swissmedic

Date: 7 February 2025
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Manufacturing procedure for "Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale"

International non-proprietary name: faecal microbiota

Pharmaceutical form: rectal suspension

Dosage strength(s): 1 vial of 250 mL is equivalent to 70 g of faecal matter

Route(s) of administration: by colonoscopy, by rectal enema, or by nasojejunal/nasoduodenal tube

Marketing authorisation holder: Centre Hospitalier Universitaire Vaudois (CHUV)

Marketing authorisation no.: 68581

Decision and decision date: approved on 12.12.2024

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

CDI	*Clostridioides difficile* infections
ECDC	European Centre for Disease Prevention and Control
EDQM	European Directorate for the Quality of Medicines & HealthCare
FMT	Faecal microbiota transplantation
HAI	Healthcare-associated infections
PASS	Post-authorisation safety study
rCDI	Recurrent *C. difficile* infection
RMP	Risk management plan
SAE	Serious adverse event
SoC	Standard of care
SwissPAR	Swiss Public Assessment Report
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s)

Authorisation of a manufacturing process for non-standardised medicinal products in accordance with Article 33 and 34 TPO
The applicant requested the authorisation of a manufacturing process for the non-standardised medicinal product "Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale" in accordance with Article 33 and 34 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Clostridioides difficile infections

2.2.2 Approved indication

Multiple recurrent infection with *Clostridioides difficile* (formerly known as *Clostridium difficile*) in adult patients (≥ 18 years) after prior specific antibiotic treatment according to current recommendations.

2.2.3 Requested dosage

A single administration of 50 to 250 mL (administration by colonoscopy, by rectal enema, or by nasojejunal/nasoduodenal tube)

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	30 June 2021
Additional documentation	29 April 2022
Formal control completed	13 July 2022
List of Questions (LoQ)	23 January 2023
Response to LoQ	17 May 2023
Preliminary decision	18 August 2023
Response to preliminary decision	15 December 2023
Preliminary decision no. 2	27 March 2024
Response to preliminary decision no. 2	24 May 2024
Preliminary decision no. 3	23 August 2024
Response to preliminary decision no. 3	12 September 2024
Final decision	12 December 2024
Decision	approval

3 Medical context

Clostridioides difficile (*C. difficile*) is a gram-positive anaerobic and spore-forming bacterium that can cause *C. difficile* infections (CDI), a potentially life-threatening disease resulting in diarrhoea and significant inflammation of the colon.
Clostridioides difficile is the most common cause of healthcare-associated infectious diarrhoea in the developed world and is responsible for 4.3% of all healthcare-associated infections (HAI) in Switzerland[1].
The incidence and severity of CDI have risen recently, with a significant impact in terms of morbidity, mortality, and financial cost. The 30-day mortality ranges from 6 to 11%, and even higher in intensive care unit (ICU) patients. The most recent ECDC report for 2016–2017 indicated an incidence rate of 3.48 CDI episodes per 10,000 patient-days[2]. In Switzerland, the mean incidence rate reported was 3.8 CDI episodes per 10,000 patient-days for 2022[3].
Three parameters are key to the development of infection: acquisition of *C. difficile* (from the environment); gut dysbiosis; and host susceptibility to infection. Despite treatment with antibiotics, recurrence affects up to 30% of *C. difficile* infection patients (with increasing risk of recurrence after the previous recurrence episode).

4 Quality aspects

4.1 Drug substance

The drug substance of “Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale” is a preparation of human stool received through a donation from a healthy donor.
The specifications include donor screening according to the EDQM guide (Guide to the quality and safety of tissues and cells for human application).
No drug substance shelf life has been established since the drug substance is immediately introduced into the drug product manufacturing process.

4.2 Drug product

The finished drug product is a faecal suspension contained in a bottle for intestinal or rectal administration after reconditioning. One bottle is equivalent to 70 g of drug substance formulated with 0.9% saline and glycerol.
The composition of the drug product (faecal microbiota) varies from donor to donor and is thus classified as a non-standardised medicinal product.
The drug product is stored at ≤ -80 °C in a polycarbonate bottle. A shelf life of 24 months has been accepted.

4.3 Quality conclusions

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

[1] Swissnoso. Point Prevalence Survey 2017 of Healthcare-Associated Infections and Antimicrobial Use in Swiss Acute Care Hospitals 2018. Available online: https://www.swissnoso.ch/fileadmin/swissnoso/Dokumente/5_Forschung_und_Entwicklung/2_Punktpraevalenzstudie/Report_Point_Prevalence_Survey_2017_of_HAI_and_antimicrobial_use_in_Swiss_acute_care_hospitals.pdf (accessed on 21 March 2024).
[2] Dey A. ECDC - Annual epidemiological report for 2016-2017. *Clostridioides (Clostridium) difficile* infections. Annual epidemiological report for 2016–2017.
[3] Swiss Med Wkly. 2024;154:3571

5 Nonclinical aspects

No nonclinical studies were performed. This can be accepted as faecal microbiota transplantations (FMT) are based on highly complex, variable, individualised, and non-standardisable products derived from human donor faeces. The proof-of-concept of the treatment of *Clostridioides difficile* infection (CDI) by FMT has been established in multiple clinical studies. The risks of the FMT are minimised by adhering to defined requirements of donor screening and, during manufacturing, by adequate microbiological safety analysis.

6 Clinical aspects

6.1 Clinical pharmacology

n. a.

6.2 Dose finding and dose recommendation

n. a.

6.3 Efficacy

Multiple systematic reviews, meta-analyses, and a Cochrane review[4] have been published on the efficacy and safety of faecal microbiota transplantation (FMT) for the treatment of recurrent *C. difficile* infections (rCDI) with products similar to “Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale” (“FMT CHUV”).
The evidence for the efficacy of “FMT CHUV” as treatment for rCDI was based on a systematic review, meta-analyses, and a Cochrane review of 6 RCTs in published articles. The majority of the controlled studies included in these analyses suggest a benefit of FMT in recurrent *C. difficile* infection in terms of the proportion of participants with a resolution of rCDI. Nonetheless, the evidence is limited, as many controlled trials included in reviews that have compared FMT to antibiotic therapy have a short median follow-up of 11 weeks, as well as antibiotic treatment regimens that are non-compliant with current guidelines. Many studies had an open design. In addition, the clinical studies contribute highly heterogeneous data, as delivery treatments (procedural aspects of FMT preparation and delivery) and patient populations differed significantly.
Notwithstanding these limitations, the totality of the evidence based on the literature suggests that the FMT is superior with respect to the resolution of rCDI compared to alternative treatments, including antibiotics such as vancomycin, which are commonly prescribed for this infection.
Observational data on patients treated with the “FMT CHUV” product have been requested by Swissmedic and have been provided by the CHUV. Observational efficacy data from 86 patients treated with “FMT CHUV” (modified-release capsule and rectal suspension) are consistent, in terms of rCDI, with the suggested benefits observed in the literature.

6.4 Safety

Mild transient events, such as abdominal pain, bloating, nausea, vomiting, flatulence, constipation, fatigue, and diarrhoea were reported in clinical trials and in the observational data from the CHUV. Data on serious adverse events (the Cochrane review states that FMT likely leads to a small decrease in SAEs, although these events were few) and all-cause mortality (the Cochrane review states that FMT may result in a reduction in all-cause mortality, although the number of events was small, and the confidence intervals of the summary estimate from the studies were wide) showed that FMT may be safe in the short term for the treatment of rCDI. Data on the long-term safety of FMT remain limited and will be collected in a register (post-approval measures).
The major risk associated with the “FMT CHUV” procedure is insufficient donor screening covering only partially known and as yet unknown infectious agents, which inadvertently may be transferred to the recipient. To date, no transmission of pathogens, diseases that may be mediated by the microbiota, or deaths related to FMT have been reported by the CHUV in the follow-up of patients treated with “FMT CHUV”.

6.5 Final clinical benefit-risk assessment

For rCDI, conclusive evidence on the safety and effectiveness is limited by the relative lack of controlled studies with a sufficient level of evidence. The generalisability of the results to the “FMT CHUV” product has not been directly demonstrated. Meta-analyses and a Cochrane review suggest a benefit of FMT compared to standard of care (SoC) in immunocompetent adults with rCDI, and this is also supported by observational data from the CHUV. The available data did not allow us to draw any

[4] Minkoff NZ, Aslam S, Medina M, Tanner-Smith EE, Zackular JP, Acra S, Nicholson MR, Imdad A. Fecal microbiota transplantation for the treatment of recurrent *Clostridioides difficile (Clostridium difficile)*. Cochrane Database of Systematic Reviews 2023, Issue 4.

conclusion on the benefits or potential harms of FMT for rCDI in the immunocompromised population. As requested by Swissmedic, these aspects have been appropriately reflected in the Information for healthcare professionals.
The major risk associated with the “FMT CHUV” procedure is insufficient donor screening covering only partially known and as yet unknown infectious agents, which inadvertently may be transferred to the recipient. The Information for healthcare professionals and the risk management plan adequately mitigates this risk.
Currently, the benefit-risk profile for the second recurrence of CDI is considered positive. The authorisation was granted on the basis of the high medical need, the manageable toxicity profile, and the benefit compared to SoC. The major conditions to be fulfilled by the CHUV in the post-marketing phase include additional data from a registry study of patients treated with “FMT CHUV” and annual updates on any new information concerning the safety and efficacy of “FMT CHUV”.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for “Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale” was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale

Composition

Active substances

Faecal microbiota

Excipients

(For 250 mL): Sodium chloride (1.5g), Glycerol E422 (24g), Aqua purificata
250 mL of rectal suspension contains 600 mg of sodium.

Pharmaceutical form and active substance quantity per unit

Rectal suspension
250 mL bottle, equivalent to 70g of faeces.

Indications/Uses

Multiple recurrent infection with *Clostridioides difficile* (formerly known as *Clostridium difficile*) in adult patients (≥ 18 years) after prior specific antibiotic treatment according to current recommendations.

Dosage/Administration

Dosage depends on the route of administration and on the clinical form.
The prescription and supervision of the administration of Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale is restricted exclusively to specialised professionals in the hospital setting. Each administration is entered in the CHUV register and the patient is monitored for 5 years (see below).

Usual doses
50 to 250 mL injection of Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale depending on the route and the procedure of administration.

Most of the time, a single dose is sufficient. In case of a new episode within 8 weeks or a procedure failure, a second treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale may be required.

Specific patient populations

Paediatric population

There is no sufficient clinical data on the use of Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale in children and adolescents. Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale is not authorised for the use in the paediatric population.

Immunodeficient patients

There are insufficient data in the available literature to determine whether safety or efficacy in immunodeficient population are different from those in the general population.

Method of administration

Depending on the patient's clinical situation, the treatment can be administered on an inpatient or an outpatient setting.

For the traceability, a stool and a blood sample of the receiving patient are taken before the first treatment (stored in biobanks at -80°C).

By colonoscopy

Before the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale: A short hospitalisation is sometimes required (1 to 3 days). Anti-*C.difficile* specific antibiotic therapy (fidaxomicin or vancomycin) is interrupted 24 to 48 hours before the faecal microbiota transfer (FMT).

During the 2 days before the colonoscopy, the patients must be on a fibre-free diet.

The day before, a bowel preparation solution is prescribed, using a procedure adapted to the patient's clinical situation, ideally in divided doses (the day before and the day of treatment).

The day of treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale, the patient can take his/her usual necessary medication with a small amount of water.

The patient must be fasting for 4 hours before the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale: The efficacy of the bowel preparation solution's must be assessed (Boston Bowel Preparation Scale). The colonoscopy is made with a premedication (sedation).

A volume between 50-250mL is directly injected in the colon during the endoscopy.

The duration of faecal microbiota transfer via colonoscopy is typically 30 to 40 minutes. The patient then remains under post-colonoscopy monitoring according to current recommendations.

By enema for rectal administration

Before the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale: a verification of the patient's ability to control his/her anal sphincter is essential before proceeding the FMT by this route of administration.

A bowel preparation solution is prescribed with a procedure which is adapted to the patient's clinical situation.

The day of treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale: the enema is performed at least 2 hours apart from a meal.

For the treatment the patient lies on his/her left side. The doctor inserts a lubricated tube into the rectum and makes the tube go up about 10 cm in the intestine. Then, a volume of 50 to 150mL of "Faecal Microbiota Transfer for allogenic use, CHUV, rectal suspension" is administered during 5 to 15 minutes. The patient must be able to control his/her anal sphincter to keep the enema. The patient must remain on his/her left side as long as possible, at least 30 minutes, while retaining the enema. After evacuation, a small toilet is performed.

The patient remains under supervision, in a laying position for at least one hour after treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale.

By nasojejunal tube or nasoduodenal tube

Before the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale: A bowel preparation solution, adapted to the patient's clinical situation, is made the day before the faecal microbiota transfer.

The day of treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale, the patient can take his/her usual necessary medication with a small amount of water. The patient must be fasting for 6 hours before the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale:

The positioning of the tube must be checked before the administration of the Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale. The patient remains in a sitting position for the duration of treatment. The doctor introduces the preparation in the nasojejunal or nasoduodenal tube with the help of 50mL syringes. If the patient already has a jejunostomy, this route of administration will be preferred. The contents of each syringe are injected for one to two minutes depending on the patient's tolerance. The standard dose for this route of administration is between 50 and 250 ml (1-5 syringes of 50 mL).

The patient must remain in a sitting or standing position for about 3 to 4 hours after the faecal microbiota transfer. The patient is allowed to eat one hour after the treatment.

Patients monitoring

After the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale by colonoscopy, enema, nasojejunal tube or nasoduodenal tube: There is no particular diet to follow. Treatment with vancomycin or fidaxomicin must not be resumed.
To assess efficacy, the patient's intestinal transit must be monitored with the help of a bowel movement record to complete daily for at least eight weeks. This calendar is analysed during follow-up consultations. Two appointments are planned: 15 days and 2 months after the treatment. Also, phone consultations or in-person consultations are planned at 6 months and once yearly for 5 years in the scope of a systematic follow-up and data collection in the CHUV FMT registry.
The patient monitoring is the same regardless of associated comorbidities.

Recommendations in case of acute diarrhoea within 8 weeks following faecal microbiota transfer
If, after the faecal microbiota transfer, the patient has more than 3 liquid/watery stools (Bristol Stool Scale: 6-7) per day for more than 48 hours, it is necessary to search for *C. difficile*.
If the diagnosis of a *C. difficile* infection is retained in accordance with current recommendations, an antibiotic treatment active against *C.difficile* (fidaxomicin or vancomycin) is prescribed. A new faecal microbiota transfer must be considered.

Recommendations in case of antibiotic use
If the patient must take antibiotics after the faecal microbiota transfer, the intestinal transit must be monitored (see recommendations in case of diarrhoea).

Contraindications

Severe allergic reactions to one of the components and/or excipients.
Patients treated with systemic antibiotics (except the antibiotics that are indicated for *C. difficile* infections).
Acute intestinal perforation.
Severe immunodepression, agranulocytosis or severe neutropenia.
Contraindications for administration procedures by endoscopy or enema must be observed.

Warnings and precautions

Mild/moderate immunodeficient patients
Data in mild/moderate immunodeficient patients are limited. Therefore, it is not possible to determine the benefit/risk in this population. The risk of developing complications after the potential transfer of pathogens is likely to be increased in immunodeficient patients. As a precautionary measure, additional screening tests are performed on donors, including stool and blood tests, for mild/moderate immunocompromised patients.

Inflammatory Bowel disease (IBD)

If the patient is known for an *Inflammatory Bowel disease (IBD),* it is most often necessary to strengthen the IBD management before and after the FMT because a risk of post-transfer flare-up was described. The accountability of the FMT on these flare-ups has not been proven. It remains infrequent (less than 5%).

Treatment with systemic antibiotic

In case of a systemic antibiotic treatment, the Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale must be delayed because the antibiotic use can cancel the faecal microbiota transfer's effect. If an antibiotic therapy is scheduled (e.g. antibiotic prophylaxis for surgery or dental treatment), it is advisable to postpone the FMT until after the surgery or, if not, to perform it with an interval of at least one month between the FMT and the scheduled antibiotic therapy.

In case of an antibiotic prophylaxis with sulfamethoxazole-trimethoprim (Bactrim) in immunodeficient patients to prevent opportunistic infections with *Pneumocystis jirovecii*, alternative therapies may be considered. Depending on the risk-benefit ratio and the absence of alternatives, sulfamethoxazole-trimethoprim is ideally resumed between 72 hours and one week after FMT.

Transmissible infectious agents

Despite strict selection criteria for the donors, a potential risk of transmission of a disease or an infection cannot be totally excluded. To date, these events are exceptional. A rigorous selection of donors serves to minimize this risk.

Potential presence of food allergens

This product is made from human faeces and may contain food allergens. The risk of the faecal microbiota transfer to cause adverse reactions due to food allergens is unknown.

Excipients of particular interest

This medicine contains glycerol and may cause headaches, stomach-aches and diarrhoeas.

This medicine contains 600 mg of sodium per treatment (if all 250 mL are administrated), which is equivalent to 30% of the WHO-recommended maximum daily dietary intake of 2g of sodium per adult.

Interactions

Antibiotics that have an impact on the function and composition of the intestinal microbiota should be avoided (as far as possible) in the days following the treatment with Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale.

- If an antibiotic therapy is planned (e.g antibiotic prophylaxis for dental procedure/care), it is advisable to delay the faecal microbiota transfer until after the procedure. Or, if not possible, to perform it with an interval of at least one month between the FMT and the scheduled antibiotic therapy
- In the case of an antibiotic prophylaxis with sulfamethoxazole-trimethoprim (Bactrim) to prevent opportunistic infection from *Pneumocystis jirovecii* in immunodeficient patients, alternatives such as oral administration of atovaquone or monthly aerosol of pentacarinat (for a duration of 1 month) should be discussed. In the absence of alternatives, the treatment with sulfamethoxazole-trimethoprim is ideally resumed between 72h and one week after the FMT, considering the benefit-risk balance for the patient.

Pregnancy, lactation

There is no sufficient clinical data on Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale use in pregnant women. In the literature, only a few cases are reported and there are no specific clinical trials on FMT and pregnancy. Therefore, the Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale is not recommended during pregnancy and lactation, unless there are no therapeutic alternatives.

Effects on ability to drive and use machines

No corresponding studies have been performed.

Undesirable effects

The summary of the safety profile is based on a systematic review, made on 20 randomized trials and research (*C. difficile* infections and non-C. *difficile* infections) including 4241 patients who received one or more faecal microbiota transfer(s) (n = 5688). (Systematic review: The global incidence of faecal microbiota transplantation-related adverse reactions from 2000 to 2020. DOI: 10.1111/apt.16148)

Summary of the safety profile

The most frequent adverse reactions are gastrointestinal (diarrhoea, abdominal discomfort, constipation, flatulence, bloating, nausea) and are mainly of grade 1 and 2 (mild and moderate). They are reversible and more frequent timely after the faecal microbiota transfer, i.e., the day after the transfer or up to a week afterwards.

List of adverse reactions

"Very common" (≥1/10), "common" (≥1/100, <1/10), "uncommon" (≥1/1000, <1/100), "rare" (≥1/10,000, <1/1000), "very rare" (<1/10,000).

System organ classes	*Frequency*	*Adverse reaction from clinical trials*
Gastrointestinal disorders		
	Very common	Diarrhoeas
	Common	Abdominal discomfort, constipation, flatulence, bloating, nausea
	Very rare	Worsening or relapse of chronic inflammatory bowel disease
Infections and infestations		
	Rare	Transmission of pathogenic micro-organisms without signs of severity or of variable severity
	Very rare	Transmission of pathogenic micro-organisms leading to severe infection
General disorders and administration site abnormalities	Uncommon	Fever with a spontaneously favourable evolution

Description of specific adverse reactions and additional information

Severe adverse reactions, including severe infections and deaths, that are possibly, probably or certainly imputable to the faecal microbiota transfer are very rare. They are almost all linked to the method of administration by endoscopy of the upper airway or linked to poor clinical practices (such as insufficient screening for certain microorganisms in the donor).

Transmission of microorganisms and/or microbiota-mediated pathologies

- Transmission of microorganisms that are unknown to this day or that may later cause a disease. No unconventional pathogens were transmitted by a faecal microbiota transfer, including in severe immunodeficient patients in the long term.
- Transmission of SARS-CoV-2. This risk has not been proven yet. A rigorous and specific screening is done on every donor (questionnaires, stool analyses) to address this potential risk.
- Pathologies mediated by the donor's intestinal microbiota (e.g., obesity, diabetes, colon cancer, other cancers, autoimmune diseases, etc.): During donor selection, this risk is minimized by excluding donors with comorbidities and/or a family history of these pathologies.

Adverse reactions that are identified after the granting of the marketing authorisation

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

No cases of overdose have been reported.

Properties/Effects

ATC code

No ATC code was assigned.

Mechanism of action

Mechanisms of action of the faecal microbiota transfer are imperfectly known. Schematically, the symbiosis of the gut microbiota ensures with the host a “barrier effect” against *C.difficile by e*nsuring intestinal homeostasis, special and nutrient competition and is involved in bile acids metabolism (important role in the pathophysiological mechanism of this infection). The faecal microbiota transfer would make it possible to intervene on these different mechanisms, thus participating in the healing and prevention of new episodes of *C. difficile* infection.

Pharmacodynamics

There are no pharmacokinetic or pharmacodynamic studies for the Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale.

Clinical efficacy

The effectiveness of the “Faecal Microbiota Transfer, for allogenic use CHUV, rectal suspension” in the indication of multiple recurrent *Clostridioides difficile* infections is suggested by several meta-analysis and a Cochrane review. Observational efficacy data from 86 patients treated with “FMT CHUV” (modified release capsule and rectal suspension) are consistent with the benefits observed in the literature.

These observational data from patients treated at CHUV did not suggest a significant difference in terms of efficacy:

- In sub-populations (patients with inflammatory bowel disease) compared to the general population.
- Between the fresh preparation and the frozen one (at -80°C).

- Between oral and endoscopic administration.

Faecal microbiota transfers that are administered by enema (rectal route of administration) have lower effectiveness linked to procedure failure (immediate evacuation of the enema after the transfer because of a bad sphincter control). Selecting patients can significatively improve the effectiveness of this route of administration and avoid treatment failure and the need to repeat the treatment.

Pharmacokinetics

Absorption

Not applicable.

Distribution

Not applicable.

Metabolism

Not applicable.

Elimination

The excretion is made at 100% by the faecal route.

Linearity/non-linearity

Not applicable.

Kinetic in some groups of patients

Not applicable.

Liver function disorders

Not applicable.

Renal function disorders

Not applicable.

Elderly patients

Not applicable.

Children and teenagers

Not applicable.

Genetic polymorphisms

Not applicable.

Preclinical data

The Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale has not been assessed in terms of carcinogenicity, genotoxicity, mutagenic potential or impairment of male or female fertility in animals.

Other information

Shelf life

The medicine must not be taken beyond the date written after the mention “EXP” on the packaging.

Stability after thawing:

Maximum 6 hours in the fridge at 2-8°C after complete thawing.

Special precautions for storage

Store in the freezer (below -80°C).
Store in the fridge (2-8°C) for a maximum of 24 hours (including thawing).

Instructions for handling

Preparation of syringes

- Thawing steps: 2 procedures are possible
  1- Let the suspension defrost in the bottle for 15 minutes at ambient temperature on a sterile field, rinse the bottle with cold water and place the bottle in the bain-marie (temperature between 20°C et 35°C) until the complete thawed.
  2- Let the suspension slowly defrost in the refrigerator at 2-8°C (during the night)
- Filtration through a sterile gauze.
- Conditioning in sterile syringes of 50 mL and labelling.

The syringes that are prepared from Transfert de microbiote fécal pour utilisation allogénique CHUV, suspension rectale for an administration by colonoscopy, enema, nasojejunal tube or nasoduodenal tube, must be stored in a refrigerator at 2-8°C and administered to the patients within 6 hours of complete thawing.

Authorisation number

68581 (Swissmedic)

Packs

1 bottle of 250 ml [A]
Only for hospital use according to article 26, Al.4 OMéd (Ordinance on Medicinal Products, Swiss Law).

Marketing authorisation holder

CHUV, Lausanne University Hospital, Switzerland

Manufacturer

CHUV, Pharmacy department, Lausanne University Hospital, Switzerland

Date of revision of the text

December 2024