

FDA approves Novartis Scemblix® (asciminib), with novel mechanism of action for the treatment of chronic myeloid leukemia

Nov 01, 2021

- Scemblix provides much-needed and long-awaited new option for patients with chronic myeloid leukemia (CML) who suffer with intolerance or inadequate response after at least two previous tyrosine kinase inhibitor (TKI) treatments¹
- In the pivotal Phase III ASCEMBL trial, Scemblix demonstrated significant and clinically meaningful superiority in major molecular response (MMR) rate vs. Bosulif®* (bosutinib) (25% vs. 13%) at 24 weeks, and more than three times lower discontinuation rates due to side effects (7% vs. 25%)^{2,3}
- Additional Phase I data in patients with CML with the T315I mutation supported the FDA approval for a second indication in this patient population⁴
- With a new mechanism of action known in scientific literature as a STAMP inhibitor and clinical trials across treatment lines - including in the first-line setting -, Scemblix reinforces Novartis' two-decade commitment to bring transformative therapies to people living with CML²⁻¹⁸

EAST HANOVER, N.J., Nov. 1, 2021 - Novartis announced today that the US Food and Drug Administration (FDA) approved Scemblix® (asciminib) for the treatment of chronic myeloid leukemia (CML) in two distinct indications. The FDA granted Scemblix accelerated approval for adult patients with Philadelphia chromosome-positive CML in chronic phase (Ph+ CML-CP), previously treated with two or more tyrosine kinase inhibitors (TKIs), based on major molecular response (MMR) rate at 24 weeks; and full approval for adult patients with Ph+ CML-CP with the T315I mutation¹. In accordance with the Accelerated Approval Program, continued approval for the first indication may be contingent upon verification and description of clinical benefit from confirmatory evidence¹. Scemblix is the first FDA-approved CML treatment that works by binding to the ABL myristoyl pocket and represents an important development for patients who experience resistance and/or intolerance to currently available TKI therapies¹⁻³. Also known as a STAMP inhibitor in scientific literature, Scemblix is being studied across multiple treatment lines for CML-CP, including the ASC4FIRST Phase III study evaluating Scemblix as a first-line treatment²⁻¹⁸.

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"The introduction of TKIs twenty years ago revolutionized treatment for CML; however, there remain many patients who do not respond adequately to at least two available treatments and often experience challenging side effects that add a burden to their daily lives," said Lee Greenberger, Chief Scientific Officer at The Leukemia & Lymphoma Society. "The approval of Scemblix may offer hope to patients by addressing gaps in CML care."

For many patients, current treatment for CML may be limited by intolerance or resistance, and sequential use of available TKIs is associated with increased failure rates¹⁹⁻²⁶. In an analysis of patients with CML treated

with two prior TKIs, approximately 55% reported intolerance to previous treatment²⁷. Additionally, a pooled analysis in the second-line setting showed that up to 70% of patients are unable to achieve major molecular response (MMR) within two years of follow-up²⁸⁻³⁰. Moreover, patients who develop the T315I mutation are resistant to most available TKIs, leaving them at an increased risk of disease progression⁴.

"CML can be difficult to treat when currently available treatments fail patients, when treatment side effects cannot be tolerated, or sometimes both," expressed Dr. Michael J. Mauro**, Hematologist and Myeloproliferative Neoplasms Program Leader at Memorial Sloan Kettering Cancer Center (MSK). "The addition of Scemblix into the CML treatment landscape gives us a novel approach to combat this blood cancer, helping address clinical challenges in patients struggling after switching to a second treatment, as well as in patients who develop the T315I mutation and face significantly worse outcomes."

The FDA approval of Scemblix is based on results from the Phase III ASCEMBL trial and a Phase I (NCT02081378) study that included patients with Ph+ CML-CP with the T315I mutation.

In patients with Ph+ CML-CP who had experienced resistance or intolerance to at least two TKIs, the ASCEMBL trial showed that¹⁻³:

- Scemblix nearly doubled the MMR rate vs. Bosulif® (bosutinib)* at 24 weeks (25% vs. 13% [P=0.029])
- The proportion of patients who discontinued treatment due to adverse reactions was more than three times lower in the Scemblix arm (n = 156) vs. patients in the Bosulif arm (n = 76) (7% vs. 25%)
- The most common (incidence ≥ 20%) adverse reactions and laboratory abnormalities in the Scemblix arm were, respectively: upper respiratory tract infections and musculoskeletal pain; decrease in platelet and neutrophil counts, decrease in hemoglobin; increase in triglycerides, creatine kinase and alanine aminotransferase (ALT)

"After more than two decades of reimagining CML care, we continue to boldly push the boundaries of innovation to transform the standard-of-care and help even more patients living with this disease," said Susanne Schaffert, PhD, President, Novartis Oncology. "We would like to thank all those who have been involved in helping to advance this new and important breakthrough."

Scemblix is currently available for physicians to prescribe to appropriate patients in the US.

Additional efficacy and safety details for Scemblix, including data on patients with the T315I mutation, and full Prescribing Information can be found at

<https://www.novartis.us/sites/www.novartis.us/files/scemblix.pdf>.

About Scemblix® (asciminib)

Scemblix (asciminib) is indicated for the treatment of adult patients with Ph+ CML-CP pre-treated with two or more TKIs, as well as adult patients with Ph+ CML-CP with the T315I mutation¹. The first indication is approved under the US FDA Accelerated Approval Program based on MMR rate at 24 weeks; continued approval for the first indication may be contingent upon verification and description of clinical benefit from confirmatory evidence.

Scemblix is the first FDA-approved CML treatment that binds to the ABL myristoyl pocket¹. 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 cells²⁻¹¹. Scemblix has also been shown

to limit off-target activity in pre-clinical studies³¹.

Novartis has initiated regulatory filings for Scemblix in multiple countries and regions across the globe.

Scemblix represents an important development for patients who experience resistance and/or intolerance to currently available TKI therapies, and it is being studied across multiple treatment lines for CML-CP²⁻¹⁸. Specifically, the ASC4FIRST Phase III study (NCT04971226) evaluates Scemblix as a first-line treatment and is in the recruitment phase¹³.

About 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. Despite these advancements, we're not standing still. We continue to research ways to target the disease, seeking to address the 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.

Indication

SCSEMBLIX[®] (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 SCSEMBLIX 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 SCSEMBLIX live longer or if their symptoms improve. Ongoing studies exist to find out how SCSEMBLIX works over a longer period of time.

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

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

Important Safety Information

SCSEMBLIX[®] (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. SCSEMBLIX 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 SCSEMBLIX, 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 SCSEMBLIX, they should stop taking SCSEMBLIX 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. SCSEMBLIX 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>.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 15,000 people in the United States. For more information, please visit <https://www.novartis.us>.

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