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Public Assessment Report

Scientific discussion

Dualux 50 micrograms/mL + 5 mg/mL eye drops, solution in single-dose container

(latanoprost, timolol maleate)

ES/H/0935/001/DC

Applicant: Laboratorios Salvat S.A.

This module reflects the scientific discussion for the approval of Dualux 50 micrograms/ml + 5 mg/ml eye drops, solution in single-dose container. The procedure was finalised at 03 July 2025. 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 Dualux 50 micrograms/mL + 5 mg/mL eye drops, solution in single-dose container from Laboratorios Salvat S.A.

The product in indicated:

- Reduction of intraocular pressure (IOP) in adults (including the elderly) with open angle glaucoma and ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues

II. QUALITY ASPECTS

II.1 Introduction

The finished product is presented as eye drops solution containing 50 mcg/ml of Latanoprost and 5 mg/ml of timolol.
The maximum daily dose is one eye drop in the affected eye(s) once daily.
The product is available in single-dose translucent low density polyethylene (LDPE) containers. Each single-dose container contains 0.4 ml solution.

II.2 Drug Substance

Drug Substance Latanoprost

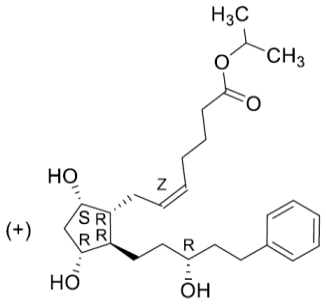
The ASMF procedure is used to support the quality of the drug substance.

General Information

Nomenclature:

INN:	Latanoprost
Chemical name:	Propan-2-yl (5Z)-7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-hept-5-enoate
CAS-No:	*130209-82-4*

Structure:



Molecular formula : $C_{26}H_{40}O_5$
Molecular weight : 432.6

General Properties:

Latanoprost is a colorless to yellow thick oil, very soluble in ethanol (96 %), chloroform, acetonitrile and dimethylsulfoxide and very slightly soluble in water. It contains six stereogenic centers. Latanoprost is hygroscopic.

Manufacture, process controls and characterisation
The description of the manufacturing process is properly detailed. The specifications of the materials used in the synthesis are sufficient and adequate. The profiles of impurities, including residual solvents, of these materials which can influence the quality of the active substance are well defined and controlled. The acceptance criteria for the critical stages and the information on the quality and control of intermediates are adequate.

Specification, analytical procedures, batch analysis
Active substance specifications are considered appropriate and limits justified. Analytical methods are correctly described and validation carried out according to ICH. Batch results support consistent production.

Container closure system
The active substance is packaged in small bottles made of high density polyethylene (HDPE Purell PE GF 4760) with a leakproof polypropylene (PP HF840MO) closure. The choice of the container closure system is properly justified. Compliance with the relevant requirements and/or regulations is confirmed.

Stability
Stability studies have been performed in accordance with current guidelines. Protocol, controlled parameters and test methods are considered adequate. The packaging material is similar to that proposed for storage. Proposed re-test period and storage conditions are justified.

Drug Substance Timolol Maleate

The active substance Timolol Maleate is sourced by OLON S.P.A. and the quality is supported by CEP. The quality of the drug substance Timolol Maleate supplied by the manufacturer is controlled in compliance with the corresponding monograph of the Ph. Eur. 572. The active substance has a certificate of suitability of the European pharmacopoeia: R1-CEP 2003-239-Rev 05. This certificate of suitability issued on 16th of March 2021 is considered valid according to EDQM database.

II.3 Medicinal Product

Description of the product

The drug product Latanoprost 50 micrograms/ml + timolol 5 mg/ml eye drops, solution in single dose container (Latanoprost + timolol SD), is a clear, colorless, sterile, aqueous solution packed in a low-density polyethylene (LDPE) single dose container via blow-fill-seal (BFS) manufacturing technology for ophthalmic use.

The quantitative composition and function of each excipient of Latanoprost + timolol SD is provided.

The excipients are Sodium dihydrogen phosphate monohydrate, sodium chloride, disodium hydrogen phosphate anhydrous, benzalkonium chloride, sodium hydroxide and hydrochloric acid (to adjust pH) and water for injection. The drug product is packaged in a low-density translucent polyethylene (LDPE) single-dose container with a deliverable volume of approximately 0.4 ml. As these containers are semi-permeable, they will be contained in an aluminium foil overwrap pouch or sachet and a carton box for protection with a folded patient information leaflet.

Pharmaceutical Development
The development of the product has been described, the choice of excipients is justified and their functions explained.

The physicochemical characteristics of the active substance that may affect the pharmaceutical form are identified and their control strategy is justified.
The proposed method of sterilization has been appropriately justified.

Manufacture of the product
The manufacturing process is fully described and in-process controls are appropriate considering the nature of the product and the manufacturing process. The industrial batch size is well-defined. Sufficient validation data are provided.

Excipients

Excipients used are well known and of appropriate quality.

None of the excipients is of animal origin.

Product specification, analytical procedures, batch analysis

The finished product specifications are adequate to control the finished product. Provided description and validation data for the analytical methods are adequate. Batch analysis data have been submitted and the results show that the finished product meets the proposed release specification.

Container closure system

The finished product is packaged in a 0.5 ml translucent low-density polyethylene (LDPE) container. The single –dose ampoules are packed into pre-printed aluminium foil overwrap pouches and heat-sealed. The choice of the container closure system is justified considering the nature of the finished product. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. The proposed protocol is considered adequate. The packaging material is the same as that intended for marketing. Proposed shelf-life and storage conditions are properly established.

Shelf-life: 24 months.

Storage conditions: This product does not require any special storage conditions.

III. NON-CLINICAL ASPECTS

III.1. Critical evaluation of the Non-Clinical Overview

Pharmacodynamic, pharmacokinetic and toxicological properties of latanoprost and timolol maleate are well known. As latanoprost and timolol maleate are widely used, well-known active substances, the applicant has not provided additional studies, and further studies are not required. Overview based on literature review is, thus, appropriate.

III.2. Ecotoxicity/environmental risk assessment (ERA)

Both latanoprost and timolol maleate PEC surface water values are below the action limit of 0.01 µg/L and are not PBT substances as log Kow values do not exceed 4.5.

Summary of main study results

Substance (INN/Invented Name): latanoprost			
CAS-number (if available): 130209-82-4			
PBT screening		Result	**Conclusion**
Bioaccumulation potential- log K_{ow}	OECD107	4.0	Potential PBT/vPvB: N
Phase I			
Calculation	**Value**	**Unit**	**Conclusion**
PEC surface water, default	0.0002	µg/L	> 0.01 threshold: N

Substance (INN/Invented Name): timolol maleate			
CAS-number (if available): 26921-17-5			
PBT screening		Result	**Conclusion**
Bioaccumulation potential- log K_{ow}	OECD107	-1.2 at pH 5 -0.4 at pH 7.4 1.2 at pH 9	Potential PBT/vPvB: N
Phase I			
Calculation	**Value**	**Unit**	**Conclusion**
PEC surface water, default	0.000015	µg/L	> 0.01 threshold: N

IV.CLINICAL ASPECTS

IV.1. Introduction

Latanoprost and timolol are a well-known actives substances with established efficacy and safety. A clinical overview has been provided, which is based on scientific literature. The clinical overview justifies that there no need to generate additional clinical data.

The PI documents has been amended according to the RMS and CMSs comments, and it is fully aligned with the reference product and the guidelines of application.

The Applicant did not conduct any clinical studies to support this application (please refer to biowaiver section).

IV.2. Pharmacokinetics

Biowaiver
The current application consists in a medicinal product for local use intended to act at the site of application.

A biowaiver is requested according to the *Guideline on the Investigation of Bioequivalence* (CPMP/QWP/EWP/1401/98 Rev. 1, Corr*). As the product under evaluation is the same type of solution (aqueous) than the reference product and only minor differences in the excipient composition is found, a waiver of the need to provide equivalence data is considered acceptable.

The bioequivalence between the test and the reference product can be assumed.

IV.3. Pharmacodynamics

No new studies on pharmacodynamics have been submitted, which is acceptable for this hybrid application.

IV.4. Clinical efficacy

No new studies on pharmacodynamics have been submitted, which is acceptable for this hybrid application.

IV.5. Clinical safety

No new studies on pharmacodynamics have been submitted, which is acceptable for this hybrid application.

IV.6. Risk Management Plan

The MAH has submitted a risk management plan (version 0.2, 21 January 2025), 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 Dualux 50 mcg/ml + 5 mg/ml eye drops solution in single-dose container.

The MAH has proposed the following summary of safety concerns:

Important identified risks	*None*
Important potential risks	*None*
Missing information	*None*

There are neither proposed additional pharmacovigilance activities nor proposed additional risk minimisation measures planned for Dualux 50 mcg/ml + 5 mg/ml eye drops solution in single-dose container.

IV.7. Discussion on the clinical aspects

The efficacy and safety of the active substances latanoprost and timolol are established and documented for the reference product. The bioequivalence between the test and the reference product can be assumed (please refer to section IV.2).

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

The test consisted of a pilot test with 3 participants, followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the hybrid product Dualux 50 micrograms/mL + 5 mg/mL eye drops, solution in single-dose container is found adequate. There are no objections to the approval of Dualux 50 micrograms/mL + 5 mg/mL eye drops, solution in single-dose container from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.