PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN (CH)

TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV

(faecal microbiota)

Modified release capsules, hard (2 x 20 capsules)

Rectal suspension (250 mL)

Based on Part VI of EU RMP version 05.2 (dated 05/02/2025)

Marketing Authorization holder:

CHUV, Centre hospitalier universitaire vaudois, Rue du Bugnon 46, 1011 Lausanne, Switzerland

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LIST OF ABREVIATIONS

CHUV	Centre Hospitalier Universitaire Vaudois
FMT	Faecal Microbiota Transfer
HCPs	HealthCare Professionals
IBD	Inflammatory Bowel Disease
IT	Information Technology
PL	Package Leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan

Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV is a concise document and does not claim to be exhaustive.

Please note that the reference document which is valid and relevant for the effective and safe use of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV in Switzerland is the "Arzneimittelinformation/Information sur le médicament" (see swissmedic.ch) approved and authorized by Swissmedic. CHUV, Centre hospitalier universitaire vaudois, Rue du Bugnon 46, 1011 Lausanne, Switzerland is fully responsible for the accuracy and correctness of the content of the published summary RMP of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV.

SUMMARY OF RISK MANAGEMENTPLAN FOR TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV

This is a summary of the RMP for TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV. The RMP details important risks of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV, how these risks can be minimised, and how more information will be obtained about TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV risks and uncertainties (missing information).

TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV information for healthcare professional gives essential information to healthcare professionals (HCPs) and patients on how TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV should be used.

Important new concerns or changes to the current ones will be included in updates of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV's RMP.

I. The medicine and what it is used for

TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV is authorized for the treatment of multi-recurrent *Clostridoides difficile* infection (formerly called *Clostridium difficile* infection) in adult patients (≥18years), after prior specific antibiotic treatment according to current recommendations. It contains of faecal material which is the active substance. The rectal suspension of FMT is administered by colonoscopy, by rectal enema, nasojejunal tube or nasoduodenal tube (administration of up to 250 mL rectal suspension, equivalent to 70 g of faecal materiel). The modified release capsules, hard are orally administered (up to 2 x 20 modified release capsules, hard, 1 capsule is equivalent to 1 g faecal material).

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV, together with measures to minimise such risks and the proposed studies for learning more about TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the information for healthcare professional addressed to patients and healthcare professionals.
- Important advice on the medicine's packaging.
- The authorised pack size – the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly.
- The medicine's legal status – the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV, these measures are supplemented with an additional risk minimization measure mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*, extended by donors' and recipients' registries. If important information that may affect the safe use of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

Table 1. List of important risks and missing information.

Important identified risks	• Severe infections (transmission of pathogenic microorganisms via the donor's faecal microbiota). • Serious adverse events related to the administration procedure via endoscopic route. • Flare-ups of inflammatory bowel disease post-FMT in patients with a known history of this condition.
Important potential risks	• Transmission of microbiota-mediated diseases to the recipient via the donor's faecal microbiota. • Infection caused by the transmission of an unidentified pathogenic microorganism or one whose faecal transmission route was not previously known. • Serious adverse events related to oral administration.
Missing information	• Use in pregnant and breastfeeding women. • Use in children. • Use in immunocompromised individuals. • Long-term safety and efficacy data.

II.B. Summary of important risks

Table 2. Important identified risks : Severe infections (transmission of pathogenic microorganisms via the donor's faecal microbiota)

Evidence for linking the risk to the medicine	Some infections are secondary to a transmission of pathogenic microorganisms from the donor to the recipient. Before the faecal microbiota transfer, these microorganisms are absent from the recipient's faecal microbiota. A potential transfer can be demonstrated through analytical methods to confirm the link between the faecal microbiota transfer and the transmission of microorganisms.
Risk factors and risk groups	None.
Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional - warnings and precautions; undesirable effects • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Rigorous and standardized selection of the donors. • Regular update of screening procedures • Use of diagnostic tests to limit the risk of false negatives (superior in sensibility). • IT alert on biological check-up. • Quarantine of the batches followed by a multidisciplinary validation for final eligibility of the donor and batch release. • Production of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV, from a single donor and from a single donation. • Literature monitoring and international collaboration with other faecal microbiota transfer centres with the aim of adapting donor procedures in real time • Standardized monitoring of the donors and recipients. • Traceability system for the donors and recipients with retention of biological samples. (biobank)
Additional pharmacovigilance activities	• Systematic reporting of adverse events according to Swissmedic' procedure. • Donor and recipient registry • In the registry: Notification of all adverse events even those that do not warrant reporting to Swissmedic, in accordance with ICH E2 recommendations.

Table 3. Important identified risks : Serious adverse events related to the administration procedure via endoscopic route

Evidence for linking the risk to the medicine	Post-FMT pneumonia after inhalation <u>under sedation</u> that can lead to death (naso-gastric tube, naso-gastric endoscopy, lower endoscopy). Post-FMT pneumonia after inhalation of faecal microbiota by the naso-gastric administration (identification of faecal microbiota in the lungs).
Risk factors and risk groups	Administration volume > 150 mL by the naso-gastric route Administration by an upper route, in a lying position. Sedation or impaired alertness.

Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional - undesirable effects and complementary information according to way of administration. • Prescription only medicine. • Assessment of the benefit-risk balance to choose the procedure of administration. <u>Additional risk minimisation measures:</u> • Implementation of procedures for each route of administration • Avoidance of general anaesthesia for performing TMF • Eviction, if possible, of sedation, except in particular cases with verification of the benefit-risk balance. • If possible, eviction of the nasogastric route (administration via the nasojejunal route if upper route is required) • If using the nasogastric route: reduction of volumes (<100 mL) • If using the upper route: ensure the patient is seated at a 90° angle • If performing a colonoscopy or recto-sigmoidoscopy: verification of contraindications or risk factors for complications
Additional pharmacovigilance activities	• Systematic reporting of adverse events according to the Swissmedic' procedure. • Specific notification in the recipient's registry.

Table 4. Important identified risk: Flare-ups of inflammatory bowel disease post-FMT in patients with a known history of this condition

Evidence for linking the risk to the medicine	The implication of the faecal microbiota in flare-ups has not been fully ascertained.
Risk factors and risk groups	Patients who are known to have an Inflammatory Bowel Disease.
Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional - warnings and precautions - Inflammatory Bowel disease (IBD). • Prescription only medicine. <u>Additional risk minimisation measures:</u> • If possible, evaluation of the disease's activity by endoscopy before the faecal microbiota transfer. • Mode of administration preferably via the upper route. • Adjustment of the treatment of the Inflammatory Bowel Disease before and after the faecal microbiota transfer.
Additional pharmacovigilance activities	• Systematic and standardized reporting in the recipient registry, with a minimum follow-up of 5 years, in accordance with ICH E2 recommendations for all pathologies. • Reporting of adverse events according to the Swissmedic procedure, with an assessment of causality.

Table 5. Important potential risk: Transmission of microbiota-mediated diseases to the recipient via the donor's faecal microbiota

Evidence for linking the risk to the medicine	The link between FMT and a pathology is difficult to establish as the causes of a pathology are usually multifactorial. Up to now, there are no signs on a probable or proven causality, over the last ten years, based on available literature. Evidence for linking the risk to the medicine may be achived by long-term cohort evaluation, registries, and biobanks.
Risk factors and risk groups	Risk factors and risk groups vary depending on the pathologies and the recipients.
Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional – Adverse effects - Transmission of microorganisms and/or microbiota-mediated pathologies • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Eligibility of donors based on the absence of known pathology linked to the faecal microbiota in the donors or in their families. • Exclusion of donors who are over the age of 50, because of the risk of colorectal cancer and other comorbidities.
Additional pharmacovigilance activities	• Systematic and standardized reporting in the recipient registry, with a minimum follow-up of 5 years, in accordance with ICH E2 recommendations for all pathologies. • Reporting of adverse events according to the Swissmedic procedure, with an assessment of causality.

Table 6. Important potential risk: Infection caused by the transmission of an unidentified pathogenic microorganism or one whose faecal transmission route was not previously known.

Evidence for linking the risk to the medicine	Linkage by biokank and registry: Reanalysis of the presence of the unidentified microorganism in faecal matter of the donor, in the product, as well as post-TMF in the recipient's stool. Retrospective detection of the unknown microorganism after the establishment of the analysis method (e.g., PCR) in faecal matter, in the product, as well as post-TMF in the recipient's stool.
Risk factors and risk groups	Donors: history of infections over the last eight weeks, proven contagion in the donor’s entourage. Potential risk varying based on epidemiological trends.
Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional – Adverse effects - Transmission of microorganisms and/or microbiota-mediated pathologies • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Rigorous and standardized selection of the donors. • Literature monitoring and international collaboration with other faecal microbiota transfer centres.

Additional pharmacovigilance activities	In case of suspicion of an unidentified pathogenic microorganism (e.g., case of SARS-CoV-2) or one whose faecal transmission route was not previously known: • Notification to Swissmedic • If confirmed: suspension of the production and, if necessary, implementation of additional measures • Resumption of production after Swissmedic' validation of the additional measures

Table 7. Important potential risk: Serious adverse events related to oral administration.

Evidence for linking the risk to the medicine	Risk is a false route The size of modified-release capsules and the number to be swallowed are important.
Risk factors and risk groups	Age dysphagia swallowing disorders
Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professional – Method of administration; Contraindications • Prescription only medicine. • Assessment of the benefit-risk balance to choose the procedure of administration. <u>Additional risk minimisation measures:</u> • Verification of the absence of swallowing difficulties or dysphagia. • Be mindful of the patient's position, whether standing or sitting at a 90-degree angle.
Additional pharmacovigilance activities	• Systematic reporting of adverse events according to the Swissmedic' procedure. • Specific notification in the recipient's registry.

Table 8. Missing information: Use in pregnant and breastfeeding women

Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professionals – pregnancy and breastfeeding. • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Literature monitoring and international collaboration with other faecal microbiota transfer centres. • Systematic monitoring of the recipient and the child over 5 years (registry)
Additional pharmacovigilance activities	The PSUR/PBRER will mention treated pregnant and breastfeeding women, their associated characteristics, and any observed adverse events.

Table 9. Missing information: Use in children

Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professionals – paediatric population. • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Literature monitoring and international collaboration with other faecal microbiota transfer centres. • To be used only in the absence of a therapeutic alternative. • Long-term follow-up of recipients (registry and biobank).
Additional pharmacovigilance activities	The PSUR/PBRER will mention treated pediatric patients, their associated characteristics, and any observed adverse events.

Table 10. Missing information: Use in immunocompromised individuals

Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professionals – Immunodeficient patients; Warnings and precautions; Contraindications • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Literature monitoring and international collaboration with other TMF centres. • Evaluation of the benefit-risk balance. • Donor screening is adapted based on the recipient's level of immunosuppression and serology.. • Long-term follow-up of recipients (registry and biobank).
Additional pharmacovigilance activities	The PSUR/PBRER will mention treated immunocompromised patients, their associated characteristics, and any observed adverse events.

Table 11. Missing information: Long-term safety and efficacy data

Risk minimisation measures	<u>Routine risk communication:</u> • Information for healthcare professionals – Dosage/Administration - Patients monitoring over 5 years • Prescription only medicine. <u>Additional risk minimisation measures:</u> • Literature monitoring and international collaboration with other faecal microbiota transfer centres. • Long-term follow-up of donors and recipients (registry and biobank).
Additional pharmacovigilance activities	• Donors and recipients' registries. • Annual updates on any new information on safety and efficacy. • Annual interim reports of registry data (with yearly reassessment) • PSUR/PBRER submitted annually to Swissmedic.

II.C. Post-authorisation development plan

II.C.1. Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV.

II.C.2. Other studies in post-authorisation development plan

There are no studies required for TRANSFERT DE MICROBIOTE FECAL POUR UTILISATION ALLOGENIQUE CHUV.