20 October 2025
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Scemblix (asciminib)
Treatment of chronic myeloid leukaemia
EU/3/20/2261

Sponsor: Novartis Europharm Limited

Note

Assessment report as adopted by the COMP with all information of a commercially confidential nature deleted.

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1. Product and administrative information

Product	
Designated active substance	Asciminib
Other name	-
INN	Asciminib
Tradename	Scemblix
Orphan condition	Treatment of chronic myeloid leukaemia
Sponsor's details:	Novartis Europharm Limited Vista Building Elm Park Merrion Road Dublin 4 D04 A9N6 Ireland
Orphan medicinal product designation procedural history	
Sponsor/applicant	Novartis Europharm Limited
COMP opinion	20 February 2020
EC decision	24 March 2020
EC registration number	EU/3/20/2261
Post-designation procedural history	
COMP opinion on review of orphan designation at the time of marketing authorisation	14 July 2022
Type II variation procedural history	
Rapporteur / Co-rapporteur	Janet Koenig / Peter Mol
Applicant	Novartis Europharm Limited
Application submission	7 April 2025
Procedure start	26 April 2025
Procedure number	EMA/VR/0000265010
Invented name	Scemblix
Proposed therapeutic indication	Scemblix is indicated for the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP). Further information can be found in the European public assessment report (EPAR) on the Agency's website https://www.ema.europa.eu/en/medicines/human/EPAR/Scemblix
CHMP opinion	16 October 2025
COMP review of orphan medicinal product designation procedural history	
COMP rapporteurs	Frauke Naumann-Winter /Karri Penttila
Sponsor's report submission	20 May 2025
COMP opinion (adoption via written procedure)	20 October 2025

2. Grounds for the COMP opinion

2.1. Orphan medicinal product designation

The COMP opinion that was the basis for the initial orphan medicinal designation in 2020 was based on the following grounds:

Having examined the application, the COMP considered that the sponsor has established the following:

- the intention to treat the condition with the medicinal product containing asciminib was considered justified based on preliminary clinical data demonstrating anti-tumour response in patients affected by the condition;
- the condition is life threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, such as intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, and the risk of severe infections;
- the condition was estimated to be affecting approximately 1.2 in 10,000 persons in the European Union, at the time the application was made.

Thus, the requirements under Article 3(1)(a) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing asciminib will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data demonstrating anti-tumour response in patients affected by the condition, who have failed all currently authorised therapies. The Committee considered that this constitutes a clinically relevant advantage.

Thus, the requirement under Article 3(1)(b) of Regulation (EC) No 141/2000 on orphan medicinal products is fulfilled.

The COMP concludes that the requirements laid down in Article (3)(1) (a) and (b) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled. The COMP therefore recommends the designation of this medicinal product, containing asciminib as an orphan medicinal product for the orphan condition: treatment of chronic myeloid leukaemia.

2.2. Review of orphan medicinal product designation at the time of marketing authorisation

The COMP opinion on the initial review of the orphan medicinal product designation in 2022 was based on the following grounds:

- the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated Orphan Medicinal Product.
- the prevalence of chronic myeloid leukaemia (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 1.4 in 10,000 persons in the European Union, at the time of the review of the designation criteria;
- the condition is life threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, and the risk of severe infections;

- although satisfactory methods for the treatment of the condition have been authorised in the European Union, the assumption that Scemblix may be of significant benefit is supported with data showing that Scemblix offers benefit in patients treated in third line or later, irrespective of ponatinib pre-treatment.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that:

- the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied;
- the criteria for designation as set out in Article 3(1)(b) are satisfied.

The Committee for Orphan Medicinal Products has recommended that Scemblix, asciminib, for treatment of chronic myeloid leukaemia (EU/3/20/2261) is not removed from the Community Register of Orphan Medicinal Products.

3. Review of criteria for orphan designation at the time of type II variation

Article 3(1)(a) of Regulation (EC) No 141/2000

Intention to diagnose, prevent or treat a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand people in the Community when the application is made

Condition

Chronic myeloid leukaemia (CML) is a clonal myeloproliferative disorder of transformed hematopoietic progenitor cells characterized by overproduction of immature myeloid cells and mature granulocytes in the spleen, bone marrow, and peripheral blood. The hallmark of CML is the Philadelphia (Ph) chromosome found in up to 95% of patients (Seong et al 1999). The Ph chromosome results from a reciprocal translocation t(9;22)(q34;q11) which fuses a portion of the Abelson (ABL1) gene on chromosome 9 with a portion of the breakpoint cluster region (BCR) gene on chromosome 22. The resulting fusion gene encodes a chimeric protein (BCR::ABL1), resulting in a constitutively active tyrosine kinase domain (Soverini et al 2019). This oncoprotein promotes cell growth and replication through downstream signalling pathways such as RAS, RAF, JUN kinase, MYC, and STAT (Jabbour, Kantarjian 2022).

The natural history of CML is characterized by a triphasic course. Clinically, most patients are diagnosed in the chronic phase (CP), characterized by anaemia, splenomegaly, and leucocytosis with generally few constitutional symptoms like fatigue, weight loss, malaise, easy satiety, and left upper quadrant fullness or pain. If CML-CP remains untreated, or is not controlled with available therapies, patients will progress to an intermediate phase known as accelerated phase (AP), marked by the presence of primitive blast cells in the bone marrow and peripheral blood. Most patients with CML-AP eventually progress to a blast phase (BP), a condition resembling acute leukaemia in which myeloid or lymphoid blasts proliferate in an uncontrolled manner (Apperley 2015).

It is the BCR::ABL1 protein, in particular its constitutively active tyrosine kinase activity, that is the main driver of Ph+ CML-CP. Therefore, this underlying pathology of CML remains unchanged across lines of treatment.

The approved therapeutic indication "Scemblix is indicated for the treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP)" falls within the scope of the designated orphan condition "treatment of chronic myeloid leukaemia".

Intention to diagnose, prevent or treat

The medical plausibility is confirmed by the positive benefit/risk assessment of the CHMP.

Chronically debilitating and/or life-threatening nature

The sponsor argued that there have been no changes in the chronically debilitating or life-threatening nature of the condition since the orphan designation of asciminib on 24-March-2020 nor the initial marketing authorisation in 2022.

The sponsor discussed the life-threatening nature of the condition. In patients progressing to CML-BP, the expected median overall and failure-free survivals are limited to 12 and 5 months, respectively (Jain et al 2017). The primary aim for treatment of these patients is to achieve early optimal response to prevent disease progression, maintain quality of life and reduce the likelihood of serious and irreversible side-effects. In second line (2L) treatment specifically, appropriate treatment selection can also avoid sequentially switching of TKIs, which has been linked to lower response rates, worse overall survival (OS), and overlapping toxicities (Cortes, Lang 2021).

The sponsor did not discuss the chronically debilitating nature of the condition. The COMP concluded that the condition is life threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, the risk of severe infections or progression of disease into the accelerated or blast phase (AML).

Number of people affected or at risk

The sponsor proposed a prevalence of 1.74 in 10.000 persons.

This was based on literature review and rare disease databases provided either partial or complete prevalence estimates of CML: Nordic Cancer Registries (NORDCAN), Global Cancer Observatory (GLOBOGAN) and European Cancer Information System (ECIS).

- Literature review

Eight studies published since 2020 were identified with information on the epidemiology of CML. Only two of these studies included prevalence estimates, which varied from 1.49 per 10,000 in a study from Germany (Saussele et al 2022) to 2.3 per 10,000 in a study from Italy (Polverelli et al 2024). As data on the prevalence of CML in the overall targeted EU/EEA region were not directly available from the published literature, it was indirectly estimated using the prevalence reported in these two studies. Assigning weights based on the population of each country (Germany and Italy) to the two prevalence estimates and assuming that the prevalence of CML in the other countries in the targeted EU/EEA region was the equal to the higher of the two published estimates, the prevalence in the overall targeted EU/EEA region was estimated to be 2.15 per 10,000. Although based on two very recent studies, a major limitation of this estimate is that it is derived from data on only two countries in the EU and therefore may not be representative of the entire EU/EEA region.

- Rare disease databases

Information on prevalence of CML in the Nordic countries was available from NORDCAN. The complete prevalence of CML in the Nordic region was 1.26 per 10,000 in 2022 and ranged from 0.91 per 10,000 to 1.46 per 10,000 in the individual Nordic countries. NORDCAN is considered a robust source of epidemiology data on cancer. However, data on the overall targeted EU/EEA region were not available.

Table 1. Prevalence of CML in Nordic countries in 2022

	Prevalence per 10,000				
	1-year	3-years	5-years	10-years	Complete prevalence
NORDIC countries	0.11	0.31	0.48	0.77	1.26
Denmark	0.17	0.45	0.64	0.96	1.46
Finland	0.06	0.18	0.3	0.5	0.91
Iceland	0.07	0.25	0.38	0.64	1.14
Norway	0.12	0.33	0.53	0.79	1.26
Sweden	0.1	0.29	0.47	0.81	1.35

According to the ECIS data from 2020, CML affects 1.43 per 10,000 people in the EU-27 and the prevalence ranged from 0.68 to 2.11 per 10,000 in the individual countries. While ECIS is also considered to be a robust source of epidemiology data on cancer, prevalence estimates for the overall targeted EU/EEA region (including Iceland, Liechtenstein, and Norway) were not directly available from ECIS.

Table 2. Prevalence of CML across Europe in 2020

Country	**Cumulative prevalence per 10,000**	**Age-standardized cumulative prevalence per 10,000**
Austria	1.34	1.33
Belgium	2.08	2.07
Croatia	0.83	0.78
Cyprus	1.06	1.11
Czechia	0.81	0.8
Denmark	1.42	1.41
Estonia	0.68	0.67
Finland	0.96	0.91
France	2.11	2.07
Germany	1.43	1.36
Greece	1.52	1.45
Hungary	0.85	0.84
Iceland	1.67	1.87
Ireland	1.13	1.31
Italy	1.7	1.59
Latvia	1.46	1.43
Lithuania	1.34	1.31
Luxembourg	1.5	1.65
Malta	0.86	0.9

Netherlands	1.3	1.28
Norway	1.22	1.28
Poland	0.8	0.8
Portugal	1.07	1.03
Romania	0.84	0.84
Slovakia	0.95	0.98
Slovenia	0.8	0.77
Spain	1.47	1.45
Sweden	1.19	1.21
EU27	1.43	1.39

Data on the prevalence of leukaemia in 2022 were available from GLOBOCAN. The 5-year and complete prevalence estimates of CML in the targeted EU/EEA region were indirectly calculated using information on the 5-year prevalence of all leukaemia from GLOBOCAN 2022, the proportion of CML among all leukaemia's estimated from NORDCAN, and the ratio of complete prevalence to 5-year prevalence from NORDCAN. These calculations resulted in a complete prevalence estimate of 1.74 per 10,000.

Table 3. 5-year and complete prevalence of CML per 10,000 derived from the prevalence of all leukemias in Europe, 2022

Country	**5-year prevalence of all leukemias per 10,000**	**Estimated CML prevalence per 10,000**	
		5-year prevalence	**Complete prevalence**
Austria	4.25	0.57	1.50
Belgium	6.22	0.83	2.18
Bulgaria	2.77	0.37	0.97
Croatia	4.88	0.65	1.71
Cyprus	5.39	0.72	1.89
Czechia	4.74	0.63	1.65
Denmark	6.40	0.85	2.23
Estonia	5.43	0.72	1.89
Finland	4.63	0.62	1.63
France	6.17	0.82	2.15
Germany	5.41	0.72	1.89
Greece	5.32	0.71	1.86
Hungary	4.43	0.59	1.55
Iceland	3.65	0.49	1.29
Ireland	3.83	0.51	1.31
Italy	5.20	0.69	1.81
Latvia	4.74	0.63	1.65
Lithuania	5.21	0.69	1.81
Luxembourg	3.38	0.45	1.18
Malta	3.47	0.46	1.21
Netherlands	6.10	0.81	2.13
Norway	5.67	0.75	1.97
Poland	4.00	0.53	1.39

Portugal	4.36	0.58	1.52
Romania	3.12	0.42	1.10
Slovakia	3.98	0.53	1.39
Slovenia	5.61	0.75	1.97
Spain	3.81	0.51	1.34
Sweden	5.23	0.70	1.84
EU-27+Iceland+ Norway (no data from Liechtenstein)	4.99	0.66	1.74

The COMP concluded that ECIS provides a more accurate direct estimate of CML prevalence in the EU27 compared to the indirect estimation derived from the proportion of CML within leukaemia in GLOBOCAN. In view of the above, the complete prevalence estimate 1.4 in 10,000 persons is agreed.

Article 3(1)(b) of Regulation (EC) No 141/2000

Existence of no satisfactory methods of diagnosis prevention or treatment of the condition in question, or, if such methods exist, the medicinal product will be of significant benefit to those affected by the condition.

Existing methods

The sponsor has provided a list with the medicinal products which are authorised for the applied condition. The table has been revised to include also information on whether these medicinal products are considered as satisfactory methods or not for this extension of indication.

Table 4. Authorised TKIs for the treatment of CML

Authorised TKI	Date of original market authorisation	Indication	Satisfactory method
Imatinib (Glivec)	07-Nov-2001	Glivec is indicated for the treatment of • adult and pediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive(Ph+) chronic myeloid leukemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment, • adult and pediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis.	Glivec is not considered as satisfactory method since Glivec does not cover 2L Ph+ CML-CP after any other TKI.
Nilotinib (Tasigna)	19-Nov-2011	Tasigna is indicated for the treatment of: • adult and pediatric patients with newly diagnosed Philadelphia chromosome positive chronic myelogenous leukemia (CML) in the chronic phase, • adult patients with chronic phase and accelerated phase Philadelphia chromosome positive CML with	Tasigna is not considered as satisfactory method since Tasigna covers 2L Ph+ CML-CP after imatinib only and not the other TKIs.

Authorised TKI	Date of original market authorisation	Indication	Satisfactory method
		resistance or intolerance to prior therapy including imatinib. Efficacy data in patients with CML in blast crisis are not available, • pediatric patients with chronic phase Philadelphia chromosome positive CML with resistance or intolerance to prior therapy including imatinib.	
Dasatinib (Sprycel)	20-Nov-2006	SPRYCEL is indicated for the treatment of adult patients with: • newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in the chronic phase, • chronic, accelerated or blast phase CML with resistance or intolerance to prior therapy including imatinib, • Ph+ acute lymphoblastic leukemia (ALL) and lymphoid blast CML with resistance or intolerance to prior therapy. SPRYCEL is indicated for the treatment of pediatric patients with: • newly diagnosed Ph+ CML in chronic phase (Ph+ CML-CP) or Ph+ CML-CP resistant or intolerant to prior therapy including imatinib.	Sprycel is not considered as satisfactory method since Sprycel covers 2L Ph+ CML-CP after imatinib only and not the other TKIs
Bosutinib (Bosulif)	27-Mar-2013	Bosulif is indicated for the treatment of adult patients with: • newly diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML), • CP, accelerated phase (AP), and blast phase (BP) Ph+ CML previously treated with one or more tyrosine kinase inhibitor(s) [TKI(s)] and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.	Bosulif is not considered as satisfactory method because Bosulif does not seem to cover 2L Ph+ CML-CP for patients for whom imatinib, nilotinib and dasatinib may be considered appropriate treatment options
Ponatinib (Iclusig)	01-Jul-2013	Iclusig is indicated in adult patients with: • chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation, • Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.	Iclusig is not considered as satisfactory method Iclusig covers only 1L Ph+ CML-CP patients with T315I mutation.

Based on the above, the COMP considered that there are no satisfactory methods vis-à-vis Scemblix in the context of this extension of indication.

Significant benefit

Not applicable.

4. COMP list of issues

Not applicable.

5. COMP position adopted on 20 October 2025

The COMP concluded that:

- the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated Orphan Medicinal Product.
- the prevalence of chronic myeloid leukaemia (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 1.4 in 10,000 persons in the European Union, at the time of the review of the designation criteria;
- the condition is life threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, the risk of severe infections and progression of disease to accelerated or blast phase;
- at present, no satisfactory method for the entirety of the patient population targeted by asciminib has been authorised in the European Union for patients affected by the condition.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that:

- the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied;
- the criteria for designation as set out in Article 3(1)(b) are satisfied.

The Committee for Orphan Medicinal Products has recommended that Scemblix, asciminib for treatment of chronic myeloid leukaemia (EU/3/20/2261) is not removed from the Community Register of Orphan Medicinal Products.