NOVARTIS

SOTAURIC

(midostaurin)

25 mg soft gelatine capsule

Patient Information Leaflet

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SOTAURIC® 25 mg soft capsules

(midostaurin)

This medicine is subject to additional monitoring information. This will allow quick identification of new safety information. You can help by reporting any side effects you may get.

Read all of this leaflet carefully before you start taking SOTAURIC

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse or other health care provider.
- SOTAURIC 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 SOTAURIC is and what it is used for

What SOTAURIC is

SOTAURIC contains the active substance midostaurin. It belongs to a class of medicines called protein kinase inhibitors.

What SOTAURIC is used for

SOTAURIC is used to treat acute myeloid leukaemia (AML) in adults who have a defect in a gene called FLT3. Acute myeloid leukaemia is a form of cancer of certain white blood cells (called myeloid cells) in which the body over produces an abnormal type of these cells.

SOTAURIC is also used in adults to treat aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM AHN), or mast cell leukaemia (MCL). These are disorders in which the body produces too many mast cells, a type of white

blood cell. Symptoms are caused when too many mast cells enter organs such as the liver, bone marrow or spleen, and release substances such as histamine into the blood.

How SOTAURIC works

Midostaurin blocks the action of some enzymes (kinases) in the abnormal cells and stops their division and growth.

At the start of treatment in AML SOTAURIC is always used together with chemotherapy (medicines for treating cancer).

If you have any questions about how SOTAURIC works or why this medicine has been prescribed for you, ask your doctor, pharmacist or nurse.

2. What you need to know before you take SOTAURIC

Follow the doctor's instructions carefully.

Do not take SOTAURIC:

- if you are allergic to midostaurin or to any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice.
- if you are already taking any of the following medicines:
    - medicines used to treat tuberculosis, such as rifampicin;

- medicines used to treat epilepsy, such as carbamazepine or phenytoin;
- enzalutamide, a medicine used to treat prostate cancer;
- St. John's Wort (also known as *Hypericum perforatum*), a herbal medicine used to treat depression.

These medicines must be avoided during treatment with SOTAURIC. Talk to your doctor if you are told that you have to start taking one of them during SOTAURIC treatment.

- If you have severe heart failure, had a heart attack (myocardial infarction) within the previous 6 months, diagnosed with congenital or acquired conditions called heart conduction blocks or very prolonged QT time on your heart rate and rhythm tracing (ECG). If you are pregnant or breast feeding your baby.
- If you are pregnant or breast feeding your baby

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking SOTAURIC:

- if you have any infections;
- if you have a heart disorder (see 'Do not take SOTAURIC');
- if you have problems with your lungs or problems breathing.

Tell your doctor, pharmacist or nurse straight away if you get any of these symptoms during treatment with SOTAURIC:

- if you have fever, sore throat or mouth ulcers, because these may indicate that your white blood cell count is low;
- if you have new or worsening symptoms such as fever, cough with or without mucous, chest pain, trouble breathing or shortness of breath, because these may be signs of lung problems;
- if you have or experience chest pain or discomfort, light headedness, fainting, dizziness, blue discolouration of your lips, hands or feet, shortness of breath, or swelling of your lower limbs (oedema) or skin, because these may be signs of heart problems.

Your doctor may need to adjust, temporarily stop or completely discontinue your treatment with SOTAURIC.

Monitoring during treatment with SOTAURIC

Your doctor will perform regular blood tests during treatment with SOTAURIC in order to monitor the amount of blood cells (white blood cells, red blood cells and platelets) and electrolytes (e.g. calcium, potassium, magnesium) in your body. Your heart and lung function will also be checked regularly.

Children and adolescents

SOTAURIC should not be used in children and adolescents below 18 years of age as safety and efficacy have not established in this age group. In children and adolescents who are also receiving other chemotherapy, SOUTAURIC could cause a severe reduction of certain types of blood cells.

Other medicines and SOTAURIC

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because SOTAURIC can affect the way some medicines work. Some other medicines can also affect how SOTAURIC works.

The following medicines **must be avoided** during treatment with SOTAURIC:

- medicines used to treat tuberculosis, such as rifampicin;
- medicines used to treat epilepsy, such as carbamazepine or phenytoin;
- enzalutamide, a medicine used to treat prostate cancer;
- St. John's Wort (also known as *Hypericum perforatum*), a herbal medicine used to treat depression.

Tell your doctor or pharmacist if you are taking any of the following medicines:

- some medicines used to treat infections, such as ketoconazole or clarithromycin;
- some medicines used to treat HIV, such as ritonavir or efavirenz;
- nefazadone, a medicine used to treat depression;
- some medicines used to stop the body from rejecting organ transplants, such as tacrolimus;
- some medicines used to treat cancer, such as paclitaxel or cyclophosphomide
- some medicines used to control levels of fat in your blood, such as atorvastatin;

- digoxin, a medicine used to treat heart failure;
- warfarin, a medicine used to treat and prevent thrombosis;
- tizanidine, a medicine used to relax muscles;
- codeine, a medicine used to treat pain;
- omeprazole, a medicine to treat excessive stomach acid, ulcers and heartburn;
- chlorzoxazone, a medicine used for treating discomfort caused by muscle spasms.

If you are taking any of these medicines, your doctor might prescribe a different medicine for you during your treatment with SOTAURIC.

You should also tell you doctor if you are already taking SOTAURIC and you are prescribed a new medicine that you have not previously taken during treatment.

Ask your doctor or pharmacist if you are not sure whether your medicine is one of the medicines listed above.

Pregnancy and breast-feeding

SOTAURIC may harm your unborn baby and you should not be treated with SOTAURIC during pregnancy (see ‘Do not take SOTAURIC’). If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

SOTAURIC could harm your baby. You should not breast feed during treatment with

SOTAURIC and for at least 4 months after stopping the treatment (see 'Do not take SOTAURIC').

Contraception in women

If you become pregnant while taking SOTAURIC, it may harm your baby. Your doctor will ask you to take a pregnancy test before you start treatment with SOTAURIC to make sure you are not pregnant. You must use an effective method of contraception while taking SOTAURIC and for at least 4 months after you have stopped taking it. Your doctor will discuss with you the most suitable method of contraception for you to use.

If you become pregnant or think you are pregnant, tell your doctor right away.

Fertility

SOTAURIC may reduce fertility in men and women. You should discuss this with your doctor before starting treatment.

Driving and using machines

Take special care when driving and using machines as you may develop dizziness and vertigo while you are taking SOTAURIC.

SOTAURIC contains ethanol anhydrous (alcohol)

SOTAURIC contains about 14 vol. % ethanol anhydrous, which corresponds to up to 333 mg alcohol per dose. This is equivalent to 8.4 ml beer or 3.5 ml wine. Alcohol may be harmful if you have alcohol related problems, epilepsy or liver problems, or if you are pregnant or breast feeding.

SOTAURIC contains macrogolglycerol hydroxystearate (castor oil)

SOTAURIC contains macrogolglycerol hydroxystearate, which may cause stomach discomfort and diarrhoea.

3. How to take SOTAURIC

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Do not exceed the dose prescribed by your doctor.

How much SOTAURIC to take

Your doctor will tell you exactly how many capsules to take.

- *Patients with AML*

  The usual daily dose is 50 mg (2 capsules) twice daily.

- *Patients with ASM, SM-AHN or MCL*

  The usual daily dose is 100 mg (4 capsules) twice daily

Depending on how you respond to SOTAURIC, your doctor may lower your dose or temporarily interrupt the treatment.

Taking SOTAURIC

- Taking SOTAURIC at the same time each day will help you to remember to take your medicine.
- Take SOTAURIC twice a day at about 12 hour intervals (for example, with breakfast and with your evening meal).
- Take SOTAURIC with food.
- Swallow the capsules whole with a glass of water. Do not open, crush or chew them to ensure proper dosing and avoid the unpleasant taste of the capsule content.
- For patients with AML, SOTAURIC is taken with chemotherapy medicines. It is very important to follow your doctor’s recommendations.
- If you vomit after you swallow the capsules, do not take any more capsules until your next scheduled dose.

How long to take SOTAURIC

- Continue taking SOTAURIC for as long as your doctor tells you. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.
- If you are being treated for AML, after you finish taking SOTAURIC with chemotherapy medicines, you will receive SOTAURIC alone for up to 12 months.
- If you are being treated for ASM, SM AHN or MCL, you will receive SOTAURIC as a long-term treatment, possibly lasting for months or years.

If you have any questions about how long to take SOTAURIC, talk to your doctor or pharmacist.

If you take more SOTAURIC than you should

If you take more capsules than you should, or if someone else takes your medicine, talk to a doctor or go to a hospital straight away, taking the pack with you, as medical treatment may be necessary.

If you forget to take SOTAURIC

If you forget to take SOTAURIC, skip the missed dose and take your next dose at the usual time. Do not take a double dose to make up for a forgotten dose. Instead, wait until it is time for your next dose.

If you stop taking SOTAURIC

Stopping your treatment with SOTAURIC may cause your condition to become worse. Do not stop taking your medicine unless your doctor tells you to do so.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

SOTAURIC can cause side effects.

Stop taking SOTAURIC and tell your doctor straight away if you notice any of the following as these could be signs of an allergic reaction:

- difficulty breathing or swallowing;
- dizziness;
- swelling of the face, lips, tongue or throat;
- severe itching of the skin, with red rash or raised bumps.

Some side effects in patients with AML could be serious.

Tell your doctor, pharmacist or nurse straight away if you notice any of the following:

- weakness, spontaneous bleeding or bruising, frequent infections with signs such as fever, chills, sore throat or mouth ulcers (signs of a low level of blood cells);
- fever, cough with or without mucus, chest pain, trouble breathing or shortness of breath (signs of non-infectious interstitial lung disease or pneumonitis)

- severe shortness of breath, laboured and unusually rapid breathing, dizziness, light headedness, confusion and extreme tiredness (signs of acute respiratory distress syndrome);
- infections, fever, low blood pressure, decreased urination, rapid pulse, rapid breathing (signs of sepsis or neutropenic sepsis).

Other possible side effects in patients with AML

Other side effects include those listed below. If any of these side effects become severe, tell your doctor or pharmacist.

Most of the side effects are mild to moderate and will generally disappear after a few weeks of treatment.

Frequent (may affect more than 1 in 10 people)

- infection at catheter site;
- red or purple, flat, pinhead spots under the skin (petechiae);
- problems falling asleep (insomnia);
- headache;
- shortness of breath, laboured breathing (dyspnoea);
- abnormal electrocardiogram (QT prolongation);
- dizziness, light headedness (low blood pressure);
- nose bleeds;

- throat pain (laryngeal pain);
- mouth sores (stomatitis);
- nausea, vomiting;
- upper abdominal pain;
- haemorrhoids (piles);
- excessive sweating;
- skin rash with flaking or peeling (exfoliative dermatitis);
- back pain;
- joint pain (arthralgia);
- fever;
- thirst, high urine output, dark urine, dry flushed skin (signs of high levels of sugar in the blood, known as hyperglycaemia);
- muscle weakness, drowsiness, confusion, convulsions, impaired consciousness;
- muscle weakness, muscle spasms, abnormal heart rhythm (signs of low levels of potassium in the blood, known as hypokalaemia);
- bruising and bleeding (defect in blood clotting);
- abnormal blood test results which can indicate to your doctor how well certain parts of your body are functioning: high levels of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (indicative of liver function).

Less frequent (may affect up to 1 in every 10 people)

- upper respiratory tract infection;

- nausea, vomiting, constipation, stomach pain, frequent urination, thirst, muscle weakness and twitching (signs of high levels of calcium in the blood, known as hypercalcaemia);
- fainting;
- involuntary shaking of the body;
- headache, dizziness (high blood pressure);
- fast heart beat (sinus tachycardia);
- collection of fluid around the heart, which, if severe, can decrease the heart's ability to pump blood (pericardial effusion);
- fluid collection in the lungs/chest cavity, which, if severe, could make you breathless (pleural effusion);
- sore throat and a runny nose;
- swelling of the eyelid;
- discomfort in the anus and rectum;
- abdominal pain, nausea, vomiting, constipation (abdominal discomfort);
- dry skin;
- eye pain, blurred vision, intolerance to light (keratitis);
- neck pain;
- bone pain;
- pain in limbs;
- increased weight;
- blood clotted in the catheter;

- abnormal blood test results which can indicate to your doctor how well certain parts of your body are functioning: high levels of uric acid.

Not known (frequency cannot be estimated from the available data)

- Raised, painful, red to dark reddish-purple skin patches or sores that appear mainly on the limbs, face and neck, with a fever (signs of acute febrile neutrophilic dermatosis or Sweet syndrome)

Some side effects in patients with ASM, SM AHN and MCL could be serious.

Tell your doctor, pharmacist or nurse straight away if you notice any of the following:

- weakness, spontaneous bleeding or bruising, frequent infections with signs such as fever, chills, sore throat or mouth ulcers (signs of a low level of blood cells);
- fever, cough, difficult or painful breathing, wheezing, chest in pain when breathing (signs of pneumonia);
- infections, fever, dizziness, light headedness, decreased urination, rapid pulse, rapid breathing (signs of sepsis or neutropenic sepsis);
- vomiting of blood, black or bloody stools (signs of gastrointestinal bleeding).

Other possible side effects in patients with ASM, SM AHN and MCL

Other side effects include those listed below. If any of these side effects become severe, tell your doctor or pharmacist.

Frequent (may affect more than 1 in 10 people)

- urinary tract infection;
- upper respiratory tract infection;
- headache;
- dizziness;
- shortness of breath, laboured breathing (dyspnoea);
- cough;
- fluid collection in the lungs/chest cavity, which, if severe, could make you breathless (pleural effusion);
- nose bleeds;
- nausea, vomiting;
- diarrhoea;
- constipation;
- rapid weight gain, swelling of the limbs (calves, ankles);
- feeling very tired (fatigue);
- fever;
- thirst, high urine output, dark urine, dry flushed skin (signs of high levels of sugar in the blood, known as hyperglycaemia);
- yellow skin and eyes (sign of high bilirubin in the blood);
- abnormal blood test results which indicate possible problems with the pancreas (high levels of lipase or amylase) and liver (high levels of alanine aminotransferase (ALT) or spartate aminotransferase (AST)).

Less frequent (may affect up to 1 in every 10 people)

- involuntary shaking of the body;
- cough with phlegm, chest pain, fever (bronchitis);
- cold sores in the mouth due to viral infection (oral herpes);
- painful and frequent urination (cystitis);
- feeling of pressure or pain in the cheeks and forehead (sinusitis);
- red, swollen painful rash on any part of the skin (erysipelas);
- shingles (herpes zoster);
- disturbance in attention;
- feeling dizzy with spinning sensation (vertigo);
- bruising (haematoma);
- upset stomach, indigestion;
- feeling weak (asthenia);
- chills;
- generalised swelling (oedema);
- increased weight;
- contusion (bruises);
- falls;
- dizziness, light headedness (low blood pressure);
- sore throat.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of SOTAURIC.

5. How to store SOTAURIC

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and the blister foil after EXP. The expiry date refers to the last day of that month.
- Store at or below 30 °C.
- Store in the original container in order to protect from moisture.
- Do not use this medicine if you notice any damage to the packaging or if there are any signs of tampering.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What SOTAURIC contains

- The active substance is midostaurin. Each soft capsule contains 25 mg midostaurin.
- The other ingredients are: macrogolglycerol hydroxystearate, gelatin, macrogol, glycerol, ethanol anhydrous, maize oil mono-di-triglycerides, titanium dioxide (E171), all-rac-alpha-tocopherol, iron oxide yellow (E172), iron oxide red (E172), carmine (E120), hypromellose, propylene glycol, purified water.

What SOTAURIC looks like and contents of the pack

SOTAURIC 25 mg soft capsules are pale orange, oblong capsules with red imprint “PKC NVR”.

The capsules are provided in blisters and are available in packs containing 28, 56 or 112 soft capsules.

Not all pack sizes and types may be marketed.

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