الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Libsa®

Type of Application: New Drug Application.

Type of Product: Human Generic Drug.

Active Pharmaceutical Ingredient(s): Rivaroxaban

ATC code: B01AF01

Dosage Form: Film-coated tablet

Dosage Strength: 10 mg, 15 mg, 20 mg

Pack Size: 10 mg (10,30 tabs) 15 mg (30 tabs), 20 mg (30 tabs)

Shelf life: 24 months

Storage Conditions: Store below 30°C.

Reference Product in SA (if applicable): Xarelto

Marketing Authorization Holder: Alpha Pharma Industry

Note: The Saudi PAR is a final document, which provides information relating to a submission at a particular point in time and will not be updated after publication.

Manufacturer: Alpha Pharma Industry

Registration No.: 2301233150 , 2301233148 , 2301233149 , 2301233147

Date of Decision: 15/01/2023 -23/01/2023 – 16/01/2023

Proposed Indications:

Libsa®10 mg :

Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Libsa® 15&20 mg :

- Adults

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

- Pediatric population

Treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years and weighing more than 50 kg after at least 5 days of initial parenteral anticoagulation treatment.

Product Background

This product is considered as a human generic drug for Saudi regulatory purposes qualified to follow the SFDA's regulatory Regular pathway.

The SFDA approval for Libsa® is based on a review of the quality, safety and efficacy of the product provided as an e-CTD in accordance with the relevant guidelines, basic product information summarized hereinafter:

Drug Substance

- Rivaroxaban is a white or yellowish powder. Rivaroxaban is insoluble in acetone, practically insoluble in methanol, very slightly soluble in tetrahydrofuran, slightly soluble in acetonitrile and glacial acetic acid and soluble in dimethylformamide and dimethyl sulfoxide.. Polymorphism has been observed (Polymorph I).
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of the API has been fully elucidated using several spectroscopic techniques.
- The drug substance specification includes relevant tests for proper quality control. Whereas 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 drug product is available in three strengths:
    1. 10 mg Pink, round shaped, biconvex film-coated tablets, debossed JS51 on one side and plain on other side.
    2. 15 mg Red, round shaped, biconvex film-coated tablets, debossed JS52 on one side and plain on other side.
    3. 20 mg Dark Red, round shaped, biconvex film-coated tablets, debossed JS53 on one side and plain on other side.
- Each tablet contains 10 mg 15 mg and 20 mg of Rivaroxaban. 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 (Alu – PVC/PVDC Blisters. : 30 Tablets (10 tablets/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 shelf life.

Clinical Aspects

Bioequivalence Study

For 20mg:

Ratio and 90% Confidence Intervals (CI) of Libsa® (Rivaroxaban) 20 mg versus Xarelto® (Rivaroxaban) 20 mg Film-coated tablets:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}	95.01	91.12 - 99.06
AUC_{0-t}	97.74	94.83 - 100.73
$AUC_{0-\infty}$	97.74	94.91 - 100.66

Based on the results obtained in this study, Libsa® (Rivaroxaban) 20 mg of Alpha pharma industries, Saudi Arabia, is **bioequivalent** to Xarelto® (Rivaroxaban) 20 mg of Bayer AG Leverkusen, Germany, under fed Conditions.

For 10mg:

Ratio and 90% Confidence Intervals (CI) of Libsa® (Rivaroxaban) 10 mg versus Xarelto® (Rivaroxaban) 10 mg Film-coated tablets:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}	97.61	91.48 - 104.15
AUC_{0-t}	97.71	93.75 - 101.83
$AUC_{0-\infty}$	98.01	94.07 - 102.11

Based on the results obtained in this study, Libsa® (Rivaroxaban) 10 mg of Alpha pharma industries, Saudi Arabia, is **bioequivalent** to Xarelto® (Rivaroxaban) 10 mg of Bayer AG Leverkusen, Germany, 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