Report SKYSONA® elivaldogene autotemcel

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: elivaldogene autotemcel **Brand Name:** SKYSONA® **Originator/licensee:** bluebird bio (Netherlands) B.V. **Classification:** NCE **ATC code:** not yet assigned **Orphan Status:** **Eu:** Yes **Us:** Yes **Mechanism of action:** elivaldogene autotemcel is made specifically for each pt, using the pt'shaematopoietic stem cells. The stem cells are modified in a laboratory to insert a working gene for making human ALDP. When the pts receives elivaldogene autotemcel, which is made up of these modified cells, the cells start making ALDP, which will then break down the very long chain fatty acids that build-up in pts with CALD. [1]	**Authorized Indication:** **EMA:** elivaldogene autotemcel is indicated for the treatment of early CALD in pts less than 18 years of age, with an ABCD1 genetic mutation, and for whom an HLAmatched sibling HSC donor is not available [1]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 20/5/2021 **FDA M.A. date: ---** **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway: ---** --- **ABBREVIATIONS:** **AEs:** Adverse Events **ALDP:**Adrenoleukodystrophy protein **CALD:** Cerebral Adrenoleuko-dystrophy **CHMP:** Committee for Medicinal Products for Human Use **HLA:** Human leukocyte antigen **HSC:**Haematopoietic Stem Cell **M.A.:** Marketing Authorization **MRI:**Magnetic Resonance Imaging **P.O.:** Positive Opinion **pt:** patient **SAEs:** Serious Adverse Events	**Summary of clinical EFFICACY:** **STARBEAM (NCT01896102)**: is a single-group, open-label, phase 2–3 safety and efficacy study.Eligible pts (n=17) were male, ≤17 years who had gadolinium enhancement on MRI due to CALD and had the following signs of early-stage disease: CALD score* 0 or 1 (for severity of gross neurologic dysfunction) and a Loes score** of 0.5-9.0 (used to assess the extent of lesions on MRI of the head).Pts who had an HLA-matched sibling HSC donor for transplantation were excluded.Pts received conditioning with busulfan and cyclophosphamide, after which elivaldogene autotemcel and were followed for two years. Enrollment in a 13-year long-term follow-up study was offered to pts that had completed the study. The primary efficacy end point was being alive and having no major functional disabilities at 24 months.15/17 pts (88%) were alive and free of major functional disabilities (maintained a CALD score of 0 or 1). Twopts had neurologic disease progression (one withdrew from the study and the other died 22 months after the infusion due to complication of a viral infection).Loes score had stabilized in 12/17 pts (71%). 14 pts were enrolled in the long-term follow-up study. [2] *CALD score: 0-25 which ranges from 0 to 25, with higher scores indicating more severe deficits. **Loes score: which ranges from 0 to 34, with higher scores indicating an increased extent of lesions on MRI **Summary of clinical SAFETY:** Most AEs associated with the treatment occurred during the conditioning phase or the first two weeks after the infusion (generally associated with myeloablative chemotherapy).One pts had tachycardia and one pts had hemorrhagic cystitis (associated with BK virus - human polyomavirus) on day 42 possibly related to elivaldogene autotemcel. [2] **Ongoing studies:** ● ***For the same indication:***Yes [3,4] ● ***For other indications:***No **Discontinued studies (for the same indication):**No --- **References:** 1.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/skysona;(Accessed 26 Jul 2021). 2.Eichler F, Duncan C, Musolino PL, Orchard PJ, De Oliveira S, Thrasher AJ, et al. Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy. N Engl J Med. 2017 Oct 26;377(17):1630-1638. 3.https://clinicaltrials.gov/ct2/show/NCT03852498?term=elivaldogene&cond=Cerebral+Adrenoleukodystrophy&draw=2&rank=1(Accessed 26 Jul 2021). 4.https://clinicaltrials.gov/ct2/show/NCT02698579?term=elivaldogene&cond=Cerebral+Adrenoleukodystrophy&draw=2&rank=3(Accessed 26 Jul 2021). 5.https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=IT&data_id=16884&MISSING%20CONTENT=Adrenoleucodistrofia-legata-all-X--forma-cerebrale&search=Disease_Search_Simple; (Accessed 26 Jul 2021). 6.Mallack EJ, van de Stadt S, Caruso PA, et al. Clinical and radiographic course of arrested cerebral adrenoleukodystrophy. Neurology. 2020;94(24):e2499-e2507. 7.https://clinicaltrials.gov/ct2/show/NCT04528706?recrs=abdef&cond=Cerebral+Adrenoleukodystrophy&phase=12&draw=2&rank=3(Accessed 26 Jul 2021).	**Cost of therapy:** not yet available **Epidemiology:** Adrenoleukodystrophy has an estimated world birth prevalence of 1/20,000,35% of males develop CALD in childhood (the most severe form of the disease)[5,6]. **POSSIBLE PLACE IN THERAPY** Allogeneic transplantation is the only effective therapy for CALD that has been identified to date.[2, 5] **OTHER INDICATIONS IN DEVELOPMENT:** No **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** / **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION** MIN-102 [7] *Service reorganization Yes *Possible off label use No

Issued on July 2021