Report Scemblix® - asciminib hydrochloride

Product & Mechanism of action

Substance: asciminib hydrochloride

Brand Name: Scemblix

Originator/licensee: Novartis Europharm Limited

Classification: NCE

ATC code: L01EA

Orphan Status:
Eu: Yes
Us: Yes

Mechanism of action:
asciminib is an antineoplastic agent which is a potent allosteric inhibitor of the tyrosine kinase BCR-ABL1 kinase activity [1,2].

ABBREVIATIONS:
AE: adverse event
ALT: alanine aminotransferase
BID: twice a day
CCF: Cardiac failure congestive
CHMP: Committee for Medicinal Products for Human Use
CI: confidence interval
CML: chronic myeloid leukaemia
CP: chronic phase
M.A.: marketing authorization
MAT: mesenteric artery thrombosis
MCyR: major cytogenetic response
MMR: Major Molecular Response
P: p-value
Ph+: Philadelphia chromosome-positive
Pts: patients
QD: once daily
TEAE: Treatment emergent adverse events
TKI: tyrosine kinase inhibitors
URTI: upper respiratory tract infections
UTIs: Urinary tract infection

Authorized indications Licensing status

Authorized Indication:
EMA: asciminib is indicated for the treatment of adult patients with Ph+ CML-CP previously treated with two or more TKIs [1].

Route of administration: OS

Licensing status
EU CHMP P.O. date: 23/06/2022
EU M.A. date:
FDA M.A. date: 29/10/2021

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: Yes

References:
[1]. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/scemblix
[2]. https://www.io.nihr.ac.uk/wp-content/uploads/2022/01/23792-Asciminib-for-Chronic-Myeloid-Leukaemia-V1.0-MAY2020-NON-CONF.pdf
[3]. https://adisinsight.springer.com/trials/700283706
[4]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215358s000Orig1lbl.pdf
[5]. https://ashpublications.org/blood/article/138/21/2031/476601/A-phase-3-open-label-randomized-study-of-asciminib
[6]. https://adisinsight.springer.com/drugs/800040192
[7]. https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=IT&data_id=3705&Disease_Disease_Search_diseaseGroup=521&Disease_Disease_Search_diseaseType=ORPHA&Disease(s)/group%20of%20diseases=Chronic-myeloid-leukemia&title=Chronic%20myeloid%20leukemia&search=Disease_Search_Simple#:~:text=La%20leucemia%20mieloide%20cronica%20(LMC,la%20prevalenza%20in%201%2F17.000.
[8]. https://www.clinicaltrials.gov/

Essential therapeutic features

Summary of clinical EFFICACY:
(NCT03106779) ASCEMBL is a phase III, multi-center, randomized, open-label study to compare the efficacy of asciminib vs bosutinib in the treatment of adult pts (≥ 18 yrs) with CML-CP previously treated with a minimum of two ATP-binding site TKIs. A total of 233 pts were randomized in a 2:1 ratio and stratified according to MCyR status to receive either asciminib 40mg BID (n=156) or bosutinib 500mg QD (n=76). The primary endpoint was the number of pts with MMR* rate at week 24. The MMR rate at week 24 was 25.5% with asciminib and 13.2% with bosutinib. The difference in MMR rate between treatment arms, after adjusting for MCyR at baseline, was 12.2% (95% confidence interval, 2-sided P=0.029) [3-5].

**MMR was defined as a ≥ 3.0 log reduction in BCR-ABL1 transcripts compared to the standardized baseline equivalent to ≤ 0.1% BCR-ABL1/ABL% by IS as measured by RQ-PCR*

Figure 1: Summary of efficacy results in pts with Ph+CML-CP

	SCEMBLIX 40 mg BID	Bosutinib 500 mg QD	Difference (95% CI)	P-value
MMR rate, % (95% CI) At 24 week	N=156 25 (19, 33)	N=76 13 (6.5, 23)	12[a] (2.2, 22)	0.029[b]

[a]Estimated using a common risk difference stratified by baseline major cytogenetic response status.
[b]Estimated using a Cochrane-Mantel-Haenszel two-sided test stratified by baseline major cytogenetic response status.

Summary of clinical SAFETY:
The proportion of pts who experienced AEs, TEAEs and AEs leading to treatment discontinuation was lower with asciminib than with bosutinib. The most common AEs leading to treatment discontinuation included thrombocytopenia (all-grade, 3.2%; grade ≥3, 3.2%) with asciminib and increased ALT (all-grade, 5.3%; grade ≥3, 3.9%) with bosutinib.
SAEs included pyrexia, cardiac congestive failure, thrombocytopenia and urinary tract infection. In the asciminib arm, two deaths occurred due to arterial embolism and ischemic stroke (one each) (defined as death occurring during treatment or within 30 days after the end of treatment). Two deaths occurred after asciminib discontinuation during survival follow-up (both from CML). In the bosutinib arm, one patient died on treatment from septic shock [5].

Figure 2: Summary of clinical safety

	All-grade AEs	TEAEs	AEs leading to treatment discontinuation	Death
Asciminib	140 (90%)	99 (64%)	6%	4 (3%)
Bosutinib	73 (96%)	67 (88%)	21%	1 (1%)

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** Yes

Discontinued studies (for the same indication): Yes [6]

NHS impact

Cost of therapy:
Price not available yet.

Epidemiology:
Chronic myeloid leukemia (CML) is the most common myeloproliferative disease, representing 15-20% of leukemia cases. The annual incidence was estimated at 1-1.5 cases per 100,000 people and the prevalence at 1/17,000 subjects [7].

POSSIBLE PLACE IN THERAPY
The current pharmacological treatment option for third line treatment of CML-CP are: Imatinib, Nilotinib, Dasatinib, Bosutinib, Ponatinib [2].

OTHER INDICATIONS IN DEVELOPMENT: Yes

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: Yes

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION
Dasatinib, Ponatinib, Nilotinib, Asciminib, Pioglitazone […] [8]

*Service reorganization: No
*Possible off label use: Yes

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