الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

TRANSLARNA®

Type of Application: New drug application.

Type of Product: New chemical entity.

Active Pharmaceutical Ingredient(s): Ataluren.

ATC code: M09AX.

Dosage Form: Granules for oral suspension.

Dosage Strength: 125 – 250 – 1000 mg.

Pack Size: 30.

Shelf life: 48 months**.**

Storage Conditions: Store below 30°C.

Reference Product in SA (if applicable): NA.

Marketing Authorization Holder: PTC Therapeutics International Limited.

Manufacturer: Rovi Pharma Industrial Service.

Registration No.: 1-5481-20.

Date of Decision: Approved on 14/04/2021.

Proposed Indications:

Translarna is indicated for the treatment of Duchenne muscular dystrophy (DMD) resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 5 years and older. Efficacy has not been demonstrated in non-ambulatory patients. The presence of a nonsense mutation in the dystrophin gene should be determined by genetic testing.

Product Background

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

The SFDA approval for Translarna® (Ataluren, 125, 250 and 1000 mg) is based on a review of the quality, safety and efficacy as summarised hereinafter:

Quality Aspects

Drug Substance

- Ataluren is a white to off-white powder. Ataluren is very slightly soluble in acetonitrile, slightly soluble in acetone and methanol and practically insoluble in water (pH 6.6). Ataluren does not have chirality. polymorphism has been observed.
- The drug substance (DS) is manufactured by a multiple-step chemical synthesis.
- The structure of Ataluren 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.

Drug Product

- Translarna drug product (DP) is available in three strengths:
    1. 125 mg White to off-white powder.
    2. 250 mg White to off-white powder.
    3. 1000 mg White to off-white powder.
- Each sachet contains 125,250 or 1000 mg of Translarna. 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 which 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 heat-sealed aluminum foil sachet.

- 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 proposed shelf life (48 months).

Clinical Aspects

Efficacy and Safety

The clinical development program for Translarna consisted of two efficacy and safety clinical studies: PTC124-GD-007-DMD and PTC124-GD-020-DMD. And one pharmacokinetic study: PTC124-GD-004-DMD

Summary of the clinical studies presented hereafter:

1: PTC124-GD-007-DMD, This was a Phase 2b, international, multicenter, randomized, double-blind, placebo-controlled, dose-ranging study to evaluate the efficacy and safety of Ataluren in ambulatory males ≥5 years old with nonsense mutation dystrophinopathy (N=174). Patients were stratified by age, corticosteroid use, and baseline 6MWD and were randomized in a 1:1:1 ratio to receive placebo; 10, 10, 20 mg/kg of Ataluren; or 20, 20, 40 mg/kg of Ataluren three times per day (TID) at morning, midday, and evening for 48 weeks. The primary endpoint was to evaluate the effect of ataluren on ambulation as assessed by 6-minute walk distance (6MWD).

2: PTC124-GD-020-DMD, this was a Phase 2, multicenter, open-label, sequential dose-ranging study to evaluate the clinical activity, safety, and pharmacokinetics of Ataluren in patients with nonsense mutation DMD (nmDMD) (N=38). The study consisted of a 21-day screening period, followed by a single 56-day cycle of therapy comprising a 28-day Ataluren treatment period and a 28-day post-treatment follow-up period. The primary endpoint was to determine whether Ataluren could safely provide pharmacological activity, as measured by immunofluorescence evidence of an increase in dystrophin production on extensor digitorum brevis (EDB) or tibialis anterior (TA) muscle biopsy.

3: PTC124-GD-020-DMD, This was a Phase 3, international, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of Ataluren in ambulatory males ≥7 to ≤16 years old with nonsense mutation Duchenne muscular dystrophy (nmDMD) (N=320). Patients were stratified by age, duration of corticosteroid use prior to baseline, and baseline 6MWD and were randomized in a 1:1 ratio to receive placebo or 10, 10, 20 mg/kg of Ataluren three times per day (TID) at morning, midday, and evening for 48 weeks. The primary endpoint was to determine the effect of Ataluren on ambulation as assessed by change in 6-minute walk distance (6MWD).

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

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