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Public Assessment Report

Scientific discussion

Pantoprazole Olikla
Pantoprazole sodium sesquihydrate

SK/H/0301/001/DC

Date: 02/09/2024

This module reflects the scientific discussion for the approval of Pantoprazole Olikla. The procedure was finalised at 25.04.2024/ Day 210. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Pantoprazole Olikla 40mg, powder for solution for injection, from Olikla s.r.o..
The product is indicated for*:*

- Reflux oesophagitis.

- Gastric and duodenal ulcer.

- Zollinger–Ellison Syndrome and other pathological hypersecretory conditions.

A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

The finished product was developed as a generic to Controloc i.v., 40 mg powder for solution for injection (DE/H/0268/003, MA-holder Takeda GmbH). The proposed product has the same qualitative and quantitative composition in the active substance, the same pharmaceutical form and similar composition and content of excipients. A bioequivalence study is not necessary for the generic medicine since it is intended to be administered via intravenous route.
The pharmaceutical form of the medicinal product is white or almost white powder for solution for injection with 40 mg pantoprazole as the drug substance (as 44.94 mg pantoprazole sodium sesquihydrate), which is a proton-pump inhibitor working by decreasing the amount of acid made in the stomach used to treat gastroesophageal reflux disease and conditions where the stomach produces too much acid.
The following packaging materials are used for the medicinal product:

- Type I glass vial with enough capacity to contain 10 ml (Ph. Eur. current edition)
- Chlorobutyl stopper type I special for freeze-dried products (Ph. Eur. current edition)
- Flip-off seal made of aluminium
- Vial label (white paper, high gloss, permanent adhesive, cut according to appropriate size)
- Package leaflet
- Cardboard box

II.2 Drug Substance

Name of the drug substance (INN): Pantoprazole sodium sesquihydrate
Chemical name: 1H-Benzimidazole, 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridyl)methyl]sulfinyl]-,sodium salt, hydrate (2:3)

The drug substance pantoprazole sodium sesquihydrate is described in the European Pharmacopoeia monograph. CEP certificates were submitted for all active substance sources.

II.3 Medicinal Product

The development of the product has been described, the choice of excipients is justified and their functions explained. The finished product is manufactured in one strength 40 mg, using a sterile filtration process followed by lyophilisation. The description of the manufacturing process has been provided in the dossier. Process validation was performed on three batches with size of 132,000 vials which is the batch size proposed for commercial manufacture. The results of the validation study confirmed that the manufacturing process is controlled and capable of providing a product that complies with the established specifications.

The medicinal product contains disodium edetate, sodium hydroxide and water for injection as excipients. All excipients used are well known and widely used for the manufacture of pharmaceutical products and comply with relevant pharmacopoeia monographs. The active ingredient was found to be compatible with all the excipients used in formulation.

The relevant stability data were provided are adequate. The approved shelf-life of the medicinal product is 24 months. Storage conditions: This medicinal product does not require any special temperature storage conditions. The vials should be kept in the outer carton in order to protect from light. After reconstitution, or reconstitution and dilution, chemical and physical in-use stability has been demonstrated for 12 hours at 25 °C.
From a microbiological point of view, the product should be used immediately.
If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 12 hours, at no more than 25 °C.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The chemical-pharmaceutical documentation in relation to the drug substance pantoprazole sodium sesquihydrate is of sufficient quality in view of the present European regulatory requirements. Information on development, manufacture and control of the finished product was presented in a suitable manner.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of pantoprazole are well known. As pantoprazole is a widely used, well-known active substance, the Applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

The non-clinical safety data contained in the proposed SmPC reflect the characteristics of the substance and are in line with the reference product´s SmPC CONTROLOC i.v. 40 mg powder for solution for injection.

III.2 Ecotoxicity/environmental risk assessment (ERA)

Since Pantoprazole Olikla 40 mg powder for solution for injection is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental

risk assessment is therefore not deemed necessary.

III.3 Discussion on the non-clinical aspects

There are no objections to the dossier of Pantoprazole Olikla 40 mg powder for solution for injection from a non-clinical point of view.

IV. CLINICAL ASPECTS

The clinical overview on the clinical pharmacology, efficacy and safety is adequate.

No new data has been presented by the Applicant and this is acceptable since this application is provided under Article 10(1) of Directive 2001/83/EC so called "generic application". Bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product. The product is powder for solution for injection and has the same indications and method administration as the reference product.

The Applicant submitted a waiver justification to support the generic application in line with the BEQ guideline (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr) based on similar quantitative and qualitative composition of the powder for solution containing the same acrive substance as the currently approved product "Anagastra 40 mg powder for solution for injection" (Controloc i.v.).

Since this medicinal product is to be administered as an aqueous intravenous solution containing the same active substance as reference product and the content of excipients is similar, it can be concluded that a waiver justification is considered appropriate as support of the generic application.

The SmPC is in accordance with SmPC of the reference product.

IV.1 Risk Management Plan

The Applicant has submitted a Risk management plan version 1.0 signed 19.02.2024 with data lock point for this RMP 01.10.2022, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Pantoprazole Olikla.

Safety specification

Table: Summary of safety concerns proposed by the Applicant in RMP version 1.0

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

The submitted Risk Management Plan, version 1.0 with data lock point for this RMP 01.10.2022 and signed 19.02.2024 is considered acceptable.

Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the Applicant, which is endorsed.

V. USER CONSULTATION

A bridging report was submitted and is considered acceptable. The results of the testing of the package information leaflet for Controloc 40 mg, powder for solution for injection also shows that after close comparison that potential users of Pantoprazole Olikla 40 mg, powder for solution for injection are able to find, understand and act upon information contained in the leaflet. The products have the same indication, route of administration, the same special precaution and safety issues are identified, belongs to the same drug class, have the same pharmaceutical form (powder for solution for injection, powder for solution for injection), have the same writing style, will be used by the same patient population and the PIL is in the same format as for Controloc 40 mg, powder for solution for injection.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

There are no objections to the dossier of Pantoprazole Olikla 40 mg powder for solution for injection from a non-clinical point of view.
From the clinical perspective, submitted clinical data are adequate to support the indication.
From the quality perspective the dossier is sufficient. The quality of the product is considered acceptable when used in accordance with the conditions defined in the SmPC.
The benefit/risk assessment is considered positive.