Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

fecal microbiota (TBC)

(Ferring Canada Inc.)

Indication: Indicated to prevent recurrence of Clostridioides difficile infection (CDI) in adults following antibiotic treatment for recurrent CDI.

January 17, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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By filing with CDA-AMC, the submitting organization or individual agrees to the full disclosure of the information. CDA-AMC does not edit the content of the submissions received.

CDA-AMC does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting group and all conflicts of interest information from individuals who contributed to the

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: RBX2660
Indication: Clostridioides difficile infection, prevention
Name of Patient Group: Canadian Digestive Health Foundation
Author of Submission: Kelsey Cheyne, Executive Director

1. About Your Patient Group

We are the Canadian Digestive Health Foundation, Canada's trusted resource on digestive health. Committed to providing useful, up-to-date information and research to help Canadians better manage digestive conditions and live healthier lives. Our mission is to reduce suffering and improve quality of life by providing trusted, accessible, and accurate information about digestive health and disease. Patients can access information for free, anytime at CDHF.ca

2. Information Gathering

CDHF creates content on our website CDHF.ca and disseminates it through our newsletter of 10k subscribers, and our social channels. The information from patients below that we have gathered have been from patients who have emailed, and have commented on our social posts when it comes to c.diff content.

3. Disease Experience

Clostridioides difficile, more commonly known as C. diff for short, is a type of bacteria that causes irritation and swelling of the colon (colitis) leading to gastrointestinal issues such as nausea, vomiting, abdominal pain and diarrhea.

Controlling **C. diff infection** involves prioritizing symptom management, infection eradication, and preventing complications. Managing severe diarrhea and dehydration is critical to avoid life-threatening outcomes, while targeted antibiotics or advanced therapies like FMT are essential to eliminate the infection and reduce the high risk of recurrence. Preventing transmission is equally important, requiring strict hygiene practices and surface disinfection to protect others. Monitoring for complications is also important, alongside supporting nutrition and gut health through a gentle diet and probiotics to aid recovery. Addressing the mental and emotional toll on patients and caregivers is also key, with education, counseling, and support systems helping improve quality of life and reduce stigma.

Recurrent Clostridioides difficile infection (rCDI) presents a significant challenge for individuals, families, and the healthcare system. rCDI causes debilitating symptoms, including severe diarrhea, abdominal pain, and fatigue, which can significantly disrupt daily life. Recurrent episodes can lead to anxiety about future infections, reduced quality of life, and difficulty in returning to normal activities. The chronic nature and high recurrence rate mean prolonged periods of lifestyle adjustment and emotional toll.

CDHFs audience has commented on our social posts, and through email, and have indicated the following, which addresses the burden of this disease.

- I had C.diff. Never been so sick in my life

- I went through C-dff and came awfully close to death. It was not a good thing. I am well again and grateful to the team who helped me get better.
- I went through this. I went to see an infectious disease specialist for some time. Ended up on intravenous antibiotic drip for 6 weeks. It was the worst time of my ilfe. I got it from my roommate in hospital.

4. Experiences With Currently Available Treatments

Treatment for **C. difficile infection (CDI)** focuses on eradicating the infection, preventing recurrence, and managing symptoms. First-line antibiotics include **fidaxomicin** and **vancomycin**. For recurrent CDI, extended or pulsed regimens of these antibiotics and adjunctive therapies like **bezlotoxumab** (a monoclonal antibody) are used to reduce relapse. Severe or recurrent cases may benefit from **fecal microbiota transplantation (FMT)** to restore healthy gut flora.

We know that antibiotics can negatively affect the gut microbiota. The antibiotics that are currently out there for c.diff address the acute infection but do not restore the diverse composition of the gut microbiome, which can cause reoccurrence.

Probiotics can help maintain gut health and reduce the rate of c.diff recurrence.

More comments from our social channels from patients on treatment options:

- I had it during pregnancy. Was very complicated to treat. Took vancomycin and Florastor.
- I don’t understand why patients are not told about a fecal transplant. Simple, fast, and painless. That’s what cured me after months of Vancomycin- thousands of dollars worth and morphine for pain.

5. Improved Outcomes

Do not have this information

6. Experience With Drug Under Review

Do not have this information

7. Companion Diagnostic Test

Do not have this information.

8. Anything Else?

Appendix: Patient Group Conflict of Interest Declaration

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   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Ferring Pharmaceuticals	X $0			

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Kelsey Cheyne
Position: Executive Director
Patient Group: Canadian Digestive Health Foundation
Date:Nov 26th, 2024

FERRING
PHARMACEUTICALS

Placeholder for organization's logo

Canadian Digestive Health Foundation

224-1540 Cornwall Rd.
Oakville, ON L6J 7W5

Project Number: SR0850-000

We are the Canadian Digestive Health Foundation, Canada's trusted resource on digestive health. Committed to providing useful, up-to-date information and research to help Canadians better manage digestive conditions and live healthier lives. Our mission is to reduce suffering and improve quality of life by providing trusted, accessible, and accurate information about digestive health and disease. Patients can access information for free, anytime at CDHF.ca

As a privately-owned, biopharma company, Ferring Pharmaceuticals (Ferring) is grounded in a commitment to science and research, developing life-changing innovative therapies that help people live better lives. Ferring is focused on transforming the potential of microbiome restoration into novel live biotherapeutics. In November 2022, Ferring received US FDA approval for RBX2660, a novel first-in-class microbiota-based live biotherapeutic indicated for the prevention of recurrence of Clostridioides difficile (C. diff) infection (CDI) in adults following antibiotic treatment.

Ferring Canada submitted their drug treatment to Health Canada in March 2024. The next few months following potential Health Canada approval will be focused on Health Technology Assessment (HTA) submissions and provincial level negotiations. Visit Ferring's dedicated microsite that focuses on microbiome developments for additional information on progress to date and upcoming milestones: https://microbiome.ferring.com/

Recurrent Clostridioides difficile infection (rCDI) presents a significant challenge for individuals, families, and the healthcare system. rCDI causes debilitating symptoms, including severe diarrhea, abdominal pain, and fatigue, which can significantly disrupt daily life. Recurrent episodes can lead to anxiety about future infections, reduced quality of life, and difficulty in returning to normal activities.

Ferring's innovative treatment, designed to prevent rCDI recurrence following antibiotic treatment, addresses an unmet need in managing this challenging condition. By reducing the risk of relapse, this therapy:

- Helps patients regain control over their health and return to their daily routines.
- Provides peace of mind for caregivers, alleviating the emotional toll of recurrent infections.
- Reduces healthcare system burdens by preventing recurrent hospital visits and associated costs.

The Canadian Digestive Health Foundation is committed to supporting individuals with C.diff and raising awareness about advances that can improve patient care. CDHF will let our 50k+ audience know of this treatment option, through our newsletter and social channels.

Sincerely,

FERRING
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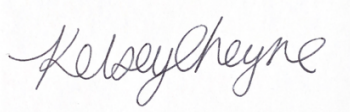
Placeholder for organization's logo



Kelsey Cheyne

Executive Director

Canadian Digestive Health Foundation

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: TBC
Indication: *Clostridioides difficile* infection, prevention
Name of Patient Group: Gastrointestinal Society
Author of Submission: Jaymee Maaghop

1. About Your Patient Group

The GI (Gastrointestinal) Society is committed to improving the lives of people with GI and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health, including obesity.

We are a national charity formed in 2008 on the groundwork of its partner organization, the Canadian Society of Intestinal Research (CSIR), which was founded in Vancouver in 1976. We receive national and international attention, simply because we have earned the respect of both the gastrointestinal medical community and Canadians who battle these issues daily. Our website, available in English and French, received 9,329,479 pageviews in 2023.

All our programs and services focus on providing Canadians with trusted, commercial-free, medically-sound information on a wide variety of topics related to obesity, gut, and liver diseases and disorders in both official languages. Our BadGut® lectures, quarterly *Inside Tract*® newsletter, pamphlets, support groups, and educational videos arm Canadians with the information they require to better understand and manage their specific needs. We also work closely with healthcare professionals and governments at all levels toward system-wide improvements in care and treatment.

2. Information Gathering

The information we used to complete this submission was obtained primarily through questionnaires and interviews:

1. 2024 international survey on *C. difficile* infection (CDI) or recurrent CDI completed by 166 respondents, including patients and caregivers from Canada (63%), the US (21%), and other countries; the results will be available on our website later in the year
2. 2022 focus group of individuals who have recurrent CDI so we could map the patient journey and animate it (pictured here), which is available on our website at www.badgut.org/patient-journeys, and we encourage your reviewers to watch this short video
3. 2020 stakeholder feedback to CADTH Environmental Scan ES0341 on access to fecal microbiota transplant https://badgut.org/fmt-cdi-2020/
4. 2017 survey on *Clostridioides difficile* infection (CDI) completed by 167 qualifying respondents living in Canada, 119 from patients and 48 caregiver responses; results were published in a peer-reviewed journal available at https://badgut.org/cdi-study-published/
5. We also had contact with individuals affected by CDI through recent phone/email/social media interactions and stories submitted over time.

3. Disease Experience

Clostridioides difficile infection, formerly known as *Clostridium difficile* infection (CDI), occurs when the *Clostridioides difficile* (*C. diff*) bacteria grow out of control in the digestive tract. The bacterium and its spores are often found in hospitals, long-term care facilities, or other healthcare settings in the feces of infected people, which can then spread to surfaces if a person with CDI does not wash their hands or if there are no stringent cleaning protocols in place. Strict cleaning protocols and adequate handwashing are paramount since *C. diff* is resistant to many cleaning methods.

The main symptom of CDI is diarrhea, and it can be debilitating as it typically involves at least six watery stools in 36 hours or at least three within 24 hours. Other symptoms may also appear, such as dehydration, fever, appetite loss, abdominal pain or tenderness, or fatigue, and CDI can often cause major distress and pain among patients.

Unfortunately, CDI can lead to death in very serious cases. A person might also not have any symptoms and still be able to spread the *C. diff* bacteria, and others can become infected if they touch these contaminated surfaces, then do not wash their hands thoroughly, and ingest the bacteria or spores. Certain populations are at a higher risk of contracting CDI. This includes individuals who are older than 65 years of age, are taking antibiotics, especially over a prolonged period, are receiving chemotherapy, or are taking immunocompromising medications or proton pump inhibitors.

Sadly, those who have had a previous episode of CDI have an increased risk of reinfection, called recurrent CDI (rCDI). While most individuals infected with *C. difficile* recover with treatment, around 25% experience a recurrence of symptoms within two months. These recurrences can happen repeatedly.

Complications from CDI can be severe, with some patients requiring partial or full removal of their colon (colectomy or ileostomy) due to the infection. Sepsis, a life-threatening response to infection, can also occur. CDI can have long-lasting effects on a patient's life. Many continue to suffer from lingering symptoms, such as pseudomembranous colitis or post-infectious irritable bowel syndrome, long after treatment.

The impact of CDI extends beyond just the infection and its symptoms, significantly affecting patients' mental health. Many report feelings of shame, embarrassment, and anxiety. For some, the emotional toll is so profound that it leads to post-traumatic stress disorder (PTSD), with patients describing a heightened sense of vulnerability and fear following their experience with the illness. Many feel shame and embarrassment as CDI is a highly-stigmatized condition. The psychological burden of CDI can be as debilitating as the physical symptoms, leaving patients grappling with lasting emotional scars long after their recovery.

Some individuals also need support to get through daily activities, which puts their caregivers at risk of contracting the infection as well. This condition puts a person's life on hold, impacting their ability to work or socialize, due to the devastating effects of CDI and because individuals must isolate to prevent the spread of disease.

The following quotes are what individuals shared with us on what it feels like to suffer with CDI and recurrent CDI:

- "Between my 2 bouts with *C. diff* I was out of work 7 months with bout 1 and 13 months with bout 2. I can no longer work as a result of post infectious bowel that never went away."
- "Once you've had *C. diff*, it's always in the back of your mind… with *C. diff*, **you just stink and you can't be around people**. It's like having COVID all the time and you just have to be separated from everybody all the time because you don't want to infect people. And **you just keep cleaning everything**."
- "I have to be careful **not to get an infection** – even a sinus infection or anything else. Because he (the doctor) doesn't want to put me on antibiotics because that could trigger it to come back. It's always there."
- "I was very conscious of the fact that **this is something that kills people**, people in the hospital. It is **infectious** and that's why hospitals are so scared of it and trying to put a stop to it. I don't think it's something to be taken lightly."
- "If I was travelling any more than 15 minutes away from the house, I would pack a little carry bag with underwear and pants…For the first five months, I basically didn't go anywhere unless it was to do the doctor... **I didn't feel comfortable leaving the house**. So yes, it **totally disrupted my life**. And even a year after I had it, if I had any disruption in my bowel movement, I would think, 'Oh no, do I have it?' It was always on my mind and two years after, I still get concerned about it. It changes your psychology. Instead of physical, it became a **psychological battle** to say, yes, I am better. I don't have to worry about it."
- "I wish that there would be more knowledge given to people when they are first diagnosed with *C. difficile*, that it is infectious and that it's a sort of a **life sentence** when you have it."

These are only a few glimpses into the experiences patients have shared about the debilitating effects of CDI and its risks of recurrence. The mental and emotional toll, marked by ongoing fear and anxiety of recurrence, reveals a significant and overlooked gap in care.

4. Experiences With Currently Available Treatments

If antibiotic use played a role in contracting CDI, the main treatment is discontinuing that medication and then receiving specific antibiotics to resolve symptoms and eradicate the infection. Vancomycin or metronidazole are typically what physicians have used to treat CDI, with a regimen of taking the antibiotic for 10-14 days, or if there is a recurrence, possibly for longer as part of a pulse/taper schedule. However, the extensive use of vancomycin has also led to some *C. difficile* strains becoming resistant, especially if a patient

has been repeatedly re-infected. Metronidazole circulates through the entire body when taken and has limited effectiveness against more severe disease, and its side effects may preclude long-term use.

Fecal microbiota transfer (FMT) is a treatment option that involves taking material from a healthy person's intestinal microbiota (via stool) and transferring it to the individual with an infection, via enema or capsule, with the goal of improving the recipient's gut microbiome. However, FMT is relatively new and limited in availability across Canada, leading to barriers in access for patients who need alternative options to treat CDI. Unfortunately, this has led to some individuals attempting to conduct their own fecal transplants, (e.g., Designer $hit) which can lead to worse outcomes. However, this simply speaks to the significant lack of effective and accessible treatments for CDI. Patients are desperate for effective treatment options!

Individuals might need to take other medications, depending on their risk factors and symptoms, and in some extreme cases, they might also require surgery for intestinal perforation. Probiotics and/or prebiotics can be helpful in improving the balance of the microbiome, but these can incur high out-of-pocket costs for patients and research is still uncovering their efficacy in CDI management.

In our 2024 survey, the majority of respondents had their CDI treated with antibiotics, with some also incorporating probiotics into their care. Fecal transplants, a newer and less commonly used treatment, were reported by only a small percentage of individuals during their first or only episode of CDI. However, the use of fecal transplants was more prevalent during recurrent infections.

5. Improved Outcomes

Patients urgently need access to more effective treatment options, especially those that can prevent recurrence. In our 2024 survey, four respondents completed the survey on behalf of loved ones who unfortunately passed away from CDI. Additionally, individuals with recurrent CDI reported experiencing significantly higher levels of pain. On average, those with a single episode rated their worst pain at 5.8/10, while those with recurrent CDI rated it at 6.9/10. The impact of pain from CDI and the illness itself, particularly in cases of recurrence, can be profound and far-reaching. It can severely affect their ability to perform routine tasks, maintain social connections and family life, and engage in activities they once enjoyed. Pain can also lead to physical exhaustion, emotional distress, and a diminished quality of life.

Individuals who contracted the infection have increased anxieties and fears that they will not have any way to combat this condition if it comes back again. Lack of availability and access to effective medication results in preventable patient suffering (e.g., continual, debilitating disease symptoms; secondary illnesses such as depression and anxiety disorders; and isolation). It also leads to unnecessary usage of healthcare resources (e.g., hospital stays, surgeries, other medications) and a ripple effect of financial burden on the government and taxpayers (e.g., inability to work), as well as an overall negative affect on society

6. Experience With Drug Under Review

One patient in our survey shared her experience with fecal microbiota transplant (FMT), which is available in the US under the brand name Rebyota®. After suffering through four recurrences, the 63-year-old patient reported immediate relief following the procedure. The procedure was quick, offering a remarkable improvement and lasting results despite having multiple recurrences. She shared that, "… recurrence is torturous and very scary. It's been a year since my Rebyota but if I get cdiff again I'm going to ask my GI to skip all the antibiotic regimens, Zinplava and go straight to Rebyota."

In our 2024 survey, 100 respondents experienced a recurrence. Of those who had recurrent CDI, 25% had 1 recurrence, 19% had 2 recurrences, 19% had 3 recurrences, and 20% had 4 or more recurrences. This is a significant number of patients grappling with recurrent infections. Recurrence is a constant fear that brings about anxiety for patients, and it can linger long after they have recovered from the infection. This ongoing concern underscores the urgent need for effective preventive options to help reduce the likelihood of recurrence and provide patients with a sense of stability and relief.

7. Companion Diagnostic Test

Physicians use stool tests to provide a definite diagnosis of *C. difficile* as they can detect toxins produced by the infection. However, patients have expressed concerns regarding lack of awareness with testing among healthcare professionals, including the need to test more than one strain for *C. difficile*. Many patients emphasized the importance of quicker identification, particularly in cases of recurrence, knowing when to test, and recognizing symptoms to ensure rapid diagnosis, early treatment, and preventing transmission.

Doctors and dentists need to be more vigilant about the risk of CDI when prescribing antibiotics. One caregiver shared in our 2024 survey that her mother's recurrent CDI was not diagnosed until much later, despite their advocacy for testing. Sadly, she passed away two months later.

8. Anything Else?

No.

Appendix: Patient Group Conflict of Interest Declaration

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Ferring Canada Inc.				x

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Name: Jaymee Maaghop
Position: Health Policy & Outreach Manager
Patient Group: Gastrointestinal Society
Date: **2025-01-17**

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: fecal microbiota live-JSLM (Rebyota)
Indication: Recurrent C. difficile Infection
Name of Patient Group: Peggy Lillis Foundation
Author of Submission: Christian John Lillis

1. About Your Patient Group

Peggy Lillis Foundation for C. diff Education & Advocacy (PLF) is the leading C. difficile patient education and advocacy nonprofit. Founded in response to the April 2010 death of 56-year-old kindergarten teacher Peggy Lillis, PLF is pursuing a vision where C. difficile is rare, treatable, and survivable. Our mission is to build a C. diff movement by educating the public, empowering advocates and shaping policy. Learn more at cdiff.org.

2. Information Gathering

As a US-based, patient-centered organization, PLF has collected over 180 (170 from the US; 10 international; 144 women and 36 men) C. diff stories since 2010. Our team has looked through these stories and identified themes related to diagnosis, treatment, socio-economic impact, and the impact of recurrent C. diff on quality of life. We also host a Facebook support group that has over 5,000 members, who regularly share the challenges of dealing with rCDI. We have also hosted numerous scientific and policy gatherings where data and studies on C. diff have been presented. Through these gatherings, personal stories, and external research, we understand recurrent C. diff to be a torturous disease that impacts the patient's physical health and socio-emotional well-being and even has financial impacts. A 2020 study in the *Journal of Patient Reported Outcomes* collected information from one hundred fifteen participants (33%) who reported current CDI and 235 (67%) reported Past CDI"[1] More recently, Infectious Disease Therapy published the first systemic review of patient experience of CDI and rCDI[2].

3. Disease Experience

Recurrent C. diff infections (rCDI) are highly burdensome for patients and caregivers. During just one occurrence of C. diff, patients are likely to experience extreme discomfort or pain, prolific diarrhea, and other common symptoms of infections. With each further recurrence, patients' pain and discomfort worsens their ability to leave their homes and care for themselves decreases, and the likelihood of experiencing another recurrence increases.

Outside of the physical manifestations of the illness, rCDI takes a severe toll on mental health and isolates patients from their social support systems. Individuals suffering from rCDI feel afraid to go out in public for fear of soiling themselves and/or infecting other people. Patients and caregivers alike also struggle with infection prevention in the form of household cleaning and segregated bathroom use, which can range from difficult to impossible depending on living arrangements.

Recurrent C. diff infections' burden of frequent and uncontrollable bowel movements, socioemotional consequences, and fears around infection spread and recurrence are easily the aspects most in need of control or amelioration.

[1] Lurienne, L., Bandinelli, PA., Galvain, T. et al. Perception of quality of life in people experiencing or having experienced a Clostridioides difficile infection: a US population survey. J Patient Rep Outcomes 4, 14 (2020). https://doi.org/10.1186/s41687-020-0179-1

[2] Armstrong EP, Malone DC, Franic DM, Pham SV, Gratie D, Amin A. Patient Experiences with Clostridioides difficile Infection and Its Treatment: A Systematic Literature Review. Infect Dis Ther. 2023 Jul;12(7):1775-1795. doi: 10.1007/s40121-023-00833-x. Epub 2023 Jul 3. PMID: 37395984; PMCID: PMC10390453.

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4. Experiences With Currently Available Treatments

For rCDI, there are a handful of treatments currently able to cure the infection or prevent a recurrence. These therapeutics include antimicrobials (vancomycin, fidaxomicin, or metronidazole); microbiome restoration therapies approved for use in the United States (fecal microbiota live-JSLM, fecal microbiota spores live-BRPK, and traditional fecal microbiota transplant); as well as adjunctive therapies like bezlotoxumab (in the U.S.) and intravenous immunoglobulin that support patients' immune responses and are associated with improved outcomes.

Antimicrobials are the easiest of the therapies mentioned above to access, although prescribers can be slow to adapt to changes in clinical practice guidelines; for example, many patients are still prescribed metronidazole for CDI and rCDI, years after ID and GI guidelines were updated to advise a shift away from the drug's use. And while these therapies are often the least expensive options, a course of the newest targeted antibiotic, fidaxomicin, can still bear a heavy cost burden for the patient.

Microbiome therapeutics, where they have been approved for use, can be challenging to access. Prescribers may be unwilling to risk their patients' health on novel therapies or uncomfortable with the procedure to administer them. Time and financial costs for the patient are issues here as well. Dysphagia may prohibit patients from receiving oral options, while the inability of a patient to tolerate an enema or colonoscopy can preclude other methods. The specific requirements for initiating microbiome therapies (usually within a certain number of days after concluding antibiotic treatment) can also present a barrier to access.

Some drugs are known to carry side effects. Still, the greatest risk remains the possibility that using antibiotics to treat C. diff (especially if prescribed a broader-spectrum drug) can actually worsen the patient's condition by further destabilizing the gut's microbial ecology.

5. Improved Outcomes

Patients and caregivers struggle with feeling truly well or healthy after a recurrence is treated. Because of the disruptions to the intestinal microbial balance caused by rCDI and some of the treatments for rCDI, patients often continue to feel unwell or experience persistent diarrhea, discomfort or pain, and an inability to tolerate food–even after the infection is considered to be cured. As such, outcomes that are most desired by patients are those tied to the stabilization of the microbiome. If a treatment is able to improve the microbial balance and help in cessation of diarrhea and GI upset, patients and caregivers receive an immense boost to quality of life–they feel comfortable leaving the house, the feel less fear of recurring again, and are able to nourish and hydrate themselves in ways they could not during active infection.

There are limited trade-offs patients and caregivers consider around choosing rCDI therapies, mostly due to the sparse treatment options. Most patients are concerned with the cost of rCDI treatment and the uncertainty around the therapies' ability to truly eradicate the infection and alleviate symptoms. Microbiome therapeutics are often a more attractive, if more expensive, option for consumers due to the appeal of reestablishing a healthy balance of gut microbes. These therapies also tend to lend patients and caregivers more security around preventing further recurrence.

6. Experience With Drug Under Review

PLF has been working with Ferring and its predecessor company throughout the development of fecal microbiota live-JSLM. Several of our patients who had traditional FMT or were otherwise treated testified at the US Food & Drug Administration Advisory Committee about the significant unmet need for rCDI treatments. In the US, traditional FMT is considered an experimental therapy and a treatment of last resort, severely limiting access. We have an estimated 180,000 rCDI cases annually, only ~10,000 of which were treated by FMT. Those who did receive it had to endure months or years of failed antibiotic treatments before being eligible. Since Rebyota's approval in the US, rCDI patients' access to fecal microbiota live-JSLM has greatly increased. Most patients can get it paid for by private insurance or Medicare Part B. For those without coverage, patient assistance programs have made the product available. Every patient who received Rebyota only did so after standard antibiotic therapy had failed to prevent recurrences.

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Based on patient responses through our stories, peer support and Facebook support group programs, the product is found to be easily accessible and to have minimal side effects. Many patients wish it was offered at the first recurrence. For example, Sherry H. from our Facebook support group says “I did Rebyota. It’s a life saver!” Most patients find Rebyota easier to take than vancomycin since it’s administered once by enema or colonoscopy. Tom P. said “Rebyota is an easier treatment, no bowel prep.” Many patients find vancomycin, particularly long doses, to be very difficult to tolerate. It also fails to address the microbiome dysbiosis, leaving them vulnerable to recurrences for months or years. Kimberly M. says, “Rebyota worked! It was super simple and noninvasive. There’s no prep before. I had it done in the office by a nurse and it took a total of about 30 minutes from start to finish. I had some slight cramping after wards but that was about it.”

In summary, fecal microbiota live-JSLM has had significant benefits to rCDI patients in terms of access, ease of administration, and with very few side effects. As a patient-centered organization, this product provides significant benefits with minimal adverse events.

7. Companion Diagnostic Test

Not applicable.

8. Anything Else?

No.

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2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it. **Not beyond reference to existing studies.**

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

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Ferring				X
Merck			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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Name: Christian John Lillis
Position: CEO
Patient Group: Peggy Lillis Foundation
Date: January 15, 2024

Clinician Group Input

No clinician group input was received for this review.