Saudi Public Assessment Report

(Summary Report)

Buvidal®

Type of Application: New drug application.

Type of Product: New chemical entity.

Active Pharmaceutical Ingredient(s): Buprenorphine.

ATC code: N07BC01.

Dosage Form: Solution for injection.

Dosage Strength: 24 – 16 – 8 – 64 – 32 – 128 – 96 mg.

Pack Size: 1.

Shelf life: 24 months.

Storage Conditions: Do not store above 30°C.

Reference Product in SA (if applicable): NA**.**

Marketing Authorization Holder: Camurus AB.

Manufacturer: Rechon Life Science AB.

Registration No.: 0808222428 – 0808222427 – 0808222426 – 0808222430 0808222429 – 0808222431 – 2908222557.

Date of Decision: Approved on 15/08/2022.

Proposed Indications: Treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over.

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 verification approval.

The SFDA approval for Buvidal® (BUPRENORPHINE 24, 16, 8, 64, 32, 128, 96 mg) is based on a review of the quality, safety and efficacy as summarised hereinafter:

Quality Aspects

Drug Substance

General Information:

Buprenorphine is a white or almost white crystalline powder. It is very slightly soluble in water, it is soluble in methanol and ethanol. Polymorphism has been observed. The structure has been fully elucidated using several spectroscopic techniques.

Manufacture, characterization and process controls:

Buprenorphineis is manufactured by Siegfried PharmaChemikalien Minden GmbH, Minden, Germany through a multiple steps chemical synthesis. A list of the reagents and solvents used in the manufacturing process with identification of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) classification for solvents as well as the respective specifications has been submitted. The specifications for raw materials are acceptable. Potential and actual impurities were identified and assessed according to international guidelines and references on impurities.

Control of the drug substance:

The drug substance (DS) specification includes tests for assay, appearance, identification, impurities, loss on drying, specific optical rotation, bacterial endotoxins and microbial tests. All methods and acceptance criteria included in the drug substance specifications have been described, justified and accepted. Batch analysis data and CoA have been presented by the drug substance manufacturer demonstrating compliance of the submitted batches with the drug substance specification. The analytical methods used have been adequately described and non-compendial methods appropriately validated in accordance with the international guidelines. Satisfactory information regarding the reference standards used for assay and impurities testing has been presented.

Container closure system:

The primary packaging is a double polyethylene bag. The materials comply with pharmacopeia and regulatory requirements. The choice of the container closure system has been validated by stability data and it is adequate for the intended use of the product.

Stability:

Appropriate stability data have been presented and justify the established re-test period.

Drug Product

Description of the product and Pharmaceutical Development:

The drug product (DP) is presented as a Prolonged-release solution for injection. Yellowish to yellow clear liquid. All excipients are well known pharmaceutical ingredients and their quality is compliant with international standards. The list of excipients is included in section 6.1 of the Summary of Product Characteristics (SPC). The compatibility of the drug substance with the excipients has been adequately demonstrated. The development of the formulation composition including the formulation design, choices of product components (e.g., properties of the drug substance, excipients, container and closure system), and manufacturing process has been adequately described.

Manufacture of the product:

The manufacturing process of the drug product consists of eight main steps: weighing, dissolving, sterile filtration, filling, closing, visual inspection, labelling, assembly in safety device and secondary packaging. The process is considered to be a standard manufacturing process.

The manufacturing process has been validated. It has been demonstrated that the manufacturing process is capable of producing the finished product of intended quality in a reproducible manner. Process controls with their control limits for the finished product manufacturing process has been provided and accepted.

Product control:

The drug product specifications (release and shelf life) include appropriate tests for this kind of dosage form: identification, appearance, assay, degradation products water content, viscosity, in vitro release, gelling properties, uniformity of dosage units, fill volume, sub-visible particles, break-loose force, gliding force, sterility, bacterial endotoxins and container closure integrity. All methods and acceptance criteria included in the drug product specifications have been described, justified and accepted. The analytical methods used have been adequately described and non-compendial methods appropriately validated in accordance with the international guidelines. Satisfactory information regarding the reference standards used for assay and impurities testing has been presented.

Batch analysis:

Batch analysis data and CoA have been presented by the drug product manufacturer demonstrating compliance of the submitted batches with the drug product specification.

Container Closure System:

The primary packaging is a Type I, clear glass ready to fill syringe (RTF), stainless steel staked needle and rubber needle shield and a bromobutyl plunger stopper. The materials comply with pharmacopeia and regulatory requirements. The choice of the container closure system has been validated by stability data and it is adequate for the intended use of the product. The secondary packaging is a carton box.

Stability of the product:

Stability data was provided on commercial scale batches of drug product for each strength from the proposed manufacturer stored in the intended commercial package for 24 months under long term conditions .30ºC ±2 ºC/65% RH and on commercial scale batches for 6 months under accelerated conditions (40 ºC / 75% RH) according to the SFDA Guidelines for Stability Testing of Active Pharmaceutical Ingredients and Finished Pharmaceutical Products. Photostability has been performed. The following parameters were tested: identification, appearance, assay, degradation products water content, viscosity, in vitro release, gelling properties, uniformity of dosage units, fill volume, sub-visible particles, break-loose force, gliding force, sterility, bacterial endotoxins and container closure integrity. All batches remained stable at long-term, photostability conditions, and no significant changes or out-of-spec trends were observed. The stability results indicate that the drug product manufactured by Rechon Life Science AB, Sweden is sufficiently stable. The stability results justify the proposed shelf life of 24 months in the proposed container.

Clinical Aspects

The clinical development program for Buvidal® consisted of one pivotal clinical study: HS-11-421 efficacy and safety study.

Summary of the presented clinical study:

- HS-11-421: A randomized, double-blind, double-dummy, active-controlled, parallel-group, multi-center phase III study in untreated outpatients with moderate-to-severe opioid dependence as defined by DSM-5 criteria. The study was designed to evaluate the non-inferiority of long-acting subcutaneous injectable depot of buprenorphine (CAM2038) compared to an existing standard of care sublingual buprenorphine/naloxone (SL BPN/NX). Total of 428 subjects were randomized to SL BPN/NX tablets plus subcutaneous (SC) placebo injections or SC injections of CAM2038 plus SL placebo tablets at 1:1 ratio. Randomized subjects received flexible dosing with weekly CAM2038 q1w (first 12 weeks; Phase 1) and monthly CAM2038 q1w (last 12 weeks; Phase 2) or daily SL BPN/NX, the primary endpoint was the percentage of negative urine samples for illicit opioids.

The clinical pharmacology, efficacy and safety results from the aforementioned study was assessed by the SFDA efficacy and safety department. Based on the review of the submitted evidence, the

benefit/risk balance of Buvidal® is considered positive. Therefore, we recommend the approval of the marketing authorization of Buvidal®.

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