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

Scemblix® 20 mg
Scemblix® 40 mg
Film-coated tablets

Active ingredient
Scemblix 20 mg: each film-coated tablet contains asciminib hydrochloride, equivalent to asciminib 20 mg.
Scemblix 40 mg: each film-coated tablet contains asciminib hydrochloride, equivalent to asciminib 40 mg

Inactive ingredients and allergens in the medicine - see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.
Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your 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 to yours.

1. What is this medicine intended for?
For the treatment of adult patients with:
- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs)
- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) with the T315I mutation.

Therapeutic group: Antineoplastic agents, tyrosine kinase inhibitors (TKIs)

2. Before using this medicine
Do not use this medicine if:
- You are sensitive (allergic) to the active ingredient asciminib or to any of the other ingredients in this medicine (see section 6).

Special warnings about using this medicine
Before starting treatment with Scemblix, tell your doctor about all of your medical conditions, including if:
- You have a low blood cell count (myelosuppression)
- You have previously had inflammation of the pancreas (pancreatitis) and/or increased levels of enzymes called amylase and lipase in the blood
- You have high blood pressure (hypertension)
- You have allergic reactions (hypersensitivity)
- You have previously had heart problems or blood clots in arteries and veins (types of blood vessels)
- You are pregnant or plan to become pregnant
- You are breastfeeding or plan to breastfeed

See section 4 'Side effects' and section 2 'Pregnancy, breastfeeding and fertility'.

Children and adolescents
Scemblix is not indicated for use in children and adolescents under 18 years of age.
There is no information regarding the safety and efficacy of this medicine in children and adolescents.

Tests and follow-up
During treatment with Scemblix, you will undergo periodic blood tests and blood pressure checks.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

Effect of other medicines on Scemblix
Strong CYP3A4 inhibitors
Giving Scemblix in combination with a strong CYP3A4 inhibitor (e.g. clarithromycin, telithromycin, telaprevir, itraconazole, ketoconazole, voriconazole, ritonavir, indinavir, nelfinavir or saquinavir) increases asciminib levels in the blood, which may increase the risk of side effects. In case of treatment with Scemblix at 200 mg twice daily combined with a strong CYP3A4 inhibitor, the doctor will need to closely monitor you for side effects.

Itraconazole oral solution containing hydroxypropyl-β-cyclodextrin
Giving Scemblix in combination with an itraconazole oral solution containing hydroxypropyl-β-cyclodextrin decreases asciminib levels in the blood, which may reduce Scemblix efficacy. Avoid combined use of Scemblix at all recommended doses with itraconazole oral solution containing hydroxypropyl-β-cyclodextrin.

Effect of Scemblix on other medicines
Certain CYP3A4 substrates
Giving Scemblix in combination with CYP3A4 substrates (e.g. fentanyl, alfentanil, dihydroergotamine, or ergotamine) increases the levels of certain CYP3A4 substrates in the blood, which may increase the risk of side effects of these substrates.
In case of treatment with Scemblix at 80 mg daily dose combined with certain CYP3A4 substrates, where minimal concentration changes may lead to serious side effects, the doctor will need to closely monitor you for side effects.
Avoid combined use of Scemblix at 200 mg twice daily with certain CYP3A4 substrates, where minimal concentration changes may lead to serious side effects.

CYP2C9 substrates
Giving Scemblix in combination with CYP2C9 substrates (e.g. phenytoin or warfarin) increases the levels of certain CYP2C9 substrates in the blood, which may increase the risk of side effects. Avoid treatment with Scemblix at 80 mg daily dose combined with certain CYP2C9 substrates, where minimal concentration changes may lead to serious side effects. If combined treatment cannot be avoided, the doctor will instruct you to reduce the dosage of the CYP2C9 substrates.
Avoid combined use of Scemblix at 200 mg twice daily with sensitive CYP2C9 substrates and certain CYP2C9 substrates, where minimal concentration changes may lead to serious side effects. If combined treatment cannot be avoided, the doctor will instruct you to consider alternative therapy with a non-CYP2C9 substrate.

Certain P-gp substrates
Giving Scemblix in combination with P-gp substrates (e.g. digoxin) increases the levels of P-gp substrates in the blood, which may increase the risk of side effects of these substrates.
In case of treatment with Scemblix at 80 mg daily dose combined with P-gp substrates, the doctor will need to closely monitor you for side effects.

Substrates of OATP1B or BCRP
Giving Scemblix in combination with OATP1B and BCRP substrates (e.g. sulfasalazine, methotrexate, pravastatin, atorvastatin, pitavastatin, rosuvastatin and simvastatin) increases the level of OATP1B and BCRP substrates in the blood, which may increase the risk of adverse reactions of these substrates.
Avoid combined use of Scemblix at all recommended doses with rosuvastatin and atorvastatin.
For other OATP1B and BCRP substrates, if combined treatment with Scemblix at all recommended doses cannot be avoided, the doctor will need to closely monitor you for side effects and may instruct you to reduce the dosage of OATP1B and BCRP substrates as recommended in their leaflets.

Using this medicine and food
Take Scemblix without food. **Avoid eating** for at least 2 hours before and 1 hour after taking Scemblix.

Pregnancy, breastfeeding and fertility
Pregnancy
Tell your doctor if you are pregnant or plan to become pregnant. Scemblix can harm your unborn baby.
- Your doctor will perform a pregnancy test before you start treatment with Scemblix.
- **Females** who are able to become pregnant should use effective birth control during treatment and for 1 week after the last dose of Scemblix. Talk to your doctor about birth control methods that may be right for you.
- Tell your doctor right away if you become pregnant or think you may be pregnant during treatment with Scemblix.

Breastfeeding
Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Scemblix passes into breast milk. Do not breastfeed during treatment and for 1 week after the last dose of Scemblix.

Fertility
Scemblix may cause fertility problems in females. This may affect your ability to become pregnant. Talk to your doctor if this is a concern for you.

Driving and using machines
Asciminib has no or negligible effect on the ability to drive and operate machines.
If you experience dizziness, fatigue or other side effects which may affect the ability to drive carefully or use machines after taking the medicine, avoid these activities until the effect disappears.

Important information about some of this medicine's ingredients
Scemblix contains lactose
If you have been told by your doctor that you have an intolerance to certain sugars, contact your doctor before taking this medicine.
Scemblix contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

The standard regular dosage in patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) is:
80 mg once a day at regular time or 40 mg twice a day at intervals of about 12 hours.

The standard regular dosage in patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) with the T315I mutation is:
200 mg twice a day at intervals of about 12 hours.

Take Scemblix without food. **Avoid eating** for at least 2 hours before and 1 hour after taking Scemblix.

Do not change your dosage or schedule or stop taking Scemblix unless your doctor tells you to.
Your doctor may change your dosage or temporarily or permanently stop the treatment if you have certain side effects.

Do not exceed the recommended dose.
Swallow Scemblix tablets whole. **Do not** break, crush, or chew Scemblix tablets.

If you have accidentally taken a higher dose
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
- If you take Scemblix **once a day** and miss a dose by more than 12 hours, skip the missed dose and take the next dose at the regular time.
- If you take Scemblix **twice a day** and miss a dose by more than 6 hours, skip the missed dose and take the next dose at the regular time.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects
Like with all medicines, using Scemblix may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Scemblix may cause serious side effects, including:
- **Low blood cell counts.** Scemblix may cause low platelet counts (thrombocytopenia), low white blood cell counts (neutropenia), and low red blood cell counts (anemia). Your doctor will perform blood tests to check your blood cell counts every 2 weeks for the first 3 months of treatment, and then monthly or as needed during treatment with Scemblix. Tell your doctor right away if you have unexpected bleeding or easy bruising, notice blood in urine or stool, have fever or any signs of infection.
- **Pancreas problems.** Scemblix may cause increased levels of enzymes called amylase and lipase in the blood, which may be a sign of pancreatitis. Your doctor may perform blood tests monthly or as needed during treatment with Scemblix to diagnose pancreas problems. Tell your doctor right away if you have sudden pain or discomfort in the stomach area, nausea or vomiting.
- **High blood pressure.** Your doctor may check your blood pressure and treat high blood pressure during treatment with Scemblix as needed. Tell your doctor if you develop elevated blood pressure or symptoms of high blood pressure, including confusion, headaches, dizziness, chest pain or shortness of breath.
- **Allergic reaction.** Stop taking Scemblix and get medical help right away if you develop any signs or symptoms of an allergic reaction, including:
  - difficulty breathing or swallowing
  - swelling of the face, lips, or tongue
  - skin rash or flushing of the skin
  - feeling dizzy or faint
  - fever
  - fast heartbeat
- **Heart and blood vessel (cardiovascular) problems.** Scemblix may cause heart and blood vessel problems, including heart attack, stroke, blood clots or blockage of arteries, heart failure and abnormal heartbeat, which can be serious and may sometimes lead to death. These heart and blood vessel problems can occur in people with risk factors or a history of these problems, and/or in people previously treated with other TKI medicines. Your doctor may monitor you for heart and blood vessel problems and treat you as needed during treatment with Scemblix. Tell your doctor or get medical help right away if you develop:
  - shortness of breath
  - chest pain or pressure
  - feeling like your heart is beating too fast or you feel abnormal heartbeats
  - swelling of the ankles or feet
  - dizziness
  - weight gain
  - numbness or weakness on one side of the body
  - decreased vision or loss of vision
  - trouble talking
  - pain in the arms, legs, back, neck or jaw
  - headache
  - severe stomach-area pain
- **Fever**
- **Urinary tract infection**
- **Headache**
- **Abdominal pain**
- **Vomiting**
- **Lung infection (pneumonia)**
- **Muscle, bone, or joint pain**
- **Bleeding**
- **Constipation**
- **Chest pain, cough, hiccups, rapid breathing, fluid collection between the lungs and chest cavity which, if severe, could make you breathless (pleural effusion)**

The most common side effects of Scemblix include (affect one or more in 10 users):
- Nose, throat or sinus (upper respiratory tract) infections
- Muscle, bone, or joint pain
- Headache
- Tiredness
- Nausea
- Rash
- Diarrhea
- Vomiting
- Bleeding
- Joint pain (arthralgia)
- Generalized swelling (edema)
- Itching
- Cough
- High blood pressure (Hypertension)
- Abdominal pain

Hematology
- Decreased platelet counts, white blood cell counts and red blood cell counts

Biochemistry
- Increased blood fat (triglycerides, cholesterol) levels
- Increased blood creatine kinase levels
- Increased blood liver enzyme levels
- Increased blood pancreas enzyme (amylase and lipase) levels
- Increased blood uric acid levels
- Decreased phosphate levels
- Decreased corrected calcium levels
- Increased blood creatinine levels
- Increased blood alkaline phosphatase levels
- Increased blood bilirubin levels
- Increased or decreased blood potassium levels

Additional side effects include:
- Heart failure
- Fever
- Urinary tract infection
- Lung infection (pneumonia)
- Constipation
- Abnormal heartbeat, including changes in the electrical activity of the heart (arrhythmia, including prolonged QT in ECG)
- Chest pain, cough, hiccups, rapid breathing, fluid collection between the lungs and chest cavity which, if severe, could make you breathless (pleural effusion)
- Shortness of breath, labored breathing
- Dizziness
- High levels of fats/lipids (dyslipidemia)
- Decreased appetite
- Itchy rash (urticaria)
- Lung and bronchi (lower respiratory tract) infection
- Flu (influenza)
- Feeling of fast and hard heartbeats (palpitations)
- Vision blurred
- Dry eye
- Underactive thyroid gland with possible weight gain, fluid retention, constipation, sensitivity to cold (hypothyroidism)
- Fever above 38°C associated with a low level of white blood cells (febrile neutropenia)
- Pancreas inflammation (pancreatitis)
- Nerve damage (neuropathy peripheral)
- Hypersensitivity

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

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

5. How to store the medicine?
- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package and blister. The expiry date refers to the last day of that month.
- **Storage conditions:** Do not store above 25°C. Store in the original package in order to protect from moisture.

6. Additional information
In addition to the active ingredient, this medicine also contains:
Core-tablet: microcrystalline cellulose (E460i), hydroxypropylcellulose, low-substituted (E463),croscarmellose sodium (E468), polyvinyl alcohol-part hydrolyzed (E1203), titanium dioxide (E171), magnesium stearate, talc (E553b), colloidal silicon dioxide, lecithin (E522), xanthan gum (E415), iron oxide red (E172)

In addition, 20 mg film-coated tablets contain:
iron oxide yellow (E172)

In addition, 40 mg film-coated tablets contain:
iron oxide black (E172)

See section 2 under 'Important information about some of this medicine's ingredients'.

What the medicine looks like and contents of the pack:
Scemblix 20 mg: round, unscored, bicnvex with beveled edges, pale yellow, approximately 6.2 mm diameter film-coated tablet. Each tablet is debossed with '20' on one side and the 'Novartis' logo on the other side.
Scemblix 40 mg: round, unscored, bicnvex with beveled edges, violet white, approximately 8.2 mm diameter film-coated tablet. Each tablet is debossed with '40' on one side and the 'Novartis' logo on the other side.

Each package contains 20 or 60 film-coated tablets.
Not all pack sizes may be marketed.

Registration holder and importer and its address: Novartis Israel Ltd., P.O.B. 7126, Tel Aviv.

Revised in December 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Scemblix 20 mg: 172-84-37483-99
Scemblix 40 mg: 172-85-37484-99