الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Phesgo®

Type of Product: Combination of two humanized (IgG1, kappa) monoclonal antibodies.

Active Pharmaceutical Ingredient(s): Pertuzumab and Trastuzumab.

ATC code: L01XY02.

Dosage Form: Solution for injection.

Dosage Strength:

- 600 mg / 600 mg – 10 ml vial.
- 1200 mg / 600 mg – 15 ml vial.

Pack Size: 1.

Shelf life: 18 Months.

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

Reference Product in SA (if applicable): NA.

Marketing Authorization Holder: F. Hoffmann-La Roche Ltd.

Manufacturer: F. Hoffmann-La Roche Ltd.

Registration No.: 2308222531 – 2408222551.

Date of Decision: Approved on15/08/2022.

Proposed Indications: Treatment of patients with human epidermal growth factor receptor 2 (HER2) positive metastatic breast cancer, in combination with chemotherapy, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease as well as indicated for use in combination with chemotherapy in the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.

Product Background

This product is considered as a new biologic drug for Saudi regulatory purposes qualified to follow the SFDA's verification registration as a fact track regulatory pathway as it is containing Trastuzumab for SC administration, co-formulated with recombinant human hyaluronidase (rHuPH20, vorhyaluronidase alfa) under the name of Herceptin® which has been approved by SFDA and Pertuzumab concentrate for solution for infusion which has been approved by SFDA as well under the trade name Perjeta®.

The SFDA approved Phesgo® for marketing authorization to Saudi Arabia based on a review of the quality, safety and efficacy to meet the last version of SFDA's Data Requirements for Human Drugs Submission as summarised hereinafter:

Quality Aspects

Phesgo® quality submission included detalied information about the quality of pertuzumab and trastuzumab as an active drug substances and the Phesgo dosage form as a drug product in addition torecombinant human hyaluronidase (rHuPH20, vorhyaluronidase alfa) as a co-formulated factor functioning as a facilitator of subcutaneous adminstration for the proposed large volume solution (more than 5ml).

Pertuzumab and trastuzumab are recombinant, humanized monoclonal antibodies based on the human IgG1 (κ) framework sequences produced in Chinese hamster ovary (CHO) cell cultures and then purified extensively using standard chromatographic and filtration methods. No bovine-derived raw materials are used in their manufacture.

The active ingredient in **pertuzumab SC drug substance** is pertuzumab, a humanized mAb based on a human IgG1(κ) framework. The recombinant antibody is produced in CHO cells and consists of two HCs (449 amino acid residues each) and two LCs (214 amino acid residues each). As is typical for IgG1 antibodies, pertuzumab contains an N-linked glycosylation site at Asn299 on each of the two HCs. The calculated molecular mass of the 448-residue HC form is 145,197 Da (without HC glycosylation or C-terminal lysine), detailed description and comparison of the manufacturing process development is provided in addition to physicochemical structure. The physicochemical and biological characteristics are confirmed in characterization section accordingly through an acceptable impurity profile. All other justifications of specification for the manufacture of trastuzumab SC drug substance are described in sufficient details.

Trastuzumab subcutaneous (SC) drug substance and appendices sections submitted to the trastuzumab SC were determined to be applicable from the regulatory point of view.

Pertuzumab and trastuzumab drug products are presented a ready-to-usesolution for subcutaneous injection in two formulations (600 mg / 600 mg – 10 ml vial) and (1200 mg / 600 mg – 15 ml vial). The drug product consists of a solution at a nominal formulation of either 80 mg/mL pertuzumab

and 40 mg/mL trastuzumab in recombinant human hyaluronidase (rHuPH20), L-Histidine, L-Histidine hydrochloride monohydrate, α, α-Trehalose dehydrate, Sucrose, Polysorbate 20, L-Methionine, and Water for Injection, filled into 15 mL type I borosilicate glass vial tapered with fluororesin-laminated rubber stopper or 60 mg/mL pertuzumab and 60 mg/mL trastuzumab in rHuPH20, L-Histidine, L-Histidine hydrochloride monohydrate, α, α-Trehalose dehydrate, Sucrose, Polysorbate 20, L-Methionine, and Water for Injection , filled into 20 mL type I borosilicate glass vial tapered with fluororesin-laminated rubber stopper. Contribution from both trastuzumab SC drug substance and pertuzumab SC drug substance was taken into consideration when setting acceptance criteria for bacterial endotoxins, host cell DNA, host cell protein, and leached protein A. The pharmaceutical development of fixed dose combination (FDC) drug product as detailed in the P.2 sections and the Quality Target Product Profile (QTPP). The dosage forms, formulations, manufacturing processes, container closure systems, microbiological attributes, and compatibility with disposable syringes are suitable for the intended use of FDC drug product.

The primary packaging for products consist of a 20 mL (LD) and 15 mL (MD) colourless Type I glass vial, sealed with a rubber stopper and crimped with an aluminum seal fitted with a plastic flip-off disk.

There are no quality 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 validated.

Clinical Aspects

Efficacy and Safety

- The clinical development program for Phesgo consisted of a pivotal clinical study: (WO40324 – FeDeriCa), the study assesed the efficacy and saftey of the product.

<u>Summary of the clinical studies presented hereafter:</u>

- WO40324 – FeDeriCa

  FeDeriCa is an ongoing pivotal phase III, two-arm, open-label randomised study investigating the pharmacokinetics, efficacy, and safety of PH FDC SC compared with P+H IV, in combination with chemotherapy, in patients with HER2-positive EBC in the neoadjuvant/adjuvant settings.

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

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