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

The medicine is dispensed with a doctor's prescription only

Glivec® 100 ma

Composition:

Glivec[®] 400 ma

Film-coated Tablets

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

Film-coated Tablets

Fach film-coated tablet contains: Imatinib (as mesylate) 400 mg

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 (GIST).

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 myelodysplastic diseases (MDS/MPD) associated with genetic changes in the PDGF receptor.

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

you are allergic (hypersensitive) to imatinib or any of the additional ingredients contained in the medicine detailed in section 6 "Further Information" in this leaflet. If this applies to you tell your doctor without taking Glivec.

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 problem.
- 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 (TMA).

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 for children.

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 fluid retention

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 taker together. They 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, saguinavi or nelfinavir.

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

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

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 disorders;

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;

voriconazole:

some medicines from the statin family, which treat high cholesterol level, such as: simvastatin; some medicines to treat mental disorders, such as: benzodiazepines or pimozide

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 treatment
- 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

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 you feel well.

Children should be cautioned against riding a bicycle or playing near roads and the like.

3. HOW SHOULD YOU USE THE MEDICINE?

The doctor has prescribed Glivec for you because you suffer from a serious 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 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:

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

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 (ALL): 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

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):

The recommended dosage is 800 mg per day, to be taken as 400 mg in the morning and 400 mg in the evening. 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 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 of 100 mg. 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 600 mg.

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

Take Glivec every day, until your doctor instructs you to stop.

Method of administration

- Take Glivec with a meal. This will help protect you from stomach problems while taking Glivec.
- Swallow the tablets whole with a large glass of water.
- If you are unable to swallow the tablets, you can dissolve them into a glass of water or apple juice in the following manner:
- Use approximately 50 ml for each 100 mg tablet or 200 ml for each 400 mg tablet.
- Stir with a spoon until the tablet(s) is/are completely dissolved. · After the tablet(s) dissolve/s, drink the entire contents of the whole glass immediately. Traces

of the dissolved tablet(s) may be left in the glass. The Glivec 100 mg tablet is divisible; the 400 mg tablet is not divisible.

If you accidentally took a higher dosage

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 supervision

If you forgot to take the medicine

- If you forgot to take this medicine at the designated time, take it as soon as you remember.
- However, if it is almost time to take the next dose, do not take the forgotten dose
- Thereafter, continue taking the medicine as per the regular schedule.
- Do not take a double dose to compensate for a forgotten dose. Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting a doctor.

If you are unable to take the medicine as prescribed by the doctor or if you feel you no longer need it, consult the doctor immediately. Do not take medicines in the dark! Check the label and the dose each time you take

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 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 them. Side effects are usually mild to moderate Some side effects may be serious. Refer to a doctor immediately if you experience any of the side effects listed below:

Very common (occur in more than 1 user in 10) or common (occur in 1-10 users in 100) side

- · Rapid weight gain. Glivec may cause your body to retain water (severe fluid retention); 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 easily; Unexpected bleeding or signs of bruising (when you have not been injured). 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 disorders);
- · Light-headedness, dizziness or fainting (signs of low blood pressure); · Nausea with loss of appetite, dark-colored urine, yellowing of the eyes or skin (signs of liver disorders):
- · Rash, red skin with blisters on the lips, eyes, 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 gastrointestinal disorders):
- Blood in the urine:
- · Severely decreased urine output, feeling thirsty (signs of kidney disorders);
- · Nausea with diarrhea and vomiting, abdominal pain or fever (signs of bowel disorders); Severe headache, weakness or paralysis of the limbs or face, difficulty speaking, sudden loss of
- consciousness (signs of nervous system problems such as bleeding or swelling in skull/brain);
- Pale skin, tiredness, breathlessness and dark urine (signs of low levels 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;

· Signs of bruising;

- Muscle weakness and muscle spasms with an abnormal heart rhythm (signs of changes in the level of blood potassium);
- · 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 levels in the blood):
- Blood clots in small blood vessels (thrombotic microangiopathy).
- Side effects of unknown frequency (effects whose frequency has not yet been established): · Combination of a widespread severe rash, nausea, fever, high levels of certain white blood cells or yellow skin or eyes (signs of jaundice) with breathlessness, chest pain/discomfort, severely decreased urine output and feeling of thirst (signs of a treatment-related allergic reaction);
- 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) · Headache or feeling tired: Nausea, vomiting, diarrhea or indigestion, abdominal pain;

treatment with Glivec:

Chronic renal failure

- Rash: · Muscle cramps, muscle, bone or joint pain during treatment with Glivec or after discontinuing
- · Swelling, e.g., around the ankles or puffy eyes;
- · Weight gain; • Anemia (reduced red blood cells).

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

- · Anorexia, weight loss or a disturbed sense of taste;
- · Feeling dizzy or weak;
- · Sleeping difficulties (insomnia); Discharge from the eye with itching, redness and swelling (conjunctivitis), watery eyes or blurred
- vision, swollen eyelids; Nosebleeds
- Pain or swelling in the abdomen, flatulence, heartburn or constipation;

- Numbness of the hands or feet, paresthesia:

- · Dry mouth, skin or eyes;
- · Hot flushes, chills or night sweats;
- · Ervthema:
- · Shortness of breath, cough;

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 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 throat, with or without headache (signs of upper respiratory tract infection); severe headache felt as a throbbing pain or pulsing sensation, usually on 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 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 feeling of sadness and loss of interest, which stops you carrying out your 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; 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 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 urination, sexual intercourse or ejaculation, blood in urine (signs of edema of the testicles); inability to get or keep an erection (erectile dysfunction); heavy or irregular menstrual period; difficulty achieving/maintaining sexual arousal; decreased sexual desire; nipple pain; generally feeling unwell (malaise); viral infection such as cold sore; lower back pain resulting from kidney disorder; increased frequency of passing urine; increase in appetite; pain or burning sensation in upper abdomen or chest (heartburn), nausea, vomiting, acid reflux, feeling of fullness and bloating, black-colored stools (signs of stomach ulcer); joint and muscle stiffness; abnormal laboratory test results; eye irritation, eye pain or redness, swelling/itching of the evelids; excessive heartheats; peripheral coldness; thickened red patches around the elbows and knees (psoriasis); darkening of the skin; chest pain (angina pectoris); swollen lymph nodes

Rare side effects (occur in 1-10 users in 10,000): Confusion; nail discoloration; fungal infection;

Side effects whose frequency is unknown (effects whose frequency has not yet been

- accompanied by a tingling sensation and burning pain;
- Slowed growth in children and adolescents

Side effects in patients with aggressive systemic mastocytosis (ASM)

Patients with aggressive systemic mastocytosis (ASM) experienced at least one side effect at some point.

Side effects that were reported at the highest frequency were: diarrhea, nausea, ascites, muscle cramps, shortness of breath, tiredness, peripheral edema, anemia, itch, rash and lower respiratory

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

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

Store in the original package.

Protect from moisture.

dispose of medicines that are no longer in use. These measures will help protect the environment. 6. FURTHER INFORMATION

n addition to the active ingredient, the medicine also contains:

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

What the medicine looks like and the contents of the package: Glivec 100 mg - round, film-coated tablets with a score line on one side, dark yellow to orange-brown in color, biconvex with beveled edges. NVR is printed on one side of the tablets

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

The medicine is available in packages of 10 or 30 tablets (not all package sizes may be marketed). Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B. 7126, Tel Aviv.

Glivec 400 mg film-coated tablets: 129 92 30790

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- Unusual hair loss or thinning;

- · Mouth ulcers:
- . Pain with swelling of the joints:
- · Decreased or increased skin sensitivity;

- · Increased liver enzymes

Uncommon side effects (occur in 1-10 users in 1,000):

cardiac arrest: seizures: glaucoma: cataract: arthritis

- Reddening and/or swelling on the palms of the hands and soles of the feet, which may be
- Skin lesions that are painful and/or covered with blisters;

- to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il 5. HOW TO STORE THE MEDICINE?
- date refers to the last day of that month Do not store above 30°C.

Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to

Inactive ingredients:

Do not use if the package is damaged or shows signs of tampering.

The film-coating contains:

and SA on the other side (with a score line between the letters).

The leaflet was revised in May 2022 according to the MOH guidelines.

Glivec 400 mg - oval, film-coated tablets without a score line, dark yellow to orange-brown in color, biconvex with beveled edges. NVR is printed on one side of the tablets and SL on the other side

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health: Glivec 100 mg film-coated tablets: 129 91 30789