# Saudi Public Assessment Report

# Erloz®

**Active Pharmaceutical Ingredient(s):** Erlotinib HCL

**ATC code/CAS no.:** L01XE03

**Pharmaceutical/Dosage Form:** Film coated tablet

**Dosage Strength:** 100 mg - 150 mg

**Marketing Authorization Holder:** Saudi Hetero Lab Co, Ltd.

**Shelf life:** 36 months

**Storage conditions**: Store below 30ºC.

**Registration No.:** 1111211298-1111211299

**Decision and Decision Date**: Approved o~~O~~n 12/3/1443H

# Table of Contents

# 1. Terms, Definitions, Abbreviations

| | |
|---|---|
| **EGFR** | Epidermal Growth Factor Receptor |
| **GCP** | Good Clinical Practice |
| **GLP** | Good Laboratory Practices |
| **IHC** | Immunohistochemistry |
| **INN** | International Nonproprietary Names |
| **NSCLC** | Non-Small Cell Lung Cancer |
| **SA** | Saudi Arabia |
| **SDI** | Saudi Drug Information System |
| **SPC** | Summary of Product Characteristics |
| **USAN** | United States Adopted Names |

Erloz ®

# 2. Background

## 2.1 Submission Details

Type of submission: human generic drug

Reference product in SA: Tarceva

Pharmacological class: Antineoplastic agent, protein kinase inhibitor.

Submitted Indications:

- Non-Small Cell Lung Cancer (NSCLC)
  - First-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR activating mutations.
  - Switch maintenance treatment in patients with locally advanced or metastatic NSCLC with EGFR activating mutations and stable disease after first-line chemotherapy.
  - Treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen. In patients with tumours without EGFR activating mutations.

  Erlotinib Hydrochloride is indicated when other treatment options are not considered suitable. When prescribing Erlotinib Hydrochloride, factors associated with prolonged survival should be taken into account.

  *No survival benefit or other clinically relevant effects of the treatment have been demonstrated in patients with Epidermal Growth Factor Receptor (EGFR)-IHC negative tumours.*
- Pancreatic cancer: Erlotinib Hydrochloride in combination with gemcitabine is indicated for the treatment of patients with metastatic pancreatic cancer. When prescribing Erlotinib Hydrochloride, factors associated with prolonged survival should be taken into account.

  *No survival advantage could be shown for patients with locally advanced disease.*

Submitted Dosage: 100mg - 150mg

## 2.2 Regulatory Background

This product is considered a human generic drug for Saudi regulatory purposes.

This product is qualified for the following regulatory pathway:

☒ Normal submission

☐ Abridged

☐ Verification

☐ Priority

## 2.3 Product Information

The officially approved Summary of Product Characteristics (SPC) can be accessed via Saudi Drug Information System (SDI) at: https://sdi.sfda.gov.sa/

# 3. Scientific discussion about the product:

## 3.1 Quality Aspects

### 3.1.1 Drug Substance

- Erlotinib Hydrochloride is white to an off-white crystalline powder. Erlotinib Hydrochloride is very slightly soluble in methanol. Erlotinib Hydrochloride does not have any chiral centers. Polymorphism has been observed.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Erlotinib Hydrochloride 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.

### 3.1.2 Drug Product

- Erlotinib Hydrochloride drug product is available in two strengths:
  1. 100 mg tablet: white colored, round biconvex, debossed with 'H' on one side and '21' on the other side.

2. 150 mg tablet: white colored, round biconvex, debossed with 'H' on one side and '22' on the other side.

- Each tablet contains Erlotinib Hydrochloride equivalent to 100 mg or 150 mg Erlotinib. 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 a consistent quality of the drug product.
- The drug product is packaged in a carton box, containing 3 Alu- Alu\ PVC\ OPA blisters, 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 shelf life.

## 3.2 Clinical Aspects

### 3.2.1 Bioequivalence study

A randomized, open label, two-treatment, two-period, two-sequence, single dose, crossover, bioequivalence study of Erloz® (Erlotinib) 150 mg of Hetero Labs Limited, India, and Tarceva® (Erlotinib) 150 mg of Roche Registration Limited, United Kingdom, in healthy human adult subjects, under fasting condition. The study was conducted in accordance with GCC Guidelines for Bioequivalence, standards of Good Clinical Practice (GCP) and Good Laboratory Practices (GLP).

Blood samples were taken pre-dose (0.0) and at a specified time points up to 96 hours after administration of test or reference product. Plasma levels of Erlotinib were detected by a validated HPLC-MS/MS method.

Fifty-one (51) subjects completed the study and all data were analyzed. No significant protocol deviations were reported. There were no serious adverse events reported in the study.

The ratio and 90% Confidence Intervals of Test versus Reference for Erlotinib are tabulated below:

Table 1: Ratio and 90% Confidence Intervals (C.I) of Test versus Reference for Erlotinib:

| **Pharmacokinetic Parameter** | **Point Estimate** | **90% Confidence Intervals (%)** |
|---|---|---|
| $C_{max}$ | 108.8 | 96.35 - 122.85 |
| $AUC_{0-t}$ | 100.6 | 90.41 - 111.84 |
| $AUC_{0-\infty}$ | 100.9 | 90.76 - 112.14 |

Based on the results obtained in this study, Erloz® (Erlotinib) 150 mg of Hetero Labs Limited, India, is **bioequivalent** to Tarceva® (Erlotinib) 150 mg of Roche Registration Limited, United Kingdom, under fasting conditions.

## 4. Risk Management Plan

### 4.1 Artwork and Trade Name assessment (Artwork available in appendix)

| **Proposed trade Name** | **Dosage Form** |
|---|---|
| Erloz | Film coated tablet |

**Look –alike/Sound-alike (LA/SA) Error Risk Potential:**

Erloz ®

Erloz name LA/SA confusion risk potential has been assessed based on the evaluation of LA/SA similarities from our data sources (SFDA registered Drug List, Martindale, ISMP Confused Drug Name List, INN International Nonproprietary Names and USAN United States Adopted Names STEM) and the pharmaceutical characteristic of the product:

| LA/SA for Product name | SFDA | Shared File/ Excel Sheet | Martindale | Stem Book 2018 |
|---|---|---|---|---|
| Erloz | NO | NO | NO | NO |

**Trade Name Recommendation:**

Based on the submitted data, the proposed name Erloz is accepted.

**Outer and Inner Package:**

Based on the submitted data, the proposed artwork is accepted.

## 5. Overall Conclusion

Based on a review of data on quality, safety and efficacy, SFDA considered that the benefit/risk profile of Erloz was favorable and decided to grant the marketing authorization of Erloz, which is indicated for:

- Non-Small Cell Lung Cancer (NSCLC)
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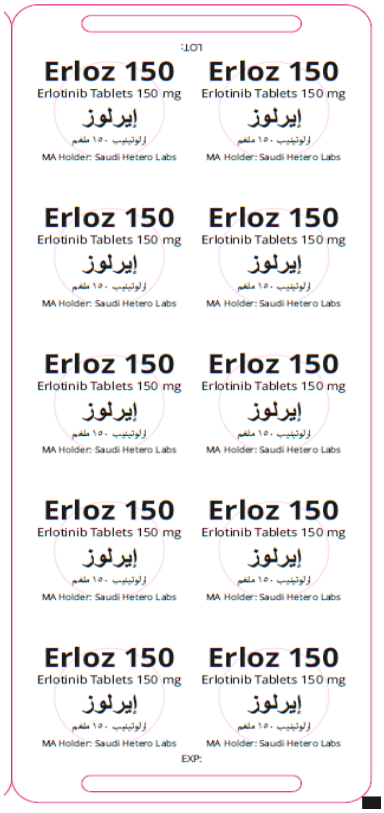
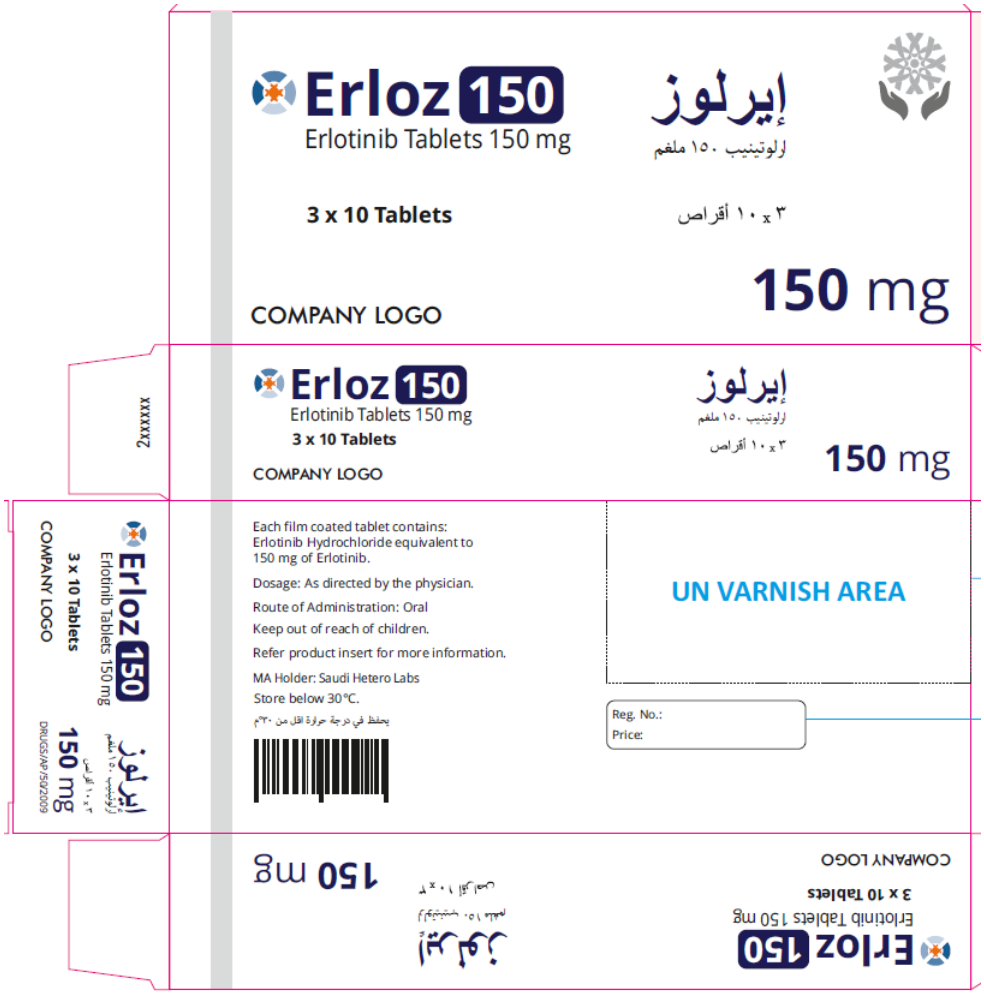
# 6. Appendix

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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 only at SDI.

*For inquiry and feedback regarding Saudi PAR, please contact us at* [Saudi.PAR@sdfa.gov.sa](mailto:Saudi.PAR@sdfa.gov.sa)

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