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

This medicine is dispensed with a physician's prescription only

| **Trajenta Duo®**<br>**2.5 mg/500 mg** | **Trajenta Duo®**<br>**2.5 mg/850 mg** | **Trajenta Duo®**<br>**2.5 mg/1000 mg** |
| --- | --- | --- |
| **Film-coated tablets** | | |
| Each **Trajenta Duo 2.5 mg/500 mg** film-coated tablet contains:<br><br>2.5 mg linagliptin,<br>500 mg metformin hydrochloride | Each **Trajenta Duo 2.5 mg/850 mg** film-coated tablet contains:<br><br>2.5 mg linagliptin,<br>850 mg metformin hydrochloride | Each **Trajenta Duo 2.5 mg/1000 mg** film-coated tablet contains:<br><br>2.5 mg linagliptin,<br>1000 mg metformin hydrochloride |

Inactive ingredients and allergens in this medicine – see 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, contact your physician 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 illness is similar to yours.

**Important information:**

Metformin, one of the ingredients in Trajenta Duo, can cause a rare but serious side effect called lactic acidosis (a build-up of lactic acid in the blood) which may cause death. Lactic acidosis is a medical emergency and must be treated in hospital. Stop taking Trajenta Duo and contact your physician right away or go to the nearest hospital emergency room if you experience symptoms of lactic acidosis (see also section 4 - 'Side effects').

## 1. What is this medicine intended for?

Trajenta Duo is intended, in addition to diet and physical exercise, to improve control of blood sugar levels in adults with type 2 diabetes mellitus for whom combined treatment with two active ingredients, linagliptin and metformin hydrochloride, is appropriate.

**Limitations of use:** Trajenta Duo should not be used for the treatment of type 1 diabetes or for the treatment of diabetic ketoacidosis, because Trajenta Duo is not effective with these conditions.

Trajenta Duo has not been studied in patients who have previously had pancreatitis. It is unknown whether patients who have previously had pancreatitis are at an increased risk of developing pancreatitis during treatment with Trajenta Duo.

**Therapeutic groups:**

Linagliptin: DPP-4 (dipeptidyl peptidase-4) inhibitor.

Metformin: biguanides.

## 2. Before using this medicine

**Do not use this medicine if:**

- you are sensitive (allergic) to the active ingredients or to any of the other ingredients in this medicine (for a list of inactive ingredients, see section 6). Symptoms of a serious allergic reaction to Trajenta Duo may include:
    - skin rash, itching, flaking or peeling
    - raised red patches on your skin (hives)
    - swelling of your face, lips, tongue and throat that may cause difficulty in breathing or swallowing
    - difficulty with swallowing or breathing

  If you experience any of these symptoms, stop taking Trajenta Duo and contact your physician right away or go to the nearest hospital emergency room.
- you have severely reduced kidney function (your physician will establish the level of damage to your kidney function)
- you have type 1 diabetes (your body does not make insulin)
- you have a medical condition called metabolic acidosis or diabetic ketoacidosis (increased levels of ketones in your blood or urine).

**Special warnings about using this medicine:**

**Before taking Trajenta Duo, tell your physician about your medical condition, including if:**

- you have or have had inflammation of your pancreas (pancreatitis)
- you have kidney problems
- you have liver problems
- you have heart problems, including heart failure
- you are 65 years of age or older
- you drink alcohol very often or drink a lot of alcohol in a short time ("binge" drinking) (see the section 'Using this medicine and alcohol consumption')
- you are going to get an injection of dye or contrast agents for an x-ray procedure. You may need to stop taking Trajenta Duo for a short time. Consult your physician about when you should stop Trajenta Duo and when you should start taking it again.
- you have type 1 diabetes. Trajenta Duo is not intended for use in patients with type 1 diabetes.
- you have low vitamin $B_{12}$ blood levels. See the section 'Tests and follow-up'.
- you are pregnant or plan to become pregnant. See the section 'Pregnancy, breastfeeding, and fertility'.
- you are breastfeeding or plan to breastfeed. See the section 'Pregnancy, breastfeeding, and fertility'.
- you are a woman who has not gone through menopause (premenopausal) who does not have periods regularly or at all. See the section 'Pregnancy, breastfeeding, and fertility'.

For special additional warnings about the following serious side effects, see section 4, 'Side Effects'.

- lactic acidosis
- pancreatitis
- low blood sugar levels (hypoglycemia)
- allergic reactions (hypersensitivity)
- low vitamin $B_{12}$ (vitamin $B_{12}$ deficiency)
- severe and disabling joint pain
- skin reaction

- heart failure

**Children and adolescents**
Effectiveness and safety of this medicine have not been tested in children and adolescents under 18 years old.

**Tests and follow-up**
- During treatment, your blood sugar levels must be tested, as instructed by your physician.
- Taking metformin hydrochloride (one of the ingredients in Trajenta Duo) may cause a decrease in the levels of vitamin $B_{12}$ in your blood, so your physician may ask you to perform blood tests to check your vitamin $B_{12}$ levels.
- Your physician may refer you for blood tests to check your kidney function before and during your treatment with Trajenta Duo.

**Interactions with other medicines**
**If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your physician or pharmacist.**
Trajenta Duo may affect the way other medicines work, and other medicines may affect how Trajenta Duo works. Tell your physician, particularly if you are taking:
- insulin or other blood sugar lowering medicines, especially sulfonylurea or insulin medicines. Taking these other medicines with Trajenta Duo increases your risk of getting low blood sugar (hypoglycemia). See section 4, 'Side Effects'.
- diuretics, corticosteroids, phenothiazines, thyroid medicines, estrogen products, oral contraceptives, phenytoin, nicotinic acid, sympathomimetic medicines, calcium channel blocking medicines, and isoniazid. These medicines may cause high blood sugar (hyperglycemia) and lead to loss of control of blood sugar levels.
- rifampicin, an antibiotic for treating tuberculosis. This combination may reduce the effectiveness of Trajenta Duo.
- ranolazine, vandetanib, dolutegravir, and cimetidine: the combination may increase the levels of metformin (one of the ingredients in Trajenta Duo) in your blood and increase the risk of lactic acidosis.
- topiramate (a medicine used to treat epileptic seizures), zonisamide, acetazolamide, or dichlorphenamide: the combination may increase the risk of lactic acidosis (see also section 4, 'Side effects').

Know the medicines you take. Keep a list of them to show your physician and the pharmacist when you get a new medicine.

**Using this medicine and food**
Take this medicine with meals. Taking this medicine with food can lower your chance of having an upset stomach.

**Using this medicine and alcohol consumption**
Avoid consuming alcohol very often or drinking a lot of alcohol in a short period of time ("binge" drinking). Alcohol consumption increases your risk of experiencing side effects.

**Pregnancy, breastfeeding, and fertility**
If you are pregnant, plan to become pregnant, breastfeeding or plan to breastfeed, consult your physician before taking this medicine.
- It is not known if Trajenta Duo will harm your unborn baby. If you are pregnant, talk to your physician about the best way to control your blood sugar while you are pregnant.
- Trajenta Duo may pass into your breast milk and may harm your baby. Talk with your physician about the best way to feed your baby if you take Trajenta Duo.

- If you are a woman who has not gone through menopause (premenopausal) and who does not have periods regularly or at all, consult your physician before treatment with Trajenta Duo. Trajenta Duo can cause the release of an egg from an ovary (ovulation). This can increase your chance of getting pregnant. Tell your physician right away if you become pregnant while taking Trajenta Duo.

## 3. How to use this medicine?

Always use this medicine according to your physician's instructions. Check with your physician or pharmacist if you are not sure about your dose or about how to take this medicine. The dosage and treatment will be determined only by the physician.
The usually recommended dosage is one tablet twice a day with meals. If you have reduced kidney function, your physician may prescribe you a lower dosage.
Taking this medicine with a meal can help lower your chance of having an upset stomach.
**Do not exceed the recommended dose.**
Swallow the medicine with water. There is no information about crushing/splitting/chewing the tablets.

Your physician may instruct you to take Trajenta Duo along with other diabetes medicines. Low blood sugar may occur more often when Trajenta Duo is taken with certain other diabetes medicines.
See section 4, 'Side Effects'.

**If you have accidentally taken a higher dose:** If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a physician or go to a hospital emergency room and bring the medicine package with you.

**If you forget to take the medicine** at the scheduled time, take it with food as soon as you remember. If you do not remember until it is time to take the next dose, skip the forgotten dose and go back to your regular schedule. Do not take two doses of Trajenta Duo together.

Adhere to the treatment as recommended by your physician.

Even if your health improves, do not stop taking this medicine without consulting your physician.
**If you stop taking this medicine**, your blood sugar levels may increase.

**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 physician or pharmacist.**

## 4. Side effects

As with any medicine, using Trajenta Duo may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

**Trajenta Duo can cause serious side effects, including:**

- **Lactic acidosis:**
  **Metformin hydrochloride, one of the ingredients of Trajenta Duo, can cause a rare but serious side effect called lactic acidosis (a build-up of lactic acid in the blood) that can cause death. Lactic acidosis is a medical emergency and must be treated in a hospital.**

**Stop taking Trajenta Duo and contact your physician right away or go to the nearest hospital emergency room if you experience any of the following symptoms of lactic acidosis:**

- feel very weak and tired
- have unusual (not normal) muscle pain
- have trouble breathing
- have unexplained stomach or intestinal problems with nausea and vomiting, or diarrhea
- have unusual sleepiness or sleep longer than usual
- feel cold, especially in your arms and legs
- feel dizzy
- have a slow or irregular heartbeat

**You have a higher chance of getting lactic acidosis with Trajenta Duo if you:**

- have severe kidney problems
- have liver problems
- drink a lot of alcohol (very often or a lot in a short period of time ("binge drinking")) (see the section 'Using this medicine and alcohol consumption')
- 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 during activity or exercise and do not drink enough fluids.
- undergo certain x-ray tests with injectable dyes or contrast agents
- have surgery or other procedures for which you need to restrict the amount of food and liquid you eat and drink
- have congestive heart failure
- have a heart attack, severe infection, or stroke
- are 65 years of age or older

Tell your physician if you have any of the problems in the list above. Tell your physician that you are taking Trajenta Duo before you have surgery or x-ray tests. Your physician may decide to stop your Trajenta Duo for a while if you have surgery or certain x-ray tests.

- **Inflammation of the pancreas (pancreatitis) which may be severe and lead to death** (an uncommon side effect – affects 1–10 in 1000 users)
  Certain medical problems increase your risk of pancreatitis.
  **Before you start taking Trajenta Duo, tell your physician if you have ever had:**
  - inflammation of the pancreas (pancreatitis)
  - a history of alcoholism
  - stones in your gallbladder
  - high blood triglyceride levels

  Stop taking Trajenta Duo and contact your physician right away if you have pain in your stomach area (abdomen) that is severe and will not go away. The pain may be felt going from your abdomen to your back. The pain may happen with or without vomiting. These may be symptoms of pancreatitis.

- **Low blood sugar (hypoglycemia)** (a common side effect – affects 1–10 in 100 users)
  If you take Trajenta Duo with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take Trajenta Duo. Signs and symptoms of low blood sugar may include headache, fast heartbeat, irritability, dizziness, drowsiness, sweating, hunger, confusion, weakness, shaking or

feeling jittery. If you notice any of these signs, check your blood sugar levels, treat them if they are low, and contact your physician.

- **Allergic reactions (hypersensitivity)** (unknown frequency). Serious allergic reactions have happened in people who are taking Trajenta Duo. Symptoms may include:
  - swelling of your face, lips, tongue, throat, and other areas on your skin
  - raised, red areas on your skin (hives)
  - difficulty with swallowing or breathing
  - skin rash, itching, flaking or peeling

  If you get any of these symptoms, stop taking Trajenta Duo and contact your physician right away or go to the nearest hospital emergency room.

- **Low vitamin $B_{12}$ (vitamin $B_{12}$ deficiency)** (a common side effect – affects 1–10 in 100 users)
  Using metformin for long periods of time may cause a decrease in the amount of vitamin $B_{12}$ in your blood, especially if you have had low vitamin $B_{12}$ blood levels previously. Your physician may refer you for blood tests to check your vitamin $B_{12}$ levels.

- **Severe and disabling joint pain** (unknown frequency). Some patients who take linagliptin, one of the ingredients in Trajenta Duo, may develop joint pain that can be severe and disabling. Contact your physician if you have severe joint pain.

- **Skin reaction** (an uncommon side effect – affects 1–10 in 1000 users).
  Some patients who take medicines called DPP-4 inhibitors, one of the ingredients in Trajenta Duo, may develop a skin reaction called bullous pemphigoid that can require treatment in a hospital. Contact your physician immediately if you develop blisters or sores on the outer layer of your skin (erosion). Your physician may tell you to stop taking Trajenta Duo.

- **Heart failure** (unknown frequency). Heart failure means your heart does not pump blood well enough.
  **Before you start taking Trajenta Duo**, tell your physician if you have ever had heart failure or have problems with your kidneys. Contact your physician right away if you have any of the following symptoms:
  - increasing shortness of breath or trouble breathing, especially when you lie down
  - swelling or fluid retention, especially in the feet, ankles or legs
  - an unusually fast increase in weight
  - unusual tiredness

  These may be symptoms of heart failure.

**Common side effects (affect 1–10 in 100 users):**
- stuffy or runny nose and sore throat
- diarrhea
- cough
- urinary tract infection
- high level of blood triglycerides
- hyperlipidemia (excess fat in the blood)
- increase in weight
- constipation
- in laboratory tests: increase in uric acid, increase in enzymes that break down fat (lipase), increase in amylase
- nausea

- vomiting
- flatulence
- abdominal discomfort
- indigestion
- weakness
- headache

**Additional side effects:**
- decreased appetite
- itching
- muscle pain

**Side effects of unknown frequency (the frequency of these effects has not been established yet):**
- mouth ulcers
- inflammation of the mouth (stomatitis)
- breakdown of muscle (rhabdomyolysis)
- rash
- liver injury

**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 physician.**

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or 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 your physician.
- 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 below 25˚C.

## 6. Additional information

- In addition to the active ingredients, this medicine also contains the following inactive ingredients:
  copovidone, maize starch, arginine, magnesium stearate, silica colloidal anhydrous, hypromellose, titanium dioxide, talc, propylene glycol.
  Trajenta Duo 2.5 mg/500 mg and Trajenta Duo 2.5 mg/850 mg also contain: iron oxide, yellow.
  Trajenta Duo 2.5 mg/850 mg and Trajenta Duo 2.5 mg/1000 mg also contain: iron oxide, red.

- What the medicine looks like and contents of the pack:
  Trajenta Duo 2.5 mg/500 mg is an oval, light yellow, biconvex tablet debossed with D2/500 on one side and the Boehringer Ingelheim symbol on the other side.
  Trajenta Duo 2.5 mg/850 mg is an oval, light orange, biconvex tablet debossed with D2/850 on one side and the Boehringer Ingelheim symbol on the other side.
  Trajenta Duo 2.5 mg/1000 mg is an oval, light pink, biconvex tablet debossed with D2/1000 on one side and the Boehringer Ingelheim symbol on the other side.
  Packs contain blister trays of either 7 or 10 tablets. Each pack contains either 14 or 60 film-coated tablets.
  Not all pack sizes may be marketed.

- **Registration holder and importer's name and address:**
  Boehringer Ingelheim Israel Ltd., 89 Medinat HaYehudim St., P.O. Box 4124, Herzliya Pituach 4676672.

**This leaflet was revised in September 2023 according to MOH guidelines.**

**Registration number of the medicine in the Ministry of Health's National Drug Registry:**
Trajenta Duo 2.5 mg/500 mg: 150-17-33739
Trajenta Duo 2.5 mg/850 mg: 150-18-33740
Trajenta Duo 2.5 mg/1000 mg: 150-19-33741