Saudi Public Assessment Report

Resepta™

Active Pharmaceutical Ingredient(s): Mycophenolic Acid (as mycophenolate sodium)

ATC code/CAS no.: L04AA06

Pharmaceutical/Dosage Form: Gastro resistant Tablets

Dosage Strength: 180 mg – 360 mg

Marketing Authorization Holder: Accord Healthcare Limited

Shelf life: 36 months

Storage conditions: Store below 30 °C

Registration No.: 2406210830 - 2406210831

Decision and Decision Date: Approved on 05/04/2021

Table of Contents

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
CI	Confidence Intervals
C_{max}	Maximum serum concentration
GCC	Gulf Cooperation Council
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
INN	International Nonproprietary Names
KSA	Kingdom of Saudi Arabia
SA	Saudi Arabia
SDI	Saudi Drug Information System
SFDA	Saudi Food and Drug Authority
SPC	Summary of Product Characteristics
USAN	United States Adopted Names
GR tablet	Gastro-resistant tablet

2. Background

2.1 Submission Details

Type of submission: Human Generic Drug

Reference product in SA: MYFORTIC Gastro-resistant tablet

Pharmacological class: Immunosuppressant

Submitted Indication:

Resepta is indicated in combination with Ciclosporin and Corticosteroids for the prophylaxis of acute transplant rejection in adult patients receiving allogeneic renal transplants.

Submitted Dosage: 180 mg – 360 mg

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

- Mycophenolate Sodium is a white or almost white, crystalline powder. Mycophenolate Sodium is slightly soluble in water and anhydrous ethanol, very slightly soluble in heptane. Mycophenolate Sodium does not have any chiral centers. Polymorphism has been observed.
- The drug substance is manufactured by multiple-step chemical synthesis.
- The structure of Mycophenolate Sodium 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

- Resepta is available in two strengths:

  1. 180 mg GR tablets: Lime Green colored, round shaped, biconvex beveled edged enteric-coated tablets imprinted with M1 on one side with black ink and plain on the other side.
  2. 360 mg GR tablets: Peach colored, oblong shaped, biconvex, enteric-coated tablets imprinted with M2 on one side with black ink and plain on the other side.

- Each tablet contains 180 mg or 360 mg of Mycophenolic Acid (as Mycophenolate Sodium). 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 12 cold formable Alu-Alu triple laminated foil blisters, with 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

Resepta™ (Mycophenolic Acid) 360 mg Gastro Resistant Tablets

Bioequivalence study (under fasting condition):

A randomized, open label, balanced, two-treatment, three-period, three-sequence, single oral dose, reference replicated crossover, bioequivalence study of Resepta™ (Mycophenolic Acid) 360 mg of Intas Pharmaceuticals Ltd., India and Myfortic® (Mycophenolic Acid) 360 mg of Novartis Pharma GmbH, Germany, in healthy human

adult subjects, under fasting condition. The study was conducted in accordance with Gulf Cooperation Council (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 Mycophenolate were detected by a validated LC-MS/MS method.

Forty-one (41) 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 Mycophenolate are tabulated below:

Table 1: Ratio and 90% Confidence Intervals (CI) of Test versus Reference for Mycophenolic acid:

Pharmacokinetic Parameter	**Point Estimate (%)**	**90% Confidence Intervals (%)**
C_{max} (ng /mL)	109.7	96.02 – 125.42
AUC_{0-t} (ng.h /mL)	99.3	95.25 – 103.59
$AUC_{0-\infty}$ (ng.h /mL)	99.8	95.81 – 103.96

Bioequivalence study (under fed condition):

A randomized, open label, balanced, two-treatment, three-period, three-sequence, single oral dose, crossover, bioequivalence study of Resepta™ (Mycophenolic Acid) 360 mg of Intas Pharmaceuticals Ltd., India and Myfortic® (Mycophenolic Acid) 360 mg of Novartis Pharma GmbH, Germany, 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 a specified time points up to 96 hours after administration of test or reference product. Plasma levels of Mycophenolate were detected by a validated LC-MS/MS method.

Forty-one (41) 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 Mycophenolate are tabulated below:

Table 2: Ratio and 90% Confidence Intervals (CI) of Test versus Reference for Mycophenolic acid:

Pharmacokinetic Parameter	Point Estimate (%)	90% Confidence Intervals (%)
C_{max} (ng/mL)	93.8	77.15 – 114.02
AUC_{0-t} (ng.h /mL)	92.4	85.77 – 99.48
$AUC_{0-\infty}$ (ng.h /mL)	92.6	86.33 – 99.42

Based on the results obtained in these studies, Resepta™ (Mycophenolic Acid) 360 mg of Intas Pharmaceuticals Ltd., India, is **bioequivalent** to Myfortic® (Mycophenolic Acid) 360 mg of Novartis Pharma GmbH, Germany, under fasting & fed conditions.

Resepta™ (Mycophenolic Acid) 180 mg Gastro Resistant Tablets

A randomized, open label, balanced, two-treatment, three-period, three-sequence, single oral dose, crossover, bioequivalence study of Resepta™ (Mycophenolic Acid) 180 mg of Intas Pharmaceuticals Ltd., India and Myfortic® (Mycophenolic Acid) 180 mg of Novartis Pharma GmbH, Germany, 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 Mycophenolate were detected by a validated LC-MS/MS method.

Forty-two (42) 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 Mycophenolate are tabulated below:

Table 3: Ratio and 90% Confidence Intervals (CI) of Test versus Reference for Mycophenolic acid:

Pharmacokinetic Parameter	Point Estimate (%)	90% Confidence Intervals (%)
C_{max} (ng/mL)	97.1	87.24 – 108.12
AUC_{0-t} (ng.h/mL)	99.8	96.81 – 102.90
$AUC_{0-\infty}$ (ng.h/mL)	98.4	95.08 – 101.83

Based on the results obtained in this study, Resepta™ (Mycophenolic Acid) 180 mg of Intas Pharmaceuticals Ltd., India, is **bioequivalent** to Myfortic® (Mycophenolic Acid) 180 mg of Novartis Pharma GmbH, Germany, under fasting condition.

4. Risk Management Plan

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

Proposed trade Name	Dosage Form
Resepta	Gastro-resistant Tablets

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

Resepta 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
Resepta	NO	NO	NO	NO

Trade Name Recommendation:

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

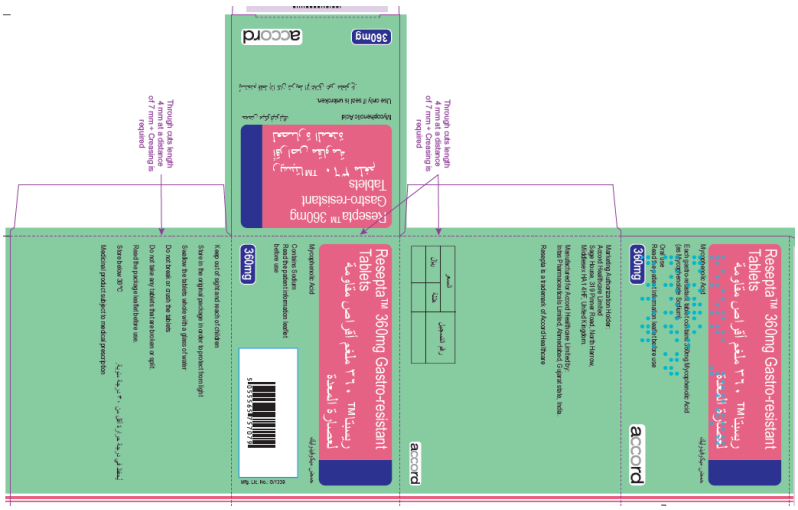
Outer and Inner Package:

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

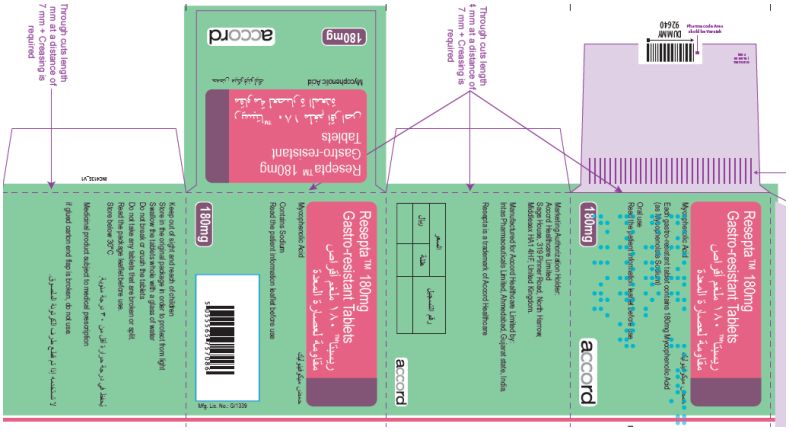
5. Overall Conclusion

Based on data reviewed from a quality, safety and efficacy perspective, the SFDA considered that the benefit/risk profile of Resepta was favorable and decided to grant the marketing authorization of Resepta in combination with Ciclosporin and Corticosteroids for the prophylaxis of acute transplant rejection in adult patients receiving allogeneic renal transplants.

6. Appendix


Resepta™ 360mg Gastro-resistant Tablets
ريسبتا™ ٣٦٠ ملغم أقراص مقاومة
accord
360mg
Through cuts length 4 mm at a distance of 7 mm + Creasing is required


Resepta™ 360mg
Gastro-resistant tablets
Mycophenolic Acid
ريسبتا™ ٣٦٠ ملغم
أقراص مقاومة لعصارة المعدة
حمض ميكوفينوليك
LOT:
EXP:


Resepta™ 180mg Gastro-resistant Tablets
ريسبتا™ ١٨٠ ملغم أقراص مقاومة
accord
180mg
Through cuts length 4 mm at a distance of 7 mm + Creasing is required


Resepta™ 180mg
Gastro-resistant tablets
Mycophenolic Acid
ريسبتا™ ١٨٠ ملغم
أقراص مقاومة لعصارة المعدة
حمض ميكوفينوليك
LOT:
MFG:
EXP:
accord

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