PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Tabrecta™ 150 mg
Tabrecta™ 200 mg

Film-coated Tablets

Active ingredient:
Capmatinib as dihydrochloride monohydrate.
Each tablet contains 150 mg or 200 mg of capmatinib.

Inactive ingredients: see section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Tabrecta is intended for the treatment of adults suffering from a type of lung cancer called non-small cell lung cancer (NSCLC) that is metastatic (has spread to other parts of the body), with a mutation that leads to skipping of exon 14 in the mesenchymal epithelial transition (MET) gene, detected by an approved test.

Therapeutic group: Anticancer medicines, a protein kinase inhibitor.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient or to any of the additional ingredients contained in the medicine (see section 6).

Special warnings regarding use of the medicine
Before treatment with Tabrecta, tell the doctor about your medical condition, including if:
- You suffer or have suffered from lung problems or breathing problems other than lung cancer.
- You suffer or have suffered from liver problems.
- You are pregnant, planning to become pregnant or are breastfeeding (see also the section "Pregnancy, breastfeeding and fertility" below).
- You are a man with a partner who can become pregnant (see also the section "Pregnancy, breastfeeding and fertility" below).

Lung or breathing problems. Tabrecta could cause inflammation of the lungs, which could cause death. Inform the doctor immediately if you develop any new or worsening symptoms (see section 4).

Liver problems. Tabrecta could cause abnormal results in liver function blood tests. The doctor will perform blood tests in order to check liver function before starting treatment as well as during treatment with Tabrecta. Inform the doctor immediately if you develop any signs or symptoms of liver problems (see section 4).

Risk of sensitivity to sunlight (photosensitivity). Your skin may be sensitive to the sun (photosensitivity) during treatment with Tabrecta. Use a sunscreen or wear clothes that cover your skin during treatment with Tabrecta in order to limit direct sunlight exposure.

Children and adolescents
Tabrecta is not intended for use in children and adolescents. There is no information about the safety and efficacy of the use of this product in children and adolescents.

Tests and follow-up
The doctor will perform blood tests in order to check liver function before starting treatment and during treatment with Tabrecta.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
Tabrecta and other medicines taken concomitantly could affect each other and cause side effects. In particular if you are taking:

Effect of other medicines on Tabrecta
Strong CYP3A inhibitors
Giving Tabrecta in combination with a strong CYP3A inhibitor (e.g., itraconazole, ketoconazole, clarithromycin, nefazodone, lopinavir/ritonavir) increases the blood concentration of capmatinib, which could increase the incidence and severity of side effects of Tabrecta. In such a case, the doctor will need to closely monitor for side effects.

Strong and moderate CYP3A inducers
Giving Tabrecta in combination with a strong CYP3A inducer [e.g., rifampicin, phenytoin, carbamazepine, St. John's wort (also known as *Hypericum perforatum*)] decreases the blood concentration of capmatinib. Similarly, giving Tabrecta in combination with a moderate CYP3A inducer (e.g., efavirenz, phenobarbital) may also decrease the concentration of capmatinib. A reduced blood concentration of capmatinib could reduce the anticancer activity of Tabrecta. Avoid the combined use of Tabrecta with strong and moderate CYP3A inducers.

Effect of Tabrecta on other medicines
CYP1A2 substrates
Administration in combination with Tabrecta increases the blood concentration of CYP1A2 substrates (e.g., tizanidine, theophyllin), which could increase the side effects of these substrates. If administration of Tabrecta in combination with CYP1A2 substrates cannot be avoided, the doctor will instruct you to reduce the dose of the CYP1A2 substrate.

P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP) substrates
Administration in combination with Tabrecta increases the blood concentration of P-gp substrates (e.g., digoxin, fexofenadine) and of BCRP substrates (e.g., rosuvastatin, sulfasalazine), which could increase the side effects of these substrates. If administration of Tabrecta in combination with P-gp or BCRP substrates cannot be avoided, the doctor will instruct you to reduce the dose of the P-gp or BCRP substrate.

MATE1 and MATE2K substrates
Administration in combination with Tabrecta may increase the blood concentration of MATE1 and MATE2K substrates (e.g., cimetidine, pyrimethamine), which could increase the side effects of these substrates. If the administration of Tabrecta in combination with MATE1 or MATE2K substrates cannot be avoided, the doctor will instruct you to reduce the dose of the MATE1 or MATE2K substrate.

Use of the medicine and food
The medicine may be taken with or without food. Adequate fluid intake is recommended.

Pregnancy, breastfeeding and fertility
Do not use the medicine without consulting a doctor before beginning treatment if you are pregnant, planning to become pregnant or are breastfeeding.

Pregnancy
Tabrecta can harm your unborn baby.
Women who are able to become pregnant:
- The doctor should do a pregnancy test before starting treatment with Tabrecta.
- You should use an effective method of birth control during treatment and for one week after your last dose of Tabrecta. Talk to your doctor about the types of birth control that may be suitable for you during this period of time.
- Inform the doctor immediately if you become pregnant or if you think you may be pregnant during treatment with Tabrecta.

Men who have partners who can become pregnant:
- You should use an effective method of birth control during treatment and for one week after your last dose of Tabrecta.

Breastfeeding
Do not breastfeed during treatment and for one week after your last dose of Tabrecta.
If you are breastfeeding or planning to breastfeed, inform the doctor. It is not known whether Tabrecta passes into breast milk.

Driving and operating machinery
Tabrecta is not expected to affect your ability to drive or operate machines.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally 400 mg of Tabrecta twice per day, with or without food. Adequate fluid intake is recommended.

Do not exceed the recommended dose.

Swallow Tabrecta tablets whole. Do not break, chew or crush Tabrecta tablets.
The doctor may change your dose, temporarily or permanently stop treatment with Tabrecta if you suffer from certain side effects.
Do not change the dose or stop taking Tabrecta unless instructed by the doctor.

If you forgot to take this medicine at the designated time or you vomited your dose of Tabrecta, **do not** take a double dose. Take the next dose at the usual time and consult the doctor.

Adhere to the treatment regimen as recommended by the doctor.

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 further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Tabrecta may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Tabrecta may cause serious side effects, including:
- **Lung or breathing problems** (interstitial lung disease, inflammation of the lungs). Tabrecta could cause inflammation of the lungs, which could cause death. Inform the doctor immediately if you develop any new or worsening symptoms, including:
  - Cough
  - Fever
  - Difficulty breathing or shortness of breath
- **Liver problems.** Tabrecta could cause abnormal results for liver function blood tests (such as a high level of alanine aminotransferase and/or aspartate aminotransferase and/or bilirubin). The doctor will perform blood tests in order to check liver function before starting treatment and during treatment with Tabrecta. Inform the doctor immediately if you develop any signs and symptoms of liver problems, including:
  - Your skin or the whites of your eyes turn yellow (jaundice)
  - Loss of appetite for several days or for a longer period of time
  - Dark or tea-colored urine
  - Nausea and vomiting
  - Light-colored stools
  - Pain or tenderness on the right side of your abdominal area
  - Confusion
  - Tiredness
  - Weakness
  - Swelling in the abdominal area
- **Risk of sensitivity to sunlight (photosensitivity).** See section 2 "Special warnings regarding use of the medicine".

Very common side effects (may affect more than one in 10 users):
- Swelling of the hands or feet
- Vomiting
- Nausea
- Muscle or bone pain
- Loss of appetite
- Tiredness and weakness
- Trouble breathing
- Pneumonia
- Elevated body temperature
- Weight loss
- Constipation
- Diarrhea
- Cough
- Skin rash
- Dizziness
- Changes in certain blood tests:

Chemistry
Low albumin level
High creatinine level
High alkaline phosphatase level
High amylase level
High gamma-glutamyl transferase level
High lipase level
Low sodium level
Low phosphorus level
High potassium level
Low glucose level
Hematology
Low lymphocyte level
Low hemoglobin level
Low leukocyte level

Additional side effects
Itching (allergic and widespread), cellulitis, acute kidney injury (including kidney failure), hives and acute inflammation of the pancreas.

These are not all of the possible side effects of Tabrecta. Refer to the doctor for medical advice about side effects. Your doctor may change your dose, temporarily stop, or permanently stop treatment with Tabrecta, if you develop certain side effects.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package/blister pack. The expiry date refers to the last day of that month.
- **Storage conditions**
  Do not store above 25°C. Store in the original package in order to protect from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Tablet core:
Microcrystalline cellulose, mannitol, crospovidone (type A), povidone (K30), magnesium stearate, colloidal silicon dioxide and sodium lauryl sulfate.
Tablet coating (150 mg):
Hypromellose, titanium dioxide (E171), talc, polyethylene glycol (PEG) 4000, ferric oxide yellow, ferric oxide red, ferric oxide black.
Tablet coating (200 mg):
Hypromellose, titanium dioxide (E171), polyethylene glycol (PEG) 4000, talc, ferric oxide yellow.

What the medicine looks like and the contents of the package:
Tabrecta 150 mg: A light orange-brown-colored, film-coated, elliptical tablet, curved with beveled edges, debossed with DU on one side and NVR on the other side. Each package contains 120 film-coated tablets.
Tabrecta 200 mg: A yellow-colored, film-coated, elliptical tablet, curved with beveled edges, debossed with LO on one side and NVR on the other side. Each package contains 120 film-coated tablets.

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B. 7126, Tel Aviv.

Revised in September 2022 according to MOH guidelines.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
169-19-36653
169-20-36654