **are breastfeeding or plan to breastfeed.** It is not known if ACTOPLUS MET passes into your milk and if it can harm your baby. You should not take ACTOPLUS MET if you breastfeed your baby. Talk to your doctor about the best way to control your blood glucose levels while breastfeeding.

Tell your doctor about all the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. ACTOPLUS MET and some of your other medicines can affect each other. You may need to have your dose of ACTOPLUS MET or certain other medicines adjusted. Certain other medicines can affect your blood sugar (glucose) control.

Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist before you start a new medicine. They will tell you if it is okay to take ACTOPLUS MET with other medicines.

How should I take ACTOPLUS MET?

- Take ACTOPLUS MET exactly as prescribed. Your doctor will tell you how many ACTOPLUS MET tablets to take and how often you should take them. Your doctor may need to change your dose of ACTOPLUS MET to control your blood glucose. Do not change your dose unless told to do so by your doctor.
- Take ACTOPLUS MET with meals to lower your chance of an upset stomach.
- If you miss a dose of ACTOPLUS MET, take your next dose as prescribed unless your doctor tells you differently. Do not take two doses at one time the next day.
- If you take too much ACTOPLUS MET, call your doctor or poison control center right away.
- If your body is under stress, for example: due to fever, infection, trauma (such as a car accident), or surgery, the dose of your diabetes medicines may need to be changed. Call your doctor right away.
- Stay on your diet and exercise programs and test your blood sugar regularly while taking ACTOPLUS MET.
- Your doctor should do blood tests before starting ACTOPLUS MET and from time to time to check your liver, kidneys, and blood cells.
- Your doctor should also do regular blood tests (for example, hemoglobin A1C) to check how well your blood sugar is controlled with ACTOPLUS MET.
- Your doctor should check your eyes regularly. Some people have had vision changes due to swelling in the back of the eye, called macular edema, while taking ACTOPLUS MET.
- It may take 2-3 months to see the full effect on your blood sugar level.

You may need to stop ACTOPLUS MET for a short time. Call your doctor for instructions if you:

- are sick with severe vomiting, diarrhea, or fever or if you drink a much lower amount of liquid than normal.
- plan to have surgery.
- are having an x-ray procedure with injection of dye.

What are other possible side effects of ACTOPLUS MET?

ACTOPLUS MET can cause other serious side effects including:

- **Weight gain.** Pioglitazone, one of the medicines in ACTOPLUS MET, can cause weight gain that may be due to fluid retention or extra body fat. Weight gain due to fluid retention can be a serious problem for people with certain conditions, including heart problems. See "What is the most important information I should know about ACTOPLUS MET?".
- **Liver problems.** It is important for your liver to be working normally when you take ACTOPLUS MET. Your doctor should do blood tests to check your liver before you start taking ACTOPLUS MET and during treatment as needed. Call your doctor right away if you have unexplained symptoms such as:
 - nausea or vomiting.
 - stomach pain.
 - unusual or unexplained tiredness.
 - loss of appetite.
 - dark urine.
 - yellowing of your skin or the whites of your eyes.
- **Macular edema** (diabetic eye disease with swelling in the back of the eye). Tell your doctor right away if you have any changes in your vision. Your doctor should check your eyes regularly.
- **Fractures (broken bones)**, usually in the hand, upper arm, or foot in women. Talk to your doctor for advice on how to keep your bones healthy. It is not known if ACTOPLUS MET can affect the bones of children.
- **Low red blood cell count (anemia).**

- **Low blood sugar (hypoglycemia).** Lightheadedness, dizziness, shakiness, or hunger may indicate that your blood sugar is too low. This can happen if you skip meals, if you use another medicine that lowers blood sugar, or if you have certain medical problems. Call your doctor if low blood sugar levels are a problem for you.
- **Ovulation** (release of an egg from an ovary in a woman) leading to pregnancy. Ovulation may happen when premenopausal women who do not have regular monthly periods take ACTOPLUS MET. This can increase the chance of pregnancy. See “What should I tell my doctor before taking ACTOPLUS MET?”.

In studies of pioglitazone (one of the medicines in ACTOPLUS MET), bladder cancer occurred in a few more people who were taking pioglitazone than in people who were taking other diabetes medicines. There were too few cases to know if the bladder cancer was related to pioglitazone.

The most common side effects of ACTOPLUS MET reported in clinical trials included diarrhea, nausea, and upset stomach. These side effects usually happen during the first few weeks of treatment. Taking ACTOPLUS MET with meals can help lessen these side effects. However, if you have unusual or unexpected stomach problems, talk with your doctor. Stomach problems that start up later during treatment may be a sign of something more serious.

Other common side effects of ACTOPLUS MET are:

- cold-like symptoms (upper respiratory infection),
- headache,
- urinary tract infection,
- dizziness,
- sinus infection,
- anemia.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the side effects of ACTOPLUS MET. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ACTOPLUS MET?

- Store ACTOPLUS MET at 59° to 86°F (15° to 30°C). Keep ACTOPLUS MET in the original container to protect from light.
- Keep the ACTOPLUS MET bottle tightly closed and protect from getting wet (away from moisture and humidity).

Keep ACTOPLUS MET and all medicines out of the reach of children.

General information about ACTOPLUS MET

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ACTOPLUS MET for a condition for which it is not prescribed. Do not give ACTOPLUS MET to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about ACTOPLUS MET. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about ACTOPLUS MET that is written for healthcare professionals. For more information, go to www.actoplusmet.com or call 1-877-825-3327.

What are the ingredients in ACTOPLUS MET?

Active Ingredients: pioglitazone hydrochloride and metformin hydrochloride

Inactive Ingredients: povidone, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, hypromellose 2910, polyethylene glycol 8000, titanium dioxide, and talc.

Always check to make sure that the medicine you are taking is the correct one. ACTOPLUS MET tablets look like this:

- 15 mg/500 mg strength tablets—white to off-white, oblong tablet with “15/500” on one side and “4833M” on the other.
- 15 mg/850 mg strength tablets—white to off-white, oblong tablet with “15/850” on one side and “4833M” on the other.

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