Report ZEMCELPRO® - Dorocubicel / Allogeneic umbilical cord-derived CD34- cells, non-expanded

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Dorocubicel / Allogeneic umbilical cord-derived CD34- cells, non-expanded **Brand Name:** Zemcelpro **Originator/licensee:** Cordex Biologics International Limited **Classification:** NCE **ATC code:** B05AX04 **Orphan Status:** **Eu:** Yes **Us:** / **Mechanism of action:** Dorocubicel and non-expanded CD34- cells are stem cells from umbilical cord blood. Dorocubicel consists of CD34+ cells expanded ex-vivo. The medicine will be available as a ≥0.23 x 10^6 viable CD34+ cells/ml / ≥0.53 x 10^6 viable CD3+ cells/ml dispersion for infusion. Once infused to the pt., the cells from the drug migrate to the bone marrow where they divide, mature and differentiate in all haematological cell lineages [1].	**Authorized Indication:** **EMA**: Dorocubicel and non-expanded CD34- cells is indicated for the treatment of adults with haematological malignancies requiring an allogeneic HSCT following myeloablative conditioning for whom no other type of suitable donor cells is available [1]. **FDA:** / **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 19/06/2025 **FDA M.A. date:** / **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** / --- **ABBREVIATIONS:** **AE**: Adverse Event **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **GVHD**: Graft-versus-host disease **HR**: Hazard Ratio **HSCT**: Haematopoietic stem cell transplantation **IV**: Intravenously **M.A.:** Marketing Authorization **OS**: Oral administration **PFS**: Progression-Free Survival **P.O.**: Positive Opinion **PS**: Performance Status **Pts**: Patients **SAE**: Serious adverse events **TRAE**: Treatment related AEs **WHO**: World Health Organization	The efficacy and safety of dorocubicel and non-expanded CD34- cells were evaluated in two single-arm, open-label, phase 2 clinical studies: the first assessed the safety and feasibility of the treatment, while the second examined T cell reconstitution in pts. enrolled in the initial trial. **Summary of clinical EFFICACY:** **NCT02668315** was a single-arm, open-label, phase 1-2 safety and feasibility study conducted in Canada. The study had two parts: in part one, pts. received two cord blood units (one expanded with UM171 and one unmanipulated cord blood) until UM171-expanded cord blood demonstrated engraftment. Once engraftment was documented part 2 was initiated in which pts. received a single UM171-expanded cord blood unit with a dose de-escalation design to determine the minimal cord blood unit cell dose that achieved prompt engraftment. Eligible pts. were aged 3-64 years, who weighed 12 Kg or more, with a haematological malignancy with an indication for allogeneic HSCT, did not have a suitable HLA-matched donor, had adequate organ function, and had a Karnofsky PS score of ≥70%. Twenty-seventy pts. were enrolled, 23 out of them were enrolled in part two to receive a single UM171-expanded cord blood transplant and 22 patients received a single UM171-expanded cord blood transplantation. No paediatric pts. (<18 years) were recruited. The primary endpoints were safety, feasibility, kinetics of haematopoietic reconstitution and identification of minimal pre-expansion cord blood unit cell dose that ensures prompt engraftment. After a median follow-up of 18 months, the lowest cell dose of the cord blood unit at thaw that resulted in prompt engraftment as a single cord transplant following UM171 expansion was 0.52 × 10^5 CD34-positive cells. The expansion of cord blood units with UM171 achieved a success rate of 96% [2,3]. **Summary of clinical SAFETY:** The most common non-hematologic grade ≥3 AEs were febrile neutropenia (73% of pts.) and bacteraemia (41% of patients). Other grade 3 or higher adverse events included: increased creatinine levels (32%), mucositis (27%), cytomegalovirus viremia (23%), GVHD syndrome (18%), and cryptogenic organizing pneumonia (14%). Two pts. (9%) experienced diffuse alveolar haemorrhage, both requiring mechanical ventilation; one pt. died due to respiratory failure related to this complication. The incidence of transplant-related mortality at 1 year was 5% (95% CI 1–31). Out of 22 patients, three (14%) died by the data cutoff date: two due to disease progression and one due to diffuse alveolar haemorrhage. The cumulative incidence of grade 3-4 acute GVHD at 1 year was 10%. No patient experienced steroid-refractory acute GVHD. The cumulative incidence of chronic GVHD at 1 year was 17%, with no cases of moderate to severe chronic GVHD [2,3]. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** No **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/zemcelpro [2] https://www.sciencedirect.com/science/article/pii/S1083879120306248 [3] https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(19)30202-9/abstract [4] https://ashpublications.org/blood/article/116/19/3724/28018/Incidence-of-hematologic-malignancies-in-Europe-by [5] https://www.mdpi.com/2072-6694/14/1/87	**Cost of therapy:** The price is not available yet. **Epidemiology:** In Europe, the age-standardized incidence rate for lymphoid malignancies is 24.5 per 100,000, and 7.55 per 100,000 for myeloid malignancies. The overall age-standardized incidence of haematological malignancies is lower in Eastern Europe [4]. --- **POSSIBLE PLACE IN THERAPY**: Treatment options are broadly divided into two main categories: small molecule anticancer drugs (e.g., tyrosine kinase inhibitors, multi-kinase inhibitors, phosphoinositide 3-kinase inhibitors, etc.) and macromolecules (e.g., monoclonal antibodies, antibody-drug conjugates). Advanced therapies such as CAR-T cells may also be considered. HSCT—particularly autologous stem cell transplantation —is a relevant treatment modality for certain haematological malignancies [5]. **OTHER INDICATIONS IN DEVELOPMENT: -** **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Omidubicel (NCT02730299) *Service reorganization: No *Possible off label use: Yes

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