MEDICATION GUIDE
ACTOPLUS MET (ak-TŌ-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.
  - Do not take ACTOPLUS MET if you have severe heart failure
  - 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
- **Lactic Acidosis.** 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.

  Call your doctor right away if you have any of the following symptoms which could be signs of lactic acidosis:
  - you feel 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

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 have not had your kidneys tested

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.

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

What is ACTOPLUS MET?
ACTOPLUS MET contains 2 prescription diabetes medicines called pioglitazone hydrochloride (ACTOS) and metformin hydrochloride (GLUCOPHAGE). ACTOPLUS MET can be used with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes.

ACTOPLUS MET is not for people with type 1 diabetes

ACTOPLUS MET is not for people with diabetic ketoacidosis (increased ketones in your blood or urine).

It is not known if ACTOPLUS MET is safe and effective in children.

Who should not take ACTOPLUS MET?
See “What is the most important information I should know about ACTOPLUS MET?”

Do not take ACTOPLUS MET if you:
- have severe heart failure
- are allergic to pioglitazone, metformin or 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

Tell your doctor before taking ACTOPLUS MET if you have any of these conditions.

What should I tell my doctor before taking ACTOPLUS MET?
Before you start taking ACTOPLUS MET, tell your doctor 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**
- **will be undergoing a surgical procedure**
- **drink a lot of alcohol** (all the time or short binge drinking)
- **have type 1 (“juvenile”) diabetes or had diabetic ketoacidosis**
- **have a type of diabetic eye disease that causes swelling in the back of the eye (macular edema)**
- **have liver problems**

- **are pregnant or plan to become pregnant.** It is not known if ACTOPLUS MET will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant 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 breast-feeding or plan to breast-feed.** It is not known if ACTOPLUS MET passes into your breast milk. You and your doctor should decide if you will take ACTOPLUS MET or breastfeed. You should not do both. 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 changed.

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 your doctor tells you to take it.
- Your doctor may need to change your dose of ACTOPLUS MET. Do not change your ACTOPLUS MET dose unless your doctor tells you to
- ACTOPLUS MET may be prescribed alone or with other diabetes medicines. This will depend on how well your blood sugar is controlled
- 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 go to the nearest hospital emergency room right away
- If your body is under stress such as from a fever, infection, 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 certain blood tests before you start and while you take ACTOPLUS MET
- Your doctor should also do hemoglobin A1C testing to check how well your blood sugar is controlled with ACTOPLUS MET
- Your doctor should check your eyes regularly while you take ACTOPLUS MET

What are the possible side effects of ACTOPLUS MET?
ACTOPLUS MET may cause serious side effects including:

- **See "What is the most important information I should know about ACTOPLUS MET?"**

- **liver problems.** Call your doctor right away if you have:
  - nausea or vomiting
  - stomach pain
  - unusual or unexplained tiredness
  - loss of appetite
  - dark urine
  - yellowing of your skin or the whites of your eyes
- **broken bones (fractures).** Usually in the hand, upper arm, or foot in women. Talk to your doctor for advice on how to keep your bones healthy
- **bladder cancer.** There may be an increased chance of having bladder cancer when you take ACTOPLUS MET. You should not take ACTOPLUS MET if you are receiving treatment for bladder cancer. Tell your doctor right away if you have any of the following symptoms of bladder cancer:
  - blood or a red color in your urine
  - an increased need to urinate
  - pain while you urinate
- **low blood sugar (hypoglycemia).** This can happen if you skip meals, if you also use another medicine that lowers blood sugar, or if you have certain medical problems. Lightheadedness, dizziness, shakiness, or hunger may happen if your blood sugar is too low. Call your doctor if low blood sugar levels are a problem for you
- **diabetic eye disease with swelling in the back of the eye (macular edema)**. Tell your doctor right away if you have any changes in your vision. Your doctor should check your eyes regularly
- **release of an egg from an ovary in a woman (ovulation) leading to pregnancy.** Ovulation may happen when premenopausal women who do not have regular monthly periods take ACTOPLUS MET. This can increase your chance of getting pregnant.
- **low red blood cell count (anemia).**

The most common side effects of ACTOPLUS MET include:
- cold-like symptoms (upper respiratory tract infection)
- swelling (edema)
- diarrhea
- headache
- increased weight

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°F to 86°F (15°C to 30°C). Keep ACTOPLUS MET in the original container and 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 the safe and effective use of 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 was 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

ACTOS and ACTOPLUS MET are trademarks of Takeda Pharmaceutical Company Limited registered with the U.S. Patent and Trademark Office and used under license by Takeda Pharmaceuticals America, Inc.

All other trademarks are the property of their respective owners.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Distributed by:
Takeda Pharmaceuticals America, Inc.
Deerfield, IL 60015

© 2009, 2011-2012 Takeda Pharmaceuticals America, Inc.

April 2012
APM001 R10