Saudi Public Assessment Report

(Summary Report)

ELIVE®

Type of Application: New Drug Application

Type of Product: Human Generic Drug

Active Pharmaceutical Ingredient(s): Entecavir monohydrate

ATC code: QJ05AF10

Dosage Form: Film-Coated Tablet

Dosage Strength: 0.5 mg - 1 mg

Pack Size: 30 Blister

Shelf life: 24 Months

Storage Conditions: Store below 30°c

Reference Product in SA (if applicable): BARACLUDE 1 mg Tablet

Marketing Authorization Holder: Aja Pharmaceutical Industries

Manufacturer: Aja Pharmaceutical Industries

Registration No.: 2704221994 - 2704221993

Date of Decision: Approved on 28/02/2022

Proposed Indications: ELIVE is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with:

- Compensated liver disease and evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis.
- Decompensated liver disease.

- For both compensated and decompensated liver disease, this indication is based on clinical trial data in nucleoside naive patients with HBeAg positive and HBeAg negative HBV infection, with a respect to patients with lamivudine-refractory hepatitis B.
- ELIVE is also indicated for the treatment of chronic HBV infection in nucleoside naive pediatric patients from 2 to < 18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum ALT levels, or histological evidence of moderate to severe inflammation and/or fibrosis, with a respect to the decision to initiate treatment in pediatric patients.

Product Background

This product is considered as a human generic drug, for Saudi regulatory purposes. Furthermore, this product is qualified to follow the SFDA's normal submission regulatory pathway.

The SFDA approval for ELIVE® (Entecavir 0.5 mg - 1 mg) is based on a review of the quality, safety and efficacy as summarized hereinafter:

Quality Aspects

Drug Substance

- Entecavir monohydrate is a white or almost white crystalline powder. Entecavir monohydrate is practically insoluble in acetonitrile and n-heptane, slightly soluble in methanol, ethanol and water, sparingly soluble in N, N-dimethylformamide, soluble in N, N-dimethylacetamide. Entecavir monohydrate does have three chiral centers. Polymorphism has been observed.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Entecavir monohydrate has been fully elucidated using several spectroscopic techniques.
- The drug substance specification includes relevant tests for proper quality control. The control methods are validated according to international guidelines.
- Appropriate stability data have been presented and justify the established re-test period.

Drug Product

- The finished drug product is available in two strengths:

    1. 1 mg FCT: Pink oval-shaped tablet with a break line on both sides.
    2. 0.5 mg FCT: White oval-shaped tablet with a break line on both sides.

- Each tablet contains 1mg or 0.5mg of Entecavir monohydrate. The composition of the drug product is adequately described, qualitatively and quantitatively. Suitable pharmaceutical development data have been provided for the finished product composition and manufacturing process.
- The manufacturing process is described narratively and in sufficient detail, taking into account pharmaceutical development data. Batch manufacturing formulas and in-process controls are included.
- The drug product specification covers appropriate parameters for this dosage form which allow for proper control of the finished drug product. The control methods are validated according to international guidelines. Batch data show consistent quality of the drug product.

- The drug product is packaged in a carton box, containing 3 Alu/Alu blister packs, containing 10 tablets in each blister.
- Appropriate stability data have been generated in the packaging material intended for commercial use and following relevant international guidelines. The data show good stability of the finished product and support the proposed shelf life.

Clinical Aspects

Bioequivalence Study

Ratio and 90% Confidence Intervals (CI) of Elive® (Entecavir) 1 mg versus Baraclude® (Entecavir) 1 mg:

Pharmacokinetic Parameter	Point Estimate	CI 90%
C_{max} (pg/mL)	101.58	95.09 – 108.52
AUC_{0-72} (pg/mL)	99.13	97.47 – 100.81

Based on the results obtained in this study, Elive® (Entecavir) 1 mg of Zentiva, Turkey, is **bioequivalent** to Baraclude® (Entecavir) 1 mg Bristol-Myers Squibb S.r.L, Italy, under fasting Conditions.

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