MEDICATION GUIDE
DUETACT® (doo-et' -ăct)
(pioglitazone hydrochloride and glimepiride) tablets

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

What is the most important information I should know about DUETACT?
DUETACT can cause serious side effects, including **new or worse heart failure.**

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

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

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

DUETACT contains 2 prescription diabetes medicines called, pioglitazone hydrochloride (ACTOS) and glimepiride, a sulfonylurea.

Your doctor will decide if you should take DUETACT.

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.

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

Who should not take DUETACT?
Do not take DUETACT if you:
- are allergic to any of the ingredients in DUETACT. See the end of this Medication Guide for a complete list of ingredients in DUETACT.
- have a condition called diabetic ketoacidosis. Diabetic ketoacidosis should be treated with insulin.

People with severe heart failure should not start taking DUETACT. See "What is the most important information I should know about DUETACT?".

What should I tell my doctor before taking DUETACT?
Before starting DUETACT, 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.**
- **have type 1 ("juvenile") diabetes or had diabetic ketoacidosis.** These conditions should be treated with insulin.
- **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 DUETACT and during treatment as needed.
- **are pregnant or planning to become pregnant.** DUETACT should not be used during pregnancy. It is not known if DUETACT 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.** DUETACT may increase your chance of becoming pregnant. Talk to your doctor about birth control choices while taking DUETACT. Tell your doctor right away if you become pregnant while taking DUETACT.
- **are breastfeeding or plan to breastfeed.** It is not known if DUETACT passes into your milk and if it can harm your baby. You should not take DUETACT if you breastfeed your baby. Talk to your doctor about the best way to control your blood glucose levels while breastfeeding.
- **have G6PD deficiency** (an inherited condition where you don't produce enough of the enzyme (G6PD). Taking glimepiride, one of the medicines in DUETACT, with this condition may cause your red blood cells to be destroyed too quickly (hemolytic anemia).

Tell your doctor about all the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. DUETACT and some of your other medicines can affect each other. You may need to have your dose of DUETACT 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 DUETACT with other medicines.

How should I take DUETACT?
- Take DUETACT exactly as prescribed.
- Your doctor may need to change your dose of DUETACT to control your blood glucose. Do not change your dose unless told to do so by your doctor.

- DUETACT may be prescribed alone or with other diabetes medicines. This will depend on how well your blood sugar is controlled.
- Take DUETACT one time each day with the first meal.
- If you miss a dose of DUETACT, 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 DUETACT, 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 DUETACT.
- Your doctor should do blood tests before starting DUETACT 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 DUETACT.
- 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 DUETACT.
- It may take 2-3 months to see the full effect on your blood sugar level.

What are other possible side effects of DUETACT?
DUETACT can cause other serious side effects including:

- **The chance of death from serious heart or blood vessel problems may be higher** when using a sulfonylurea, an ingredient in DUETACT. The risk may be higher when compared to using diet alone or diet and insulin to control blood sugar levels.
- **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.
- **Weight gain.** Pioglitazone, one of the medicines in DUETACT, 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 heart problems. See "What is the most important information I should know about DUETACT?".
- **Liver problems**. It is important for your liver to be working normally when you take DUETACT. Your doctor should do blood tests to check your liver before you start taking DUETACT 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 DUETACT can affect the bones of children.
- **Low red blood cell count (anemia).**

- **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 DUETACT. This can increase the chance of pregnancy. See "What should I tell my doctor before taking DUETACT?".

In studies of pioglitazone (one of the medicines in DUETACT), 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.

Other common side effects of DUETACT are:
- cold-like symptoms (upper respiratory infection),
- headache,
- urinary tract infection,
- diarrhea,
- nausea,
- arm or leg pain.

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

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

General information about DUETACT
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use DUETACT for a condition for which it is not prescribed. Do not give DUETACT 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 DUETACT. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about DUETACT that is written for healthcare professionals. For more information, go to www.duetact.com or call 1-877-825-3327.

What are the ingredients in DUETACT?
Active Ingredients: pioglitazone hydrochloride and glimepiride
Inactive Ingredients: croscarmellose sodium, lactose monohydrate, magnesium stearate, hydroxypropyl cellulose, polysorbate 80, and microcrystalline cellulose.

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

- 30 mg/2 mg strength tablets—white to off-white, round tablet with “30/2” on one side and “4833G” on the other.
- 30 mg/4 mg strength tablets—white to off-white, round tablet with “30/4” on one side and “4833G” on the other.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Distributed by:
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Deerfield, IL 60015

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NDA 21-925 DUETACT (pioglitazone HCl plus glimepiride fixed-dose combination) tablets

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675 N. Field Road, Lake Forest, IL 60045

PROPOSED RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL:

The goal of this REMS is to communicate the risks of DUETACT.

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with each DUETACT prescription. The Medication Guide will be included at the end of the prescribing information as a perforated attachment. Each packaging configuration including bottles, sample cards and trays will contain a Medication Guide.

Because the Medication Guide is included as part of the packaging and provided by additional means for DUETACT, Takeda has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

B. Communication Plan

The REMS for DUETACT does not include a Communication Plan.

C. Elements To Assure Safe Use

This REMS for DUETACT does not include elements to assure safe use.

D. Implementation System

Because this REMS for DUETACT does not include elements to assure safe use, an implementation system is not required.

E. Timetable for Submission of Assessments

The Timetable for Assessments is as follows:
1st FDAAA assessment: March 2011 18 months from approval of REMS
2nd FDAAA assessment: September 2012 3 years from approval of REMS
3rd FDAAA assessment: September 2016 7 years from approval of REMS

Takeda will submit the assessments within 60 days of the close of the intervals as noted above.