Saudi Public Assessment Report

(Summary Report)

Opsumit®

Type of Application: New Drug Application

Type of Product: New Chemical Entity

Active Pharmaceutical Ingredient(s): Macitentan

ATC code: C02KX04

Dosage Form: Film-Coated Tablets

Dosage Strength: 10 mg

Pack Size: 30 Tablets

Shelf life: 60 Months

Storage Conditions: Do not store above 30 ºC

Marketing Authorization Holder: Actelion Pharmaceuticals Ltd

Manufacturer: Excella GmbH & Co KG,

Registration No.: 1505222025

Decision and Decision Date: Approved on 7/03/2022

Proposed Indications: As monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension PAH in adult patients of WHO Functional Class FC II to III to reduce morbidity and the risk of mortality.

Product Background

This product is considered a new chemical entity for Saudi regulatory purposes. Furthermore, this product is qualified to follow the SFDA's normal submission regulatory pathway.

The SFDA approval for Opsumit® (Macitentan) is based on a review of the quality, safety and efficacy as summarized hereinafter:

Quality Aspects

Drug Substance

- Macitentan is non-hygroscopic white to off-white crystalline powder. Macitentan is practically insoluble in Water. Macitentan does not have chirality. Polymorphism has been observed.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Macitentan has been fully elucidated using several spectroscopic techniques.
- The drug substance specification includes relevant tests for proper quality control. Whereas 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 finished product is available as Biconvex round white film-coated tablet, debossed with 10 mg on both sides. Each tablet contains 10 mg of Macitentan. 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. Satisfactory validation data pertaining to the commercial manufacturing process are provided.
- The drug product specification covers appropriate parameters for this dosage form. They 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 a carton box, containing 2 (PVC/PE/PVdC) blisters, each blister contain 15 tablets.
- 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

The clinical development program for OPSUMIT consisted of one pivotal clinical study: (Study AC-055-302/SERAPHIN [D-12.425] assessing the efficacy and safety of the product).

Summary of the clinical studies presented hereafter:

- Study AC-055-302/SERAPHIN [D-12.425]: a pivotal placebo-controlled, global phase III study, which enrolled 742 patients with symptomatic pulmonary arterial hypertension (PAH), randomized in a 1:1:1 ratio to macitentan 3 mg O.D., macitentan 10 mg O.D., or placebo. The primary objective of the long-term, event driven SERAPHIN study was to demonstrate that macitentan reduces the risk of morbidity and mortality events during treatment in patients with PAH. An open-label (OL) extension study is ongoing. There are no other ongoing studies in the targeted indication.

The clinical pharmacology, efficacy and safety results from the above mentioned study were assessed by the SFDA efficacy and safety department. Based on the efficacy and safety review of the submitted evidence, the benefit/risk balance of OPSUMIT is considered positive. Therefore, we recommend the approval of the marketing authorization of OPSUMIT.

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