Štátny ústav pre kontrolu liečiv, Kvetná 11, 825 08 Bratislava

Public Assessment Report

Scientific discussion

ISOPRINOSINE FORTE 1000 mg tablety

Inosine acedoben dimepranol

2023/05862-REG

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This module reflects the scientific discussion for the approval of ISOPRINOSINE FORTE 1000 mg tablety (ISOPRINOSINE FORTE 1000 mg tablets). The procedure was finalised on 17.09.2025. For information on changes after this date please refer to the module 'Update'.

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I INTRODUCTION

Based on the review of the quality, safety and efficacy data, the State Institute for Drug Control has granted a marketing authorisation for **ISOPRINOSINE FORTE 1000 mg tablets** from Ewopharma International, s.r.o., Slovenská republika.

The product is indicated for treatment or management of cell-mediated immunity depression or dysfunction, and of clinical symptoms associated with:

- Viral respiratory infections caused by respiratory viruses such as adenovirus, parainfluenza virus types 1-3, respiratory syncytial virus (RSV), etc.
- Infections caused by Herpes viruses: herpes simplex virus type 1 and 2 (HSV), varicella zoster virus (VZV).
- Genital warts (condyloma accuminata) – external lesions (excluding perianal or meatal sites) as monotherapy or as an adjunct to conventional topical or surgical therapy.
- Mucocutaneous, vulvovaginal (subclinical) or endocervical-associated HPV infections (human papillomavirus infections).
- Viral hepatitis.
- Subacute sclerosis panencephalitis (SSPE).

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

The marketing authorisation has been granted pursuant to Article 10a of Directive 2001/83/EC, which corresponds to Article 49 (1) b) of Law on medicinal products and medical devices No. 362/2011.

II EXECUTIVE SUMMARY

II.1 About the product

Presented drug product contains inosine acedoben dimepranol as a drug substance, sometimes also called inosine pranobex. The drug product is indicated for the treatment or modification of reduced or non-functional cellular immunity (ATC-code J05AX05).

The finished product is presented as an oblong white to off-white tablet with a score line on one side to half the tablet into equal doses. Primary packaging consists of PVC/PVdC/Al-blister strips.

II.2 General comments on the submitted dossier

This is a national application for marketing authorization of ISOPRINOSINE FORTE 1000 mg; tablets made in accordance with the Article 10a well-established use application of the European directive 2001/83/EC as amended.

The application is a line-extension to medicinal product Isoprinosine 500 mg tablety, authorisation number 42/0198/81-CS. Other pharmaceutical forms already authorised by the applicant are Isoprinosine 1000 mg granulát na perorálny roztok vo vrecku (registration number 42/0398/19-S), Isoprinosine 50 mg/ml sirup (registration number 42/0868/09-S).

ASMF procedure is followed for the drug substance.

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.

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.2 Non clinical aspects

Applicant submitted the non-clinical overview, summarising the results published in 85 literature references. The Non-Clinical Overview on the pre-clinical pharmacology, pharmacokinetics and toxicology was adequate. The information about summary of non-clinical data is adequately presented in section 5.3 of the SmPC.

III.3 Clinical aspects

Applicant submitted the clinical overview, summarising the results published in 158 literature references. As this was a line-extension procedure of already registered product, clinical assessment concentrated mostly on acceptance of new pharmaceutical form. Application is approvable from clinical point of view.

Pharmacokinetics
Applicant submitted marketing authorisation application for new pharmaceutical form and strength, 1000 mg tablet. In order to show the bridge between the previous, already registered formulation, and a 1000 mg tablet, the applicant supported the applicaton by biowaiver, which is fully based on ICH M9 guideline on biopharmaceutics classification system-based biowaivers EMA/CHMP/ICH/493213/2018). The BCS-based biowaiver can be applicable to this immediate release, solid, orally administered dosage form (tablet).

Isoprinosine tablets 1000 mg is an immediate release, solid, orally administered dosage form designed to deliver the drug to the systemic circulation. There is no narrow therapeutic index applied for inosine pranobex. Inosine pranobex generally exhibits high solubility and high permeability, thus it belongs to BCS Class I, as was already confirmed by scientific literature and various marketing authorisation procedures across EU.

Both products (tablets 500 mg and 1000 mg) contain similar excipients. Excipients of the formulation are well known and widely used in pharmaceutical industry and have pharmacopoeia monographs.

A comparative dissolution study has been carried out between Isoprinosine 500 mg tablets and Isoprinosine 1000 mg tablets. The dissolution profiles and analysis were performed according to the analytical method registered for Isoprinosine 500 mg and proposed also for Isoprinosine 1000 mg.

Clinical efficacy
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Since this is a line extension and the bioequivalence with the already registered 500 mg tablet has been

demonstrated, additional data is not necessary.

Summary Pharmacovigilance system
The Applicant has submitted a signed Summary of the Applicant's and 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 **ISOPRINOSINE FORTE 1000 mg, tablets.**

- Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	Safety in pregnancy/breast-feeding

IV BENEFIT RISK ASSESSMENT

This was a MAA of medicinal product for human use as it is defined in Article 10(a) (bibliographic application) of the European Directive 2001/83/EC as amended corresponding to Article 49 (1) b) of Law on medicinal products and medical devices No. 362/2011 as amended. MAA was submitted via national procedure according to Article 52 of Law on medicinal products and medical devices as amended.

From a (non-)clinical point of view, the application contained adequate (non-)clinical data that supported chosen legal basis – bibliographic application.

Quality aspects of the dossier were adequately described.

Based on submitted data referring to published scientific literature applicant adequately addressed the requirements for a bibliographical application and sufficiently demonstrated the quality of a medicinal product in the scope of this MAA. Therefore, the State Institute for Drug Control granted the marketing authorisation on 17.09.2025.

V RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 Summary of Product Characteristics (SmPC)

The approved SmPC is available on the website of State Institute for Drug Control.

V.2 Package Leaflet (PL)

V.2.1 Package Leaflet

The approved PL is available on the website of State Institute for Drug Control.

V.2.2 Assessment of User Testing

The results of the user consultation with target patient groups on the package leaflet submitted by the applicant 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

V.3 Labelling

The approved Labelling is available on the website of State Institute for Drug Control.