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DIFFBIOME

Service Overview

For healthcare professionals

Orally administered lyophilized human microbiota transplantation graft capsule for recurrent *Clostridioides difficile* infection

MicroBiome Bank

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This document is the official service overview of DiffBiome: it summarises the indications, the method of use, the manufacturing and quality control steps and the regulatory status. It is written for healthcare professionals and for distribution and procurement partners. It is not a patient information leaflet and not a summary of product characteristics: it does not replace the treating physician's individual judgement.

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Document details

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What is this document about? Chapter I states the name of the service, its variations and a short description. Chapter II covers the indications, the active substance and the mechanism of action, and Chapter III the method of use, packaging, storage, dosage and tapering. Chapter IV lists the advantages, and Chapter V the pricing, quantity discounts and product bundles. Chapter VI addresses donor screening, drug interactions, known side effects and precautions, and Chapter VII the manufacturing process and quality control. Chapter VIII covers special populations, and Chapter IX the regulatory classification, prescribing and dispensing conditions and the pharmacovigilance reporting obligation.

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I. Service Overview, General Information

I.1 Name of Service

DiffBiome

I.2 Full Name of Service

DiffBiome standardized intestinal microbiota graft for MTT

I.3 Service variations

DiffBiome 30(V)+, where the Arabic number (30) stands for the number of capsules within the container, while the Roman number (V) indicates the dosage level, derived from the dry matter content of the lyophilized material. The "+" sign indicates that the preparation contains a homogenized mixture of raw materials collected over several days from the same donor.

- **DiffBiome 30(V)+** — V (5×) density, 30 capsules. The only home preparation. Homogenised graft in capsule form, collected over several days from the same donor.

No other preparation may be administered in the home setting. DiffBiome exists only in the "+" version. The former DiffBiome 30(V) and DiffBiome 15(V) packs have been withdrawn and can no longer be ordered.

I.4 Description

DiffBiome is an orally administered lyophilized human microbiota transplantation (MTT) graft capsule developed to restore healthy gut microbiota in patients experiencing recurrent *Clostridioides difficile* (*C. difficile*) infections (rCDI). Each capsule contains a standardized intestinal microbiota graft, optimized for scalable treatment protocols to ensure consistent therapeutic outcomes. Initially designed as part of the TransferBiome protocol, DiffBiome is specifically formulated to enhance microbiota diversity and functionality. The procedure is carried out under stringent safety and efficacy standards, providing a dependable and effective solution for microbiota transfer therapy (MTT).

II. Scope of Use, Active Ingredients, Mechanism of Action

II.1 Indications

DiffBiome is specifically designed for the treatment of patients with *Clostridioides difficile* infections (CDI) at home. It is particularly recommended for individuals who have not responded adequately to antibiotic therapy or have experienced multiple recurrences of CDI. The service supports the restoration of gut health by introducing a highly diverse and well-balanced microbiota concentrate that helps suppress the overgrowth of pathogenic organisms.

II.2 Active Substance

DiffBiome contains a biologically active substance obtained from carefully screened human donors, specifically designed for use in microbiome transfer therapy. Its main component is a standardized suspension of human colon-derived microbiota in a lyophilized form, prepared in accordance with strict quality and safety guidelines.

II.3 Mechanism of action

The active component in DiffBiome is a diverse community of live gut microorganisms derived from healthy, screened donor stool. When ingested, these microorganisms colonize the patient's gastrointestinal tract, restoring microbial diversity and balance, which helps suppress the overgrowth of pathogenic bacteria like *C. difficile*.

III. Method of Use, Packaging, Storage, Dosage and Tapering

III.1 Method of use

- Oral Administration: DiffBiome capsules should primarily be taken orally without chewing or opening them, on an empty stomach, accompanied by plenty of fluids. Thirty minutes after taking the capsules, additional fluids should be consumed to ensure proper hydration and optimal colonization conditions. Following this, other medications can be taken, and the regular daily routine may resume.
- Timing: capsules should be taken first thing in the morning. Avoid simultaneous consumption with alcoholic beverages or hot liquids.

III.2 Packaging

Dark Glass Containers: DiffBiome capsules are supplied in dark glass bottles to ensure effective protection from light and maintain quality. This packaging is designed to preserve the viability of the microorganisms and ensure consistent therapeutic efficacy throughout the treatment period.

Each bottle contains 30 capsules; this is what we refer to as the packaging unit. How many bottles a course requires is decided by the SIS band: 1 box at level 2, 1–2 at level 3, 2 at level 4 and 3–5 at level 5 — calculated with a 10-day starting phase and a one-capsule reduction every 3–4 days; escalation and the LOT switch increase it.

Moisture and Contaminant Control:

- Tamper-Evident Seal: each container is equipped with a tamper-evident closure to safeguard capsule integrity and ensure they remain uncompromised.
- Child-Resistant Closure: in compliance with local regulations, a child-resistant cap may be included to enhance safety and prevent unauthorized access. The product you ordered is equipped with a child-resistant closure if it is required by the regulations in your country.

Labeling:

- The label clearly displays the product name, the number of capsules, the batch number, the expiration date and storage instructions for clear reference.
- It includes a designated area for healthcare providers or pharmacists to record the dispensing date if required.

III.3 Storage

Room Temperature (up to 25°C / 77°F): a transport and transitional tolerance, not a mode of storage. Store in the unopened, original packaging. The capsules remain stable for up to 6 months (180 days) when kept away from excessive heat and direct sunlight. The capsule is not damaged by brief periods at room temperature, but its place of storage is the refrigerator.

- Refrigerated (+4°C to +8°C / 39–46°F): when stored in a sealed, dark glass container, the capsules are stable for up to 24 months.
- Deep Freeze (below –20°C / –4°F): properly sealed and protected from light, the capsules can be stored for up to 20 years.

Handling Recommendations:

- Ensure the container is tightly closed when not in use.
- Store in an upright position to reduce the risk of capsule damage.
- Minimize frequent opening and closing, as this may alter humidity levels inside the container.

III.4 Dosage

The protocol fixes the dose in daily density units, from which the capsule count is derived. 1 density unit = 1 capsule of 1× density, that is, 1/1200 of the dry-matter content of the 150 g reference donation; daily

density units = daily capsule count × density factor (for DiffBiome 30(V)+, V = 5×). When changing preparation — in escalation and in dose reduction alike — the clinician calculates the density equivalent (density × capsule count) and raises or lowers within that.

Level	SIS	Starting dose	Band max.	Density units
1	0–24	—	—	—
2	25–39	**1**/day	2/day	**5 → 10**
3	40–49	**2**/day	3/day	**10 → 15**
4	50–59	**3**/day	4/day	**15 → 20**
5	60–69	**4**/day	6/day	**20 → 30**

At level 1 (SIS 0–24) no capsule is required. Administration of the starting dose is mandatory — the course begins with it, and it is this that goes into the patient recommendation. The band maximum is exclusively an escalation value, in the case of non-response within the band. In the home bands the band maximum and the starting dose of the next level coincide: the non-responding patient may be raised up to the starting dose of the next level; beyond that, reclassification is required, not a further dose increase.

The course of escalation in the home bands (levels 2–5):

Step	Trigger	Action
1	—	Start at the starting dose of the band.
2	Beyond 48 hours the daily stool count does not decrease	Raise to the band maximum.
3	There is no response even at the band maximum	Two equivalent options, both may be attempted: dose increase up to the starting dose of the next level, or LOT switch.
4	There is no response even after these	Re-administration of the SIS and reclassification — not a further dose increase.
5	Non-response persisting at 10 capsules/day (50 units)	Institutional referral.

- Minimum course length: 10 days at the starting (or escalated) dose in every band. Below this, dose reduction is not recommended, regardless of how quickly the patient improves.
- The absolute home ceiling: 10 capsules/day (50 density units). This is not a band dose but a hard upper limit; it arises only in exceptional situations, under medical supervision.
- Physician's Discretion: the exact dosage and duration should be determined by the treating physician, customized to the patient's clinical status, medical history, and tolerance.

III.5 Tapering

Reduction may only be initiated once **every** condition of the symptomatic gate is met:

Criterion	Requirement
Elapsed time	≥ 10 days at the starting dose
Bristol trend	Has moved persistently from the baseline 6–7 range towards 5–6, and then 4–5
Stool volume / count	The extreme daily stool count has substantially decreased compared with baseline
Blood in the stool	None

The trend of the Bristol scale and the stool count are to be read together: the improvement of the Bristol value in itself, without a decreasing stool count, is not sufficient.

- The course of dose reduction: −1 capsule every 3–4 days, as long as the gate holds.
- Relapse: if, according to the Bristol scale, the stool consistency returns to level 6–7, or the stool count rises, the dose must be returned to the band maximum, held there, and a LOT switch should be considered.
- Clinical Monitoring: patients should be closely observed during the tapering process for any signs of symptom recurrence or adverse reactions. If a relapse occurs, the dose must be returned to the band maximum, and the treatment protocol may be repeated. After completing the repeat treatment, it is strongly recommended to switch to a different LOT.
- Follow-Up: A post-treatment follow-up, typically conducted within 1–2 weeks after the final dose, is recommended to evaluate therapeutic outcomes and ensure patient recovery.

IV. Advantages

IV.1 Non-Invasive Delivery

Oral capsule administration provides a minimally invasive alternative to traditional MTT methods, such as colonoscopy or enema, reducing both patient discomfort and procedural risks.

IV.2 High Efficacy

Clinical evidence demonstrates that MTT capsules can significantly lower recurrence rates of *C. difficile* infections by effectively restoring microbial diversity and inhibiting the overgrowth of harmful pathogens.

IV.3 Ready-to-Use Therapy

DiffBiome is delivered as a fully prepared, rigorously tested product that can be directly administered by healthcare providers for home treatment. It eliminates the need for in-house stool processing, donor screening, or complex MTT preparation steps, ensuring standardized, high-quality therapy while saving time and resources.

IV.4 Convenience

Oral capsules are easy to store and administer, making them suitable for outpatient settings. This reduces logistical challenges for healthcare facilities and decreases dependence on specialized procedures. The capsule form significantly enhances patient adherence to therapy.

V. Pricing, Quantity Discounts, and Packaging Options

V.1 Pricing

The final cost of DiffBiome may vary depending on distributor agreements and local regulations. The treatment volume is given by the SIS classification: 1 box at level 2, 1–2 at level 3, 2 at level 4 and 3–5 at level 5 (30 capsules/box). Escalation and the LOT switch increase the requirement. Pricing is structured per one-day treatment unit, providing flexibility for healthcare providers to customize treatment plans.

V.2 Quantity Discounts

Discounted rates may be available for bulk purchases, offering cost savings for larger orders.

V.3 Product Bundles

DiffBiome can be ordered in bundles containing a minimum of 30 capsules, sufficient for a complete base treatment regime for one patient. Additional discounts based on packaging or volume may also be available, depending on the order size and distributor terms.

VI. Additional Information

VI.1 Donor Screening and Safety

Rigorous Screening: human microbiota of donors stool is comprehensively screened according to applicable guidelines (e.g., EMA, WGO, EAGEN, or local health authority standards).

Comprehensive Testing: stringent microbiological, serological, and parasitological tests are performed to ensure the absence of infectious pathogens.

Quality Assurance: the GMP-compliant manufacturing process includes multiple quality control checkpoints to ensure consistency and safety of DiffBiome.

VI.2 Drug Interactions

Antibiotics: concurrent antibiotic use may diminish the efficacy of DiffBiome. Administration of the antibiotic must be completed at least 48 hours before the start of the course. Antibiotic treatment started during the therapy warrants suspension of the course. Alongside antibiotics it may be administered only in a life-threatening situation, following prior consultation and at an increased dose.

Probiotics: probiotics are to be discontinued during the course, unless the treating physician orders otherwise.

VI.3 Known Side Effects

Common and Mild: gastrointestinal discomfort, bloating, flatulence, diarrhea, or constipation. These effects are usually temporary and resolve without medical intervention.

Rare but Serious: infections or allergic reactions may occur and require close monitoring. Any significant or unusual symptoms should prompt immediate medical evaluation and reporting.

VI.4 Warnings and Precautions

Immunocompromised Patients: patients with severe immunodeficiency or those on immunosuppressive therapy require close monitoring during MTT due to a higher risk of infection.

Pregnancy and Lactation: limited data is available; treatment should only be initiated after careful assessment by a healthcare provider.

Other Contraindications: patients with severe active gastrointestinal conditions (e.g., toxic megacolon, fulminant colitis) or suspected bloodstream infections should undergo thorough evaluation before initiating DiffBiome therapy.

VII. Manufacturing Process and Quality Control

VII.1 Donor Eligibility and Comprehensive Medical Evaluation

Thorough Pre-Donation Assessment: all potential donors undergo a comprehensive medical evaluation before donation, including a detailed medical history, physical examination, and standard diagnostic tests. These ensure that any diseases or conditions transmissible via microbiota transfer are excluded to the best of current medical knowledge.

Dietary and Nutritional Requirements: donors adhere to a prescribed diet recommended by medical experts, including antibiotic-free animal proteins to support a stable, healthy microbiota. Regular medical evaluations are conducted to maintain the highest quality of donated material.

VII.2 Serological Testing

Routine Screening: donors undergo at least two separate serological testing sessions 8 weeks apart to detect blood- and body-fluid-transmissible infections.

Tests Include:

- HIV 1–2 (Human Immunodeficiency Virus)
- Hepatitis A, B, C, E
- *Treponema pallidum* (syphilis)
- Inflammatory markers in blood serum and stool
- Eligibility: only donors with negative results across all repeated tests qualify for donation.

VII.3 Microbiological Testing of the Donated Stool (Donatum)

Pathogen Screening: donated stool ("donatum") is analyzed using multiplex PCR or conventional microbiological methods to detect enteric pathogens, including:

- *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*
- Enteropathogenic *E. coli* (EAEC, EPEC, ETEC, STEC, EIEC)
- *Clostridioides* species
- *Plesiomonas*, *Vibrio*
- *Cryptosporidium*, *Cyclospora*, *Entamoeba histolytica*, *Giardia lamblia*
- Adenovirus, Astrovirus, Norovirus, Rotavirus, Sapovirus, SARS-CoV-2
- *Helicobacter pylori*
- Multidrug-resistant organisms (MRSA, MRSE, VRE, ESBL, CRE)
- Results: only donor samples confirmed to be free of the specified pathogens will be utilized in the final formulation of DiffBiome capsules.

VII.4 Processing and Formulation

After pathogen clearance, donor stool is processed into a bacterial suspension, lyophilized, and encapsulated using specialized pharmaceutical techniques to ensure microorganism viability and stability.

VII.5 Excipients and Vitalization Additives

To ensure optimal bacterial viability and support manufacturing integrity, each capsule contains:

- Amylum solani (potato starch)
- Inulin (chicory-derived)
- Pyridoxal 5'-phosphate (vitamin B6)
- Cyanocobalamin (vitamin B12)
- Pteroil-monoglutamic acid (folic acid, vitamin B9)

These components have been selected to promote microbial stability, bacterial viability during storage, and ensure patient safety.

VII.6 Batch (LOT) Identification and Documentation

Each production batch is assigned a unique identifier tracking all related manufacturing data, including donor information, date of production, and raw material usage.

Mandatory tests (e.g., microbiological purity checks, viable bacterial counts and active substance content) are performed according to predefined specifications prior to release.

VII.7 Microbiological Testing and Contaminant Exclusion

Regular microbiological screening (e.g., conventional culture methods, multiplex PCR) ensures the absence of contaminants or unintended pathogens.

While the product is not manufactured under sterile conditions—given it contains live bacteria—a strict exclusion protocol is in place to rule out critical pathogens.

Testing protocols follow strict local and international guidelines (e.g., EMA, WGO, EAGEN) for microbiological quality in biological products.

VII.8 Excipients and Additional Components

All excipients (e.g., Amylum solani [potato starch], inulin) and vitamin additives (B6, B12, folic acid) undergo rigorous quality checks to confirm purity, identity, and the absence of undesirable contaminants (e.g., heavy metals, residual solvents).

Certificates of Analysis (CoA) from suppliers may be required, and spot checks or additional in-house testing can be performed to verify compliance with the relevant pharmacopeial or internal specifications.

VII.9 Ongoing Quality Oversight

Quality Assurance (QA) personnel routinely audit production processes, documentation, and QC test results to ensure compliance with GMP standards.

Any deviations or out-of-specification (OOS) results are thoroughly investigated, and corrective actions are implemented to maintain product integrity and regulatory compliance.

VIII. Special Populations

VIII.1 Elderly Patients

Due to the potential for multiple comorbidities and concurrent medication use, DiffBiome should be used with caution in elderly patients, accompanied by closer monitoring for any adverse effects or interactions.

VIII.2 Pediatric Use

Currently, there are no known conditions related to the use of DiffBiome capsules that would contraindicate the application of MTT in children under 18 years of age.

IX. Additional Considerations and Regulatory Status

IX.1 Regulatory Classification

DiffBiome is classified as a Medical Laboratory Services (869015). The finalisation of its classification by the EU regulatory authorities is in progress.

IX.2 Prescribing and Dispensing

DiffBiome should only be used under the supervision of a qualified healthcare professional. Its use may require compliance with specific protocols or special authorization, depending on regional and national regulations.

IX.3 Pharmacovigilance and Reporting

Any suspected adverse reactions must be reported to the relevant health authority (e.g., FDA, EMA, or local regulatory agencies) in line with applicable national regulations.

Note: This datasheet is provided for informational purposes and is intended for healthcare professionals and patients. Always seek advice from a healthcare professional before starting any new treatment.

Please note that MicroBiome Bank does not sell a product but facilitates the connection between donors and recipients by providing professional medical services. In accordance with applicable regulations, the capsules are provided as a service under code 869015 — Medical Laboratory Services, as defined by SCPA 2008. We handle donor recruitment, screening, fecal testing and the processing of the screened donation into capsule form through qualified laboratories. The contents of the capsules remain the property of the donor, subject to the cost of medical services, until fully paid by the recipient. The brand names of the individual services are intended solely to make them easier to remember and to simplify the ordering process.