Saudi Public Assessment Report

(Summary Report)

Dullarma®

Type of Application: New Drug Application

Type of Product: Human Generic Drug

Active Pharmaceutical Ingredient(s): Ibrutinib

ATC code: L01XE27

Dosage Form: Capsule, hard

Dosage Strength: 140 mg

Pack Size: 120 Bottle

Shelf life: 24 Months

Storage Conditions: Do not store above 30°c

Reference Product in SA (if applicable): Imbruvica 140 mg Capsule

Marketing Authorization Holder: Jazeera Pharmaceutical Industries (JPI)

Manufacturer: Jazeera Pharmaceutical Industries (JPI)

Registration No.: 1708222501

Date of Decision: Approved on 25/06/2022

Proposed Indications:

- Dullarma as a single agent is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).
- Dullarma as a single agent is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukemia (CLL).

- Dullarma as a single agent or in combination with bendamustine and rituximab (BR) is indicated for the treatment of adult patients with CLL who have received at least one prior therapy.
- Dullarma as a single agent is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first-line treatment for patients unsuitable for chemo-immunotherapy.

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 Dullarma® (Ibrutinib 140 mg) is based on a review of the quality, safety and efficacy as summarized hereinafter:

Quality Aspects

Drug Substance

- Ibrutinib is a white to off-white crystalline powder. Ibrutinib is practically insoluble in water and freely soluble in dimethyl sulfoxide and methanol. Ibrutinib does have 1 chiral center. Polymorphism has been observed.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Ibrutinib 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 product is available as white (body)/ white (cap) size (0) polished capsules imprinted with black logo: AP on the cap and 961 on the body containing white to off-white powder. Each capsule contains 140 mg of Ibrutinib. 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 an HDPE plastic bottle containing purified rayon and two desiccant bags.

- 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

Ratio and 90% Confidence Intervals (CI) of Dullarma® (Ibrutinib) 140 mg versus Imbruvica® (Ibrutinib) 140 mg:

Pharmacokinetic Parameter	Point Estimate	CI 90%
C_{max} (ng/mL)	111.95	100.13 – 125.17
AUC_{0-t} (ng/mL)	96.73	90.19 – 103.74
$AUC_{0-\infty}$ (ng/mL)	97.55	90.82 – 104.78

Based on the results obtained in this study, Dullarma® (Ibrutinib) 140 mg of Arab pharmaceutical manufacturing Co. Ltd, Jordan, is **bioequivalent** to Imbruvica® (Ibrutinib) 140 mg Janssen-Cilag International NV, Belgium, 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