Saudi Public Assessment Report

(Summary Report)

Fovepta®

Type of Product: Hepatitis B Virus Vaccine.

Active Pharmaceutical Ingredient(s): Human hepatitis B immunoglobulin.

ATC code: J06BB04.

Dosage Form: Concentrate for solution for injection.

Dosage Strength: 500 IU.

Pack Size: 1 ml.

Shelf life: 24 months.

Storage Conditions: Store in a refrigerator (2°C – 8°C), do not freeze.

Reference Product in SA (if applicable): NA.

Marketing Authorization Holder: Biotest Pharma GmbH.

Manufacturer: Biotest Pharma GmbH.

Registration No.: 3008222560.

Date of Decision: Approved on 15/08/2022.

Proposed Indications: Prevention of hepatitis B virus re-infection after liver transplantation for hepatitis B induced liver failure in adult patients.

Product Background

This product is considered as new vaccine for Saudi regulatory purposes. Furthermore, this product is qualified to follow the SFDA's regular regulatory pathway.

Fovepta® is a purified human hepatitis B immunoglobulin preparation obtained from plasma from selected and/or immunised donors having antibodies against hepatitis B surface (HBs) antigen. It is a sterile solution for subcutaneous (SC) injection containing 150 mg human plasma protein with at least 96% IgG and 500 IU/ml anti-HBs antibody. The product is considered a further development of an already approved HBIG preparation for intravenous (IV) administration (Hepatect CP) with the difference being that the intravenous product is less concentrated. Zutectra is presented in 1 ml glass syringes.

The SFDA approval for Fovepa® for marketing authorization in Saudi Arabia is based on a review of the quality, safety and efficacy referenced to the SFDA data requirement for human drug submission and relevant ICH Guidelines as summarised hereinafter:

Quality Aspects

The drug substance's starting material is human plasma for fractionation from immunized donors (HBs antibodies ≥ 10 IU/ml in the plasma pool) which compiles the requirements of the Ph.Eur. monograph no. 853 "Human plasma for fractionation", manufacturing process started from plasma pool which processed following a modified cold ethanol fractionating process to isolate and precipitate the intermediates (fraction II and fraction I/II/IIIM) In spite of clear differences in the composition of starting materials (fraction I/II/III), variation of the different process parameters within the specified limits never lead to differences in the yield or purity of the target fraction (filtrate of fraction I/III). The manufacturing process is described in sufficient details along with sufficient control for each step moreover many additional steps optionally added to increase the drug substance quality. Reproducibility and consistency of the manufacturing process in pilot scale and production scale is documented for the intermediates fraction I/II/III, fraction II, for the intermediate, caprylic acid treated and for the intermediate as well as for the final drug substance.

During the development a new plant for production is added with slight production process modifications in the combined precipitation of fibrinogen and immunoglobulins in fraction I/II/III (e.g. pH, ethanol content) for the precipitation of fraction I/II/III, fraction I/III and fraction II which lead to a higher yield of Immunoglobulin G. The required comparability studies between the production processes and control for both sites is performed concluding that new process capability to produce drug substance with needed quality is proven. Plasma related impurities were identified as critical and found to be well controlled, because undesirable effects in patients are possible (vasoactive effects, activation of the haemostatic system, digestion of the active substance or lyses of erythrocytes)

The medicinal product Fovepta is a development derived from the medical product Hepatect CP. Biotest previously SFDA's authorized product. Fovepta® is supplied as a solution for injection. The solution is clear to opalescent and colourless to pale yellow presented in syringes containing 200 IU in 0.4 ml solution for injection. Fovepta contains all four subclasses of normal human IgG in relative concentrations corresponding to their concentration in normal human plasma. A detailed analysis of the subclass distribution is given.

The container/closure system consists of type I glass syringes, type I stoppers (bromobutyl rubber), and tip caps (bromobutyl rubber) meeting the relevant Ph. Eur. Monographs. Compatibility of the drug product formulation and the container/closure material has been confirmed in stability studies. There were no significant differences in stability between storage in upright and lying position.

Clinical Aspects

Efficacy and Safety

The clinical development program for Fovepta consisted of one clinical studies:

- Study 959: efficacy and safety study.

Summary of the clinical studies presented hereafter:

- 1: Study 959, A Phase III, open label, randomised parallel study, single dose (200 IU, administered < 12 hours after birth) of Fovepta was administered by subcutaneous (SC) or intramuscular (IM) injection to 34 neonates (17 SC and 17 IM) of a gestational age ≥ 37+0 weeks born to HBsAg positive mothers. The primary efficacy variable (response rate) was defined as the proportion of infants with an anti-HBs concentration < 10 IU/L pre-dose (i.e., negative initial value) and ≥ 100 IU/L as determined post-dose during an interval of 72 hours after birth.

The clinical pharmacology, efficacy and safety results from the aforementioned studies were assessed by the SFDA efficacy and safety department. Based on the review of the submitted evidence, the benefit/risk balance of Fovepta is considered positive. Therefore, we recommend the approval of the marketing authorization of Fovepta.

Product Information

The approved Summary of Product Characteristics (SPC) with the submission can be found in Saudi Drug Information System (SDI) at: https://sdi.sfda.gov.sa/

The date of revision of this text corresponds to that of the Saudi PAR. New information concerning the authorized medicinal product in question will not be incorporated into the Saudi PAR. New findings that could impair the medicinal product's quality, efficacy, or safety are recorded and published at (SDI or Summary Saudi-PAR report).

For inquiry and feedback regarding Saudi PAR, please contact us at Saudi.PAR@sdfa.gov.sa