Date: 18 May 2022
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Colibiogen Oral

International non-proprietary name: *Escherichia coli* lysate (strain Laves)
Pharmaceutical form: oral solution
Dosage strength(s): 760 – 870 mg *Escherichia coli* lysate pro mL
Route(s) of administration: oral
Marketing Authorisation Holder: Laves Arzneimittel GmbH
Marketing Authorisation No.: 68052
Decision and Decision date: approved on 7 April 2022

Note:

Assessment Report as adopted by Swissmedic with all information of a commercially confidential nature deleted.

The SwissPAR is a “final” document, which provides information relating to a submission at a particular point in time and will not be updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
API	Active pharmaceutical ingredient
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
DSM	German collection of microorganisms
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
FDA	U.S. Food and Drug Administration
GABA	Gamma-aminobutyric acid
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing Authorisation Holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric Investigation Plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric Study Plan (US-FDA)
RMP	Risk Management Plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

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2 Background Information on the Procedure

2.1 Applicant's Request(s)

New Active Substance status
The applicant requested the status of a new active entity for the active substance *Escherichia coli* lysate (strain Laves) of the medicinal product mentioned above.

Authorisation in accordance with Art. 14 para. 1 a$^{bis-quater}$ TPA
The applicant requested a simplified authorisation in accordance with Art. 14 para. 1 a^{quater} TPA.

2.2 Indication and Dosage

2.2.1 Requested Indication

Colibiogen Oral is an intestinal mucosal- and immunotherapeutic and is used to treat irritable bowel syndrome.

2.2.2 Approved Indication

Colibiogen Oral is used for the supportive, symptomatic treatment of irritable bowel syndrome in adults.

2.2.3 Requested Dosage

Summary of the applied standard dosage:
Depending on the severity of the disease, 10 mL Colibiogen Oral should be taken 1 to 3 times daily, half an hour before meals with some liquid.
The duration of treatment depends on the symptoms and can last up to 6 months.

2.2.4 Approved Dosage

(see appendix)

2.3 Regulatory History (Milestones)

Application	2 November 2020
Formal control completed	1 December 2020
List of Questions (LoQ)	29 March 2021
Answers to LoQ	24 June 2021
Predecision	22 September 2021
Answers to Predecision	21 November 2021
Labelling corrections	20 February 2022
Final Decision	7 April 2022
Decision	approval

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3 Quality Aspects

3.1 Drug Substance

The drug substance of Colibiogen Oral is a cell-free solution of lysed *Escherichia coli* culture, strain Laves.
The manufacturing process comprises *Escherichia coli* L1931 (DSM 13792) fermentation process steps, heat inactivation and a filtration step.
The drug substance consists of components of the fermentation broth and metabolic substances of *Escherichia coli* and is thus a complex mixture of peptides, lipids, amino acids and biogenic amines.
Master and working cell banks have been established and are adequately controlled.
The specifications include e.g. tests for appearance, identity, process-related impurities, content of lead compounds (GABA and Cadaverine) and microbiological purity.
Batch analysis data of commercial-scale batches were provided and indicate a consistent manufacturing process. The analytical methods established for drug substance release are described and non-compendial methods have been validated in accordance with ICH guidelines.
No drug substance shelf life has been established since the drug substance is immediately introduced into the drug product compounding process.

3.2 Drug Product

The finished drug product is a preserved, non-sterile liquid solution intended for oral administration. One human dose is 5 mL per day but may be increased to a maximum dose per day of 30 mL. The drug product is presented in a 100 mL: brown glass bottle and is provided with a measuring cup. The drug product is formulated with sucrose, citric acid, ethanol, sodium benzoate (preservative) and orange flavour. The orange flavour contains linalool and citral.
The manufacturing process of the finished drug product is a standard process consisting of compounding, filling and sealing steps. Process validation studies were executed at commercial scale using three consecutive validation batches.
The quality of drug product is assured by employing a similar battery of tests as used for drug substance testing but also comprises release and stability specifications for the content of preservative and ethanol. The analytical procedures are validated in accordance with ICH guidelines or comply with Ph. Eur.
The claimed shelf life of 36 months when stored at room temperature (15 – 25°C) is justified based on stability studies performed according to ICH guidance. The proposed in-use shelf life of 6 weeks at room temperature is justified by Ph. Eur. antimicrobial preservation studies.

3.3 Quality Conclusions

Satisfactory and consistent quality of drug substance and drug product has been demonstrated.

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4 Nonclinical Aspects

Swissmedic has not assessed the primary data relating to nonclinical aspects of this application and relies on the assessment of the authority of canton Appenzell Ausserrhoden.

5 Clinical and Clinical Pharmacology Aspects

Swissmedic has not assessed the primary data relating to clinical aspects of this application and relies on the assessment of the authority of canton Appenzell Ausserrhoden.

6 Risk Management Plan Summary

No RMP is available for this medicinal product.

7 Information for Healthcare Professionals

Depending on the dispensing category of the medicinal product, the information for healthcare professionals is not always mandatory in Switzerland, the leaflet for patients may be sufficient. No information for healthcare professionals is available for Colibiogen Oral. Please refer to the patients leaflet published on www.swissmedicinfo.ch.

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