الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Lunia®

Type of Application: New Drug Application.

Type of Product: Human Generic Drug.

Active Pharmaceutical Ingredient(s): Ezetimibe, Simvastatin

ATC code: C10BA02

Dosage Form: Tablet

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

Pack Size: 28

Shelf life: 24 months

Storage Conditions: Store below 30°C.

Reference Product in SA (if applicable): Inegy

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.: 0203233315 , 0203233317

Date of Decision: 02/03/2023

Proposed Indications:

Prevention of Cardiovascular Events

Lunia is indicated to reduce the risk of cardiovascular events in patients with coronary heart disease(CHD) and a history of acute coronary syndrome (ACS), either previously treated with a statin or not.

Hypercholesterolemia

Lunia is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolemia or mixed hyperlipidemia where use of a combination product is appropriate:

• patients not appropriately controlled with a statin alone

• patients already treated with a statin and ezetimibe

Homozygous Familial Hypercholesterolemia (HoFH)

Lunia is indicated as adjunctive therapy to diet for use in patients with HoFH. Patients may also receive adjunctive treatments (e.g. low-density lipoprotein [LDL] apheresis).

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 Lunia® 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

Ezetimibe:

- Ezetimibe is a white to off-white crystalline powder. Ezetimibe soluble in Alcohol, soluble in acetonitrile and insoluble in hexane. Fenofibrate does have 1 chiral center. Polymorphism has been observed (Form-X).
- 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. The control methods are validated according to international guidelines.
- Appropriate stability data have been presented and justify the established re-test period.

Simvastatin:

- Simvastatin is white to off-white powder. Simvastatin is freely soluble in chloroform, methanol and alcohol, sparingly soluble in propylene glycol, very slightly soluble in hexane, practically insoluble in water. Simvastatin does have 7 chiral centers. Polymorphism has not been observed.
- 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. 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 two strengths:
    1. 10/20 mg tablets: White to off white, oblong, biconvex tablets debossed JS34 on one side and plain on another side.

2. 10/40 mg tablets: White to off white, oblong, biconvex tablets debossed JS35 on one side and plain on another side.

- Each tablet contains 10/20 mg OR 10/40 of Ezetimibe micronized and Simvastatin 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/Aclar white opaque blisters.
- 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 Lunia® (Ezetimibe / Simvastatin) 10/40mg Tablet versus Inegy® (Ezetimibe / Simvastatin) 10/40mg Tablet:

Free Ezetimibe (unconjugated)

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max} (ng/mL)	94.37	85.33-104.36
AUC_{0-t} (ng/mL)	100.54	95.15-106.22

Total Ezetimibe (ezetimibe + ezetimibe glucuronide)

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max} (ng/mL)	92.72	86.77-99.09
AUC_{0-72} (ng/mL)	97.75	92.76-103

Simvastatin

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max} (ng/mL)	96.27	87.03-106.50
AUC_{0-t} (ng/mL)	102.81	93.37-113.21

$AUC_{0-\infty}$ (ng/mL)	102.50	93.08-112.87

Simvastatin-OH acid

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max} (ng/mL)	105.80	-
AUC_{0-t} (ng/mL)	108.69	--
$AUC_{0-\infty}$ (ng/mL)	111.32	

Based on the results obtained in this study, Lunia® (Ezetimibe / Simvastatin) 10/40mg Tablet of Alpha pharma industries, King Abdullah Economic City, Saudi Arabia is **bioequivalent** to Inegy® (Ezetimibe / Simvastatin) 10/40mg Tablet of Manufactured by MSD International GmbH, Singapore, 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