الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Vyepti®

Type of Product: Monoclonal antibody (Anti- calcitonin gene-related peptide) monoclonal antibody-CGRP mAb)

Active Pharmaceutical Ingredient(s): Eptinezumab.

ATC code: N02C.

Dosage Form: Concentrate for solution for infusion.

Dosage Strength: 100 mg\ml.

Pack Size: 1.

Shelf life: 36 months.

Storage Conditions: Store in a refrigerator (2°C – 8°C), do not freeze.

Reference Product in SA (if applicable): NA.

Marketing Authorization Holder: H.Lundbeck Seattle BioPharmaceuticals Inc.

Manufacturer: Vetter Pharma-Fertigung GmbH & Co.KG.

Registration No.: 1708222503**.**

Date of Decision: Approved on 17/01/2022.

Proposed Indications: Preventive treatment of migraine in adults.

Product Background

This product is considered as a new biological drug, for Saudi regulatory purposes. Furthermore, this product is qualified to follow the SFDA's fact track (Abridge) regulatory pathway.

The SFDA approval for Vyepti® (Eptinezumab) 100 mg/mL with 36 months, store in a refrigerator (2 to 8°C) is based on the quality, safety and efficacy assessment undertaken to meet the last version of SFDA's Data Requirements for Human Drugs Submission as summarised hereinafter:

Quality Aspects

The drug substance (Eptinezumab) is an anti-calcitonin gene-related peptide (CGRP) monoclonal antibody (mAb) produced in a yeast-based (*Pichia pastoris*) expression system using a conventional upstream and downstream aligned with standard monoclonal antibody production practices. The antibody is an IgG1 kappa immunoglobulin containing human constant region sequences. The bulk drug substance is clear to slightly opalescent; colourless to brownish-yellow coloured solution formulated with histidine and sorbitol at a target pH of 5.8 in water for Injection. Lists for all raw materials including materials from biological origin used during the manufacture of Eptinezumab are provided with sufficient control. Data from 3 consecutive commercial-scale batches eptinezumab were produced in the scope of process performance qualification including the validation of intermediate qualifications.

The description of the non-compendial analytical procedures provided with a satisfactory validation including: specificity, linearity, accuracy, repeatability, intermediate precision, range, and robustness of analytical procedures.

In-house primary and working reference standards were used for monitoring the quality of the Eptinezumab drug substance along with characterization and evaluation of both reference standards.

The drug product is a sterile, nonpyrogenic, aqueous solution of eptinezumab. Each 1 mL of drug product contains 100 mg of eptinezumab and it is formulated with a target pH of 5.8. Sorbitol and histidine are added during the manufacture of the bulk drug substance whereas polysorbate 80 is added during the manufacturing of the drug product.

The manufacturing process of the finished product consists of several stages. All process parameters and in-process controls have been provided, which is considered adequate to ensure the robustness and consistency of the manufacturing process. Additionally, several process performance qualification lots have been provided to demonstrate the consistency of the manufacturing process, which was considered sufficient. The specification includes a set of testing parameters—for instance general characteristics and physicochemical properties, identity, quantity, purity and impurities, potency / biological activity and safety —that are implemented to monitor the quality of Eptinezumab at release and throughout the shelf life. Moreover, a description of all analytical procedures has been provided, beside with validation of in-house

analytical methods. Batch analysis data for several finished product lots were provided, and all results complied with the predetermined acceptance criteria, demonstrating consistency in the finished product's manufacturing process.
The results from 3 primary stability lots up to 36 months long-term and 6 months accelerated, 3 supportive commercial lots up to 24 months long-term and 6 months accelerated in addition to Photostability from 1 lot indicate the drug product is stable during the proposed shelf life (36 months) There are no issues pertaining to drug substance and drug product stability. There are no issues pertaining to drug substance and drug product specifications. All analytical procedures are sufficiently validated to grant their suitability for the intended use.

Clinical Aspects

Efficacy and Safety

- The clinical development program for Vyepti consisted of two efficacy and safety clinical studies:
  ALD403- CLIN-006 and ALD403- CLIN-011.

Summary of the clinical studies presented hereafter:

1: ALD403-CLIN-006 study: This was a Phase 3, parallel group, double-blind, randomized, placebo-controlled study. Eligible subjects were randomly assigned into 1 of 3 ALD403 dose levels (30 mg [n=224], 100 mg [n=225], and 300 mg [n=224]) or placebo [n=225] in a 1:1:1:1 ratio to evaluate the efficacy of repeat doses of ALD403 administered by intravenous (IV) infusion compared to placebo in subjects with frequent episodic migraine (FEM). The primary efficacy endpoint was the change in frequency of migraine days (Weeks 1-12).

2: ALD403-CLIN-011 study: This was a phase 3, parallel group, double-blind, randomized, placebo controlled study. Eligible subjects were randomly assigned 28 to 30 days after the screening visit into 1 of 2 ALD403 dose levels (100 mg [n= 372] or 300 mg [n= 374]) or placebo [n= 375] in a 1:1:1 ratio to evaluate the efficacy and safety of ALD403 administered intravenously in patients with chronic migraine to evaluate the efficacy of repeat doses of ALD403 administered intravenously (IV) compared to placebo in subjects with chronic migraine. The primary efficacy endpoint was the change in frequency of migraine days (Weeks 1-12).

- 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 Vyepti is considered positive. Therefore, we recommend the approval of the marketing authorization of Vyepti.

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