Saudi Public Assessment Report

Lenamid ®

Active Pharmaceutical Ingredient(s): Lenalidomide

ATC code/CAS no.: L04AX04

Pharmaceutical/Dosage Form: Capsules – (Capsule, Hard)

Dosage Strength: Capsules: 5mg, 10mg and 25mg

Capsule, Hard: 20mg 2.5 mg 15 mg

Marketing Authorization Holder: Saudi Hetero Lab Ltd

Shelf life: 24 months

Storage conditions: Store below 30°C.

Registration No.: 1008210918 - 1008210920 - 1008210921

Decision and Decision Date: Approved on 12/07/2021

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1. Terms, Definitions, Abbreviations

Terms	Definitions
AUC_{0-t}	Area under the concentration-time curve (time 0 to time of last quantifiable concentration
$AUC_{0-\infty}$	Area under the serum concentration-time curve from time 0 to infinite time
C.I	Confidence Intervals
C_{max}	Maximum serum concentration
GCC	Gulf Cooperation Council
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
INN	International Nonproprietary Names
SFDA	Saudi Food and Drug Authority
SA	Saudi Arabia
SDI	Saudi Drug Information System
SFDA	Saudi Food and Drug Authority
SPC	Summary of Product Characteristics
USAN	United States Adopted Names

2. Background

2.1 Submission Details

Type of submission: Human Generic Drug

Reference product in SA: REVLIMID

Pharmacological class: Other immunosuppressants

Submitted Indication:

Multiple myeloma

Lenalidomide capsules as monotherapy is indicated for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

Lenalidomide capsules as combination therapy with dexamethasone, or Bortezomib and Dexamethasone or melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

Lenalidomide capsules in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Myelodysplastic syndromes

Lenalidomide capsules as monotherapy is indicated for the treatment of adult patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.

Mantle cell lymphoma

Lenalidomide capsules as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.

2.2 Regulatory Background

This product is considered a human generic drug for Saudi regulatory purposes. Furthermore, this product is qualified to follow the regular review pathway.

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

- Lenalidomide is an off-white to pale-yellow powder. Lenalidomide is slightly soluble in dimethyl formamide. Lenalidomide has/possesses one stereochemical center. Polymorphism has been observed.
- The drug substance is manufactured by multiple-step chemical synthesis.
- The structure of Lenalidomide 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 justified the established re-test period.

3.1.2 Drug Product

- Lenalidomide drug product is available in three strengths:
    1. 5 mg capsule: white opaque cap and white opaque body, hard gelatin capsules imprinted with ‘H’ on cap and ‘L2’on body, filled with off white to pale yellow color powder.

2. 10 mg capsule: orange opaque cap and white opaque body, hard gelatin capsules imprinted with ‘H’ on cap and ‘L4’on body, filled with off white to pale yellow color powder.
3. 25 mg capsule: white opaque cap and white opaque body, hard gelatin capsules imprinted with ‘H’ on cap and ‘L7’on body, filled with off white to pale yellow color powder.

- Each capsules contains 5 mg, 10 mg or 25 mg of Lenalidomide. 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 blisters, with 7 capsules 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

Bioequivalence study (under fasting condition):

A randomized, open label, two-treatment, two-period, two-sequence, single dose, crossover, bioequivalence study of Lenamid® (Lenalidomide) 25 mg of Hetero Labs Limited, India, and Revlimid® (Lenalidomide) 25 mg of Celgene Corporation Summit,

USA, 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 specified time points up to 24 hours after administration of test or reference product. Plasma levels of Lenalidomide were detected by a validated LC-MS/MS method.

Forty three (43) volunteers 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 Lenalidomide are tabulated below:

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

Pharmacokinetic Parameter	**Point Estimate**	**90% Confidence Intervals (%)**
C_{max}	99.7	94.24 - 105.49
AUC_{0-t}	98.9	97.39 - 100.38
$AUC_{0-\infty}$	98.9	97.42 - 100.41

Bioequivalence study (under fed condition):

A randomized, open label, two-treatment, two-period, two-sequence, single dose, crossover, bioequivalence study of Lenamid® (Lenalidomide) 25 mg of Hetero Labs Limited, India, and Revlimid® (Lenalidomide) 25 mg of Celgene Corporation Summit, USA, in healthy human adult subjects, under fed 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 specified time points up to 24 hours after administration of test or reference product. Plasma levels of Lenalidomide were detected by a validated LC-MS/MS method.

Thirty eight (38) volunteers 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 Lenalidomide are tabulated below:

Table 2: Ratio and 90% Confidence Intervals (C.I) of Test versus Reference for Lenalidomide:

Pharmacokinetic Parameter	**Point Estimate**	**90% Confidence Intervals (%)**
C_{max}	102.3	96.46 - 108.48
AUC_{0-t}	99.7	96.61 - 102.79
$AUC_{0-\infty}$	99.7	96.70 - 102.79

Based on the results obtained in these studies, Lenamid ® (Lenalidomide) 25 mg of Hetero Labs Limited, India is **bioequivalent** to Revlimid® (Lenalidomide) 25 mg of Celgene Corporation Summit, USA under fasting and fed conditions.

4. Risk Management Plan

4.1 Artwork and Trade Name Assessment (Artwork available in appendix)

Proposed trade Name	**Dosage Form**
Lenamid	Cap

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

Lenamid 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
Lenamid	NO	NO	NO	NO

Trade Name Recommendation:

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

Outer and Inner Package:

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

5. Overall Conclusion

Based on data reviewed from a quality, safety and efficacy perspective, the SFDA considered that the benefit/risk profile of Lenamid was favorable and decided to grant the marketing authorization of Lenamid for the treatment of:

Multiple myeloma

Lenalidomide capsules as monotherapy is indicated for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

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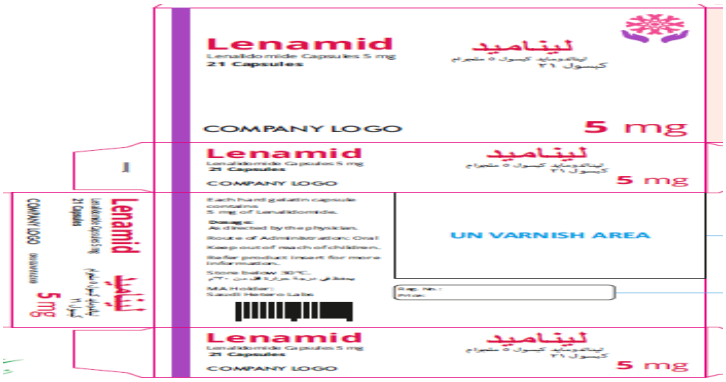
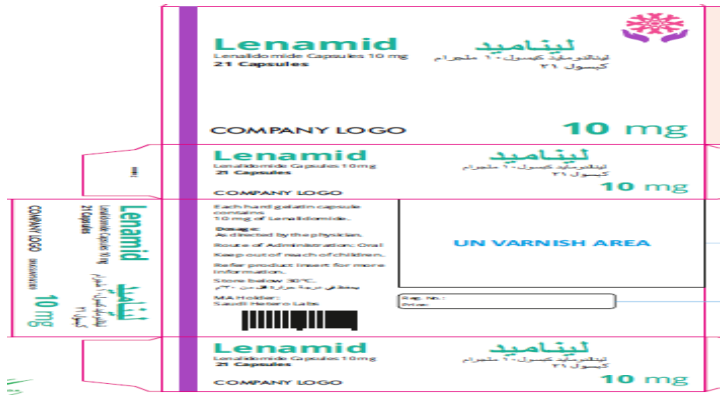
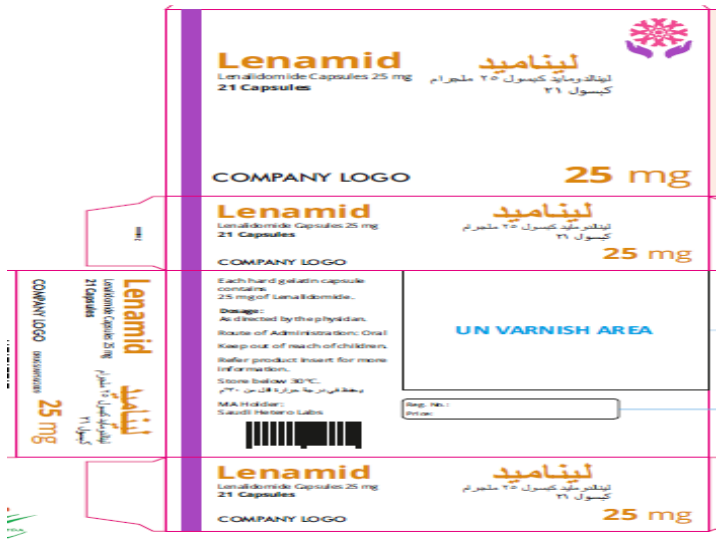
Mantle cell lymphoma

Lenalidomide capsules as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.

6. Appendix







Lenamid ®

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