Patient leaflet in accordance with the pharmacists' regulations (preparations) - 1986

This medicine is to be supplied upon physician's prescription only

Trajenta duo®
2.5/500 Tablets
2.5/850 Tablets
2.5/1000 Tablets

Each tablet of **Trajenta duo 2.5/500** contains: 2.5 mg linagliptin 500 mg metformin hydrochloride	Each tablet of **Trajenta duo 2.5/850** contains: 2.5 mg linagliptin 850 mg metformin hydrochloride	Each tablet of **Trajenta duo 2.5/1000** contains: 2.5 mg linagliptin 1000 mg metformin hydrochloride

For the list of inactive ingredients and allergens see section 6.

- Read the entire leaflet carefully before you start using this medicine.
- This leaflet contains summary information about this medicine. If you have any further questions, refer to the physician or the pharmacist.
- This medicine has been prescribed for treating your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.
- Safety and efficacy of the medicine have not been tested in children and adolescents below the age of 18.

Introduction:

- Metformin, one of the ingredients of TRAJENTA DUO, may cause a rare but a serious side effect called lactic acidosis, which is manifested by accumulation of lactic acid in the blood and may be fatal. Lactic acidosis is a medical emergency requiring treatment at the hospital (See also section 2 under "Special warnings related to the use of the medicine" and section 4 – "Side effects").
- The physician may recommend treatment with TRAJENTA DUO to control blood sugar levels as monotherapy or in combination with additional agents. If you are taking Trajenta Duo with additional medicines such as sulfonylurea or insulin, the risk of low blood sugar levels (hypoglycemia) is increased. Adjustment of the dosage of sulfonylurea or insulin may be required. See section 2 – "If you are taking other medicines" and section 4 – "Side effects."
- See section1 for limitations of use - "What is this medicine intended for" and section 2 – "Before using this medicine".

1. What is this medicine intended for?

Trajenta Duo is intended, in addition to diet and physical exercise, for control of blood sugar levels in adults with type 2 diabetes 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, since TRAJENTA DUO is not effective in these conditions.
TRAJENTA DUO has not been studied in patients who have previously suffered from pancreatitis. It is not known whether patients who have previously suffered from pancreatitis are at increased risk of developing pancreatitis during the treatment with TRAJENTA DUO.

Therapeutic group:
Linagliptin: DPP-4 (Dipeptidyl Peptidase-4) enzyme inhibitor. Metformin: Biguanide class.

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 that this medicine contains (please refer to section 6 for the list of inactive ingredients). Signs of severe allergy to TRAJENTA DUO are rash, itch, peeling of the skin, urticaria (raised red skin areas), swelling of the face, lips, tongue, throat, which may cause difficulties in breathing or swallowing.
- You have type 1 diabetes (your body does not produce insulin), or you have either acute or chronic metabolic acidosis, including diabetic ketoacidosis (increased levels of ketones in blood and/or urine). TRAJENTA DUO is not suitable for treatment of these conditions.
- You have kidney problems.

Special warnings regarding the use of the medicine:

1) **Lactic acidosis** (See details in section 4 "Side effects"). Metformin, one of the ingredients of TRAJENTA DUO, may cause a rare but a serious side effect called lactic acidosis, which is manifested by accumulation of lactic acid in the blood and may be fatal. Lactic acidosis is a medical emergency requiring treatment at the hospital. If you experience the signs of lactic acidosis, stop the treatment with TRAJENTA DUO and seek physician's assistance immediately. (See also section 4 – "Side effects").

You are at increased risk of developing lactic acidosis if you:
- Suffer from kidney or liver problems or from heart failure (requiring medication therapy).
- Drink alcohol frequently or drink a lot of alcohol in a short period of time (See section: Using the drug and alcohol consumption).
- Suffer from dehydration (excessive loss of body fluids). This may occur if you do not drink enough fluids and/or due to conditions of fever, vomiting or diarrhea. Dehydration may also occur in case of excessive sweating during regular activity or physical activity.
- Undergo certain X-ray imaging with X-ray dyes or contrast agents injected into the body.
- Undergo surgery.
- Suffer from a heart attack, severe infection or stroke.
- Are 80 years old or older and you have not performed renal function tests.

Consult a physician before receiving treatment with TRAJENTA DUO if any of the above conditions is applicable to you.

Immediately stop taking TRAJENTA DUO and consult a physician if any of the following symptoms of lactic acidosis appears: sensation of weakness and extreme fatigue, abnormal muscle pain, difficulties breathing, unusual somnolence, or abnormally prolonged sleep, sudden abdominal pain or sudden intestinal disorders accompanied by nausea and vomiting or diarrhea, sensation of cold, especially in the arms and legs, dizziness, slowing of or a change in the heart rate, decrease in blood pressure.

2) **Pancreatitis** (See details in section 4 “Side effects”) may occur in patients treated with TRAJENTA DUO, it may be severe and even life threatening. Certain medical problems may increase the risk of pancreatitis.

Consult a physician before receiving treatment with TRAJENTA DUO if you currently suffer or have previously suffered from any of the following conditions:

- Pancreatitis.
- Gallbladder stones.
- History of alcoholism.
- High blood triglyceride levels.

Stop taking TRAJENTA DUO and consult a physician immediately if persistent severe abdominal pain appears. You may experience pain which radiates from your abdomen to your back. The pain may appear with or without vomiting. These may be symptoms of pancreatitis.

Before using TRAJENTA DUO, tell your physician if:

- You have or have had impairment function of the liver, kidneys or heart (including heart failure), or any other medical condition.
- You suffer or have previously suffered from pancreatitis, gallbladder stones, alcoholism, high blood triglyceride levels.
- If you are taking additional blood sugar lowering medicines: especially medicines called “sulfonylurea” (such as glimepiride) or insulin. Combination of these medicines with TRAJENTA DUO increases the risk of low blood sugar level (hypoglycemia). The physician may want to adjust the dosage of sulfonylurea or insulin. See section 4 “Side effects”.
- You drink alcohol frequently or drink a lot of alcohol in a short period of time (binge drinking).
- You are 80 years old or older – Do not take TRAJENTA DUO before undergoing kidney function tests and receiving normal results.

You may be required to stop using TRAJENTA DUO for a while. Consult the physician regarding the date of discontinuing the treatment with TRAJENTA DUO and the date of resuming the treatment if you:

- You are going to have an injection of a dye or a contrast agent for an X-ray imaging.
- You are going to undergo surgery.
- You suffer from dehydration.

The physician will decide regarding the date of discontinuation of TRAJENTA DUO treatment and the date of resuming this treatment.

If you are taking or have recently taken other medicines including non-prescription medicines and food supplements, tell the physician or the pharmacist. Especially inform the physician or the pharmacist if you are taking:

- Other blood sugar lowering medicines: especially medicines of the sulfonylurea class or insulin, combination of these medicines with TRAJENTA DUO increases the risk of low blood sugar level (hypoglycemia). Please see section "Before using TRAJENTA DUO, tell your physician if” and section 4 – "Side effects".
- Rifampicin (antibiotic for the treatment of tuberculosis): the combination may reduce the efficacy of TRAJENTA DUO.
- Medicines such as Amiloride, Digoxin, Morphine, Procainamide, Quinidine, Quinine, Ranitidine, Triamterene, Trimethoprim, and Vancomycin: the combination may increase the blood levels of metformin (one of the ingredients of TRAJENTA DUO).
- Topiramate (a medicine for the treatment of epileptic seizures): the combination may increase the risk of lactic acidosis (See also section 2 under “Special warnings regarding the use of the medicine”).

Using the medicine and food
Take the medicine with meals. Intake with meals may reduce gastrointestinal disorders.

Using the medicine and alcohol consumption
Avoid consumption of high quantities of alcohol during treatment with TRAJENTA DUO. Alcohol consumption increases the risk of lactic acidosis (See also section 2 under “Special warnings regarding the use of the medicine”).

Pregnancy and breastfeeding
Consult a physician prior to beginning treatment, if you are pregnant, plan to become pregnant or breastfeeding.

- There is no information about the effect of the medicine on the fetus. If you are pregnant, consult your physician regarding the best way to control your sugar levels during pregnancy.
- There is no information about passage of the medicine to the breast milk. Consult your physician regarding the best way to feed your baby while using this medicine.

3. How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure.
The dosage and treatment will be determined only by the physician.

The recommended dose is usually: one tablet twice a day with food. **Do not exceed the recommended dose.** Swallow the medicine with water.
There is no information about crushing/splitting/chewing.

If you are taking TRAJENTA DUO with additional medicines such as sulfonylurea or insulin, the risk of low blood sugar levels (hypoglycemia) is increased. Adjustment of the sulfonylurea or insulin dosage may be required.

When your body is exposed to stress, such as fever, trauma (for example, a road accident), infection or surgery, the dosage of the blood sugar lowering medicine required for you may change. Immediately consult the physician if any of these conditions is applicable to you and follow the physician’s instructions.

Tests and follow-up

- During the treatment period, blood sugar levels should be tested according to the physician’s instructions.
- Continue with your diet program and your physical activity program, while taking TRAJENTA DUO.
- Your diabetes will be monitored by your physician, by performing routine blood tests, including sugar blood level and hemoglobin A1C tests.
- The physician will perform blood tests to examine your renal function prior to and during the treatment with TRAJENTA DUO.
- Consult your physician about how to prevent, identify and treat low blood sugar levels (hypoglycemia), high blood sugar levels (hyperglycemia) and diabetes complications.

There may be situations in which you will be required to stop taking the medicine for a while. Consult the physician in the following situations:

- If you suffer from dehydration (excessive loss of body fluids). This may occur if you do not drink enough fluids and/or due to conditions of fever, vomiting or diarrhea. Dehydration may also occur in case of excessive sweating during regular activity or physical activity.

- If you are going to undergo surgery.
- If you are going to have an injection of a dye or contrast agents for X-ray imaging.

If you accidently have taken a higher dosage: If you have taken an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or to a hospital emergency room and bring the medicine package with you.

If you forgot to take the medicine at the scheduled time, take the next dose immediately once you have remembered. If it is time to take the next dose, skip the forgotten dose and return to the regular intake schedule. Do not take two doses together.
Persist with the treatment as recommended by the physician.

Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the physician or the pharmacist. **If you stop taking the medicine**, your blood sugar levels may increase**.**

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any other questions regarding the use of the medicine, consult the physician or the pharmacist.

4. Adverse events

As with any medicine, use of TRAJENTA DUO may cause adverse events in some of the users. Do not be alarmed by reading the list of adverse events. You may not experience any of them.

Allergic reactions (hypersensitivity):
Severe allergic reactions may occur after taking the first dose or up to 3 months after beginning treatment with TRAJENTA DUO. The symptoms may include:
- Swelling of the face, lips, throat and other skin areas.
- Difficulty breathing or swallowing.
- Urticaria (raised red skin areas).
- Rash, itch, peeling of the skin.

If signs of a severe allergic reaction develop, stop the treatment and contact a physician immediately.

Pancreatitis:
Pancreatitis may occur in patients treated with TRAJENTA DUO, it may be severe and even life threatening. (See also section 2 “Special warnings regarding the use of the medicine”).
Stop using the medicine and contact a physician immediately if persistent severe abdominal pain develops. The pain may radiate to the back and may appear with or without vomiting. These may be symptoms of pancreatitis.

Stop using the medicine and contact a physician immediately if you develop one or more symptoms of **lactic acidosis** (See also section 2 “Special warnings regarding the use of the medicine”): feeling of weakness and extreme fatigue, unusual muscle pain, difficulties breathing, abnormal drowsiness, or sleeping for period longer than usual, sudden abdominal pain or sudden intestinal problems accompanied by nausea and vomiting or diarrhea, sensation of cold, especially in the arms and legs, dizziness, heart rate slowing or change, decrease of blood pressure.

Low blood sugar levels (Hypoglycemia): Signs and symptoms of low blood sugar level may include the following: headache, hunger, rapid heartbeats, sweating, irritability, drowsiness, weakness, dizziness, sensation of stress, confusion. If you are taking TRAJENTA DUO with other medicines which may cause low levels of blood sugar levels, such as sulfonylureas or insulin, your risk of low blood sugar levels increases. If you notice one or more of these signs, check your blood sugar levels, treat them if they are low and contact a physician.

The most common side effects occurring during treatment with TRAJENTA DUO are: congested or runny nose, sore throat and diarrhea. If these side effects do not resolve, or are causing discomfort or getting worse, consult the physician.

Additional side effects are: cough, decreased appetite, nausea, vomiting, itching.

Spontaneous post-marketing reports included reports on:

- Rash.
- Acute pancreatitis which has even led to death.

If you suffer from an adverse event not mentioned in the leaflet, or if you experience a change in your general health condition, you should consult the physician immediately.

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Store below 25˚C.

6. Additional information

- In addition to the active ingredients the medicine also contains the following inactive ingredients:
  Copovidone, maize starch, arginine, hypromellose 2910, magnesium stearate, titanium dioxide, colloidal silicon anhydrous, talc, propylene glycol.
  TRAJENTA DUO 2.5/500 and TRAJENTA DUO 2.5/850 also contains: yellow iron oxide. TRAJENTA DUO 2.5/850 and TRAJENTA DUO 2.5/1000 also contains: red iron oxide.
- What does the medicine look like and what is the content of the package:
  TRAJENTA DUO 2.5/500 is a light yellow tablet and its shape is elliptical convex. D2/500 is imprinted on one side and the logo of Boehringer Ingelheim is imprinted on the other side.

  TRAJENTA DUO 2.5/850 is a light orange tablet and its shape is elliptical convex. D2/850 is imprinted on one side and the logo of Boehringer Ingelheim is imprinted on the other side.

  TRAJENTA DUO 2.5/1000 is a light pink tablet and its shape is elliptical convex. D2/1000 is imprinted on one side and the logo of Boehringer Ingelheim is imprinted on the other side.

  The packages are supplied in blisters of 7 or 10 tablets. Each package contains 14 or 60

coated tablets.
Not all packs may be marketed.

- **Registration holder and his address:**
  Boehringer Ingelheim Israel, 89 Medinat Ha-Yehudim St., P.O.B. 4124, Hertzeliya Pituach 4676672, Israel.

- **Manufacturer:** Boehringer Ingelheim Ellas A.E., Koropi, Greece.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
TRAJENTA DUO 2.5/500: 150-17-33739
TRAJENTA DUO 2.5/850: 150-18-33740
TRAJENTA DUO 2.5/1000: 150-19-33741

This leaflet was checked and approved by the Ministry of Health in August 2014.