NOVARTIS

SCEMBLIX - Safety profile and tolerability - HCP

Prescribing information

Image

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SCEMBLIX®▼ (asciminib) is indicated for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia (Ph + CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors, and without a known T315I mutation.[1]

Safety profile and tolerability

SCEMBLIX®▼ (asciminib) resulted in fewer all-grade and grade ≥3 AEs vs bosutinib[2,3]

The ASCEMBL trial population was not restricted to Ph+ patients with CML-CP.[2] SCEMBLIX is indicated in adults with Ph+ CML-CP previously treated with two or more TKIs and without a

known T315I mutation.[1]

Patients receiving SCEMBLIX and bosutinib, respectively, experienced:

WEEK 24:[2]

	SCEMBLIX (N=156)		BOSUTINIB (N=76)	
	All grades	Grade ≥3	All grades	Grade ≥3
% of patients with ≥1 adverse event (n)	**89.7** (140)	**50.6** (79)	**96.1** (73)	**60.5** (46)

WEEK 96:[3]

	SCEMBLIX (N=156)		BOSUTINIB (N=76)	
	All grades	Grade ≥3	All grades	Grade ≥3
% of patients with ≥1 adverse event (n)*	**91** (142)	**56.4** (88)	**97.4** (74)	**68.4** (52)

WEEK 156:[4]

	SCEMBLIX (N=156)		BOSUTINIB (N=76)	
	All grades	Grade ≥3	All grades	Grade ≥3
% of patients with ≥1 adverse event (n)*	**91** (142)	**59.6** (93)	**97.4** (74)	**68.4** (52)

Most frequent all-grade AEs by Week 156 (occurring in ≥20% of patients in any treatment arm)[4]

Analysis at the end of study cut-off date: 22 March 2023.

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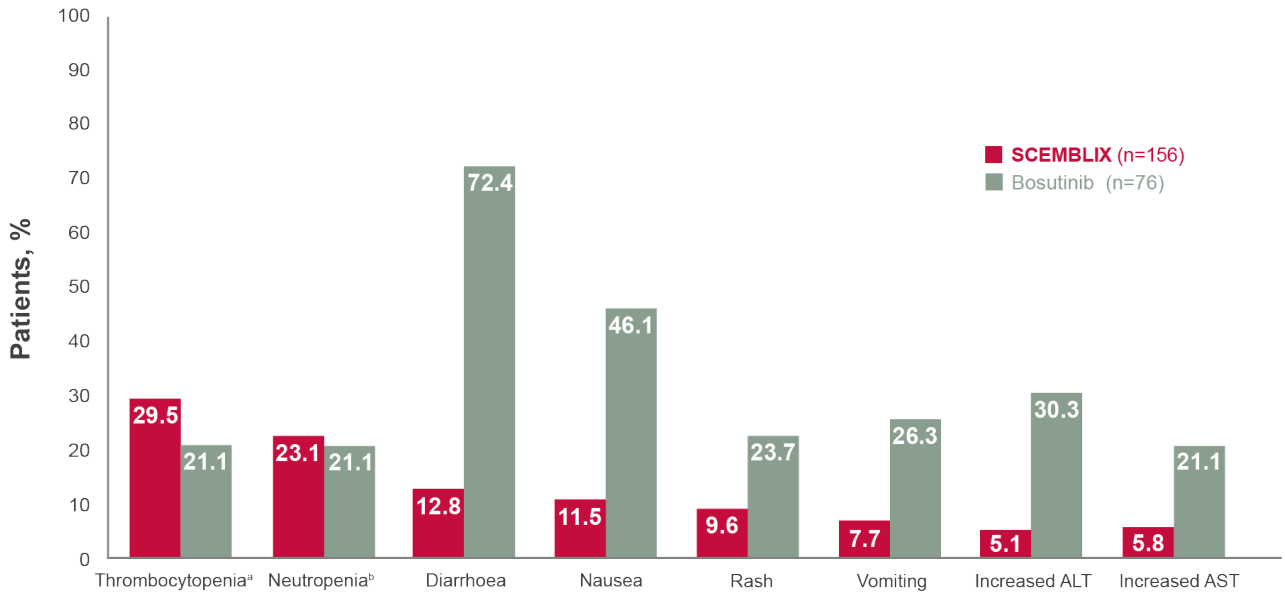

[a]Thrombocytopenia includes: thrombocytopenia and platelet count decreased.
[b]Neutropenia includes: neutropenia and neutrophil count decreased.

Adapted from Mauro MJ, et al. 2023.[4]

By Week 156, all-grade AEs leading to dose adjustment or interruption occurred in **43.6% of patients receiving SCEMBLIX** vs **64.5% of patients receiving bosutinib.**[3]

By the end of study cut-off, the median duration of exposure was **156.0 weeks with SCEMBLIX** compared to **30.5 weeks with bosutinib.**[4]

Patients on SCEMBLIX were observed to experience fewer grade ≥3 AEs vs bosutinib (59.6% vs 68.4% respectively) at week 156 and required fewer dose modifications vs bosutinib at week 96*[3,4]

*A lower proportion of patients receiving SCEMBLIX than bosutinib had dose modifications of study drug: 42.3% and 61.8% of patients, respectively, had at least one dose interruption due to AEs; 23.7% and 44.7% of patients, respectively, had at least one dose reduction due to AEs.[3]

Patients taking SCEMBLIX were observed to experience lower treatment discontinuation vs bosutinib[4]

Discontinuation rates due to AEs at Week 156[‡4]

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Patients who completed the treatment[‡4]

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Consistent with the primary analysis, the most common AEs leading to discontinuation were thrombocytopenia (3.2%) and neutropenia (2.6%) for SCEMBLIX and increased ALT (3.9%) and neutropenia (3.9%) for bosutinib at the Week 96 cut-off date.[†3] New AEs leading to discontinuation since the Week 96 analysis were pregnancy (SCEMBLIX, n=1) and diarrhoea

(bosutinib, n=1).[‡4]

AEs observed with SCEMBLIX in clinical studies[1]

System organ class	Frequency category[a]	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infection[b]
	Common	Lower respiratory tract infection,[c] influenza
Blood and lymphatic system disorders	Very common	Thrombocytopenia,[d] neutropenia,[e] anaemia[f]
	Uncommon	Febrile neutropenia, pancytopenia
Immune system disorders	Uncommon	Hypersensitivity
Metabolism and nutrition disorders	Very common	Dyslipidaemia[g]
	Common	Decreased appetite
Nervous system disorders	Very common	Headache, dizziness
Eye disorders	Common	Dry eye, vision blurred
Cardiac disorders	Common	Palpitations
Vascular disorders	Very common	Hypertension[h]
Respiratory, thoracic and mediastinal disorders	Very common	Dyspnoea, cough
	Common	Pleural effusion, non-cardiac chest pain
Gastrointestinal disorders	Very common	Pancreatic enzymes increased,[i] vomiting, diarrhoea, nausea, abdominal pain,[j] constipation
	Common	Pancreatitis[k]
Hepatobiliary disorders	Very common	Hepatic enzyme increased[l]
	Common	Blood bilirubin increased[m]
Skin and subcutaneous tissue disorders	Very common	Rash,[n] pruritus
	Common	Urticaria
Musculoskeletal and connective tissue disorders	Very common	Musculoskeletal pain,[o] arthralgia
General disorders and administration site conditions	Very common	Fatigue,[p] oedema,[q] pyrexia[r]

Investigations	Common	Electrocardiogram QT prolonged, blood creatine phosphokinase increased

[a]Frequency based on the safety pool (A2301 + X2101) SCEMBLIX all grade events (N=356).
[b]Upper respiratory tract infection includes: upper respiratory tract infection, nasopharyingitis, pharyngitis and rhinitis.
[c]Lower respiratory tract infections includes: pneumonia, bronchitis and tracheobronchitis.
[d]Thrombocytopenia includes: thrombocytopenia and platelet count decreased.
[e]Neutropenia includes: neutropenia and neutrophil count decreased.
[f]Anaemia includes: anaemia, haemoglobin decreased, normocytic anaemia.
[g]Dyslipidaemia includes: hypertriglyceridaemia, blood cholesterol increased, hypercholesterolaemia, blood triglycerides increased, hyperlipidaemia and dyslipidaemia.
[h]Hypertension includes: hypertension and blood pressure increased.
[i]Pancreatic enzymes increased includes: lipase increased, amylase increased and hyperlipasaemia.
[j]Abdominal pain includes: abdominal pain and abdominal pain upper.
[k]Pancreatitis includes: pancreatitis and pancreatitis acute.
[l]Hepatic enzymes increased includes: alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, transaminases increased and hypertransaminasaemia.
[m]Blood bilirubin increased includes: blood bilirubin increased, bilirubin conjugated increased and hyperbilirubinaemia.
[n]Rash includes: rash, rash maculopapular and rash pruritic.
[o]Musculoskeletal pain includes: pain in extremity, back pain, myalgia, bone pain, musculoskeletal pain, neck pain, musculoskeletal chest pain, musculoskeletal discomfort.
[p]Fatigue includes: fatigue and asthenia.
[q]Oedema includes: oedema and oedema peripheral.
[r]Pyrexia includes: pyrexia and body temperature increased.

Adapted from SCEMBLIX Summary of Product Characteristics.[1]

For the management of adverse reactions, the dose can be reduced based on individual safety and tolerability. Please see the Summary of Product Characteristics for further information on dose modifications for adverse events.[1]

Contrandication: Hypersensitivity to the active substance or to any of the excipients listed in the Summary of Product Characteristics.[1]

For the full safety information, including information on interactions please refer to the SmPC.

Special populations[1]

Elderly
No dose adjustment is required in patients aged 65 years or above.

Renal impairment
No dose adjustment is required in patients with mild, moderate or severe renal impairment.

Hepatic impairment

No dose adjustment is required in patients with mild, moderate or severe hepatic impairment. Since there are no data available in patients with moderate or severe hepatic impairment, caution should be exercised in these patients.

Paediatric population
The safety and efficacy of SCEMBLIX in paediatric patients aged below 18 years have not been established. No data are available.

Special warnings and precautions for use[1]

Myelosuppression

Thrombocytopenia, neutropenia and anaemia occurred in patients receiving SCEMBLIX. Severe (NCI-CTCAE grade 3 or 4) thrombocytopenia and neutropenia events were reported during treatment with SCEMBLIX. Myelosuppression was generally reversible and managed by temporarily withholding treatment. Complete blood counts should be performed every two weeks for the first 3 months of treatment and then monthly thereafter, or as clinically indicated. Patients should be monitored for signs and symptoms of myelosuppression.

Based on the severity of thrombocytopenia and/or neutropenia, the dose should be reduced, temporarily withheld or permanently discontinued.

Pancreatic toxicity

Pancreatitis and asymptomatic elevation of serum lipase and amylase, including severe reactions, occurred in patients receiving SCEMBLIX.

Serum lipase and amylase levels should be assessed monthly during treatment with SCEMBLIX, or as clinically indicated. Patients should be monitored for signs and symptoms of pancreatic toxicity. More frequent monitoring should be performed in patients with a history of pancreatitis. If serum lipase and amylase elevation are accompanied by abdominal symptoms, treatment should be temporarily withheld and appropriate diagnostic tests should be considered to exclude pancreatitis.

Based on the severity of serum lipase and amylase elevation, the dose should be temporarily withheld, reduced or permanently discontinued.

QT prolongation

QT prolongation occurred in patients receiving SCEMBLIX.

It is recommended that an electrocardiogram is performed prior to the start of treatment with SCEMBLIX, and monitored during treatment as clinically indicated. Hypokalaemia and hypomagnesaemia should be corrected prior to SCEMBLIX administration and monitored during treatment as clinically indicated.

Caution should be exercised when administering SCEMBLIX concomitantly with medicinal products with a known risk of torsades de pointes, or in patients who have a history of or predisposition for QTc prolongation or uncontrolled or significant cardiac disease including bradycardia.

Hypertension

Hypertension, including severe hypertension, occurred in patients receiving SCEMBLIX.

Hypertension should be monitored and managed using standard antihypertensive therapy during treatment with SCEMBLIX as clinically indicated.

Hepatitis B reactivation

Reactivation of hepatitis B virus (HBV) has occurred in patients who are chronic carriers of this virus following administration of other BCR-ABL1 tyrosine kinase inhibitors (TKIs). Patients should be tested for HBV infection before the start of treatment with SCEMBLIX.

HBV carriers who require treatment with SCEMBLIX should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

Lactose

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially “sodium free.”

Pregnancy and lactation[1]

Women of childbearing potential/contraception
The pregnancy status of women of childbearing potential should be verified prior to starting treatment with SCEMBLIX.

Women of childbearing potential should be advised to use effective contraception during treatment with SCEMBLIX and for at least 3 days after stopping treatment and to avoid becoming pregnant while receiving SCEMBLIX.

Pregnancy
There are no or limited amount of data from the use of SCEMBLIX in pregnant women. SCEMBLIX is not recommended for use during pregnancy, or in women of childbearing potential not using contraception. The patient should be advised of a potential risk to the foetus if SCEMBLIX is used during pregnancy or if the patient becomes pregnant while taking SCEMBLIX.

Breast-feeding
It is unknown whether SCEMBLIX is excreted in human milk. Because of the potential for serious adverse reactions in the breast-fed newborn/infant, breast-feeding is not recommended during treatment and for at least 3 days after stopping treatment with SCEMBLIX.

Patients taking SCEMBLIX were observd to experience lower treatment discontinuation vs bosutinib (50.3% vs 89.5%, respectively) at Week 156[4]

Help your patients stay on treatment with SCEMBLIX[2,3]

Learn about initiation and dosing

[†]The cut-off date for this analysis was 6 October 2021. The median duration of follow-up was 2.3 years from randomisation to data cut-off date.
[‡]The end of study cut-off date was 22 March 2023.[4]

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BCR-ABL, breakpoint cluster region and Abelson murine leukaemia viral oncogene homologue; CML-CP, chronic myeloid leukaemia in chronic phase; HBV, hepatitis B virus; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; Ph+, Philadelphia chromosome positive; QTc, corrected QT interval; TKI, tyrosine kinase inhibitor.

For further information, please refer to the Summary of Product Characteristics.

References

1. SCEMBLIX (asciminib) Summary of Product Characteristics.
2. Réa D, et al. *Blood* 2021;138(21):2031–2041.
3. Hochhaus A, et al. *Leukemia* 2023;37:617–626.
4. Mauro MJ, et al. P 4536. 65th Annual Meeting of the American Society of Hematology, 9–12 December 2023, San Diego, USA.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.

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