PRESCRIBING INFORMATION
Please consult the Summary of Product Characteristics before prescribing.

LIBMELDY™ ▼ (atidarsagene autotemcel). Gene therapy. Finished product composed of one or more infusion bags containing a dispersion for infusion of an autologous $CD34^+$ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector expressing the human arylsulfatase A (*ARSA*) gene. Quantitative information for each batch is provided in the Lot Information Sheet; concentration is 2-10 million $CD34^+$ cells/mL.

Indication: Treatment of metachromatic leukodystrophy (MLD) characterized by biallelic mutations in the arylsulfatase A gene leading to a reduction of the ARSA enzymatic activity: i) in children with late infantile or early juvenile forms, without clinical manifestations of the disease; ii) in children with the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline.

Dosage and administration: Must be administered in a qualified treatment centre by a physician with experience in Haematopoietic Stem Cell Transplantation (HSCT) and trained for administration and management of patients treated with the medicinal product. Patients are expected to enrol and be followed up in a long-term follow-up study. Libmeldy is for autologous use only and should be administered only once. Dose to be administered is defined based on the patient's body weight at the time of infusion. Minimum recommended dose is 3×10^6 $CD34^+$ cells/kg of body weight. In clinical studies doses up to 30 million $CD34^+$ cells/kg have been administered. Maximum volume to be administered should remain < 20% of the patient's estimated plasma volume. Patients must be able to donate a minimum of 8 million $CD34^+$ cells/kg from peripheral blood mobilisation (mPB) for product manufacture. A back-up collection of HSPC containing at least 2 million $CD34^+$ cells/kg is also required. The back-up cells may be harvested either through mPB apheresis or bone marrow harvest. Libmeldy is administered via intravenous (IV) infusion with an infusion rate not exceeding 5 mL/kg/hr. **Pre-treatment conditioning**: A myeloablative conditioning is required before infusion of Libmeldy. Busulfan is the recommended conditioning medicinal product. **Pre-medication:** IV chlorpheniramine administered 15-30 minutes before Libmeldy infusion is recommended. **Children:** Safety and efficacy in patients with the late juvenile form of the disease have not been established; no data available. **Elderly:** Libmeldy has not been studied in patients > 65 years of age. **Hepatic and renal impairment:** Not studied; dose adjustment is not expected to be required.

Contraindications: Hypersensitivity to the active substance or excipients; previous treatment with haematopoietic stem cells gene therapy; contraindications to the mobilisation and the myeloablative medicinal products must be considered.

Special warnings and precautions: **Autologous use:** Must not be administered to any patient other than the original $CD34^+$ cell donor. **Rapidly progressive phase:** Treatment should be performed before the disease enters its rapidly progressive phase. Eligibility to treatment with Libmeldy should initially be assessed by the treating physician via full neurological examination, motor function assessment and neurocognitive assessment, as appropriate for the patients' age. **Mobilisation and myeloablative conditioning agents:** Warnings and precautions associated with these medicinal products must be considered. **Dimethylsulfoxide** is known to possibly cause anaphylactic reactions following parenteral administration; patients without previous exposure should be observed closely**. Engraftment failure:** Failure of neutrophil engraftment is a short-term but potentially important risk defined as a failure to reach an absolute neutrophil count (ANC) > 500 cells/µL. In clinical studies no patients failed to engraft bone marrow. **Prolonged cytopenia**: Patients may exhibit severe cytopenias, including severe neutropenia [defined as ANC <500 cells/µL] and prolonged thrombocytopenia, for several weeks following myeloablative conditioning and Libmeldy infusion. Patients should be monitored for at least 6 weeks after infusion. **Risk of insertional oncogenesis**: There is a theoretical risk of leukaemia or lymphoma after treatment with Libmeldy. **Anti-ARSA antibodies**: AAA were reported in 5 patients during clinical development; titers were generally low and resolved spontaneously or after treatment with rituximab. **Serological testing:** Libmeldy has not been studied in patients with HIV-1, HIV-2, HTLV-1, HTL-2, HBV, HCV or mycoplasma infections; patients should be tested prior to mobilisation. **Interference with virological testing:** Patients who have received Libmeldy are likely to test positive by polymerase chain reaction assays for HIV due to LVV provirus insertion resulting in a false positive HIV test. **Blood, organ and tissue donation:** Patients treated with Libmeldy must not donate blood, organs, tissues and cells for transplantation. **After Libmeldy infusion**, standard procedures for patient management after HSPC transplantation should be followed.

Interactions: No pharmacokinetic interactions are expected. **Anti-retroviral use:** Patients should not take anti-retroviral medicinal products from at least one month prior to mobilisation until at least 7 days after Libmeldy infusion. **Live vaccines:** The safety of immunisation with live viral vaccines during or following treatment with Libmeldy has not been studied. Vaccination with live viral vaccines is not recommended for at least 6 weeks preceding the start of myeloablative conditioning, during Libmeldy treatment and until haematological recovery.

Fertility, pregnancy and lactation: As Libmeldy is not intended for use in adults, data on use during pregnancy or lactation and animal reproduction studies are not available. Concerning fertility, the treating physician should inform the patient's parents/carers about options for cryopreservation of spermatogonial stem cells or ovarian tissue.

Side effects: Safety was evaluated in 35 patients with a median duration of follow-up of 4.51 years with the investigational formulation (29 patients) and 0.87 years with the commercial (cryopreserved) formulation (6 patients). Given the small patient population, adverse reactions do not provide a complete perspective. **Adverse reactions attributed to Libmeldy;** Very common (≥ 1/10): Antibody test positive (anti ARSA antibody**). Adverse reactions potentially attributed to myeloablative conditioning:** Very common (≥ 1/10): Febrile neutropenia, neutropenia, metabolic acidosis, stomatitis, vomiting, hepatomegaly, veno-occlusive liver disease, ovarian failure. Common (≥ 1/100 to < 1/10): Cytomegalovirus viraemia, pneumonia, staphylococcal infection, urinary tract infection, viral infection, anaemia, thrombocytopenia, fluid overload, insomnia, headache, epistaxis, oropharyngeal pain, ascites, diarrhoea, gastrointestinal haemorrhage, nausea, hypertransaminasaemia, skin exfoliation, back pain, bone pain, oliguria, pyrexia, ALT and AST increased, aspergillus test positive. **Prescribers should consult the Summary of Product Characteristics for complete information regarding the adverse reaction profile.**

Legal category: Prescription medicine.

Marketing Authorisation (MA) number: EU/1/20/1493/001

MA Holder: Orchard Therapeutics (Netherlands) B.V., Basisweg 10, 1043JB Amsterdam, The Netherlands.

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Preparation Number: API-LIB-EMA-0622

▼**This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse events. Further information about local reporting details can be found in Section 4.8 of the Summary of Product Characteristics.**

Please also report any adverse events to Orchard Therapeutics at: **drugsafety@orchard-tx.com**

For medical enquiries, please contact Orchard Therapeutics via email at medinfo@orchard-tx.com