News Release

SERB receives positive CHMP opinion for Voraxaze® (glucarpidase) as Rescue Therapy for High Dose Methotrexate Toxicity

- Voraxaze® recommended for retention on the Community Register of Orphan Medicinal Products

LONDON – 25 November 2021 – SERB and BTG Specialty Pharmaceuticals today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending a marketing authorisation for Voraxaze® (glucarpidase) to reduce toxic plasma methotrexate concentration in adults and children (aged 28 days and older) with delayed methotrexate elimination or at risk of methotrexate toxicity.

The CHMP positive opinion is one of the final steps before marketing authorisation is granted by the European Commission, which has the authority to approve medicines for use in all members states of the European Union as well as Iceland, Liechtenstein, and Norway. Voraxaze® will be sold in these markets by SERB, which merged with BTG in March 2021.

The EMA's Committee for Orphan Medical Products (COMP) also recommended that Voraxaze® remains on the Community Register of Orphan Medicinal Products. Orphan medicines benefit from 10 years of market exclusivity upon approval as well as regulatory support for subsequent clinical development and commercialization in the European Union.

"Prolonged exposure to high concentrations of methotrexate can cause severe and potentially life-threatening toxicity," said Antoine Bernasconi, SERB Chief Commercial Officer. "This positive CHMP opinion for Voraxaze is an important step toward offering a reliable and specific rescue therapy for cancer patients in Europe who experience toxic methotrexate concentrations."

The positive opinion is based on clinical data as well as real world experience in the US where Voraxaze® has been sold by BTG Specialty Pharmaceuticals since it was approved by the FDA in January of 2012. Since its launch in the US, an estimated 2,867 patients have been treated with Voraxaze®. The efficacy of Voraxaze® has been evaluated in four open-label, multi-centre studies in patients with delayed methotrexate elimination. In patients with methotrexate concentrations measured by chromatographic methods, a median reduction of > 97% in methotrexate concentration occurred within 15 minutes following Voraxaze® administration. [i, ii]

The CHMP approval follows the news earlier this year that Japan's Ministry of Health, Labour and Welfare authorized glucarpidase to be sold in Japan as Megludase® by BTG's marketing partner, Ohara Pharmaceutical Co.

About High Dose Methotrexate Toxicity

High Dose Methotrexate (HDMTX) chemotherapy is used to treat or prevent the recurrence of certain types of cancer in adults and children, such as leukaemia, lymphoma, and osteosarcoma. Despite standard supportive measures, HDTMX may induce renal dysfunction in some patients, delaying MTX elimination. This may result in sustained elevated levels of MTX concentration which in turn may cause acute renal toxicity and other systemic adverse reactions that do not respond to standard doses of first-line therapy.

Administering Voraxaze® may quickly lower MTX levels and avoid further systemic damage. It works by breaking down methotrexate into its inactive metabolites which are then eliminated from the body by routes other than the kidney – primarily the liver. Voraxaze® is the only drug able to reduce toxic plasma methotrexate levels.

Further Development of Voraxaze®:

In addition to the current indications, Voraxaze® is being independently studied in Europe and the United States to explore whether the "planned use" of Voraxaze® in combination with high-dose methotrexate might alleviate toxicity, manage the risk to patients, and help them to complete therapy. Enrolment in these studies is ongoing. For more information about these studies, or to contact an investigator about participation, please visit ClinicalTrials.gov.

About SERB and BTG Specialty Pharmaceuticals

Together, SERB and BTG are a growing specialty pharmaceutical company and a dedicated ally to healthcare providers treating patients with critical conditions, focusing on emergency care and rare diseases. For over 30 years we have made treating these complex and life-threatening conditions possible, supporting clinicians, healthcare systems and governments while offering hope to patients and their families. As a fully integrated company, we have the experience and capabilities to acquire, develop, and manufacture our medicines to the highest standards, and make them available worldwide through our secure supply chain.

Learn more about SERB: https://serb.eu/

Learn more about BTG Specialty Pharmaceuticals: https://btgsp.com

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[i] *Widemann BC, Balis FM, Kim A, et al. Glucarpidase, leucovorin, and thymidine for high-dose methotrexate-induced renal dysfunction: clinical and pharmacologic factors affecting outcome.* J Clin Oncol. *2010;28(25):3979-3986.*

[ii] *2013 Annual Meeting of the North American Congress of Clinical Toxicology (NACCT).* Clin Toxicol. *2013;51(7):575-724.*