SAFETY, DOSING, AND ADMINISTRATION

SCEMBLIX®
(asciminib) 20 mg, 40 mg tablets

INDICATIONS

SCEMBLIX is indicated for the treatment of adult patients with:

- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with 2 or more tyrosine kinase inhibitors (TKIs)
- Ph+ CML in CP with the T315I mutation

IMPORTANT SAFETY INFORMATION for SCEMBLIX

Myelosuppression

- Thrombocytopenia, neutropenia, and anemia, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX
- Perform complete blood counts every 2 weeks for the first 3 months of treatment and monthly thereafter or as clinically indicated. Monitor patients for signs and symptoms of myelosuppression
- Based on the severity of thrombocytopenia and/or neutropenia, reduce dose, temporarily withhold, or permanently discontinue SCEMBLIX as described in the prescribing information

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

How to use this guide

1. This document summarizes the starting doses and safety profile of SCEMBLIX and offers guidance on dose modification for management of adverse reactions
2. The presented adverse reaction-management strategies are designed to be a reference and are not intended to supersede your clinical judgment in managing individual patients
3. Not all adverse reactions associated with SCEMBLIX are discussed in this guide
4. An informational section entitled Patient Counseling has been included to help you reinforce important points to counsel patients about potential adverse reactions

IMPORTANT SAFETY INFORMATION for SCEMBLIX (cont)

Pancreatic Toxicity

- Pancreatitis (including grade 3 reactions) and asymptomatic elevation in serum lipase and amylase (including grade 3/4 elevations), have occurred in patients receiving SCEMBLIX
- Assess serum lipase and amylase levels monthly during treatment with SCEMBLIX, or as clinically indicated. Monitor patients for signs and symptoms of pancreatic toxicity. Perform more frequent monitoring in patients with a history of pancreatitis
- If lipase and amylase elevation are accompanied by abdominal symptoms, temporarily withhold SCEMBLIX and consider appropriate diagnostic tests to exclude pancreatitis
- Based on the severity of lipase and amylase elevation, reduce dose, temporarily withhold, or permanently discontinue SCEMBLIX as described in the prescribing information

Hypertension

- Hypertension, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX
- Monitor and manage hypertension using standard antihypertensive therapy during treatment with SCEMBLIX as clinically indicated
- For grade 3 or higher reactions, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of hypertension

SCEMBLIX overview

In ASCEMBL, a study for patients with Ph+ CML-CP, previously treated with ≥2 TKIs

- At Week 24, SCEMBLIX demonstrated 25% MMR rate (n=157) vs 13% (n=76) with bosutinib (difference[a]: 12% [95% CI, 2.2-22; *P*=0.029[b]])[1]*
- SCEMBLIX more than doubled the MMR rate at Week 96 vs bosutinib (38% vs 16%; difference[a]: 22% [95% CI, 11-33; *P*=0.001])[1]
- More patients achieved CCyR at Week 24 with SCEMBLIX vs bosutinib (41% vs 24%; 95% CI, 3.6-31)[1,c]
- More patients achieved MR4 and MR4.5 at Week 96 with SCEMBLIX vs bosutinib (17% vs 11% and 11% vs 5%, respectively)[2]

ASCEMBL study design[1]

- Multicenter, 2:1 randomized (stratified by MCyR status), active-controlled, and open-label study for the treatment of 233 adults with Ph+ CML-CP, previously treated with 2 or more TKIs
- 157 patients received SCEMBLIX at 40 mg bid and 76 patients received bosutinib at 500 mg qd until unacceptable toxicity or treatment failure occurred
- The median duration of treatment was 24 months (range: 0 to 46 months) for patients receiving SCEMBLIX and 7 months (range: 0 to 43 months) for patients receiving bosutinib

In X2101, a study for patients with Ph+ CML-CP with the T315I mutation[1]

- By 24 weeks, 42% of patients (n=45) with Ph+ CML-CP with the T315I mutation who received SCEMBLIX at a dose of 200 mg bid achieved MMR (95% CI, 28–58)

X2101 study design in patients with Ph+ CML-CP with the T315I mutation[1]

- A multicenter, open-label study where efficacy was based on 45 patients with Ph+ CML-CP with the T315I mutation who received SCEMBLIX at a dose of 200 mg bid. Patients continued treatment until unacceptable toxicity or treatment failure occurred
- The median duration of treatment was 108 weeks (range: 2 to 215 weeks)

bid, twice daily; CCyR, complete cytogenetic response; CML, chronic myeloid leukemia; MCyR, major cytogenetic response; MMR, major molecular response; Ph+, Philadelphia chromosome-positive; qd, once daily; TKIs, tyrosine kinase inhibitors.
MMR was defined as *BCR::ABL1*^{IS} ≤0.1%.[1]
CCyR was defined as 0% of Philadelphia chromosome–positive metaphases in bone marrow aspirate with at least 20 examined.[1]
MCyR is defined as 0% to 35% Ph+ metaphases.[2]
MR4 is defined as *BCR::ABL*^{IS} ≤0.01%.[3]
MR4.5 is defined as *BCR::ABL*^{IS} ≤0.0032%.[3]
*Primary end point.
[a]Estimated using a common risk difference stratified by baseline MCyR status.
[b]Estimated using a Cochran-Mantel-Haenszel 2-sided test stratified by baseline MCyR status.
[c]CCyR analysis based on patients who were not in CCyR at baseline.

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

SCEMBLIX® (asciminib) 20 mg, 40 mg tablets

SCEMBLIX has a well-established tolerability profile over time in ASCEMBL[1]

All-grade adverse reactions (occurring in ≥10% of patients in any treatment arm) at the Week 96 analysis[1]

	SCEMBLIX (n=156)		Bosutinib (n=76)	
Adverse reaction	**All grades %**	**Grade 3 or 4 %**	**All grades %**	**Grade 3 or 4 %**
URTI[a]	26	0.6	12	1.3
Musculoskeletal pain[b]	24	2.6	17	1.3
Headache[c]	21	1.9	16	0
Fatigue[d]	20	0.6	11	1.3
Rash[e]	18	0.6	30	8
Hypertension[f]	14	7	5	3.9
Abdominal pain[g]	14	0	24	2.6
Diarrhea[h]	13	0	72	11
Arthralgia	13	0.6	3.9	0
Nausea	12	0.6	46	0

Serious adverse reactions occurred in 18% of patients who received SCEMBLIX. Serious adverse reactions in ≥1% included cardiac failure congestive (1.9%), pyrexia (1.9%), urinary tract infection (1.9%), headache (1.3%), and thrombocytopenia (1.3%). Two patients (1.3%) had a fatal adverse reaction, one each for mesenteric artery thrombosis and ischemic stroke.[1]

URTI, upper respiratory tract infection.
[a]Upper respiratory tract infection includes: nasopharyngitis, upper respiratory tract infection, rhinitis, pharyngitis, respiratory tract infection, and pharyngotonsillitis.
[b]Musculoskeletal pain includes: pain in extremity, back pain, myalgia, non-cardiac chest pain, neck pain, bone pain, spinal pain, arthritis, musculoskeletal pain, and musculoskeletal chest pain.
[c]Headache includes: headache and post-traumatic headache.
[d]Fatigue includes: fatigue and asthenia.
[e]Rash includes: rash, rash maculopapular, dermatitis acneiform, rash pustular, eczema, dermatitis, skin exfoliation, dermatitis exfoliative generalized, rash morbilliform, drug eruption, erythema multiform, and rash erythematous.
[f]Hypertension includes: hypertension and hypertensive crisis.
[g]Abdominal pain includes: abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower, abdominal tenderness, and epigastric discomfort.
[h]Diarrhea includes: diarrhea and colitis.

IMPORTANT SAFETY INFORMATION for SCEMBLIX (cont)

Hypersensitivity

- Hypersensitivity, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX. Reactions included rash, edema, and bronchospasm
- Monitor patients for signs and symptoms and initiate appropriate treatment as clinically indicated
- For grade 3 or higher reactions, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of hypersensitivity

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

Laboratory abnormalities in ASCEMBL

Select laboratory abnormalities (≥10%) that worsened from baseline at the Week 96 analysis[1]

	SCEMBLIX[a]		Bosutinib[a]	
Laboratory abnormality	**All grades %**	**Grade 3 or 4 %**	**All grades %**	**Grade 3 or 4 %**
Platelet count decreased	46	24	36	12
Triglycerides increased	44	5	30	2.6
Neutrophil count decreased	43	22	33	15
Hemoglobin decreased	37	2	54	5
Creatine kinase increased	30	2.6	24	5
ALT increased	26	0.6	50	16
Uric acid increased	21	6	18	2.6
AST increased	21	1.9	46	7
Lymphocyte count decreased	20	3.3	34	2.6
Phosphate decreased	18	6	20	7
Corrected Calcium decreased	16	0.6	22	0
Lipase increased	15	4.5	18	7
Creatinine increased	15	0	26	0
Amylase increased	13	1.3	13	0
ALP increased	13	0	12	0
Bilirubin increased	12	0	3.9	0
Cholesterol increased	12	0	8	0
Potassium decreased	11	0	9	0

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.
[a]The denominator used to calculate the rate for SCEMBLIX and bosutinib varied from 152 to 156 and 75 to 76, respectively, based on the number of patients with a baseline value and at least one post-treatment value.

SCEMBLIX safety data remained consistent between the Week 24 and Week 96 analyses.[2]

SCEMBLIX® (asciminib) 20 mg, 40 mg tablets

Safety profile in patients with the T315I mutation

All-grade adverse reactions (in ≥10% of patients)[1]	SCEMBLIX 200 mg bid (N=48)	
Adverse reaction	All grades %	Grade 3 or 4 %
Musculoskeletal pain[a]	42	4.2
Fatigue[b]	31	2.1
Nausea	27	0
Rash[c]	27	0
Diarrhea	21	2.1
Vomiting	19	6
Headache[d]	19	2.1
Abdominal pain[e]	17	8
Arthralgia	17	0
Hemorrhage[f]	15	2.1
Cough[g]	15	0
Hypertension[h]	13	8
Pruritus	13	0
URTI[i]	13	0
Edema	10	4.2

Select laboratory abnormalities (≥10%) that worsened from baseline[1]	SCEMBLIX[j] 200 mg bid	
Laboratory abnormality	All grades %	Grade 3 or 4 %
ALT increased	48	6
Potassium increased	48	2.1
Lipase increased	46	21
Triglycerides increased	46	2.1
Neutrophil count decreased	44	15
Hemoglobin decreased	44	4.2
Lymphocyte count decreased	42	4.2
Phosphate decreased	40	6
Uric acid increased	40	4.2
AST increased	35	2.1
Calcium corrected decreased	33	0
Creatinine increased	31	0
Amylase increased	29	10
Platelet count decreased	25	15
Bilirubin increased	23	0
Cholesterol increased	15	0
ALP increased	13	0

Serious adverse reactions occurred in 23% of patients who received SCEMBLIX. Serious adverse reactions in >1% included abdominal pain (4.2%), vomiting (4.2%), pneumonia (4.2%), musculoskeletal pain (2.1%), headache (2.1%), hemorrhage (2.1%), constipation (2.1%), arrhythmia (2.1%), and pleural effusion (2.1%).[1]

ALP, alkaline phosphatase.
[a]Musculoskeletal pain includes: pain in extremity, back pain, myalgia, musculoskeletal pain, noncardiac chest pain, bone pain, arthritis, and musculoskeletal chest pain.
[b]Fatigue includes: fatigue and asthenia.
[c]Rash includes: rash, rash maculopapular, dermatitis acneiform, eczema, rash papular, skin exfoliation, and dyshidrotic eczema.
[d]Headache includes: headache and migraine.
[e]Abdominal pain includes: abdominal pain and hepatic pain.
[f]Hemorrhage includes: epistaxis, ear hemorrhage, mouth hemorrhage, postprocedural hemorrhage, skin hemorrhage, and vaginal hemorrhage.
[g]Cough includes: cough and productive cough.
[h]Hypertension includes: hypertension and hypertensive crisis.
[i]URTI includes: upper respiratory tract infection, nasopharyngitis, rhinitis, and pharyngitis.
[j]The denominator used to calculate the rate was 48 based on the number of patients with a baseline value and at least one post-treatment value.

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

Dosing options to accommodate your patients[1]

Patients previously treated with ≥2 TKIs:

80 mg qd

There is also an option to take SCEMBLIX 40 mg tablets twice a day (AM + PM)

- Recommended dosage for patients who have the T315I mutation is 200 mg bid AM + PM

Patients should:

Avoid food consumption for at least 2 hours before and **1 hour after** taking SCEMBLIX[1]

Swallow SCEMBLIX whole—do not break, crush, or chew them[1]

SCEMBLIX is available as film-coated tablets: **20 mg** (6.2 mm diameter) and **40 mg** (8.2 mm diameter)[1]

Based on pharmacokinetic parameters studied in an exposure-response analysis, the predicted efficacy and safety profile of SCEMBLIX at the 80 mg qd dose is similar to that at the 40 mg bid dose.[4]

IMPORTANT SAFETY INFORMATION for SCEMBLIX (cont)

Cardiovascular Toxicity

- Cardiovascular toxicity (including ischemic cardiac and central nervous system conditions; and arterial thrombotic and embolic conditions) and cardiac failure have occurred in patients receiving SCEMBLIX. Some toxicities were grade 3/4 and 3 fatalities were reported
- Arrhythmia, including QTc prolongation, have occurred in patients receiving SCEMBLIX. Some of these arrhythmias were grade 3
- Monitor patients with a history of cardiovascular risk factors for cardiovascular signs and symptoms. Initiate appropriate treatment as clinically indicated
- For grade 3 or higher cardiovascular toxicity, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of cardiovascular toxicity

Embryo-Fetal Toxicity

- SCEMBLIX can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus if SCEMBLIX is used during pregnancy or if the patient becomes pregnant while taking SCEMBLIX

SCEMBLIX® (asciminib) 20 mg, 40 mg tablets

Dosage reductions

For the management of adverse reactions, reduce the SCEMBLIX dose as described in the table below

Recommended dosage reductions for SCEMBLIX for adverse reactions[1]

Dosage reduction	Dosage for patients with Ph+ CML-CP previously treated with ≥2 TKIs	Dosage for patients with Ph+ CML-CP who have the T315I mutation
First reduction	• **40 mg qd** OR • **20 mg bid**	**160 mg bid**
Subsequent reduction	Permanently discontinue SCEMBLIX in patients unable to tolerate **40 mg qd** OR **20 mg bid**	Permanently discontinue SCEMBLIX in patients unable to tolerate **160 mg bid**

IMPORTANT SAFETY INFORMATION for SCEMBLIX (cont)

Embryo-Fetal Toxicity (cont)

- Verify the pregnancy status of females of reproductive potential prior to starting treatment with SCEMBLIX. Advise females to use effective contraception during treatment and for at least 1 week after the last SCEMBLIX dose

ADVERSE REACTIONS

- Most common adverse reactions (≥20%) were upper respiratory tract infections, musculoskeletal pain, headache, fatigue, nausea, rash, and diarrhea
- Most common laboratory abnormalities (≥20%) were platelet count decreased, triglycerides increased, neutrophil count decreased, hemoglobin decreased, creatine kinase increased, alanine aminotransferase increased, lipase increased, amylase increased, aspartate aminotransferase increased, uric acid increased, and lymphocyte count decreased

DRUG INTERACTIONS

- Asciminib is an inhibitor of CYP3A4, CYP2C9, and P-gp. Asciminib is a CYP3A4 substrate
- Closely monitor for adverse reactions during concomitant use of strong CYP3A4 inhibitors and SCEMBLIX at 200 mg twice daily
- Avoid concomitant use of itraconazole oral solution containing hydroxypropyl-β-cyclodextrin and SCEMBLIX at all recommended doses
- Closely monitor for adverse reactions during concomitant use of certain CYP3A4 substrates and SCEMBLIX at 80 mg total daily dose. Avoid use of SCEMBLIX at 200 mg twice daily
- Avoid concomitant use of CYP2C9 substrates and SCEMBLIX at all recommended doses. If coadministration with 80 mg total daily dose is unavoidable, reduce the CYP2C9 substrate dosage as recommended in its prescribing information. If coadministration with 200 mg twice daily is unavoidable, consider alternative therapy with a non-CYP2C9 substrate
- Closely monitor for adverse reactions during concomitant use of certain P-gp substrates and SCEMBLIX at all recommended doses

Dosage modifications for the management of adverse reactions

Dose modifications for the management of adverse reactions[1]

Adverse reaction	Dosage modification
Thrombocytopenia and/or neutropenia	
ANC less than 1.0 x 10^9/L and/or PLT less than 50 x 10^9/L	Withhold SCEMBLIX until resolved to ANC greater than or equal to 1 x 10^9/L and/or PLT greater than or equal to 50 x 10^9/L. If resolved: • Within 2 weeks: Resume SCEMBLIX at starting dose • After more than 2 weeks: Resume SCEMBLIX at reduced dose For recurrent severe thrombocytopenia and/or neutropenia, withhold SCEMBLIX until resolved to ANC greater than or equal to 1 x 10^9/L and PLT greater than or equal to 50 x 10^9/L, then resume at reduced dose
Asymptomatic amylase and/or lipase elevation	
Elevation greater than 2.0 x ULN	Withhold SCEMBLIX until resolved to less than 1.5 x ULN. • If resolved, resume SCEMBLIX at reduced dose. If events reoccur at reduced dose, permanently discontinue SCEMBLIX • If not resolved, permanently discontinue SCEMBLIX. Perform diagnostic tests to exclude pancreatitis
Nonhematologic adverse reactions	
Grade 3[a] or higher	Withhold SCEMBLIX until recovery to Grade 1 or less. • If resolved, resume SCEMBLIX at reduced dose • If not resolved, permanently discontinue SCEMBLIX

Please refer to the full Prescribing Information for dose reduction, modification, and discontinuation of SCEMBLIX in the event of specific adverse reactions. Management of dosing for each patient should be based on individual benefit/risk assessment.

ANC, absolute neutrophil count; PLT, platelets; ULN, upper limit of normal.
[a]Based on Common Terminology Criteria for Adverse Events (CTCAE) v 4.03.

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

SCEMBLIX® (asciminib) 20 mg, 40 mg tablets

Patient counseling[1]

Advise patients taking SCEMBLIX to report any signs or symptoms of potential treatment-related adverse reactions. In addition, advise patients to read the FDA-approved patient labeling (Patient Information).

Myelosuppression	Inform patients of the possibility of developing low blood cell counts. Advise patients to immediately report fever, any suggestion of infection, or signs or symptoms suggestive of bleeding or easy bruising.
Pancreatic Toxicity	Inform patients of the possibility of developing pancreatitis that may be accompanied by nausea, vomiting, severe abdominal pain, or abdominal discomfort, and to promptly report these symptoms.
Hypertension	Inform patients of the possibility of developing hypertension. Advise patients to contact their health care provider for elevated blood pressure or if symptoms of hypertension occur, including confusion, headache, dizziness, chest pain, or shortness of breath.
Hypersensitivity	Advise the patient to discontinue SCEMBLIX and seek immediate medical attention if any signs or symptoms of a hypersensitivity reaction, such as rash, edema, or bronchospasm occur.
Cardiovascular Toxicity	Inform patients of the possibility of the occurrence of cardiovascular toxicity, especially those with a history of cardiovascular risk factors. Advise patients to immediately contact their health care provider or get medical help if they develop cardiovascular signs and symptoms.
Embryo-Fetal Toxicity	Advise women to inform their health care provider if they are pregnant or become pregnant. Inform female patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 week after receiving the last dose of SCEMBLIX.
Lactation	Advise women not to breastfeed during treatment with SCEMBLIX and for at least 1 week after the last dose.
Infertility	Advise women of reproductive potential of the potential for impaired fertility from SCEMBLIX.
Drug Interactions	Advise patients that SCEMBLIX and certain other medicines, including over the counter medications or herbal supplements, can interact with each other and may alter the effects of SCEMBLIX.

Drug interactions[1]

Effect of Other Drugs on SCEMBLIX

Strong CYP3A4 Inhibitors

- Asciminib is a CYP3A4 substrate. Concomitant use of SCEMBLIX with a strong CYP3A4 inhibitor increases both the asciminib C_{max} and AUC, which may increase the risk of adverse reactions
- Closely monitor for adverse reactions in patients treated with SCEMBLIX at 200 mg bid with concomitant use of strong CYP3A4 inhibitors

Itraconazole Oral Solution Containing Hydroxypropyl-β-cyclodextrin

- Concomitant use of SCEMBLIX with itraconazole oral solution containing hydroxypropyl-β-cyclodextrin decreases asciminib C_{max} and AUC, which may reduce SCEMBLIX efficacy
- Avoid coadministration of SCEMBLIX at all recommended doses with itraconazole oral solution containing hydroxypropyl-β-cyclodextrin

Effect of SCEMBLIX on Other Drugs

Certain CYP3A4 Substrates

- Asciminib is a CYP3A4 inhibitor. Concomitant use of SCEMBLIX increases the C_{max} and AUC of CYP3A4 substrates, which may increase the risk of adverse reactions of these substrates
- Closely monitor for adverse reactions in patients treated with SCEMBLIX at 80 mg total daily dose with concomitant use of certain CYP3A4 substrates, where minimal concentration changes may lead to serious adverse reactions
- Avoid coadministration of SCEMBLIX at 200 mg bid with certain CYP3A4 substrates, where minimal concentration changes may lead to serious adverse reactions

CYP2C9 Substrates

- Asciminib is a CYP2C9 inhibitor. Concomitant use of SCEMBLIX increases the C_{max} and AUC of CYP2C9 substrates, which may increase the risk of adverse reactions of these substrates
- Avoid coadministration of SCEMBLIX at 80 mg total daily dose with certain CYP2C9 substrates, where minimal concentration changes may lead to serious adverse reactions. If coadministration is unavoidable, reduce the CYP2C9 substrate dosage as recommended in its prescribing information
- Avoid coadministration of SCEMBLIX at 200 mg bid with sensitive CYP2C9 substrates and certain CYP2C9 substrates, where minimal concentration changes may lead to serious adverse reactions. If coadministration is unavoidable, consider alternative therapy with non-CYP2C9 substrate

Certain P-gp Substrates

- Asciminib is a P-gp inhibitor. Concomitant use of SCEMBLIX increases the plasma concentrations of P-gp substrates, which may increase the risk of adverse reactions of these substrates
- Closely monitor for adverse reactions in patients treated with SCEMBLIX at all recommended doses with concomitant use of P-gp substrates, where minimal concentration changes may lead to serious toxicities

IMPORTANT SAFETY INFORMATION FOR SCEMBLIX

Myelosuppression

- Thrombocytopenia, neutropenia, and anemia, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX
- Perform complete blood counts every 2 weeks for the first 3 months of treatment and monthly thereafter or as clinically indicated. Monitor patients for signs and symptoms of myelosuppression
- Based on the severity of thrombocytopenia and/or neutropenia, reduce dose, temporarily withhold, or permanently discontinue SCEMBLIX as described in the prescribing information

Pancreatic Toxicity

- Pancreatitis (including grade 3 reactions) and asymptomatic elevation in serum lipase and amylase (including grade 3/4 elevations), have occurred in patients receiving SCEMBLIX
- Assess serum lipase and amylase levels monthly during treatment with SCEMBLIX, or as clinically indicated. Monitor patients for signs and symptoms of pancreatic toxicity. Perform more frequent monitoring in patients with a history of pancreatitis
- If lipase and amylase elevation are accompanied by abdominal symptoms, temporarily withhold SCEMBLIX and consider appropriate diagnostic tests to exclude pancreatitis
- Based on the severity of lipase and amylase elevation, reduce dose, temporarily withhold, or permanently discontinue SCEMBLIX as described in the prescribing information

Hypertension

- Hypertension, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX
- Monitor and manage hypertension using standard antihypertensive therapy during treatment with SCEMBLIX as clinically indicated
- For grade 3 or higher reactions, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of hypertension

Hypersensitivity

- Hypersensitivity, including grade 3/4 reactions, have occurred in patients receiving SCEMBLIX. Reactions included rash, edema, and bronchospasm
- Monitor patients for signs and symptoms and initiate appropriate treatment as clinically indicated
- For grade 3 or higher reactions, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of hypersensitivity

Cardiovascular Toxicity

- Cardiovascular toxicity (including ischemic cardiac and central nervous system conditions; and arterial thrombotic and embolic conditions) and cardiac failure have occurred in patients receiving SCEMBLIX. Some toxicities were grade 3/4 and 3 fatalities were reported
- Arrhythmia, including QTc prolongation, have occurred in patients receiving SCEMBLIX. Some of these arrhythmias were grade 3
- Monitor patients with a history of cardiovascular risk factors for cardiovascular signs and symptoms. Initiate appropriate treatment as clinically indicated
- For grade 3 or higher cardiovascular toxicity, temporarily withhold, reduce dose, or permanently discontinue SCEMBLIX as described in the prescribing information depending on persistence of cardiovascular toxicity

Embryo-Fetal Toxicity

- SCEMBLIX can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus if SCEMBLIX is used during pregnancy or if the patient becomes pregnant while taking SCEMBLIX
- Verify the pregnancy status of females of reproductive potential prior to starting treatment with SCEMBLIX. Advise females to use effective contraception during treatment and for at least 1 week after the last SCEMBLIX dose

ADVERSE REACTIONS

- Most common adverse reactions (≥20%) were upper respiratory tract infections, musculoskeletal pain, headache, fatigue, nausea, rash, and diarrhea
- Most common laboratory abnormalities (≥20%) were platelet count decreased, triglycerides increased, neutrophil count decreased, hemoglobin decreased, creatine kinase increased, alanine aminotransferase increased, lipase increased, amylase increased, aspartate aminotransferase increased, uric acid increased, and lymphocyte count decreased

DRUG INTERACTIONS

- Asciminib is an inhibitor of CYP3A4, CYP2C9, and P-gp. Asciminib is a CYP3A4 substrate
- Closely monitor for adverse reactions during concomitant use of strong CYP3A4 inhibitors and SCEMBLIX at 200 mg twice daily
- Avoid concomitant use of itraconazole oral solution containing hydroxypropyl-β-cyclodextrin and SCEMBLIX at all recommended doses
- Closely monitor for adverse reactions during concomitant use of certain CYP3A4 substrates and SCEMBLIX at 80 mg total daily dose. Avoid use of SCEMBLIX at 200 mg twice daily
- Avoid concomitant use of CYP2C9 substrates and SCEMBLIX at all recommended doses. If coadministration with 80 mg total daily dose is unavoidable, reduce the CYP2C9 substrate dosage as recommended in its prescribing information. If coadministration with 200 mg twice daily is unavoidable, consider alternative therapy with a non-CYP2C9 substrate
- Closely monitor for adverse reactions during concomitant use of certain P-gp substrates and SCEMBLIX at all recommended doses

Please **click here** for full Prescribing Information.

References: 1. Scemblix [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. CABL001A2301 clinical study report. Novartis Pharmaceuticals Corp; 2022. **3.** Réa D, Mauro M, Boquimpani C, et al. *Blood*. 2021;138(21):2031-2041. **4.** Combes FP, Li YF, Hoch M, Ho YY, Sy SKB. *Clin Pharmacol Ther*. 2022. doi:10.1002/cpt.2699. Epub ahead of print.

SCEMBLIX: FOR ADULTS WITH Ph+ CML-CP PREVIOUSLY TREATED WITH 2 OR MORE TKIs OR WHO HAVE THE T315I MUTATION

Dosing options to accommodate your patients[1]

Patients previously treated with ≥2 TKIs:

80 mg qd

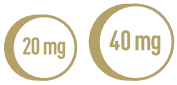
There is also an option to take SCEMBLIX 40 mg tablets twice a day (AM + PM)

- Recommended dosage for patients who have the T315I mutation is 200 mg bid AM + PM

Patients should:

Avoid food consumption for at least 2 hours before and **1 hour after** taking SCEMBLIX[1]

Swallow SCEMBLIX whole—do not break, crush, or chew them[1]



SCEMBLIX is available as film-coated tablets: **20 mg** (6.2 mm diameter) and **40 mg** (8.2 mm diameter)[1]

Based on pharmacokinetic parameters studied in an exposure-response analysis, the predicted efficacy and safety profile of SCEMBLIX at the 80 mg qd dose is similar to that at the 40 mg bid dose.[4]

Warning and Precautions for SCEMBLIX include myelosuppression, pancreatic toxicity, hypertension, hypersensitivity, cardiovascular toxicity, and embryo-fetal toxicity. The most common adverse reactions (≥20%) were upper respiratory tract infections, musculoskeletal pain, headache, fatigue, nausea, rash, and diarrhea.

Discover SCEMBLIX at scemblixinfo.com

Please see additional Important Safety Information throughout, and **click here** for full Prescribing Information for SCEMBLIX.

NOVARTIS

SCEMBLIX®
(asciminib) 20 mg, 40 mg tablets

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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