# Scemblix® (asciminib)

## Scemblix® (pronounced: Sem-blix) (asciminib) introduces a novel mechanism of action to the treatment of Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP).

Scemblix is indicated for the treatment of adult patients with[1]:

- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs)*

  **This indication is approved under the US FDA Accelerated Approval Program based on major molecular response (MMR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).*

- Ph+ CML in CP with the T315I mutation

Despite significant advances in CML care over the last few decades, many patients remain at risk of disease progression, and the sequential use of currently available TKIs is associated with treatment resistance and/or intolerance[2-6]. Moreover, some patients with CML develop mutations that cause resistance to TKI therapy – including the T315I mutation – representing a significant clinical challenge[7].

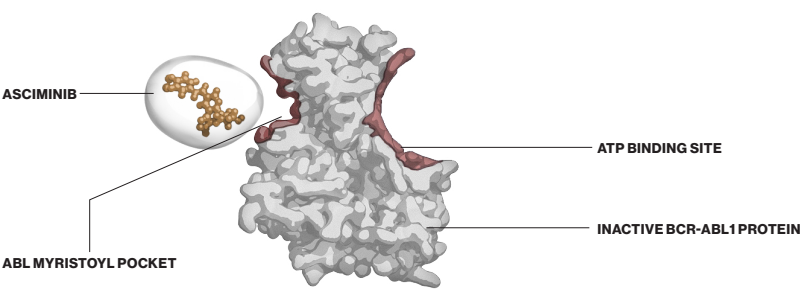
As the first FDA-approved treatment that binds to the ABL myristoyl pocket, Scemblix offers a different approach for treating Ph+ CML-CP[1,8,9].

## Mechanism of action

Scemblix is the first FDA-approved CML treatment that binds to the ABL myristoyl pocket[1,8,9]. This novel mechanism of action, also known in scientific literature as a STAMP inhibitor, may help address resistance in patients with CML previously treated with two or more TKIs and overcome mutations at the defective *BCR-ABL1* gene, which is associated with the over-production of leukemic cells [8-17].

Scemblix has been shown to limit off-target activity in pre-clinical studies[10].

**The ABL myristoyl pocket is a binding site on *BCR-ABL1* distinct from the ATP binding site. Binding at this pocket is thought to help *BCR-ABL1* regain its ability to autoregulate cell growth[11,12].**




## Development

In August 2021, the US Food and Drug Administration (FDA) granted Priority Review to Novartis for Scemblix following its submission under the FDA's Real-Time Oncology Review program. Scemblix previously received Orphan Drug, Fast Track, and two Breakthrough Therapy designations.

Scemblix is being studied in several clinical trials in the hopes of helping patients across multiple treatment lines of CML[18-24].

| Trial Name | Indication | Estimated study completion timeline (2021 2022 2023 2024 2025 2028) |
|---|---|---|
| **Phase III study of efficacy of CML-CP patients treated with ABL001 versus bosutinib, previously treated with 2 or more TKIs (ASCEMBL) (NCT03106779)** | CML-CP | 2025 |
| **Phase III study of oral ABL001 versus other TKIs in adult patients with newly diagnosed Ph+ CML-CP (ASC4FIRST) (NCT04971226)** | Ph+ CML-CP | 2028 |
| **Phase II study of efficacy and safety of ABL001 in combination with imatinib in patients with chronic myeloid leukemia in chronic phase (NCT03578367)** | CML-CP | 2022 |
| **Phase I study of oral ABL001 in patients with CML or Ph+ ALL (NCT02081378)** | CML (T315I mutation) and Ph+ ALL | 2024 |
| **Phase II study of ABL001 versus best available therapy in Chinese patients with CML-CP (NCT04795427)** | CML-CP | 2025 |
| **Phase IIIb study of ABL001 monotherapy in previously treated patients with chronic myeloid leukemia in chronic phase (CML-CP) with and without T315I mutation (NCT04666259)** | CML-CP with and without T315I mutation | 2023 |
| **Phase IIIb optimization study of asciminib in patients with chronic myelogenous leukemia in chronic phase (CML-CP) previously treated with 2 or more tyrosine kinase inhibitors (NTC04948333)** | CML-CP | 2025 |

## Novartis' commitment to CML

Novartis has a long-standing scientific commitment to patients living with CML. For more than 20 years, our bold science has helped transform CML into a chronic disease for many patients. We research ways to target the disease, seeking to address the remaining challenges with treatment resistance and/or intolerance that many patients face. Novartis also continues to reimagine CML care through its commitment to sustainable access for patients and collaboration with the global CML community.

**Indications**

SCEMBLIX® (asciminib) tablets is a prescription medicine used to treat adults with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with 2 or more tyrosine kinase inhibitor (TKI) medicines. The effectiveness of SCEMBLIX in these patients is based on a study that measured major molecular response (MMR) rates. No clinical information is available to show if these patients treated with SCEMBLIX live longer or if their symptoms improve. Ongoing studies exist to find out how SCEMBLIX works over a longer period of time.

SCEMBLIX is also approved for use in adults with Ph+ CML in CP with the T315I mutation.

It is not known if SCEMBLIX is safe and effective in children.

**Important Safety Information**

SCEMBLIX® (asciminib) tablets may cause low platelet counts (thrombocytopenia), low white blood cell counts (neutropenia), and low red blood cell counts (anemia). Patients should tell their doctor right away if they have unexpected bleeding or easy bruising; blood in their urine or stools; fever; or any signs of an infection. SCEMBLIX may increase enzymes in the patient's blood called amylase and lipase, which may be a sign of inflammation of the pancreas (pancreatitis). Patients should tell their doctor right away if they have sudden stomach-area pain or discomfort, nausea, or vomiting. During treatment with SCEMBLIX, doctors may check their patients' blood pressure and treat any high blood pressure as needed. Patients should tell their doctor if they develop elevated blood pressure or symptoms of high blood pressure including confusion, headaches, dizziness, chest pain, or shortness of breath.

If a patient has an allergic reaction while on SCEMBLIX, they should stop taking SCEMBLIX and get medical help right away. Signs or symptoms of an allergic reaction include trouble breathing or swallowing; feeling dizzy or faint; swelling of the face, lips, or tongue; fever; skin rash or flushing; or a fast heartbeat. SCEMBLIX may cause heart and blood vessel problems, including heart attack; stroke; blood clots or blockage of patient's arteries; heart failure; and abnormal heartbeat which can be serious and may sometimes lead to death. These heart and blood vessel problems can happen in people with risk factors or a history of these problems and/or previously treated with multiple TKI medicines. Patients should tell their doctor right away if they get shortness of breath; chest pain or pressure; a feeling like their heart is beating too fast or they feel abnormal heartbeats; swelling in their ankles or feet; dizziness; weight gain; numbness or weakness on one side of their body; decreased vision or loss of vision; trouble talking; pain in their arms, legs, back, neck, or jaw; headache; or severe stomach-area pain.

Before taking SCEMBLIX, patients should tell their doctor about all of their medical conditions, including if they have a history of pancreatitis; a history of heart problems; or blood clots in their arteries and veins (types of blood vessels). SCEMBLIX can harm an unborn baby. Women should tell their doctor right away if they become pregnant or think they may be pregnant during treatment with SCEMBLIX. Women who are able to become pregnant should have a pregnancy test before they start SCEMBLIX and should use effective birth control during treatment and for 1 week after the last dose of SCEMBLIX. Women should not breastfeed during treatment and for 1 week after their last dose of SCEMBLIX.

Patients should tell their doctor about all the medicines they take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements. SCEMBLIX and other medicines may affect each other, causing side effects. The most common side effects of SCEMBLIX include nose, throat, or sinus (upper respiratory tract) infections; muscle, bone, or joint pain; rash; tiredness; nausea; and diarrhea. The most common blood test abnormalities include decreased blood counts of platelets, white blood cells, and red blood cells; and increased blood levels of triglycerides, creatine kinase, liver enzymes, or pancreas enzymes (amylase and lipase).

Please see full Prescribing Information for SCEMBLIX, available at https://www.novartis.us/sites/www.novartis.us/files/scemblix.pdf.

**References:**

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NOVARTIS

**Novartis Pharma AG**
CH-4002 Basel Switzerland

10/21 146494

**Novartis Pharmaceuticals Corporation**
East Hanover, New Jersey 07936-1080