CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215358Orig1s008

PRODUCT QUALITY REVIEW(S)

Office of Lifecycle Drug Products
Division of Post-Marketing Activities I
Review of Chemistry, Manufacturing, and Controls

1. **NDA Supplement Number: NDA-215358-SUPPL-08**
   sNDA Recommendation: ☒Approval ☐Complete Response
   sNDA managed by: ☐OPQ ☒OND

2. **Submission(s) Being Reviewed**:

Submission	**Type**	**Submission Date**	**CDER Stamp Date**	**Assigned Date**	**PDUFA Goal Date**	**Review Date**
Original Supplement	PAS (Efficacy)	04/30/2024	04/30/2024	05/04/2024	10/30/2024	10/15/2024
Amendment-610		08/14/2024	08/14/2024			
Amendment-625		09/16/2024	09/16/2024			
Amendment-626		09/16/2024	09/16/2024			
Amendment-640		10/04/2024	10/04/2024			
Amendment-648		10/11/2024	10/11/2024			

3. **Provides For:**
   This efficacy supplement provides for new indication in the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP).

4. **Review #**: 1

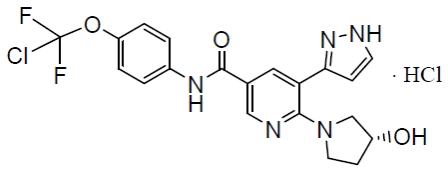
5. **Clinical Review Division**: OOD/ Division of Hematology Malignancies 1 (DHM 1)

6. **Name and Address of Applicant**:
   Tina Lertharakul, Pharm.D.
   Sr. Global Program Regulatory Manager
   Regulatory Affairs, Oncology
   Novartis Pharmaceuticals Corporation
   One Health Plaza
   East Hanover, NJ 07936-1080
   Tel: 201-919-8009
   Email: tina.lertharakul@novartis.com

7. **Drug Product:**

Drug Name	Dosage Form	Strength	Route of Administration	Rx or OTC	Orphan Designation #
Scemblix® (asciminib)	Tablet	20 and 40 mg	PO	Rx	16-5564

8. Chemical Name and Structure of Drug Substance:



USAN: Asciminib hydrochloride
Chemical name (IPPAC): N-[4-(Chloro difluoromethoxy)phenyl]-6-[(3*R*)-3-hydroxypyrrolidin-1-yl]-5-(1H pyrazol-3-yl) pyridine-3-carboxamide—hydrogen chloride
Chirality: Contains *R* enantiomer.
Molecular formula: Free base: $C_{20}H_{18}ClF_2N_5O_3$
Salt form: $C_{20}H_{18}ClF_2N_5O_3$.HCl
MW: Free base: 449.84 g/mol, salt form: 486.30 g/mol.

9. Indication:
Scemblix® (asciminib) is a kinase inhibitor indicated for the treatment of 1) Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs); 2) Ph+ CML in CP with the T315I mutation.

10. Supporting/Relating Documents: None

11. Consults: None

12. Executive Summary:
New Drug Application (NDA) 215358 for Scemblix® (asciminib, ABL001) film-coated tablets, was approved on October 29, 2021, for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs) and • Ph+ CML in CP with the T315I mutation. Asciminib is an oral and potent inhibitor of tyrosine kinase activity of ABL and BCR-ABL1 kinases. Asciminib inhibits the ABL1 kinase activity of the BCR-ABL1 fusion protein, by specifically targeting the ABL myristoyl pocket. The applicant has Orphan Designation for the above indication.

The purpose of this sNDA is to seek approval for new indication in the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP). Additionally, this sNDA is being submitted under Real-Time Oncology Review according to the RTOR submission plan submitted to the Agency in the Type B pre-sNDA briefing book on February 2, 2024, and agreed at the Type B Pre-sNDA meeting on March 4, 2024.

There are no CMC changes or new information is provided in Modules 3 and 4 of this application. The supplement provides updated PI. The Applicant proposed a change to (b) (4) After IR exchanges the applicant agreed to keep (b) (4)

as advised by the Agency. There are no other proposed changes related to the CMC section 2, 3, 11 and 16. No new quality data or documentation were generated for the purpose of this submission.

The supplement includes a Request for Categorical Exclusion from Environmental Assessment. The applicant Novartis certifies that this submission for asciminib qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(b) as the estimated environmental intake concentration of the active moieties, asciminib, will be significantly less than 1 ppb, based on the peak production estimates for the next five years. Further, the applicant Novartis states that, to the best of its knowledge, no extraordinary circumstances exist which may significantly affect the quality of the human environment and would thus require the preparation of at least an Environmental Assessment.

The previously submitted Chemistry, Manufacturing and Controls (CMC)/quality (Module 3) in NDA 215358 is considered adequate to support the proposed indication. Therefore, this supplement **is recommended for approval** from CMC standpoint.

13. Conclusions & Recommendations:
This supplement is recommended for approval.

14. Comments/Deficiencies to be Conveyed to Applicant: None

15. Primary Reviewer:
Mustafa Guzel, Ph.D., CMC reviewer, Unit 3, DPQA IV, OPQA 1, OPQ.

16. Secondary Reviewer:
Rohit Kolhatkar, Ph.D., SPQA, Unit 3, DPQA IV, OPQA 1, OPQ.

Note: *Electronic signatures for the above are appended at the end of this document.*

Mustafa Guzel

Digitally signed by Mustafa Guzel
Date: 10/15/2024 11:50:05AM
GUID: 634591a8000ae9af0f6f5f573cbe1923

Rohit Kolhatkar

Digitally signed by Rohit Kolhatkar
Date: 10/16/2024 11:30:13AM
GUID: 57bf531500b52a2eccd5395bec77ebc2
Comments: concur with approval recommendation