Applicant : Eurolab (Pty) Ltd
Proprietary name : Mivesta 100 mg & 400 mg
Dosage form and strength : Film-coated tablets
Date of submission : 26 January 2023
Approval date : 13 January 2023

APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

MIVESTA 100 mg and 400 mg film-coated tablets

Imatinib mesylate

Sugar free

Read all of this leaflet carefully before you start taking MIVESTA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- **MIVESTA** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What **MIVESTA** is and what it is used for
2. What you need to know before you take **MIVESTA**
3. How to take **MIVESTA**
4. Possible side effects
5. How to store **MIVESTA**
6. Contents of the pack and other information(

1 What MIVESTA is and what it is used for

Treatment for adults and children for:

- **Chronic myeloid leukaemia (CML):** Leukaemia is a cancer of white blood cells.

  Treatment for adults for certain other types of leukaemia or cancer of the stomach and

skin. Chronic myeloid leukaemia is a form of leukaemia in which certain abnormal white cells (named myeloid cells) start growing out of control.

- **Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph-positive ALL).** Leukaemia is a cancer of white blood cells. These white cells usually help the body to fight infection. Acute lymphoblastic leukaemia is a form of leukaemia in which certain abnormal white cells (named lymphoblasts) start growing out of control. **MIVESTA** inhibits the growth of these cells.

MIVESTA is also a treatment for adults for:

- Myelodysplastic/myeloproliferative diseases (MDS/MPD). These are a group of blood diseases in which some blood cells start growing out of control. **MIVESTA** inhibits the growth of these cells in a certain subtype of these diseases
- Systemic mastocytosis (SM) without the D816V c-Kit mutation and eosinophilia. This is a rare disorder that results in too many mast cells building up in your body.
- Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL). These are blood diseases in which some blood cells (named eosinophils) start growing out of control. **MIVESTA** inhibits the growth of these cells in a certain subtype of these diseases.
- Gastrointestinal stromal tumours (GIST). GIST is a cancer of the stomach and bowels. It arises from uncontrolled cell growth of the supporting tissues of these organs.
- Dermatofibrosarcoma protuberans (DFSP). DFSP is a cancer of the tissue beneath the skin in which some cells start growing out of control. **MIVESTA** inhibits the growth of these cells

2 What you need to know before you take MIVESTA

Do not take MIVESTA:

- if you are hypersensitive (allergic) to imatinib mesilate or any of the other ingredients of **MIVESTA** (see **What MIVESTA contains**).
- if you are pregnant, planning to become pregnant or breastfeeding your baby.

Warnings and Precautions

Take special care with **MIVESTA**:

- If you have or ever had a liver, kidney or heart disorder. In patients with liver dysfunction, blood counts and liver enzymes should be carefully monitored.
- If you are taking a medicine called levothyroxine, because your thyroid has been removed (severe fluid retention), your Thyroid-Stimulating Hormone (TSH) levels should be carefully monitored.
- If you notice any stroke-like symptoms, such as trouble walking, speaking and understanding, as well as paralysis or numbness of the face, arm or leg, weakness on one side of the body, vision problems and slurred speech.
- If you notice that you put on weight very quickly. **MIVESTA** may cause your body to retain water. You should therefore be weighed regularly.
- If you notice bleeding at the site of the tumours or bleeding from the gastrointestinal tract (dark excretions looking like ground coffee).
- If you have ever had or might now have a Hepatitis B infection (a liver infection). This is because **MIVESTA** could cause Hepatitis B to become active again, which can be fatal in some cases. You will be carefully checked by your doctor for signs of the infection before treatment is started.
- If you have any blood disorders.
- If you are dehydrated or have gout (high uric acid levels).
- If **MIVESTA** is used in children, close monitoring of growth in children is recommended.

- You should avoid sunlight when taking **MIVESTA**, as your skin or eyes can become very sensitive to sunlight or other forms of light.
- If you experience bruising, bleeding, fever, feeling tired and confusion. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA).

Children and adolescents

MIVESTA is also a treatment for children with CML. There is no experience in children with CML below 2 years of age. There is limited experience in children with Ph-positive ALL and very limited experience in children with MDS/MPD, DFSP, GIST and HES/CEL.

Some children and adolescents taking **MIVESTA** may have slower than normal growth. The doctor will monitor the growth at regular visits.

Other medicines and MIVESTA

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

Before taking **MIVESTA** tell your doctor if you are using any of the following:

- medicines that prevent the formation of blood clots (e.g. warfarin)
- some medicines that treat fungal skin infections or antibacterial medicines (e.g. ketoconazole, itraconazole, posaconazole, voriconazole, erythromycin, ~~and~~ clarithromycin and telithromycin)
- anti-inflammatory and immunosuppressant medicines (e.g. dexamethasone, ciclosporin, tacrolimus, sirolimus or pimozide)
- antiretroviral medicines (e.g. indinavir, lopinavir/ritonavir, ritonavir, saquinavir, nelfinavir)
- hepatitis C medicines (e.g. telaprevir, boceprevir)

- anticonvulsants (used to prevent seizures, e.g. primidone)
- mood-stabilising medicines (e.g. phenytoin, carbamazepine, phenobarbitone)
- rifampicin (used to treat tuberculosis)
- St. John's Wort (a herbal medicine for treating depression)
- medicines used to treat high cholesterol (e.g. simvastatin)
- ergotamine, diergotamine (to treat migraines or cluster headaches)
- powerful opioid medicines, such as fentanyl or alfentanil
- antihistamine to treat allergic conditions (e.g. terfenadine)
- anti-cancer medicine, such as bortezomib, docetaxel
- quinidine, an antiarrhythmic medicine
- metoprolol, used to treat high blood pressure
- high doses of paracetamol
- surgical removal of all or part of your thyroid gland and also taking the thyroid hormone, levothyroxine
- on chemotherapy regimen, for example using L-asparaginase

MIVESTA with food and drink

MIVESTA should be taken with food and a large glass of water to minimise the risk of upsetting your digestive system.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist, or other health care provider for advice before taking **MIVESTA**.

Pregnancy

- You should not take **MIVESTA** if you are pregnant or plan to become pregnant.
- If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **MIVESTA**.
- **MIVESTA** is not recommended during pregnancy, as it may harm your baby. Your doctor will discuss with you the possible risks of taking **MIVESTA** during pregnancy.
- You should use highly effective contraception during treatment and for at least 15 days after stopping treatment with **MIVESTA**.

Breast-feeding

- Do not breastfeed during treatment with **MIVESTA** and for 15 days after ending treatment, as it may harm your baby.

Fertility

- Patients who are concerned about their fertility while taking **MIVESTA** are advised to consult with their doctor, pharmacist or healthcare professional.

Driving and using machines

MIVESTA may cause dizziness or blurred vision and therefore may impair your ability to drive and use machinery.

It is not always possible to predict to what extent **MIVESTA** may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which **MIVESTA** affects them.

3 How to take MIVESTA

Do not share medicines prescribed for you with any other person.

Always take **MIVESTA** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will advise you on the dose you should be taking for your specific condition.

Your doctor may adjust the dosage if necessary for any of the conditions mentioned above depending on the severity of the condition and the side-effects you experience.

Recommended dose:

How much MIVESTA to take

Use in adults

Your doctor will tell you exactly how many tablets of **MIVESTA** to take.

- **If you are being treated for CML:**

  Depending on your condition the usual starting dose is either 400 mg or 600 mg to be taken once a day.

- **If you are being treated for GIST:**

  The starting dose is 400 mg, to be taken once a day.

For CML and GIST, your doctor may prescribe a higher or lower dose depending on how you respond to the treatment. If your daily dose is 800 mg, you should take 400 mg in the morning and 400 mg in the evening.

- **If you are being treated for Ph-positive ALL:**

  The starting dose is 600 mg to be taken once a day.

- **If you are being treated for MDS/MPD:**

  The starting dose is 400 mg to be taken once a day.

- **If you are being treated for SM**

- The starting dose is 100 mg to be taken once a day. Your doctor may decide to increase the dose to 400 mg, to be taken once a day, depending on how you respond to treatment.
- **If you are being treated for HES/CEL:**

  The starting dose is 100 mg, to be taken once a day. Your doctor may decide to increase the dose to 400 mg, to be taken once a day, depending on how you respond to treatment.
- **If you are being treated for DFSP:**

  The dose is 800 mg per day, to be taken as 400 mg in the morning and 400 mg in the evening.

Use in children and adolescents

The doctor will tell you how many tablets of **MIVESTA** to give to your child. The amount of **MIVESTA** given will depend on your child's condition, body weight and height. The total daily dose in children must not exceed 600 mg with CML. The treatment can either be given to your child 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).

When and how to take MIVESTA

- Take **MIVESTA** with a meal. This will help protect you from stomach problems when taking **MIVESTA**.
- Swallow the tablets whole with a large glass of water.

If you are unable to swallow the tablets, you can dissolve them in a glass of still water or apple juice:

- Use about 50 ml for each 100 mg tablet or 200 ml for each 400 mg tablet.

- Stir with a spoon until the tablets have completely dissolved.
- Once the tablet has dissolved, drink everything in the glass straight away. Traces of the dissolved tablets may be left behind in the glass.

Your doctor will tell you how long your treatment with **MIVESTA** will last. Do not stop treatment early without consulting your doctor because it may decrease the effectiveness of the treatment. If you have the impression that the effect of **MIVESTA** is too strong or to weak, tell your doctor or pharmacist.

If you take more MIVESTA than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take MIVESTA

If you have missed your dose by only a few hours, take the missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and take **MIVESTA** at the next regularly scheduled time.

Do not take a double dose to make up for forgotten individual doses.

4 Possible side effects

MIVESTA can have side effects.

Not all side effects reported for **MIVESTA** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **MIVESTA**, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop taking MIVESTA and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,
- yellowing of the skin and eyes, also called jaundice.
- Nausea, vomiting, feeling tired, dark urine, numbness, fits, hallucinations, muscle cramps and heart palpitations, as it can all be symptoms of a serious life-threatening condition called Tumour lysis syndrome, a condition that is caused by massive tumour cells killed and released in the bloodstream.
- thrombotic microangiopathy (a rare but serious medical disease - it is a pattern of damage that can occur in the smallest blood vessels inside many of your body's vital organs – most commonly the kidney and brain). Symptoms may include feeling tired, fever, confusion, weakness, headache, bleeding.
- improper beating of your heart, whether irregular, too fast or too slow. Symptoms may also include chest pain, fainting or dizziness.
- subdural haematoma is a serious condition where blood collects between the skull and the surface of the brain (symptoms include headache, confusion, vomiting, slurred speech or coma).
- vomiting blood.

These are all very serious side effects. If you have them, you may have had a serious reaction to **MIVESTA**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- chest pain,
- angina (cramping of the heart muscle),
- changes in the way your heart beats, for example, if you notice it beating faster,
- signs of recurrent infections such as fever or sore throat,
- less urine than is normal for you, blood in the urine or more frequent urinating,
- unexpected bleeding or bruising,
- blurred vision, bleeding of the blood vessels in the eye,
- glaucoma (sudden ocular pain, seeing halos around lights, red eye, very high pressure in the eye).
- lesions or pinhead-sized bumps, that starts on your face or in your armpits and groin area and then become widespread. You may also experience fever and feeling tired.
- rhabdomyolysis (a serious medical condition that can be fatal or result in permanent disability), that is caused by a breakdown of muscle tissue that releases a damaging protein into the blood. Symptoms include dark, reddish urine, a decreased amount of urine, weakness and muscle aches.
- if you experience severe pelvic pain, severe nausea, vomiting, light-headedness and weakness. These can be symptoms of a ruptured cyst.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor as soon as possible if you notice any of the following:

The following side effects occur frequently:

- weight gain, swelling of the body,
- headache, dizziness, tingling or pins and needles sensation in arms or legs, difficulty sleeping,

- nose bleeds, shortness of breath,
- red and swollen eyes, swollen eyelids, watery eyes, blurred vision, bleeding in the eye
- nausea (feeling sick), vomiting (being sick), diarrhoea (loose stools), indigestion, stomach pain, bloating, flatulence, constipation, heartburn, mouth sores,
- muscle spasm and cramps, muscle pain, joint swelling, muscle stiffness,
- tiredness, fever,
- loss of appetite,
- dry skin, hair loss, night sweats,
- lower than normal number of red and white blood cells and platelets in the blood (symptoms may include feeling tired, weakness, dizziness, trouble breathing, fast heartbeat, fever, pale skin, purple or red spots on the skin, rash, easy bruising, and abnormal bleeding)
- sleep disorder (trouble falling or staying asleep)
- taste disturbances
- numbness
- flushing or reddening of skin
- bleeding
- cough
- dry mouth
- gastritis (stomach inflammation that may cause stomach pain, nausea and vomiting)
- skin sensitivity to light,
- muscle aches and pain
- bone pain
- swelling of the skin or body
- weight loss

The following side effects occur less frequently:

- chest infection, flu-like symptoms, skin infections, bladder infections,
- throat infection, nasal-throat infection, difficulty breathing
- fungal infection
- forming of a high number of blood platelets (symptoms include headache, dizziness, chest pain, fainting, vision changes, redness, throbbing and burning pain in hands and feet)
- low white blood cell in your blood, called lymphocytes (symptoms include fever, cough, runny nose, enlarged lymph nodes, small tonsils, painful joints, skin rash, night sweats).
- haemolytic anaemia (premature destruction of red blood cells). Symptoms may include abnormal paleness, yellow skin, dark-coloured urine, fever, weakness, dizziness and confusion.
- gout (painful swelling of ankle or foot),
- increased or decreased appetite,
- severe headache, weakness or paralysis of limbs or face, difficulty speaking, sudden loss of consciousness, drowsiness, fits (seizures),
- involuntary shaking or movement
- blood clots, high or low blood pressure, flushes, coldness in fingers or toes
- blood in stools, stomach ulcers,
- liver infection
- red or purple spots on skin, increased sweating, breaking of finger or toenails, peeling of skin on the lips, skin discolouration, dry scaly patches, skin blisters,
- eye irritation, eye pain or deterioration of vision,
- ringing in the ear, difficulty hearing

- congestive heart failure (heart doesn't pump as well as it should). Symptoms include shortness of breath, feeling tired, swollen legs and rapid heartbeat
- palpitations (feeling like your heart is racing or beating too hard)
- painful swelling and sores inside the mouth
- difficulty swallowing
- pastular rash - a patch of large red bumps that have pus inside
- bruising or increased tendency to bruise
- inflammation of hair follicles
- nail discolouration
- painless swelling under the skin, due to an allergic reaction
- symmetrical, bull's-eye-shaped, red, raised skin areas that can appear all over the body
- small blood vessel inflammation
- muscular weakness
- arthritis – swelling and tenderness of one or more joints
- myopathy, a disease that affects the muscles that control voluntary movement in the body and includes muscle weakness.
- depression, anxiety, decreased sexual drive, confusion,
- breast enlargement (in men and women), nipple pain, sexual dysfunction, heavy menstrual periods in woman
- erectile dysfunction/ impotence
- irregular menstruation
- feeling unwell
- chest pain
- sudden and severe inflammation of the pancreas – symptoms may include excessive thirst, frequent urination, extreme tiredness (fatigue) or weakness, weight loss and nausea.

The following side effects may also occur:

- Reddening and/or swelling on the palms of the hands and soles of the feet which may be accompanied by tingling sensation and burning pain.
- Slowing of growth in children and adolescents
- Recurrence (reactivation) of Hepatitis B infection when you have had Hepatitis B in the past (a liver infection)
- pseudoporphyria – a condition that mimics porphyria that causes skin fragility and photosensitivity. Blisters form where the skin is exposed to the sun and are most often seen on the hands and feet.

If you notice any side-effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effect

If you get side effects, talk to your doctor. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8 By reporting side effects, you can help provide more information on the safety of **MIVESTA**.

5 How to store MIVESTA

- Store at or below 25 °C.
- Protect from moisture.
- Keep blisters in the carton until required for use.
- Store all medicines out of reach of children.
- Do not use after the expiry date printed on the label or carton.

- Return all unused medicine to your pharmacist.
- Do not use **MIVESTA** if you notice any visible signs of deterioration.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Shelf-life

36 months

6 Contents of the pack and other information

What MIVESTA contains

- The active substance is imatinib mesilate.
- The other ingredients are colloidal anhydrous silica, crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose and Opadry Yellow 03F520050 containing hypromellose, iron oxide yellow, iron oxide red, macrogol and talc.

What MIVESTA looks like and contents of the pack

MIVESTA film-coated tablets are packed into clear transparent PVC/PVdC-Alu blisters or plain matt finish Alu-Alu blisters, containing 10 tablets per blister.

Pack size: 20, 30 or 60 film-coated tablets per carton.

Holder of Certificate of Registration

Eurolab (Pty) Ltd.

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Woodmead, 2144

This leaflet was last revised

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MIVESTA 100: 49/26/0742

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