23 June 2025
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Zemcelpro (dorocubicel / allogeneic umbilical cord-derived CD34- cells, non-expanded)
Treatment in haematopoietic stem cell transplantation
EU/3/20/2271

Sponsor: Cordex Biologics International 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(s)	Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate
Other name(s)	--
International Non-Proprietary Name	Dorocubicel / Allogeneic umbilical cord-derived CD34- cells, non-expanded
Tradename	Zemcelpro
Orphan condition	Treatment in haematopoietic stem cell transplantation
Sponsor's details:	Cordex Biologics International Limited 5th Floor Block E Iveagh Court Harcourt Rd Dublin 2 D02 YT22 Ireland
Orphan medicinal product designation procedural history	
Sponsor/applicant	CATS Consultants GmbH
COMP opinion	19 March 2020
EC decision	22 April 2020
EC registration number	EU/3/20/2271
Post-designation procedural history	
Transfer of sponsorship	Transfer from CATS Consultants GmbH to Cordex Biologics International Limited – EC decision of 11 December 2023
Marketing authorisation procedural history	
Rapporteur / Co-rapporteur	Emmely de Vries / Jan Mueller-Berghaus
Applicant	Cordex Biologics International Limited
Application submission	23 November 2023
Procedure start	20 June 2023
Procedure number	EMA/H/C/005772
Invented name	Zemcelpro
Proposed therapeutic indication	Zemcelpro is indicated for the treatment of adult patients with haematological malignancies requiring an allogeneic hematopoietic stem cell transplantation following myeloablative conditioning for whom no other type of suitable donor cells is available. 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/ZEMCELPRO
CHMP opinion	19 June 2025

COMP review of orphan medicinal product designation procedural history	
COMP rapporteur(s)	Elisabeth Johanne Rook / Frauke Naumann-Winter
Sponsor's report submission	22 October 2024
COMP discussion and adoption of list of questions	10-12 June 2025
COMP opinion (adoption via written procedure)	23 June 2025

2. Grounds for the COMP opinion

Orphan medicinal product designation

The COMP opinion that was the basis for the initial orphan medicinal product in 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 haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate was considered justified based on preliminary clinical data showing improved engraftment;
- the condition is life-threatening and chronically debilitating due to susceptibility to severe infections and complications such as graft-versus-host disease;
- the condition was estimated to be affecting approximately 0.7 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 haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a better outcome than other allogenic stem cell transplantations. 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 haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate as an orphan medicinal product for the orphan condition: treatment in haematopoietic stem cell transplantation".

3. Review of criteria for orphan designation at the time of marketing authorisation

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

Haematopoietic stem cells transplantation (HCT) is an established procedure for many acquired or inherited disorders of the haematopoietic system, benign or neoplastic, including those of the immune system (Passweg et al., 2021). In comparison with alternative treatments, HCT is associated with superior outcomes in patients with haematologic malignancies (Motabi & DiPersio 2012). Accordingly, HCT has emerged as a preferred strategy for the treatment of a variety of these diseases, including myeloid malignancies like acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS), and lymphoid malignancies like MM, acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma (NHL), and Hodgkin's lymphoma (HL).

HCT can be performed as autologous HCT (auto-HCT) where the donor is the patient himself or allogeneic HCT (allo-HCT) where the donor is a healthy volunteer. Most lymphoid malignancies (like MM, HL, and NHL) are treated by auto-HCT, while most myeloid malignancies (like AML and MDS), but also ALL, are treated by allo-HCT (Passweg et al., 2021).

The approved therapeutic indication "Zemcelpro is indicated for the treatment of adult patients with haematological malignancies requiring an allogeneic hematopoietic stem cell transplantation following myeloablative conditioning for whom no other type of suitable donor cells is available." falls within the scope of the designated orphan condition "treatment in haematopoietic stem cell transplantation".

Intention to diagnose, prevent or treat

The medical plausibility has been confirmed by the positive benefit/risk assessment of the CHMP, see EPAR.

Chronically debilitating and/or life-threatening nature

Autologous haematopoietic stem cell transplantation has emerged as a preferred strategy for the treatment of a variety of chemotherapy or radiation sensitive haematologic malignancies, including leukaemias and lymphomas (Rajkumar & Kyle, 2005; Attal et. al., 1996; Bensinger et. al, 2009, Philip et al., 1991, Döhner et al., 2017). Allogeneic haematopoietic stem cell transplantation is also a preferred strategy for chemotherapy-resistant malignancies. Left untreated, these malignancies are life-threatening and patients suffering from one of these malignancies have little prospects for survival. Allogeneic stem cell transplantation itself is also associated with risk of life-threatening complications such as graft-vs-host-disease, infections, delays or failure of engraftment or loss of graft. Both short term and long-term complications show significant variation depending on several factors and can be fatal.

Number of people affected or at risk

The sponsor has noted that at the 2022 update[1], according to the (European Society for Blood and Marrow Transplantation (EBTM) the number of individuals undergoing HSCT in the EU-27, United-Kingdom, Norway and Iceland was as follows:

Table 1. Number of HSCT per country in the EU-27, United Kingdom, Norway and Iceland

Country	**Number of HSCT**	
	2017 data (Initial ODD) (Passweg et al. 2019)	**2022 data (Passweg et al. 2024)**
Austria	557	650
Belgium	942	884
Bulgaria	94	94
Croatia	235	230
Cyprus	25	40
Czech Republic	732	724
Denmark	342	321
Estonia	63	72
Finland	446	352
France	4961	4591
Germany	7682	7765
Greece	385	391
Hungary	203	345
Iceland	22	13
Ireland	268	298
Italy	4972	5285
Latvia	24	32
Lithuania	229	253
Luxembourg	23	28
The Netherlands	1494	1563
Norway	337	438
Poland	1761	1572
Portugal	525	579
Romania	258	250

Slovakia	242	267
Slovenia	144	170
Spain	3180	3493
Sweden	799	734
United Kingdom	4407	4448
Total	**35352**	**35882**

The number of inhabitants on January 1st, 2023, in the EU-27, United Kingdom, Norway, Iceland and Liechtenstein was calculated as follows:

Table 2. Number of inhabitants on January 1st, 2023 in the EU-27, United Kingdom, Norway, Iceland and Liechtenstein[2]

Country	**Number of inhabitants**	
	2017 data (Initial ODD)	**2023 data**
EU-28	513 481 698	-
EU-27	-	448 387 872
United Kingdom	-	67 736 802
Norway	5 328 212	5 488 984
Iceland	356 991	387 758
Liechtenstein	38 378	39 679
Total	**519 205 279**	**522 041 095**

The sponsor proposes that the prevalence in the European Economic Area on January 1st, 2023, is estimated to be 31434/454304293 which corresponds to 0.7 persons per 10,000 inhabitants. The COMP uses the number of transplants as a proxy for incidence, and incidence of the short-term procedure a proxy for prevalence. The COMP can accept this estimate for the purpose of a review for the maintenance of the orphan designation.

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

There are medicinal products authorised in the EU for patients undergoing HSCT. These medicines are used pre- or post- HSCT for different purpose:

- Eradication of the malignant cells / Treatment of the underlying disease.

- Preparation of the bone marrow for the transplantation.
- Immuno-stimulation: restoration of the immune system that was suppressed by antitumour medicines.
- Prevention or treatment of the complications: infections, graft-versus-host disease.

Zemcelpro is indicated for the treatment of adult patients with haematological malignancies requiring an allogeneic haematopoietic stem cell transplantation following myeloablative conditioning for whom no other type of suitable donor cells is available.

AlloSCT is performed by using stem cells from different donors (from related donors or unrelated volunteers or cryopreserved umbilical cord blood) depending on the underlying condition and the availability of sufficiently matched grafts. The selection of a suitable donor type involves careful consideration of multiple risk factors and patient-specific variables.

Zemcelpro primarily addresses the adult patients with haematological malignancies requiring an allogeneic HSCT who lack a suitable donor by offering them a therapeutic option by enabling transplantation of small cord blood units that don't meet the minimal cell dose requirements for unmanipulated single cord blood transplant. There are no other cord blood expansion technologies or alternative therapy approved that could be used to address this target patient population.

Significant benefit

Not applicable.

4. COMP position adopted on 23 June 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 treatment in haematopoietic stem cell transplantation (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 0.7 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 susceptibility to severe infections and complications such as graft-versus-host disease
- at present, no satisfactory method has been authorised in the European Union for the treatment of the entirety of patients covered by the therapeutic indication of Zemcelpro.

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 Zemcelpro, haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate, dorocubicel / allogeneic umbilical cord-derived CD34- cells, non-expanded for treatment in haematopoietic stem cell transplantation (EU/3/20/2271) is not removed from the Community Register of Orphan Medicinal Products.