الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Roneza ®

Type of Application: New Drug Application.

Type of Product: Human New Drug.

Active Pharmaceutical Ingredient(s): Rosuvastatin, Ezetimibe

ATC code: QC10BA06

Dosage Form: Film-coated tablet

Dosage Strength: 10,40 mg / 10,20 mg / 10,10 mg / 5,10 mg

Pack Size: 30

Shelf life: 36 months.

Storage Conditions: Store below 30°C**.**

Reference Product in SA (if applicable): Crestor®, Ezetrol®

Marketing Authorization Holder: Tabuk Pharmaceutical Manufacturing Company

Manufacturer: Elpen Pharmaceuticals

Registration No.: 1309222603 , 1309222600 , 1309222601 , 1309222602

Date of Decision: 13/09/2022

Proposed Indications:

It is indicated as adjunct to diet for treatment of primary hypercholesterolemia as substitution therapy in adult patients adequately controlled with the individual substances given concurrently at the same dose level as in the fixed dose combination, but as separate products.

Product Background

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

The SFDA approval for Roneza ® 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:

Quality Aspects

Drug Substance

Rosuvastatin Calcium

- Rosuvastatin Calcium is a white or almost white hygroscopic powder. Rosuvastatin Calcium is slightly soluble in water, freely soluble in methylene chloride, practically insoluble in anhydrous ethanol. The API manufacturers consistently produces the amorphous form.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Rosuvastatin Calcium 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.

Ezetimibe

- Ezetimibe is a white to an off-white crystalline powder. Ezetimibe is freely soluble in methanol and acetone, soluble in ethanol; practically insoluble in water.. Polymorphism has been observed (anhydrous crystalline).
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Ezetimibe 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 drug product is available in four strengths:
    1. 40/10 mg: White, round, biconvex film coated tablets with a diameter of 10 mm approximately and "EL 2" embossed on one side.

2. 20/10 mg: Yellow, round, biconvex film coated tablets with a diameter of 10 mm approximately and "EL 3" embossed on one side.
3. 10/10 mg: Beige, round, biconvex film coated tablets with a diameter of 10 mm approximately and "EL 4" embossed on one side
4. 5/10 mg: Light yellow, round, biconvex film coated tablets with a diameter of 10 mm approximately and "EL 5" embossed on one side.

- Each tablet contains 40/10 mg, 20/10 mg, 10/10 mg and 5/10 mg of Rosuvastatin and Ezetimibe. 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 OPA/Alu/PVC-Alu 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 Roneza® (40mg/10mg)

Ratio and 90% Confidence Intervals (CI) of Roneza® (Rosuvastatin / Ezetimibe) 40mg/10mg Tablet versus Crestor®(Rosuvastatin)40.mg and Ezetrol®(Ezetimibe)10 mg Tablet:

Rosuvastatin:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}(ng/mL)	100.26	92.07-109.17
AUC_{0-t}(ng/mL)	97.76	92.58-103.24

Total Ezetimibe:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}(ng/mL)	98.26	91.03- 106.06
AUC_{0-t}(ng/mL)	97.48	92.35-102.90-

Ezetimibe (Unconjugated):

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**

C_{max}(ng/mL)	98.70	89.14-109.29
AUC_{0-t}(ng/mL)	94.25	88.41-100.47

For Roneza® (5mg/10mg)

Ratio and 90% Confidence Intervals (CI) of Roneza® (Rosuvastatin / Ezetimibe) 5mg/10mg Tablet versus Crestor®(Rosuvastatin)5.mg and Ezetrol®(Ezetimibe)10 mg Tablet:

Rosuvastatin:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}(ng/mL)	97.27	90.84-104.16
AUC_{0-t}(ng/mL)	92.8	88.05-97.8

Total Ezetimibe:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}(ng/mL)	111.41	104.49-118.79
AUC_{0-t}(ng/mL)	99.51	95.16-104.06

Ezetimibe (Unconjugated):

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max}(ng/mL)	109.87	101.35-119.09
AUC_{0-t}(ng/mL)	101.33	95.85-107.13

Based on the results obtained in these studies, of Roneza® (Rosuvastatin/ Ezetimibe) 40mg/10mg and 5mg/10mg Tablet of ELPEN SA Pharmaceutical Industry, Greece is **bioequivalent** to Crestor®(Rosuvastatin) 40mg and Crestor®(Rosuvastatin)5mg Tablets of AstraZeneca GmbH, Germany, and Ezetrol®(Ezetimibe)10 mg of Shering-Plough Labo N.V., Belgium Tablet, 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