

MEDICATION GUIDE
AVANDAMET® (ah-VAN-duh-met)
(rosiglitazone maleate and metformin hydrochloride) Tablets

Read this Medication Guide carefully before you start taking AVANDAMET 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 AVANDAMET, ask your doctor or pharmacist.

What is the most important information I should know about AVANDAMET?

AVANDAMET is available only through the AVANDIA-Rosiglitazone Medicines Access Program. Both you and your doctor must be enrolled in the program so that you can get AVANDAMET. To enroll, you must:

- talk to your doctor,
- understand the risks and benefits of AVANDAMET, and
- agree to enroll in the program.

AVANDAMET may cause serious side effects, including:

New or worse heart failure

- Rosiglitazone, one of the medicines in AVANDAMET, 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 AVANDAMET.
- If you have heart failure with symptoms (such as shortness of breath or swelling), even if these symptoms are not severe, AVANDAMET 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

Myocardial Infarction (“Heart Attack”)

Rosiglitazone, one of the medicines in AVANDAMET, may raise the risk of heart attack. The risk of having a heart attack may be higher in people who take

AVANDAMET with insulin. Most people who take insulin should not also take AVANDAMET.

Symptoms of a heart attack can include the following:

- chest discomfort in the center of your chest that lasts for more than a few minutes, or that goes away or comes back
- chest discomfort that feels like uncomfortable pressure, squeezing, fullness or pain
- pain or discomfort in your arms, back, neck, jaw or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

Call your doctor or go to the nearest hospital emergency room right away if you think you are having a heart attack.

People with diabetes have a greater risk for heart problems. It is important to work with your doctor to manage other conditions, such as high blood pressure or high cholesterol.

Lactic acidosis

Metformin, one of the medicines in AVANDAMET, can cause a rare but serious condition called lactic acidosis (a build-up 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 AVANDAMET if you:

- have kidney problems or your kidneys are affected by certain X-ray tests that use injectable dye. People with kidney problems should not take AVANDAMET.
- 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 AVANDAMET 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
- you have trouble breathing
- you feel dizzy or lightheaded
- you have a slow or irregular heartbeat

AVANDAMET can have other serious side effects. Be sure to read the section below "What are possible side effects of AVANDAMET?".

What is AVANDAMET?

AVANDAMET contains two prescription medicines for treating diabetes, rosiglitazone maleate (AVANDIA) and metformin hydrochloride. AVANDAMET is used, with diet and exercise, to treat certain adults with type 2 ("adult-onset" or "non-insulin dependent") diabetes ("high blood sugar") who are:

- already taking rosiglitazone or rosiglitazone-containing products
- unable to control their blood sugar on other diabetes medicines, and after talking with their doctor have decided not to take pioglitazone (ACTOS) or pioglitazone-containing products (ACTOPLUS MET, ACTOPLUS MET XR, DUETACT)

Metformin works mainly by decreasing the production of sugar by your liver. Rosiglitazone helps your body respond better to its natural insulin and does not cause your body to make more insulin. These medicines work together to help control your blood sugar. AVANDAMET may be used alone or with other diabetes medicines.

AVANDAMET is not for people with type 1 diabetes mellitus or to treat a condition called diabetic ketoacidosis.

It is not known if AVANDAMET is safe and effective in children under 18 years old.

Who should not take AVANDAMET?

Do not take AVANDAMET if you:

- have kidney problems. Before you take AVANDAMET and while you take it, your doctor should test your blood to check for signs of kidney problems.
- have a condition known as metabolic acidosis, including diabetic ketoacidosis.
- 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 AVANDAMET and when to start it again.

Many people with heart failure should not start taking AVANDAMET. See “What should I tell my doctor before taking AVANDAMET?”.

What should I tell my doctor before taking AVANDAMET?

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

Before taking AVANDAMET, tell your doctor about all your medical conditions, including if you:

- **have heart problems or heart failure**
- **have kidney problems**
- **have type 1 (“juvenile”) diabetes or had diabetic ketoacidosis.** These conditions should be treated with insulin.
- **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).
- **develop a serious condition such as a heart attack, severe infection, or a stroke.**
- **are 80 years old or older.** People who are over 80 years old should not take AVANDAMET 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 AVANDAMET and during treatment as needed.
- **had liver problems while taking REZULIN[®]** (troglitazone), another medicine for diabetes.
- **are pregnant or plan to become pregnant.** AVANDAMET should not be used during pregnancy. It is not known if AVANDAMET can harm your unborn baby. You and your doctor should talk about the best way to control your diabetes during pregnancy. If you are a premenopausal woman (before the “change of

life”) who does not have regular monthly periods, AVANDAMET may increase your chances of becoming pregnant. Talk to your doctor about birth control choices while taking AVANDAMET. Tell your doctor right away if you become pregnant while taking AVANDAMET.

- **are breast-feeding or planning to breast-feed.** It is not known if AVANDAMET passes into breast milk. You should not use AVANDAMET while breast-feeding.

Tell your doctor about all the medicines you take including prescription and non-prescription medicines, vitamins or herbal supplements. AVANDAMET and certain other medicines can affect each other and may lead to serious side effects including high or low blood sugar, or heart problems. Your doctor may need to change your dose of AVANDAMET or your other medicines. Especially tell your doctor if you take:

- **insulin.**
- **any medicines for high blood pressure, high cholesterol or heart failure, or for prevention of heart disease or stroke.**

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

How should I take AVANDAMET?

- Take AVANDAMET exactly as prescribed. Your doctor may need to change your dose until your blood sugar is better controlled.
- AVANDAMET should be taken by mouth and with meals.
- AVANDAMET may be prescribed alone or with other diabetes medicines. This will depend on how well your blood sugar is controlled.
- It can take 2 weeks for AVANDAMET to start lowering your blood sugar. It may take 2 to 3 months to see the full effect on your blood sugar level.
- If you miss a dose of AVANDAMET, take it as soon as you remember, unless it is time to take your next dose. Take your next dose at the usual time. Do not take double doses to make up for a missed dose.
- If you take too much AVANDAMET, call your doctor or poison control center right away.
- Test your blood sugar regularly as your doctor tells you.
- Diet and exercise can help your body use its blood sugar better. It is important to stay on your recommended diet, lose extra weight, and get regular exercise while taking AVANDAMET.
- Your doctor should do blood tests to check your liver and kidneys before you start AVANDAMET and during treatment as needed. Your doctor should also do

regular blood sugar tests (for example, "A1C") to monitor your response to AVANDAMET.

There may be times when you will need to stop taking AVANDAMET for a short time. Tell your doctor if you:

- are sick with severe vomiting, diarrhea or fever, or if you drink a much lower amount of liquid than normal.
- are going to have dye injected into a vein for an X-ray, CAT scan, heart study or other type of scanning.
- plan to have surgery.

What should I avoid while taking AVANDAMET?

Do not drink a lot of alcohol while taking AVANDAMET. This means you should not "binge drink", and you should not drink a lot of alcohol on a regular basis. Drinking a lot of alcohol can increase the chance of getting lactic acidosis.

What are possible side effects of AVANDAMET?

AVANDAMET may cause serious side effects, including:

- **New or worse heart failure.** See "What is the most important information I should know about AVANDAMET?".
- **Heart attack.** See "What is the most important information I should know about AVANDAMET?".
- **Swelling (edema).** AVANDAMET can cause swelling due to fluid retention. See "What is the most important information I should know about AVANDAMET?".
- **Weight gain.** Rosiglitazone, one of the medicines in AVANDAMET, can cause weight gain that may be due to fluid retention or extra body fat. Metformin, the other medicine in AVANDAMET, can cause weight loss. There is little change in weight with AVANDAMET. Weight gain can be a serious problem for people with certain conditions including heart problems. See "What is the most important information I should know about AVANDAMET?".
- **Liver problems.** It is important for your liver to be working normally when you take AVANDAMET. Your doctor should do blood tests to check your liver before you start taking AVANDAMET 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** (a 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. Very rarely, some people have had vision changes due to swelling in the back of the eye while taking rosiglitazone, one of the medicines in AVANDAMET.
- **Fractures (broken bones)**, usually in the hand, upper arm or foot. Talk to your doctor for advice on how to keep your bones healthy.
- **Low red blood cell count (anemia).**
- **Low blood sugar (hypoglycemia).** Lightheadedness, dizziness, shakiness or hunger may mean 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 egg from an ovary in a woman) leading to pregnancy. Ovulation may happen in premenopausal women who do not have regular monthly periods. This can increase the chance of pregnancy. See “What should I tell my doctor before taking AVANDAMET?”.

Common side effects of AVANDAMET include:

- **Diarrhea, nausea, and upset stomach.** These side effects usually happen during the first few weeks of treatment. Taking AVANDAMET with food can help lessen these side effects. If you have unusual or unexpected stomach problems, talk with your doctor. Stomach problems that start up later during treatment with AVANDAMET may be a sign of something more serious and should be discussed with your doctor.
- **Cold-like symptoms**
- **Headache**
- **Joint aches**
- **Dizziness**

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 AVANDAMET?

- Store AVANDAMET at room temperature, 59° to 86°F (15° to 30°C).
- Keep AVANDAMET in the container it comes in. Keep the container closed tightly.
- Safely, throw away AVANDAMET that is out of date or no longer needed.

Keep AVANDAMET and all medicines out of the reach of children.

General information about AVANDAMET

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

This Medication Guide summarizes important information about AVANDAMET. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about AVANDAMET that is written for healthcare professionals. You can also find out more about AVANDAMET by calling 1-888-825-5249.

What are the ingredients in AVANDAMET?

Active Ingredients: Rosiglitazone maleate and metformin hydrochloride

Inactive Ingredients: Hypromellose 2910, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol 400, povidone 29-32, sodium starch glycolate, titanium dioxide, and 1 or more of the following: Red and yellow iron oxides.

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

- 2 mg/500 mg – pale pink, with “gsk” on one side and “2/500” on the other.
- 4 mg/500 mg – orange, with “gsk” on one side and “4/500” on the other
- 2 mg/1,000 mg – yellow, with “gsk” on one side and “2/1000” on the other
- 4 mg/1,000 mg – pink, with “gsk” on one side and “4/1000” on the other

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



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