LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Olpalan
(olopatadine hydrochloride)

SE/H/2637/001/DC

This module reflects the scientific discussion for the approval of Olpalan. The procedure was finalised at 2026-03-11. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Olpalan, 1 mg/ml, Eye drops, solution.

The active substance is olopatadine hydrochloride, olopatadine. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

The medicinal product Olopatadine G.L. Pharma 1mg/ml eye drops solution is submitted for approval as an essentially similar medicinal product of the reference product Opatanol® 1 mg/ml eye drops, solution (as hydrochloride).

Mode of action
Olopatadine hydrochloride is a tricyclic compound with multiple mechanisms of action against multiple allergic conditions. It is a potent histamine H1-receptor antagonist and a specific mast cell stabilizer, with additional anti-inflammatory properties.

Pharmacological classification
It belongs to the pharmacotherapeutic group of ophthalmologicals; decongestant and antiallergics; other antiallergics (ATC-code S01GX09).

Claimed indication
Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.

Proposed posology
The dose is one drop in the conjunctival sac of the affected eye(s) twice daily (8 hourly). Treatment may be maintained for up to four months, if considered necessary.

Use in elderly
No dosage adjustment in elderly patients is necessary.

Paediatric patients
Olopatadine G.L. Pharma may be used in paediatric patients three years of age and older at the same dose as in adults. The safety and efficacy of Olopatadine G.L. Pharma in children aged under 3 years has not been established. No data are available.

Use in hepatic and renal impairment
Olopatadine in the form of eye drops (Olopatadine G.L. Pharma) has not been studied in patients with renal or hepatic disease. However, no dosage adjustment is expected to be necessary in hepatic or renal impairment (see section 5.2).

Method of administration
For ocular use only.

II.2 General comments on the submitted dossier

The application for Olopatadin G.L. Pharma, 1 mg/ml, eye drops, solution, is a Hybrid Art. 10(3) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK as concerned member state (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Opatanol, 1 mg/ml, eye drops, solution, authorised in EU since 2002, with Novartis Europharm Limited as marketing authorisation holder.

The clinical overview has been written by L. Poulos, M.D., B.Pharm. Ph.D., independent expert. The report refers to 100+ publications up to the year 2019.

The submitted clinical overview on the clinical pharmacology, efficacy and safety of olopatadin is considered adequate.

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, 'close-out letters' or 'exchange of information' issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

GCP
Not applicable, as no clinical studies have been submitted.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

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.

Drug 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.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of olopatadine are well known. As olopatadine is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

The proposed drug product Olopatadine 1 mg/mL eye drops solution has the same qualitative and quantitative composition as the EU reference product Opatanol 1 mg/ml eye solution regarding the drug substance and the preservative and is qualitatively same to the EU Opatanol eye drops solution for the rest of the excipients. The replacement of disodium phosphate dodecahydrate (Opatanol) with disodium phosphate anhydrous is of no importance, since both dissociate to the same anion and cation (sodium and phosphates). Furthermore, the indication and posology are identical to that of the reference product.

All the excipients used are well known excipients, used the pharmaceutical industry for eye drop preparations for decades.

Impurities
One impurity is present in the drug product at levels above the ICH 3B(R2) qualification limit (1.0% or 50 µg TDI, whichever is lower). This impurity is considered adequately qualified and the specification is agreed.

Environmental Risk Assessment (ERA)
An updated ERA for Olopatadine has been provided.

Phase 1
The default $PEC_{SURFACEWATER}$ value of Olopatadine is 0.00064 µg/L which is below the trigger value. As no other concerns are available, the risk assessment can stop in Phase 1.

PBT/vPvB screening
Experimental studies have been performed for determination of pKa and $logD_{ow}$ of Olopatadine. The pKa study was performed in agreement with principles of the OECD 112 guideline. The mean pKa values for Olopatadine were found to be 4.33 (pKa1; acid) and 9.42 (pKa2; base), respectively, which are in good agreement with the respective values reported in the available literature sources. The study was not performed in compliance with GLP. However, the study plan and the study report generated for the determination of pKa1 and pka2 of Olopatadine have been provided. Overall, the quality of the study seems acceptable.

The n-octanol/water distribution coefficient study was performed at three environmentally relevant pH values, i.e. 5, 7 and 9. The method applied was developed according to OECD 107 guideline. The $logD_{n\text{-}octanol/buffer}$ of Olopatadine at pH of 5, 7 and 9 was found to be 0.312, 0.338, and 0.235, respectively, which are in good agreement with values reported in available literature sources. The study was not performed in compliance with GLP. However, he analytical method verification protocols, analytical method verification reports, partition coefficient study plans and partition coefficient study reports, generated for each investigated pH value of 5, 7 and 9, have been provided. Overall, the quality of the study seems acceptable.

The experimentally estimated n-octanol/water distribution coefficients ($logD_{n\text{-}octanol/buffer}$) of Olopatadine are well below the trigger value for a PBT/vPvB evaluation ($logK_{ow} \leq 4.5$), therefore no further assessment is required.

Summary of main study results

Substance (INN/Invented Name): Olopatadine			
CAS-number (if available): 140462-76-6			
PBT screening		Result	**Conclusion**
Bioaccumulation potential- log K_{ow}	OECD107	0.396 (pH 5) 0.341 (pH 7) 0.375 (pH 9)	Potential PBT (N)
Phase I			
Calculation	**Value**	**Unit**	**Conclusion**
$PEC_{surfacewater}$ (default)	0.00064	µg/L	> 0.01 threshold (N)

Overall summary and conclusion
Based on environmental exposure estimates for Olopatadine, this Risk Assessment is concluded in Phase 1. No other environmental concerns are apparent.

Olopatadine does not meet the trigger for a definitive PBT/vPvB assessment.

It can therefore be concluded that Olopatadine 1 mg/mL eye drops, solution is unlikely to represent a risk to the environment following its recommended usage in patients and no further risk assessment is required.

III.3 Clinical aspects

No clinical studies have been conducted to support the application. The applicant refers to the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr**) to justify an exemption from conducting a bioequivalence study. The exemption is acceptable from a clinical point of view since essential similarity with the originator product can be reasonably assumed. “Opatanol 1 mg/ml eye drops solution” has the same qualitative and quantitative composition as the EU reference product Opatanol 1 mg/ml eye solution regarding the drug substance and the preservative and is qualitatively the same as the EU Opatanol eye drops solution for the other excipients (refer to table 1). Furthermore, the indication and posology are identical to that of the reference product. The justification for a bio-waiver is therefore acceptable, also in view of the topical pharmacological effect of the product at the site of administration.

Pharmacokinetics
The applicant presents in the Clinical Overview characteristics of absorption, distribution, metabolism, excretion and pharmacokinetics in special populations of orally and ocular administered olapatadine. This is deemed acceptable.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Since essential similarity with the reference product can be reasonably assumed and because equivalence has been shown based on quality data, additional data is not considered necessary.

Pharmacovigilance system
Proposed MAH: G.L. Pharma GmbH (RMS, CMS)
The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

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 Olopatadin G.L. Pharma.

Part II Safety specification

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

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

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

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plan, version SE/H/2637/01/DC signed 22 Oct 2024 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)
Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the product, Olopatadin G.L. Pharma, is found adequate. There are no objections to approval of Olopatadin G.L. Pharma, from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Post approval commitments
N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**
  N/A

- **Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83/EC**
  N/A

- **Specific obligation to complete post-authorisation measures for the marketing authorisation under Exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC**
  N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Hydagelan film-coated tablets, AT/H/1460/001-002/DC and Olopatadine 1 mg/ml Eye drops, Solution, DE/H/5136/001/DC. The bridging report submitted by the applicant has been found acceptable.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-