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Public Assessment Report

Scientific discussion

BEOTEBAL 5 mg tablets
BEOTEBAL 10 mg tablets
biotin

SK/H/0318/001-002/DC

Date: 22.10.2025

This module reflects the scientific discussion for the approval of BEOTEBAL 5 mg and BEOTEBAL 10 mg. The procedure was finalised at 26.02.2025 (D210). 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 agreed to grant a marketing authorisation for BEOTEBAL 5 mg tablets and BEOTEBAL 10 mg tablets from Zaklady Farmaceutyczne Polpharma S.A., Poland. The concerned member states involved in this procedure were BG, CZ and HU.

The product is indicated for the treatment of biotin deficiency in adults with symptoms such as hair loss, hair and nail growth disorders and their excessive fragility, inflammation of the skin located around the eyes, nose, lips and ears, and prevention of its sequelae, after other causes have been ruled out by a doctor

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

The marketing authorisation has been granted under the legal basis of Article 10(1) of Directive 2001/83/EC. The application for BEOTEBAL, tablets is a generic application claiming essential similarity to the original products Biotebal MAX 10 mg and Biotin Polpharma 5 mg.

II. QUALITY ASPECTS

II.1 Introduction

The finished product is presented as uncoated tablet for oral use containing 5 mg or 10 mg of biotin. The two strengths are dose proportional and are differentiated by tablet diameter and engraving “10” on one side of the 10 mg strength. Excipients used in the drug product (lactose monohydrate, cellulose microcrystalline, povidone K-30, croscarmellose sodium, silica colloidal anhydrous, magnesium stearate and purified water) are well-known and of Ph. Eur. quality.
The product is packed in PVC/Aluminium blisters in a carton box.

II.2 Drug Substance

The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.
The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.
The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.
Stability studies confirm the retest period.

II.3 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.
The manufacturing process has been sufficiently described and critical steps identified.
The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.“

III. NON-CLINICAL ASPECTS

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

Biotin's long history of use in medicine, coupled with its essential role in health, means that its adverse reactions are well recognized. Consequently, non-clinical safety pharmacology studies are not typically required for biotin. The document specifies that the known adverse effects are included in the Summary of Product Characteristics (SmPC) based on available literature, thus conforming to regulatory guidelines.

Toxicological studies show that biotin has a high safety margin, with only marginal adverse effects at extremely high doses in animal models. The lack of adverse effects in humans at high doses supports the safety of biotin supplementation. The European Commission and other health bodies have not established a Tolerable Upper Intake Level (UL) due to the absence of observed health risks from biotin intake from all sources.

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since this is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

There are no objections to the dossier of BEOTEBAL 5 mg tablets and BEOTEBAL 10 mg tablets from a non-clinical point of view.

IV. CLINICAL ASPECTS

The clinical overview based on the scientific literature on the clinical pharmacology, efficacy and safety was adequate.

The theoretical criteria for BCS based biowaiver were met in solubility, permeability, absorption, PK linearity. The criteria were supported by literature references; therefore, biotin can be classified as BCS class I (highly soluble, highly permeable). Furthermore, the excipients in test and reference products are the same, quantitatively and qualitatively, for both strengths.

The submitted document showed detailed evaluation of the comparative dissolution profiles for BEOTEBAL 5 mg and BEOTEBAL 10 mg against the reference products Biotebal MAX 10 mg and Biotin Polpharma 5 mg. All tested batches of BEOTEBAL 5 mg and BEOTEBAL 10 mg tablets achieved more than 85% dissolution within 15 minutes across all tested media, including 0.1 M HCl, acetate buffer pH 4.5, and phosphate buffer pH 6.8. As a result, the

profiles are considered similar without the need for f2 mathematical evaluation, in accordance with the guideline CPMP/EWP/QWP/1401/98 Rev.1/Corr.

The dissolution conditions employed, such as the use of a paddle apparatus at 50 rpm, a temperature of 37°C ± 0.5°C, and a medium volume of 900 mL, comply with standards of guideline CPMP/EWP/QWP/1401/98 Rev.1/Corr.. The profiles align well with regulatory expectations for biowaiver applications. The tables and graphs provided in the document present detailed time-point dissolution data for each product in all media, confirming the reproducibility and robustness of the dissolution method.

In conclusion, BEOTEBAL 5 mg and BEOTEBAL 10 mg tablets demonstrated equivalence in dissolution to the reference products Biotebal MAX 10 mg and Biotin Polpharma 5 mg. This supports the claim of bioequivalence and compliance with regulatory standards.

Cumulative information about similarity of dissolution profiles is presented in the table below:

Product:	**BIOTEBAL MAX 10 mg, Batch No.: 10419 vs.**			
	Medium:	**0.1 M HCl**	**acetate buffer pH 4.5**	**phosphate buffer pH 6.8**
BIOTEBAL PRO 10 mg, Batch No.: 11118	f_2	similar*	similar*	similar*
BIOTEBAL PRO 10 mg, Batch No.: 11218	f_2	similar*	similar*	similar*
	BIOTIN POLPHARMA 5 mg, Batch No.: 10419 vs.			
BIOTEBAL PRO 5 mg, Batch No.: 11118	f_2	similar*	similar*	similar*

** more than 85% of active substance dissolved within 15 minutes for both formulations*

It was shown that dissolution profiles of biotin from BIOTEBAL MAX 10 mg and BIOTIN POLPHARMA 5 mg tablets are considered as similar with dissolution profiles of biotin from BEOTEBAL 5 mg and BEOTEBAL 10 mg in all tested media.

IV.1 Risk Management Plan

The MAH has submitted a risk management plan, 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 BEOTEBAL 5 mg and BEOTEBAL 10 mg.

Safety specification

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	Interference with clinical laboratory tests
Missing information	Use in pregnancy and during breast-feeding

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

Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Biotebal Max, MA No.25865 authorised in Poland. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

There are no objections to the dossier of BEOTEBAL 5 mg tablets and BEOTEBAL 10 mg tablets 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 SmPC, PL and labelling were satisfactory.
The benefit/risk assessment is considered positive.

Agreement between Member States was reached during the procedure. There was no discussion in the CMDh. The decentralised procedure was finalised with a positive outcome on 26.02.2025. No conditions pursuant to Article 21a or 22 of Directive 2001/83/EC have been made during the procedure.