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Public Assessment Report

Scientific discussion

Colchicine IASIS 0.25 mg/ml oral solution (colchicine)

SK/H/0304/001/DC

Date of this report:	January 2026

This module reflects the scientific discussion for the approval of Colchicine IASIS. The procedure was finalised at 13 September 2024. 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 Member States have agreed to grant a marketing authorisation for Colchicine IASIS 0.25 mg/ml oral solution.
The product is indicated for:

- the treatment of acute gout
- the prophylaxis of a gout attack during initiation of urate-lowering therapy
- the treatment of acute and recurrent pericarditis as an adjunct to aspirin/NSAID therapy
- in Familial Mediterranean Fever for prophylaxis of attacks and prevention of amyloidosis

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

II EXECUTIVE SUMMARY

II.1 Rationale for the product

N/A

II.2 About the product

Mode of action
Colchicine is an alkaloid extracted from the plant Colchicum autumnale (family *Colchinaceae*) very common in South-Central Europe and in North-Central Italy.
Its primary mechanism of action is tubulin disruption which leads to subsequent down regulation of multiple inflammatory pathways and modulation of innate immunity. Urate crystals are phagocytosed by leukocytes. Hereby inflammatory factors are released. Colchicine inhibits these processes. Other properties of colchicine, such as interaction with microtubules, could also contribute to its action.

Pharmacological classification
Pharmacotherapeutic group: Antigout preparations; preparations with no effect on uric acid metabolism
ATC code: M04AC01

Approved indications

Colchicine IASIS is indicated in adults for:

- the treatment of acute gout
- the prophylaxis of a gout attack during initiation of urate-lowering therapy
- the treatment of acute and recurrent pericarditis as an adjunct to aspirin/NSAID therapy

Adults and paediatric population
- in Familial Mediterranean Fever for prophylaxis of attacks and prevention of amyloidosis

Posology

The recommended dosage is:

- *Treatment of acute gout attack*

2 to 3 times daily 0.5 mg (2 mL oral solution), possibly preceded by an initial dose of 1 mg (4 mL oral solution). Treatment should end until the acute attack resolves, or earlier in the event of gastrointestinal symptoms and no improvement after 2 to 3 days.

No more than 6 mg (24 mL oral solution) should be taken as a course of treatment. After completion of a course, another course should not be started for at least 3 days (72 hours).
If diarrhoea or vomiting occurs, Colchicine IASIS should be discontinued immediately as these may be the first signs of an intoxication.

- *Prophylaxis of a gout attack*

0.5 – 1 mg (2 – 4 mL oral solution) per day (to be taken in the evening).

- *Treatment of acute and recurrent pericarditis*

0.5 mg (2 mL oral solution) once daily in patients of less than 70 kg of body weight or in patients with intolerance to higher doses.
0.5 mg (2 mL oral solution) twice daily in patients of more than 70 kg of body weight.

Treatment should be continued for 3 months in acute pericarditis and 6 months in recurrent pericarditis.

- *Familial Mediterranean Fever*

Adults

The dose may be given as a single dose or doses higher than 1 mg (4 mL oral solution) per day may be divided and given twice daily.
Colchicine dosage should be increased in a stepwise fashion up to a maximum of 3 mg (12 mL oral solution) per day to control disease in patients who do not clinically respond to the standard dosage. Any increase of the daily dose should be monitored closely for adverse effects.
Careful monitoring is needed in the presence of impaired renal or liver function. For these patients, the starting dose should be reduces by 50 % (e.g. ≤ 1 mg/day, 4 mL oral solution).

Paediatric population
Colchicine IASIS should only be used for Familial Mediterranean Fever in children and adolescents.

For paediatric use, colchicine should only be prescribed under the supervision of a medical specialist with the necessary knowledge and experience.

A starting dose should be administered orally based on age:
- 0.5 mg (2 mL oral solution) per day in children less than 5 years of age
- 1 mg (4 mL oral solution) per day in children from 5 to 10 years of age
- 1.5 mg (6 mL oral solution) per day in children over 10 years of age

In children with amyloid nephropathy, higher daily doses up to 2 mg (8 mL oral solution) per day might be needed.
Colchicine dosage should be increased in a stepwise fashion (e.g. 0.25 mg/step) up to a maximum of 2 mg/day to control disease in patients who do not clinically respond to the standard dosage. Any increase of the daily dose should be monitored closely for adverse effects.

Method of Administration
Oral use.
The oral solution should be considered especially for children younger than 1 year.

A graduated oral syringe and a Press-In Bottle Adaptor are provided with the drug product.

For special populations etc. see Summary of Product Characteristics.

II.3 General comments on the submitted dossier

This concerns an application for marketing authorisation for Colchicine IASIS 0.25 mg/ml oral solution according to article 10(3) of Directive 2001/83/EC, a hybrid application.

European Reference Product (ERP)
A European Reference Product is used in RMS and CMSs CY, EL and RO: Colchicine Tiofarma 0.5 mg tabletten (MAH: Tiofarma B.V.), registered in NL on 28 December 1998.

II.4 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.

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
Based on the data and documents submitted, the RMS has been assured that the study was conducted and reported in compliance with GCP: a GCP statement and audit certificate(s) were provided; monitoring report(s) and recent inspection(s) by competent authorities identified no concerns relevant to the study; and, where conducted outside the EU, compliance with the ethical requirements of Directive 2001/20/EC was confirmed. On this basis, inspection of the submitted bioequivalence study ARL/21/209 is not considered necessary.

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

The chemical-pharmaceutical documentation and Quality Overall Summary in relation to Colchicine IASIS are of sufficient quality in view of the present European regulatory requirements.

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 development of the product has adequately been performed and described.
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 control 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.
The analytical methods applied are suitably described and validated.
Batch analysis has been performed on three batches. The batch analysis results show that the finished products meet the specifications proposed.

The conditions used in the stability studies are according to the ICH stability guidelines.

III.2 Non clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of colchicine are well known. As colchicine is a widely used, well-known active substance, the applicant has not provided additional studies, and further studies were not required. An overview based on the literature review was, thus, appropriate.

The excipients were well within the described limits for use in medicinal products, considered generally safe, or also naturally occurring at physiological levels in humans.
The instructions on use of the drug product during pregnancy and lactation, the effect on fertility from a non-clinical perspective, and the preclinical safety data contained in the proposed SmPC reflect the characteristics of the API and are in line with the reference product´s SmPC.

The non clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology was adequate.

Environmental Risk Assessment (ERA)
No significant increase in consumption was noted in either RMS or CMSs. To conclude, no increase in environmental exposure was expected after the approval of the drug product on the market.

III.3 Clinical aspects

Pharmacokinetics
The drug product used for the bioequivalence study No. ARL/21/209 was Colchicin Ysat 0.5 mg Tabletten by Tiofarma B.V.
The study has demonstrated that Colchicine IASIS was bioequivalent to Colchicin Ysat under fasting conditions. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of geometric mean for the test and reference product fell within the conventional acceptance range of 80.00-125.00 %.

Pharmacodynamics
N/A

Clinical efficacy/Clinical safety
Literature data for the support of indications (“treatment of acute gout”; “prophylaxis of a gout attack during initiation of urate-lowering therapy”; “treatment of acute and recurrent pericarditis as an adjunct to aspirin/NSAID therapy”) has been provided.
Regarding the indication “treatment of acute and recurrent pericarditis as an adjunct to aspirin/NSAID therapy” a bridge based on data between Colchicine IASIS and the drug product used in the clinical studies has been provided as well.

Summary Pharmacovigilance system
The Applicant has submitted a signed Summary of the 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 Colchicine IASIS.

Safety specification

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

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.

Summary of the RMP
The submitted Risk Management Plan, version 0.1 signed 25 January 2023 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 applicant has proposed renewal date 5 years after the end of procedure. The applicant's proposal is acceptable.

IV BENEFIT RISK ASSESSMENT

This application concerns a hybrid medicinal product referencing Colchicine Tiofarma 0.5 mg tabletten. Bioequivalence with the reference medicinal product has been demonstrated. No clinically relevant differences in efficacy or safety are anticipated in the proposed indications.
Overall, the benefit–risk balance is favourable.

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

Description	Due date
N/A	N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to 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

Assessment of the User Testing is attached in the 'QRD Guidance and Checklist for the Review of User Testing Results'.

V.5 Labelling

The approved Labelling is available in the MRI Product Index.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-