Patient package insert in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Inlyta® 1 mg
Inlyta® 5 mg
Film-coated tablets

Each tablet contains: axitinib 1 mg or 5 mg.

For a list of inactive ingredients and allergens in the preparation: See section 2 under "Important information about some of this medicine's ingredients" and section 6 "Further information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, consult your doctor 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.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Inlyta® is intended for the treatment of advanced renal cell carcinoma (RCC), after the failure of other medicinal therapy.

Therapeutic group: a medicine from the tyrosine kinase inhibitor group.

2. BEFORE USING THIS 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, listed in section 6.

Special warnings regarding use of the medicine
Before treatment with Inlyta®, tell your doctor if:

- You have high blood pressure. High blood pressure can develop during treatment with Inlyta®; blood pressure must be monitored before and during treatment with Inlyta®.
- You have a history of blood clots in your arteries or veins (types of blood vessels), including stroke, heart attack, or changes in vision.
- You have a history of heart failure.
- You are suffering from bleeding (including in the digestive system). Inform the doctor if bleeding occurs.
- You plan to have surgery or have had surgery recently. Stop taking Inlyta® at least 2 days before the planned surgery, and continue using it again only after consulting with the attending doctor.
- You have digestive system disorders. Diarrhea, nausea, vomiting, and constipation may occur during treatment with Inlyta®. Refer immediately for medical attention if you experience continuous or severe abdominal pain because Inlyta® can cause a perforation in the digestive system or a fistula.
- You have thyroid gland problems. The function of the thyroid gland must be monitored before and during treatment with Inlyta®.

- You have worsening neurological function during treatment, including headache, seizures, tiredness, confusion, blindness, vision disturbances or other neurological disorders. These could be signs of a neurological disorder called reversible posterior leukoencephalopathy syndrome (RPLS).
- You have liver problems.
- You have wounds that do not heal.
- You are pregnant or plan to become pregnant.
- You are breastfeeding or plan to breastfeed.
- You have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.

Children and adolescents
It is not known if Inlyta® is effective and safe for use in children.

Tests and follow-up
Before starting to use and while using the medicine, the doctor will refer you for tests: urine, blood pressure, thyroid function, and liver enzymes.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- medicines for asthma, tuberculosis, seizures, bacterial infection, fungal infection, depression, or AIDS.
- dexamethasone (an anti-inflammatory steroid), phenytoin, carbamazepine, phenobarbital (used to treat, among others, epilepsy); rifampin, rifabutin, rifapentine (used to treat bacterial infections); St. John's wort (herbal remedy, *Hypericum*). Avoid treatment with these medicines during treatment with Inlyta® because these medicines reduce the level of the medicine in the blood.
- bosentan (used to treat pulmonary hypertension); efavirenz, etravirine (used to treat AIDS); modafinil (used to increase alertness in patients who tend to be sleepy during the day); and nafcillin (used to treat bacterial infections). It is advisable to avoid treatment with these medicines while you are taking Inlyta®, because they may reduce the level of Inlyta® in the blood.
- ketoconazole (used to treat fungal infections) increases the concentration of Inlyta® in the blood, therefore, co-administration of these two medicines should be avoided.

Using this medicine and food
Do not eat grapefruit or drink grapefruit juice together with Inlyta®. Grapefruit may increase the level of medicine in the blood.
The medicine can be taken with or without food.

Pregnancy, breastfeeding and fertility
Inform the doctor if you are pregnant or plan to become pregnant. Taking Inlyta® during pregnancy can cause birth defects or miscarriages. Do not become pregnant during treatment with Inlyta®.
Females who are able to become pregnant should have a pregnancy test before starting treatment with Inlyta®.
Use effective birth control during treatment and for one week after the last dose of Inlyta®. Consult your doctor about birth control methods that you can use to prevent pregnancy during this time.
Males with female partners who are able to become pregnant should use effective birth control during treatment and for one week after the last dose of Inlyta®. If your female partner becomes pregnant during your treatment with Inlyta®, tell your doctor right away.

Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if the medicine passes into breast milk. Do not breastfeed during treatment and for two weeks after the last dose of Inlyta®.

Inlyta® may cause fertility problems in females and males, which may affect your ability to have children. Ask your doctor for advice if you have any concerns.

Driving and using machines
If you feel dizzy and/or tired during treatment with Inlyta®, take special care when driving or using machines.

Important information about some of this medicine's ingredients
This preparation contains lactose. If you have been told by your doctor that you have an intolerance to certain sugars, contact your doctor before taking this medicine.

Inlyta® contains sodium. This medicine contains less than 1 mmol (23 mg) sodium per film-coated tablet. This means that it is essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this preparation according to your 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 your doctor only.
The standard dosage is usually: 5 mg tablet every 12 hours with or without food. Based on your response to the medicine or the side effects your doctor may adjust the dosage.
Method of administration: Swallow the medicine whole with a glass of water.

Do not exceed the recommended dose.

If you have accidentally taken a higher dosage you may experience dizziness, high blood pressure, seizures arising from increased blood pressure, or coughing up blood which may be fatal. Refer to the doctor immediately.

If you have taken an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine at the scheduled time, or you vomited after taking it, do not take a double dose. Take the next dose at the usual time and consult your doctor.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

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

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Inlyta® may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Inlyta® can cause serious side effects, including:

- **High blood pressure. High blood pressure is common with Inlyta®, and may sometimes be severe.** Your doctor will monitor your blood pressure regularly during treatment. If there is a rise in your blood pressure during the treatment, your doctor may prescribe medicine to lower the blood pressure, lower the dose of Inlyta®, or stop the treatment.
- **Blood clots in your veins or arteries.** Inlyta® can cause blood clots which may be serious and sometimes life-threatening. **Get medical help urgently and call your doctor if you get any of the following symptoms:** chest pain or pressure; pain in your arms, back, neck or jaw; shortness of breath; numbness or weakness on one side of your body; trouble talking; headache; vision changes.
- **Bleeding.** Inlyta® can cause bleeding which may be serious and sometimes life-threatening. **Call your doctor right away or get medical help if you get any of the following symptoms:**
  - ❖ unexpected bleeding or bleeding that lasts a long time, such as unusual bleeding from the gums, menstrual bleeding or vaginal bleeding that is heavier than normal, bleeding that is severe or is uncontrolled, pink or brown colored urine, red or black stools (looks like tar), bruises that happen without a known cause or get larger, coughing up blood or blood clots, vomiting blood or vomit that looks like coffee grounds.
  - ❖ unexpected pain, swelling, or joint pain.
  - ❖ headache, feeling dizzy or weak.
- **Heart failure.** Your doctor will regularly monitor you for signs and symptoms of heart failure during treatment with Inlyta®. Heart failure may be serious and can sometimes be life-threatening. Tell your doctor if you have any of the following symptoms during the treatment with Inlyta®: tiredness; swelling around the abdomen, legs, or ankles; shortness of breath; protruding neck vein.
- **Tear in the stomach or intestinal wall.** A tear in your stomach or intestinal wall can be serious and can sometimes be life-threatening. **Get medical help urgently if you get any of the following symptoms:** severe abdominal pain or abdominal pain that does not go away, vomit blood, red or black stools.
- **Thyroid gland problems.** Your doctor will perform blood tests to check your thyroid gland function before and during your treatment with Inlyta®. Tell your doctor if you have any of the following symptoms during your treatment with Inlyta®: tiredness that worsens or that does not go away; feeling hot or cold; your voice deepens; weight gain or weight loss; hair loss; muscle cramps and aches.
- **Risk of wound healing problem.** Wounds may not heal properly during Inlyta® treatment. Tell your doctor if you expect to have any surgery before starting or during treatment with Inlyta®. Stop taking Inlyta® at least two days before the planned surgery. Your doctor will tell you when you may start treatment with Inlyta® again after surgery.
- **Reversible posterior leukoencephalopathy syndrome (RPLS).** This syndrome may occur during treatment with Inlyta®. **Contact your doctor right away if you get:** headache, seizures, weakness, confusion, elevated blood pressure, blindness, changes in vision, problems thinking.
- **Increased level of protein in your urine.** Your doctor will check the urine for protein levels before and during your treatment with Inlyta®. If you develop protein in your urine, your doctor may lower the dosage of the medicine or stop the treatment.

- **Liver problems.** Your doctor will perform blood tests before and during your treatment with Inlyta®. Your doctor may delay or stop the treatment with Inlyta® if you develop severe liver problems.

The most common side effects of Inlyta® include:
- diarrhea
- high blood pressure
- feeling tired or weak
- decreased appetite
- nausea
- hoarseness
- rash, redness, itching or peeling of your skin on your hands and feet
- weight loss
- vomiting
- constipation

Additional side effects include:
hypothyroidism, joint pain, shortness of breath, abdominal pain, pain in the extremities, proteinuria, hair loss, muscle pain, nosebleed, hematuria, coughing up blood, cough, inflammation of the mucous membranes, inflammation of the oral mucosa, headache, rash, disturbed sense of taste, dry skin, digestion problems, itching, redness of the skin (erythema, redness or inflammation of the skin), changes in blood count, changes in hemoglobin levels, increase in levels of pancreas enzymes, changes in blood electrolyte levels, increased creatinine, increased liver enzymes, changes in blood glucose levels, dizziness, pain in the upper abdomen, dehydration, anemia, hemorrhoids, tinnitus (ringing in the ears), burning sensation in the mouth, pulmonary embolism, rectal bleeding, deep venous thrombosis, blocked vein of the retina, polycythemia (increased levels of hemoglobin in the blood), transient ischemic attack.

Side effects reported after product marketing (since reporting is voluntary and it is impossible to estimate the size of the relevant population, it is not always possible to estimate the incidence reliably or to establish a causal association with drug exposure):
Arterial (including the aorta) aneurysm and tear.

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 doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link:
https://sideeffects.health.gov.il

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 and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 30°C.
- After first opening the bottle the preparation can be used for up to 6 months.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**

microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, and Opadry® II red 32K15441.
The Opadry® II red 32K15441 film coating contains: lactose monohydrate, HPMC 2910/Hypromellose 15cp, titanium dioxide, triacetin (glycerol triacetate) and red iron oxide.

- **What the medicine look like and contents of the pack?**

Inlyta® 1 mg: Oval, red, film-coated tablet with the word 'Pfizer' embossed on one side, and '1' and 'XNB' on the other. The tablets are marketed in bottles of 60 or 180 tablets or in blister packs of 28 or 56 tablets.

Inlyta® 5 mg: Triangle-shaped, red, film-coated tablet with the word 'Pfizer' embossed on one side, and '5' and 'XNB' on the other. The tablets are marketed in bottles of 60 tablets or in blister packs of 28 or 56 tablets.

Not all pack sizes and types may be marketed.

- **Registration holder's name and address:** Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

- **Manufacturer's name and address:** Pfizer Manufacturing Deutschland GmbH, Mooswaldallee 1, 79090 Freiburg, Germany

- **Registration numbers of the medicines in the Ministry of Health's National Drug Registry are:**
  Inlyta® 1 mg: 149.67.33736
  Inlyta® 5 mg: 149.68.33737

Revised in 12/2020.