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

The medicine is dispensed with a doctor's prescription only

Film-coated Tablets

Each film-coated tablet contains: Imatinib (as mesvlate) 100 mg

Each film-coated tablet contains: Imatinib (as mesvlate) 400 mg

Film-coated Tablets

Inactive and allergenic ingredients in the preparation: See section 6 "Further Information"

Read this leaflet carefully in its entirety before using the medicine. Keep this leaflet. You may need to read it again. 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?

Glivec is a medicine containing an active substance called imatinib. The medicine works by inhibiting the production of the abnormal cells in the diseases listed below, some of which are certain types of cancer. Glivec is indicated for the treatment of adults and children 3 years of age and

above, with Philadelphia chromosome-positive chronic myeloid leukemia in the chronic phase, accelerated phase or blast crisis phase. Glivec is indicated for the treatment of adults with Kit-positive (CD117)

metastatic malignant and/or unresectable gastrointestinal stromal tumors Glivec is indicated as an adjunct therapy in adults after complete tumor

resection of Kit-positive (CD117) GIST

Glivec is indicated for the treatment of adults with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL). in combination with chemotherapy.

Glivec is indicated for the treatment of adults with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) as monotherapy.

Glivec is indicated for the treatment of adults with unresectable dermatofibrosarcoma protuberans (DFSP) and of adults with recurrent and/or metastatic DFSP who are not eligible for surgery.

Glivec is indicated for the treatment of adults with myeloproliferative or nyelodysplastic diseases (MDS/MPD) associated with genetic changes

Glivec is indicated for the treatment of adults with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL), with or without a mutation in FIP1L1-PDGFRa fusion kinase

Glivec is indicated for the treatment of adults with aggressive systemic mastocytosis (ASM) without the D816V c-kit mutation.

Therapeutic group: Antineoplastic

Chronic myeloid leukemia (CML) is a cancer of white blood cells. White blood cells usually help the body fight infection. In CML-type leukemia, certain abnormal white blood cells (called myeloid cells) start to grow uncontrollably. GIST are cancerous tumors of the stomach and the bowels. They arise from uncontrolled growth of the cells that support tissues of these organs. Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) is a cancer of the white blood cells. The white blood cells usually help the body fight infection. In ALL-type leukemia, certain abnormal white blood cells (called lymphoblasts) start to grow uncontrollably. Glivec inhibits growth of these cells.

Dermatofibrosarcoma protuberans (DFSP) is a malignant tumor of the tissue beneath the skin in which some cells start growing uncontrollably. Glivec inhibits growth of these cells.

Myeloproliferative or myelodysplastic diseases (MDS/MPD) is a group of blood diseases in which certain blood cells start to grow uncontrollably. Glivec inhibits growth of these cells in a certain subtype of these diseases. Hypereosinophilic syndrome or chronic eosinophilic leukemia (HES/CEL) is a group of blood diseases in which certain blood cells (called eosinophils) start to grow uncontrollably. Glivec inhibits growth of these cells in a certain subtype of these diseases.

Aggressive systemic mastocytosis (ASM) are malignant tumors which cause the body to produce too many blood cells called mast cells.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

ou are allergic (hypersensitive) to imatinib or any of the additiona gredients contained in the medicine detailed in section 6 "Further formation" in this leaflet. If this applies to you, **tell your doctor without**

If you think you may be allergic, but are uncertain, consult with your doctor.

Special warnings regarding use of the medicine Before treatment with Glivec, tell the doctor if:

- you are suffering, or have suffered in the past, from a liver, kidney or heart
- you are taking the medicine levothyroxine due to removal of the thyroid.
- you have ever had, or might now have, hepatitis B. This is because Glivec could cause hepatitis B to become active again, which can lead to death in certain cases. Patients will be carefully checked by their doctor to detect signs of this inflammation before starting treatment. you experience signs of bruising, bleeding, fever, tiredness and confusion
- during the course of treatment with Glivec, contact your doctor. This may be a sign of damage to blood vessels called thrombotic microangiopathy

If any of these apply to you, tell the doctor before taking Glivec. You may be more sensitive to the sun during treatment with Glivec. It is

important to cover sun-exposed areas of skin and use sunscreen with a high sun protection factor (high SPF). These precautions are also relevant

Glivec treatment will only be prescribed by a doctor with experience with medicines for treating blood cancer or solid tumors. Follow the doctor's instructions carefully, even if they differ from the general information

appearing in this leaflet. During treatment with Glivec, inform the doctor immediately if you gain weight very quickly. Glivec may cause your body to retain water (severe

Children and adolescents (below 18 years of age)

Glivec is given to children from the age of 3 years and above with CML. For the other indications. Glivec is not indicated for children and adolescents below 18 years of age.

In some children and adolescents taking Glivec, growth may be slower than normal. The doctor will monitor the growth at regular visits.

Tests and follow-up

The doctor will monitor your condition regularly, to check whether the desired effect of Glivec treatment is being obtained. You will be asked to regularly perform blood tests to see if you are tolerating Glivec (e.g., blood cells, liver and kidney functions, thyroid function). You will be weighed regularly during the course of treatment with Glivec.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines (such as paracetamol) and nutritional supplements (such as St. John's Wort), tell the doctor or pharmacist. Some medicines can interfere with the effect of Glivec when taken together. hey may increase or decrease the effect of Glivec, lead to worsening of side effects or make Glivec less effective. Glivec may do the same to some other medicines.

In particular, tell the doctor if you are taking:

Medicines which may increase blood Glivec levels:

some medicines used to treat AIDS (HIV), such as: indinavir, lopinavir/ ritonavir, ritonavir, saguinavir or nelfinavir:

some medicines used to treat hepatitis C, such as: telaprevir or boceprevir: and the like. some medicines used to treat fungal infections, such as; ketoconazole, itraconazole, posaconazole, voriconazole;

some medicines used to treat bacterial infections, such as: erythromycin, clarithromycin or telithromycin.

Exercise caution if you are taking a medicine which may increase blood Glivec levels.

Medicines which may lower blood Glivec levels:

dexamethasone, an anti-inflammatory steroidal medicine:

some medicines used to treat epilepsy, such as; phenytoin, carbamazepine. oxcarbazepine, phenobarbital, fosphenytoin or primidone; rifampicin, a medicine to treat tuberculosis:

Hypericum perforatum (also known as St. John's Wort) – a herbal product to treat depression and other conditions.

Use of the above medicines should be avoided during the course of treatment with Glivec. If you are taking any of the aforementioned medicines. the doctor may prescribe alternative medicines for you.

Medicines whose blood levels may increase upon use of Glivec: cyclosporine, an immunosuppressant medicine;

warfarin, a medicine to treat blood coagulation disorders (such as blood clots and thrombosis): or other medicines for treatment of blood coagulation

tacrolimus, sirolimus, medicines to prevent rejection of a transplanted organ in patients who underwent organ transplantation: fentanyl, alfentanil, medicines to treat pain:

terfenadine to treat allergy: bortezomib, docetaxel, medicines to treat cancer:

some medicines from the statin family, which treat high cholesterol level, such as: simvastatin:

some medicines to treat mental disorders, such as: benzodiazepines or

some medicines to treat hypertension or heart disorders, such as: calcium channel blockers or metoprolol;

ergotamine, diergotamine to treat migraine: paracetamol

Medicines whose blood levels may decrease following use of Glivec: Levothyroxine – a medicine given following removal of the thyroid.

In addition, inform the doctor, if you are already taking Glivec and have been prescribed a new medicine, including non-prescription medicines, that you have not taken previously during Glivec treatment.

Use of the medicine and food

Take Glivec with a meal to protect your stomach. Pregnancy, breast-feeding and fertility

- If you are pregnant or breast-feeding, think you may be pregnant or are planning a pregnancy, consult a doctor before using the medicine.
- Glivec is not recommended for use during pregnancy unless clearly necessary, as it may harm your baby. Your doctor will discuss with you the risks associated with taking Glivec during pregnancy.
- Women of child-bearing age must use effective contraception during the course of treatment with Glivec and for 15 days after completing the
- Do not breast-feed during treatment with Glivec and for 15 days after completing the treatment, as it may harm your baby.
- Patients concerned about their fertility during the course of treatment with Glivec should consult a doctor.

Driving and using machinery

If you experience dizziness or drowsiness, or if you have blurred vision while using Glivec, do not drive a vehicle or operate any tools or machines until vou feel well.

Children should be cautioned against riding a bicycle or playing near roads

3. HOW SHOULD YOU USE THE MEDICINE?

of water or apple juice in the following manner: The doctor has prescribed Glivec for you because you suffer from a serious • Use approximately 50 ml for each 100 mg tablet or 200 ml for each 400 illness. Glivec can help you fight this disease

Always use the preparation according to the doctor's instructions. It is important that you do so for as long as instructed by a doctor. Check with Stir with a spoon until the tablet(s) is/are completely dissolved the doctor or pharmacist if you are uncertain about the dosage and treatment After the tablet(s) dissolve/s, drink the entire contents of the whole glass regimen of the preparation. The dosage and treatment regimen will be immediately. Traces of the dissolved tablet(s) may be left in the glass. determined by the doctor only. The Glivec 100 mg tablet is divisible: the 400 mg tablet is **not** divisible.

The usual dosage is generally:

Use in adults

Your doctor will tell you exactly how many tablets of Glivec to take. If you are being treated for chronic myeloid leukemia (CML):

Depending on your condition, the recommended dosage is either 400 mg or 600 mg to be taken once a day. If you are being treated for gastrointestinal stromal tumors (GIST)

The recommended dosage is 400 mg, to be taken **once** a day. For treatment of CML and GIST diseases, your doctor may prescribe a

higher or lower dosage depending on how you respond to the treatment. If the doctor decides on a daily dosage of 800 mg, take 400 mg in the morning and 400 mg in the evening If you are being treated for Ph-positive acute lymphoblastic leukemia

The recommended dosage is 600 mg to be taken **once** a day.

If you are being treated for myelodysplastic/myeloproliferative diseases (MDS/MPD).

The recommended dosage is 400 mg to be taken **once** a day. If you are being treated for hypereosinophilic syndrome/chronic eosinophilic leukemia (HES/CEL):

The recommended dosage is 400 mg, to be taken once a day

In certain cases, the doctor may recommend a starting dosage of 100 mg once a day, and, if necessary, the doctor will consider increasing the dosage to 400 mg **once** a day, depending on your reaction to treatment. If you are being treated for dermatofibrosarcoma protuberans (DFSP)

Some side effects may be serious. Refer to a doctor immediately in The recommended dosage is 800 mg per day, to be taken as 400 mg in the you experience any of the side effects listed below: morning and 400 mg in the evening. Very common (occur in more than 1 user in 10) or common (occur in 1-10)

If you are being treated for aggressive systemic mastocytosis (ASM) The recommended dosage is 400 mg **once** per day.

In certain cases, the doctor may recommend a starting dosage of 100 mg **once** a day, and, if necessary, the doctor will consider increasing the dosage to 400 mg **once** a day, depending on your reaction to treatment.

A 400 mg dosage can be taken either as one tablet of 400 mg or four tablets of 100 mg

A 600 mg dosage is to be taken as one tablet of 400 mg plus two tablets

The dosage determined by the doctor may change, depending on your reaction to treatment.

Use in children and adolescents

The doctor will instruct you how many tablets of Glivec to give to your child. The dosage of Glivec given will depend on your child's condition, body weight and height.

For patients with CML, the maximal dosage for children should not exceed The treatment can be given to your child either as a once-daily dose or

alternatively, the daily dose can be split into two administrations (half in the morning and half in the evening). Do not exceed the recommended dose.

Duration of treatment

supervision.

• Severely decreased urine output, feeling thirsty (signs of kidney disorders); Take Glivec every day, until your doctor instructs you to stop. Nausea with diarrhea and vomiting, abdominal pain or fever (signs of

Method of administration

If you accidentally took a higher dosage

If you forgot to take the medicine

the medicine without consulting a doctor.

them. Side effects are usually mild to moderate.

not take the forgotten dose.

the doctor or pharmacist.

users in 100) side effects:

skin (signs of liver disorders):

gastrointestinal disorders);

Blood in the urine:

4. SIDE EFFECTS

fluid retention):

disorders)

If you took an overdose, or if a child has accidently swallowed the medicine.

refer to the doctor immediately or proceed to a hospital emergency room

and bring the package of the medicine with you. You may need medical

If you forgot to take this medicine at the designated time, take it as soon

Thereafter, continue taking the medicine as per the regular schedule.

Even if there is an improvement in your health, do not stop treatment with

If you are unable to take the medicine as prescribed by the doctor or if you

Do not take medicines in the dark! Check the label and the dose each

If you have further questions regarding use of the medicine, consult

As with any medicine, use of Glivec may cause side effects in some users.

Do not be alarmed by the list of side effects. You may not suffer from any of

- Do not take a double dose to compensate for a forgotten dose.

Adhere to the treatment regimen as recommended by the doctor.

feel you no longer need it, consult the doctor immediately.

time you take medicine. Wear glasses if you need them.

as you remember. However, if it is almost time to take the next dose, do

- Severe headache, weakness or paralysis of the limbs or face, difficulty **Take Glivec with a meal.** This will help protect you from stomach speaking, sudden loss of consciousness (signs of nervous system problems while taking Glivec.
- problems such as bleeding or swelling in skull/brain); Swallow the tablets whole with a large glass of water. Pale skin, tiredness, breathlessness and dark urine (signs of low levels) If you are unable to swallow the tablets, you can dissolve them into a glass
 - of red blood cells):
 - Eye pain or deterioration in vision, bleeding in the eyes: Pain in bones or joints (signs of osteonecrosis):
 - Blisters on skin or mucous membranes (signs of pemphigus);
 - Numbness or coldness in fingers and toes (signs of Raynaud's syndrome):
 - Sudden swelling and redness of the skin (signs of a skin inflammation) called cellulitis):
 - Difficulty hearing:

howel disorders):

- Muscle weakness and muscle spasms with an abnormal heart rhythm (signs of changes in the level of blood potassium);
- Signs of bruising:

levels in the blood):

- Stomach pain with nausea
- Muscle spasms with a fever, red-brown urine, muscle pain or weakness (signs of muscle disorders) Pelvic pain occasionally accompanied by nausea and vomiting, with
- unexpected vaginal bleeding, feeling dizzy or fainting due to low blood pressure (signs of disturbances in the ovaries or womb); Nausea, shortness of breath, irregular heartbeat, cloudy urine, tiredness. and/or joint discomfort accompanied by abnormal laboratory test results (e.g., high potassium, uric acid and calcium levels and low phosphorous
- Blood clots in small blood vessels (thrombotic microangiopathy). Side effects of unknown frequency (effects whose frequency has not
- vet been established): urination, sexual intercourse or ejaculation, blood in urine (signs of edema Combination of a widespread severe rash, nausea, fever, high levels of of the testicles); inability to get or keep an erection (erectile dysfunction); certain white blood cells or yellow skin or eyes (signs of jaundice) with heavy or irregular menstrual period; difficulty achieving/maintaining sexual breathlessness, chest pain/discomfort, severely decreased urine output
- and feeling of thirst (signs of a treatment-related allergic reaction); Chronic renal failure
- Recurrence (reactivation) of hepatitis B, if you have had hepatitis in the past (a liver infection).

If you experience any of these effects, refer to the doctor immediately. Additional side effects:

Refer to a doctor if any of the side effects listed below affect you severely:

Very common side effects (occur in more than 1 user in 10):

- Rapid weight gain. Glivec may cause your body to retain water (severe Headache or feeling tired Nausea, vomiting, diarrhea or indigestion, abdominal pain; Signs of infection such as: fever, severe chills, sore throat or mouth ulcers.
- Glivec may cause reduction in white blood cells, so you might get infections • Muscle cramps, muscle, bone or joint pain during treatment with Glivec or after discontinuing treatment with Glivec: • Unexpected bleeding or signs of bruising (when you have not been
 - Swelling, e.g., around the ankles or puffy eyes; · Weight gain;
- **Uncommon** (occur in 1-10 users in 1.000) or **rare** (occur in 1-10 users in 10.000) side effects: • Chest pain, irregular heart rhythm (signs of heart disorders); Cough, difficulty breathing, or pain when breathing (signs of lung)
 - Feeling dizzv or weak: · Sleeping difficulties (insomnia)
- Light-headedness, dizziness or fainting (signs of low blood pressure) Nausea with loss of appetite, dark-colored urine, yellowing of the eyes or
- Rash, red skin with blisters on the lips, eves, skin or mouth, peeling skin. fever, raised red or purple skin patches, itching, burning sensation, pustular rash (signs of a skin disorder);
- Severe abdominal pain, blood in vomit, black or bloody stools (signs of
- Discharge from the eve with itching, redness and swelling (conjunctivitis) watery eyes or blurred vision, swollen eyelids:
- Pain or swelling in the abdomen, flatulence, heartburn or constipation;

Common side effects (occur in 1-10 users in 100):

Anorexia, weight loss or a disturbed sense of taste;

Unusual hair loss or thinning:

Anemia (reduced red blood cells)

- Numbness of the hands or feet, paresthesia; · Mouth ulcers:

Nosebleeds:

- Pain with swelling of the joints:
- Drv mouth, skin or eves:
- Decreased or increased skin sensitivity:
- Hot flushes, chills or night sweats:
- Ervthema: Shortness of breath, cough:
- Increased liver enzymes.

pectoris): swollen lymph nodes.

has not yet been established

one side effect at some point.

Uncommon side effects (occur in 1-10 users in 1.000) Painful red lumps on the skin, skin pain, skin reddening (inflammation of

fatty tissue under the skin); cough, runny or stuffy nose, feeling of heaviness

discoloration; fungal infection; cardiac arrest; seizures; glaucoma; cataract;

Side effects whose frequency is unknown (effects whose frequency

Reddening and/or swelling on the palms of the hands and soles of the

Side effects in patients with aggressive systemic mastocytosis (ASM)

Patients with aggressive systemic mastocytosis (ASM) experienced at least

Side effects that were reported at the highest frequency were: diarrhea.

If a side effect occurs, if one of the side effects worsens, or if you suffer

from a side effect not mentioned in the 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

edema, anemia, itch, rash and lower respiratory tract inflammation.

side effects, or by entering the link: https://sideeffects.health.gov.il

nausea, ascites, muscle cramps, shortness of breath, tiredness, peripheral

Skin lesions that are painful and/or covered with blisters;

Slowed growth in children and adolescents.

feet, which may be accompanied by a tingling sensation and burning pain;

or pain on pressing the area above the eyes or on the sides of the nose. nasal congestion, sneezing, sore throat, blocked nose, sneezing, sore Store in the original package. throat, with or without headache (signs of upper respiratory tract infection); Do not use if the package is damaged or shows signs of tampering. severe headache felt as a throbbing pain or pulsing sensation, usually on Do not discard medicines in the wastewater or household waste bin. Ask the one side of the head and sometimes accompanied by nausea, vomiting and sensitivity to light or sound (signs of migraine); flu-like symptoms; pain or burning sensation while passing urine, increased body temperature, pain in 6. FURTHER INFORMATION groin or pelvic area, red- or brown-colored or cloudy urine (signs of urinary tract infection); pain and swelling of the joints (signs of arthralgia); a constant In addition to the active ingredient, the medicine also contains: feeling of sadness and loss of interest, which stops you carrying out your Inactive ingredients: normal activities (signs of depression); a feeling of apprehension and worry along with physical symptoms such as pounding heart, sweating, trembling dry mouth (signs of anxiety); sleepiness, drowsiness, excessive sleep; The film-coating contains: trembling/shaky movements (tremor): memory disorder: overwhelming urge to move the legs (restless leg syndrome); hearing noises (e.g., ringing, humming) in the ears that have no external source (tinnitus); hypertension; hematomas; burping; inflammation of the lips; difficulty swallowing; increased sweating; skin discoloration; brittle nails; red bumps or white-headed pimples around the roots of the hair, possibly with pain, itching or burning sensation (signs of inflammation of the hair follicles, also called folliculitis); skin rash line between the letters). with flaking or peeling (dermatitis); breast enlargement in men and women; dull pain or feeling of heaviness in the testicles or lower abdomen, pain during

arousal; decreased sexual desire; nipple pain; generally feeling unwell (malaise); viral infection such as cold sore; lower back pain resulting from The medicine is available in packages of 10 or 30 tablets (not all package kidney disorder: increased frequency of passing urine: increase in appetite: sizes may be marketed). pain or burning sensation in upper abdomen or chest (heartburn), nausea. Registration Holder and Importer and its address: Novartis Israel Ltd... vomiting, acid reflux, feeling of fullness and bloating, black-colored stools OB 7126 Tel Aviv (signs of stomach ulcer); joint and muscle stiffness; abnormal laboratory

excessive heartbeats; peripheral coldness; thickened red patches around f the Ministry of Health: the elbows and knees (psoriasis); darkening of the skin; chest pain (angina Glivec 100 mg film-coated tablets: 129 91 30789

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. The expiry date refers to the last day of that month.

Glivec 100 mg film-coated tablets: Do not store above 30°C.

Protect from moisture

5. HOW TO STORE THE MEDICINE?

pharmacist how to dispose of medicines that are no longer in use. These

Cellulose microcrystalline, crospovidone, hypromellose, magnesium stearate, silica colloidal anhydrous.

lypromellose, iron oxide red (E172), iron oxide vellow (E172), macrogol

Glivec 100 mg - round, film-coated tablets with a score line on one side.

The medicine is available in packages of 20 or 60 tablets (not all package sizes may be marketed).

to orange-brown in color, biconvex with beveled edges, NVR is printed on one side of the tablets and SL on the other side.

The leaflet was revised in May 2022 according to the MOH guidelines test results; eye irritation, eye pain or redness, swelling/itching of the eyelids; Registration numbers of the medicine in the National Drug Registry

Glivec 400 mg film-coated tablets: 129 92 30790 Rare side effects (occur in 1-10 users in 10.000): Confusion: nail

Storage temperature

Glivec 400 mg film-coated tablets: Store below 25°C.

neasures will help protect the environment.

What the medicine looks like and the contents of the package:

dark vellow to orange-brown in color, biconvex with beyeled edges, NVR is printed on one side of the tablets and SA on the other side (with a score

Glivec 400 mg - oval, film-coated tablets without a score line, dark vellow

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