Grafapex™ (treosulfan) – New orphan drug approval

- On December 22, 2024, Medexus Pharmaceuticals announced the FDA approval of Grafapex (treosulfan), **in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients 1 year of age and older with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS)**.

- Grafapex is an alkylating drug.

- The efficacy of Grafapex was established in a randomized active-controlled trial comparing Grafapex to busulfan in combination with fludarabine as a preparative regimen for allogeneic transplantation. The study included 570 patients with AML or MDS. Efficacy was established on the basis of overall survival (OS), defined as the time from randomization until death from any cause.

    — The hazard ratio for OS (stratified by donor type and risk group) compared to busulfan was 0.67 (95% CI: 0.51, 0.90) in the randomized population, 0.73 (95% CI: 0.51, 1.06) in patients with AML, and 0.64 (95% CI: 0.40, 1.02) in patients with MDS.

- Grafapex carries a boxed warning for **myelosuppression**.

- Additional warnings and precautions for Grafapex include seizures; skin disorders; injection site reactions and tissue necrosis; secondary malignancies; increased early morbidity and mortality at dosages higher than recommended; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Grafapex use were musculoskeletal pain, stomatitis, pyrexia, nausea, edema, infection, and vomiting. Selected grade 3 or 4 nonhematological laboratory abnormalities were increased gamma-glutamyltransferase (GGT), increased bilirubin, increased alanine transaminase (ALT), increased aspartate transferase (AST), and increased creatinine.

- The recommended dosage of Grafapex is 10 g/m^2 by intravenous infusion given daily for three days, beginning on Day -4 prior to transplantation in combination with fludarabine.

- Medexus plans to launch Grafapex in the first half of 2025. Grafapex will be available as a 1 g/vial and 5 g/vial lyophilized powder in single-dose vials.