الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Ornivoda®

Type of Application: New Drug Application.

Type of Product: Human New Chemical Entity drug.

Active Pharmaceutical Ingredient(s): Ornidazole.

ATC code: QP51AA03.

Dosage Form: Film-coated tablet.

Dosage Strength: 500mg.

Pack Size: 10 tablets.

Shelf life: 24 Month.

Storage Conditions: Do not store above 30°c.

Marketing Authorization Holder: Jazeera Pharmaceutical Industries (JPI).

Manufacturer: Jazeera Pharmaceutical Industries (JPI).

Registration No.: 0102233197.

Date of Decision: 01/02/2023

Proposed Indications: Ornidazole is an antibiotic used to treat protozoan infections.

Product Background

This product is considered as a new pharmaceutical product drug for Saudi regulatory purposes qualified to follow the SFDA's regular egulatory pathway.

The SFDA approval for Ornivoda® 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:

Quality Aspects

Drug Substance

Ornidazole is nitroimidazole derivative. It is an antiprotozoal drug that has proven to be effective against *Trichomonas vaginalis, Entoamoeba histolytica, Giardia lamblia and Helicobacter pylori*. Ornidazole drug substance is light yellowish crystalline powder soluble in methylene dichloride and in chloroform. The reduction of the nitro group and the generation of short-lived reactive intermediates are the basis of its parasiticidal activity.

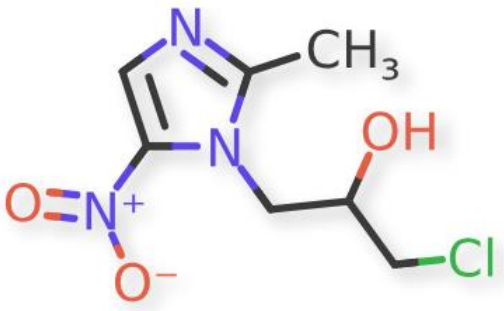

FIGURE 1:ORNIDAZOLE STRUCTURE

Ornidazole is a DNA-tropic drug with selective activity against microorganisms with enzyme systems capable of reducing the nitrogroup and catalyze the interaction between ferrodoxin proteins and nitrocompounds. After the drug penetrates the microbial cell, the mechanism of its action is based reducing the nitrogroup under the influence of the microorganism's nitroreductases and the activity of the reduced nitroimidazole.

The drug substance is manufactured by a multiple-steps chemical synthesis. The structure of Ornidazole has been fully elucidated using several spectroscopic techniques. The drug substance

specification includes relevant tests for proper quality control and met the ICH Q6A guideline. The control methods are validated according to international guidelines.

The provided stability studies protocol and stability data have been presented and justify the established re-test period.

Drug Product

Ornivoda® finished product is available as film-coated tablets. Each film-coated tablet contains 500 mg ornidazole, 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 accordingly through the pharmaceutical development data. Batch manufacturing formula and in-process controls are included. Satisfactory validation data pertaining to the commercial manufacturing process had been provided. The drug product specification established to cover all the quality attributes, all the acceptance criteria are adequately justified for this dosage form which allow proper control of release and shelf-life 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 PVC/PVDC blisters with aluminum foil.

Appropriate stability data had 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 proposed shelf life (24 months).

Clinical Aspects

Efficacy and Safety

- The clinical development program for (Ornivoda) consisted of the submitted manuscripts of published scientific literature on Ornivoda. The clinical studies review was based on four studies, all were active-control clinical trials to demonstrate the efficacy and safety of ornidazole versus the ideal comparators including Tinidazole, Metronidazole, and Clindamycin in urogenital Trichomoniasis, children, and adult with Giardia, and medico-surgical infections with sensitive anaerobic germ treatments. No full study manuscript was

provided to support the use of Ornivoda in Amoebiasis. Ornidazole 500 mg is intended for the treatment of Amoebiasis, Urogenital Trichomoniasis, Giardia and the treatment and prevention of medico-surgical infections with sensitive anaerobic germs.

Summary of the clinical studies presented hereafter:

- **Hillstrom et al. (1977),** randomized, active-control, double blind (staff and patients) study to compare the effect and tolerance of 1.5 g Ornidazole with 2 g Tinidazole administered orally. There was 88 women included in the trial, 45 women treated with 1.5 mg single dose orally Ornidazole at bedtime, and 43 women treated with 2 mg single dose orally Tinidazole at bedtime.
- **Ozbilgin et al. (2002),** active-control experimental study to compare the treatment efficacy of single dose of Ornidazole with 5 days treatments of Ornidazole and 7 days Metronidazole administered orally in children with giardiasis. A single dose of Ornidazole: 35 with 30 mg/ kg, 35 with 25 mg/ kg and 35 with 20 mg/ kg. 35 were treated with 25 mg/ kg per day of ornidazole for 5 d in 2 doses. 35 children were treated with 20 mg/ kg per day metronidazole for 7 d in 3 doses.
- **Jokipii et al. (1982),** active-control, equivalent, experimental study to compare the pharmacokinetic, therapeutic effect and safety of Ornidazole and Tinidazole as a single dose of 1.5 g in patients with giardiasis and looked for reasons for treatment failure. The trial included 100 subjects, 50 patients treated with a single dose of 1.5 g (3 500-mg tablets) of Ornidazole (Roche, Basle, Switzerland), and 50 patients treated with a single dose of 1.5 g (3 500-mg tablets) of Tinidazole (Pfizer, Brussels, Belgium).
- **Giamarellou et al. (1982),** randomized, open-label, active- control, prospective, clinic-laboratory study to evaluate the efficacy of the parental and/or oral Ornidazole if it is equals to standard parenteral Clindamycin. 67 patients received Ornidazole (Roche, Basle, Switzerland) administered at loading dose of 1000 mg and thereafter at a dose of 500 mg via intravenous (IV) infusion for 30 min every 12 h; then replaced by oral route at the same dose if the oral feeding were permitted (55 patients out of 67 treated with concomitant aminoglycoside therapy). 73 patients received Clindamycin administered only parenterally 600 mg via intravenous (IV) infusion for 30 min every 8 h (56 patients out of 73 treated with concomitant aminoglycoside therapy).

- The clinical pharmacology, efficacy and safety results from the aformentioned studies were assessed by the SFDA efficacy and safety department. Based on the review of the submitted evidence, the benefit/risk balance of (Ornivoda) is considered positive in treatment of Urogenital Trichomoniasis and Giardia only. Therfore , we recommend the approval of the marketing authorization of (Ornivoda) in treatment of Urogenital Trichomoniasis and Giardia only.

Bioequivalence Study

Ratio and 90% Confidence Intervals (CI) of Ornivoda® (Ornidazole) 500mg Tablet versus Tiberal® (Ornidazole) 500mg Tablet:

Pharmacokinetic Parameter	**Point Estimate**	**90% CI**
C_{max} (ng/mL)	97.49%	92.29% - 102.97%
AUC_{0-72} (ng/mL)	99.46%	96.99%- 102.01%

Based on the results obtained in this study, Ornivoda® (Ornidazole) 500mg of Ornivoda® (Ornidazole) 500mg, is **bioequivalent** to Tiberal® (Ornidazole) 500mg of SERB, France under fed 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