Transcript: Xifaxan Roundtable Event, April 28, 2025, Medicare Drug Price Negotiation Program Public Engagement Events

This transcript was lightly edited for readability.

Introductory Remarks

Moderator, RTI International

All right, hey, everyone. Thank you all for joining. I will be your moderator today. My name is **[MODERATOR]**, and I work for a company called RTI International. And I also want to introduce a colleague of mine who will be helping me today with today's session, **[SECONDARY MODERATOR]**. **[SECONDARY MODERATOR]** can wave for everyone to see she's here. You may hear from **[SECONDARY MODERATOR]** a couple of times today, as she has a few follow-up questions.

Today the Centers for Medicare & Medicaid Services, or CMS, is convening this patient-focused, roundtable event and others as part of the Medicare Drug Price Negotiation Program.

The purpose of today's event is to hear from you all, a group that includes patients, caregivers, and patient advocates about your experiences with the conditions and diseases treated by Xifaxan, with Xifaxan, and with other medications for the same indications.

If you wish to share input on other topics, more like policy-related topics, we do have an email address that you can send comments to. I'll show that email address at the very end of today's session. But today's session is more patient-focused and like patient experiences.

[REDACTED]

The information shared during the events will help CMS understand patients' experiences with the conditions and diseases treated by Xifaxan, patients' experiences with the drug, and patients' experiences with other drugs that are used to treat the same conditions as Xifaxan.

CMS will use this information in negotiating Medicare pricing with the manufacturers of selected drugs. Your experience and perspectives are very important to us, and we genuinely appreciate your time today. Let's watch a brief video from CMS leadership so that you can hear from them about how much they value your time and input.

CMS Remarks

00:01:49

Steph Carlton, Deputy Administrator and Chief of Staff, Centers for Medicare & Medicaid Services

Greetings, everyone. I'm Steph Carlton, the Deputy Administrator and Chief of Staff at the Centers for Medicare & Medicaid Services, or CMS. CMS administers Medicare, our country's federal insurance program, for more than 65 million older Americans and people with disabilities.

I deeply appreciate each one of you for taking the time to join us today. Lowering the cost of prescription drugs for Americans is a top priority of President Trump and his administration. As the second cycle of negotiations begins under the Trump administration, CMS is committed to engaging with stakeholders for ideas to improve the Negotiation Program.

In January 2025, CMS announced the 15 Medicare Part D drugs selected for the second cycle of price negotiations. Medicare's ability to negotiate directly with drug companies will improve access to some of the costliest drugs while fostering market competition and continuing innovation.

Our priority in negotiating with participating drug companies is to come to an agreement on a fair price for Medicare. Promoting transparency and engagement continues to be at the core of how we are implementing the Medicare Drug Price Negotiation Program. And that is why the process for negotiation engages you, the public.

This event is part of our effort to hear directly from a range of stakeholders and receive input that's relevant to the drugs selected for the second cycle of negotiations. Thank you again for joining us. Your input matters. And next, stay tuned to hear from the event moderator to give you more details on what to expect during this event.

Housekeeping

00:03:44

Moderator, RTI International

Before we begin, I want to go over what we call housekeeping items and ground rules so that everyone knows what to expect.

First, for participation, we hope that you can all contribute your perspectives throughout the session. However, if questions arise that you don't want to answer, that is totally okay. Please minimize background noises by silencing your phones and other devices, and be sure to mute yourself when you're not speaking.

This discussion today is not open to the press or the public, and I will use only your first names today during our discussion to protect your privacy. Please do not share any unnecessary personally identifying information or personal health information during the discussion.

We are going to audio and video record today, which we're doing now. But these recordings will not be shared publicly. Following the event, CMS will prepare transcripts that have participant names and identifying information removed, and these will be made available to the public.

I also want to highlight a few things to keep in mind. For video, thanks in advance for keeping your video on throughout our discussion. Today's session will last about an hour and a half. We did start 10 minutes earlier, so we may end a little early as well. I do have a monitor guide in front of me, and I may have to skip questions due to time. And if you need technical assistance, we do have this email address that's on the screen here, IRADAPStechsupport@telligen.com. If you need to take a break, feel free to take a break. If you need to step away, just turn off your camera and your microphone and come back as soon as you can. You don't need to ask for permission.

Try to speak one at a time. I may have to play traffic cop if more than one person needs to speak, and we will make sure you get a chance to speak. And finally, just looking for your honest opinions, because everyone will have different opinions. And that's okay. We want to hear from everyone.

Speaking of hearing from everyone, I actually skipped over one person. I am so sorry. We do have staff from CMS who are listening in. And, **[CMS STAFF]**, I am so sorry I didn't get a chance to introduce you. I'd like you to say hello. Say, hey, **[CMS STAFF]**.

00:05:54

CMS Staff

Thanks, **[MODERATOR]**. And hi, everyone. I wanted to go ahead and welcome you all on behalf of CMS and say, good afternoon. We are very much looking forward to learning from you all in this roundtable discussion today. And, just wanted to let you know we've got some staff here from the Medicare Drug Price Negotiations team, and we're going to be listening for the duration of the call, but are going to go off camera now, so that you all can focus on the discussion. So, thank you.

00:06:20

Moderator, RTI International

Great. Thank you so much. Okay, so I've talked a lot. I want to pause for a moment to see if you all had any questions for me before we get started. And then, if not, we'll start with the first question.

Okay. So, I'd like to do some introductions first. And I actually recognize a couple of familiar faces already, so it's good to see some of you again.

I want to begin our discussions by having you introduce yourselves. Take about 30 seconds. So quick introduction and tell me your first name. Tell me also the condition or conditions that Xifaxan treats that you have experience with either personally, or with a loved one, or as an advocate. And then, tell me whether you're going to be sharing your personal experiences, the experiences as a caregiver, or from the perspective of a patient advocate, and it could be more than one hat. And that's totally okay. So again, your first name, the condition or conditions you have experience with that Xifaxan treats, and then the perspective you'll be sharing from.

Let me start with **[Participant 1]**. Hey, **[Participant 1]**.

Discussion

00:07:23

Participant 1 (registered as a patient and representative of a patient advocacy organization)

Hi **[MODERATOR]**. Thanks again for having us here. We really appreciate the opportunity to share stories. Like I said, my name is **[Participant 1]**. I have predominantly IBS-C [irritable bowel syndrome with constipation], but I've had parts of my life where I have switched over to IBS-D [irritable bowel syndrome with diarrhea], and so I have lived through that as well. I have a daughter with IBS-D that started in high school and goes into her adulthood. She's now 27. And I'm also the **[REDACTED]** for the International Foundation for Gastrointestinal Disorders, or IFFGD, which services patients with IBS of all types, and is the sponsor of IBS Awareness Month on the National Health Observances calendar.

So, I'll be talking with all three hats today.

00:08:06

Moderator, RTI International

Okay, that sounds good. Thanks, **[Participant 1]**. **[Participant 2]**? Hey, **[Participant 2]**.

00:08:12

Participant 2 (registered as a representative of a patient advocacy organization)

Hi, **[MODERATOR]**. Hi, everyone. Thanks for having me today. My name is **[Participant 2]**. My disease state of experience is hepatic encephalopathy, due to liver damage, and that is a liver damage due to a combination of liver diseases. And they are unrelated, I will state, to any kind of alcohol use disorder or any kind of drug use. They are hereditary and also fatty liver-related, and I wear a patient hat and an advocacy hat. I currently serve as **[REDACTED]** for Global Liver Institute.

00:08:51

Moderator, RTI International

Thank you, **[Participant 2]**. **[Participant 3]**?

00:08:55

Participant 3 (registered as a representative of a patient advocacy organization and caregiver)

Hi, good afternoon, and thank you. As I add my thanks to **[Participant 1]**'s for hosting these sessions. It's so important to hear from patients and caregivers. Today I'm going to be primarily wearing the hat of an advocate. I serve as the **[REDACTED]** for the Partnership to Fight Chronic Disease. And then also, I also serve as the **[REDACTED]** for an organization called the Partnership to Fight Infectious Disease, and since this is an antibiotic, I thought it was important to represent that perspective as well.

00:09:22

Moderator, RTI International

Great thanks, **[Participant 3]**. **[Participant 4]**?

00:09:28

Participant 4 (registered as a patient)

Hi, my name is **[Participant 4]**. I am a patient living with hepatic encephalopathy from fatty liver mass-related cirrhosis, and I've been living with that since 2009. I'm also an advocate, and I run a support group with 3,500 members that are living with and/or caregivers to people with hepatic encephalopathy and have since 2010.

00:09:54

Moderator, RTI International

Thank you, **[Participant 4]**. **[Participant 5]**?

00:10:00

Participant 5 (registered as a patient)

Hi, thank you. My name is **[Participant 5]**. I'm a patient with hepatic encephalopathy due to liver disease, liver cirrhosis. It is also unrelated to alcohol or drugs or hepatitis C, or anything like that. Mine was a direct result from the damage of my liver and me needing to put in what is called a TIPS [transjugular intrahepatic portosystemic shunt] or a portosystemic shunt. And that in turn basically increases and gave me the hepatic encephalopathy. So, I'm a user of Xifaxan. Prior to this, I also have pharmacy background, so I can also speak to helping other patients navigate to get the prior authorizations and the cost of the medication itself.

00:10:48

Moderator, RTI International

Thank you, **[Participant 5]**. **[Participant 6]**, am I saying that correctly?

00:10:53

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

You are, and thank you very much for having me today. My name is **[Participant 6]**, and I am a liver cancer survivor, liver transplant recipient. I had a genetic disorder, combined with a few other things, and alcohol played a part in that whole thing. All cirrhosis, all liver disease ends in cirrhosis at the end of the day, and I just want to always make sure that we don't have stigma included. I was a user of Xifaxan. I work with patients twice a week that are users of Xifaxan. I used it quite a bit, and that was a part of me even getting to transplant, was being able to have that access to a drug that could help me understand who I was, because I didn't know that I didn't know. So, thank you for having me here today.

00:11:45

Moderator, RTI International

Thanks for coming, **[Participant 6]**. And finally, last but not least, **[Participant 7]**.

00:11:50

Participant 7 (registered as a patient)

Hi, I'm **[Participant 7]**. I am a patient with IBS-C. I was diagnosed back in 2006. I've had issues where, similarly to **[Participant 1]**, I crossed over, and it was IBS-D. I ended up with one of my flares developing something called SIBO [small intestinal bacterial overgrowth] and my doctor had decided to put me on Xifaxan when that had happened, because it was a hot mess, so I'll be wearing the hat of a patient. I do have an advocacy background for a rare neuro condition that I also have, so...

00:12:28

Moderator, RTI International

Thanks for joining, **[Participant 7]**.

00:12:30

Participant 7 (registered as a patient)

Thank you.

00:12:31

Moderator, RTI International

For our first part, we're going to use the chat window, and what I want you all to put in the chat window is a quick yes or no, which is, do you have personal experience, currently or in the past, taking Xifaxan? And you just put yes or no into the chat window. And again, do you have personal experience either now or in the past taking Xifaxan?

And I see five yeses looks like. Okay, great. That gives me a sense of where folks are coming from today. So, I want to, before we talk about Xifaxan and before we talk about the different treatments, I want to talk first about these two indications, which you all already brought up.

The first is irritable bowel syndrome with diarrhea, which I'm just going to say IBS-D, which you've all done today as well. Just so I don't trip over my words. So, IBS-D. And then we're also going to talk about hepatic encephalopathy, which you all talked about as well. And I want to talk about each indication separately for our discussion. So, apologies if you have to listen while others talk. I'll definitely come back to you.

Let's talk about IBS-D first. Not even thinking about treatments that are out there and not thinking about Xifaxan, in general, how does IBS-D affect you, your personal life or day-to-day life of people you know? So again, how does IBS-D affect your life or life of people you know? **[Participant 1]**?

00:14:00

Participant 1 (registered as a patient and representative of a patient advocacy organization)

So, honestly, IBS-D is just dreadful, mainly because you have acute bouts of diarrhea that can come on without warning. When I was at my worst, I had it infamous for always in the car on the very long stretch of road, it was highway 41, four miles from any bathroom that I take every day to go to work. And sometimes you just don't know when it's going to happen.

Speaking to many patients with IBS-D, that urgency of I have to go and I have to go now is horrendous. They have to leave early for work. Some people, up to an hour. They know where every public bathroom is on the route to work. They know all the public bathrooms in all the stores that they shop in, and won't go into a store unless they know where the bathroom is, and that it is accessible to people without a lock. So, it can be very devastating to just navigating your day-to-day life.

Also with it is severe pain and cramping that you get in your gut, which can leave people completely debilitated laying in their beds, curled up in balls for just days, when they're going through, what we call in my house, episodes of IBS. With my daughter, when she first was diagnosed with IBS-D, she was in high school. She was a competitive volleyball player on the national stage, and I remember phone calls with her because I couldn't go to every one of her national tournaments. And she one time was in **[REDACTED]**, she was curled up in a ball in the bathroom in the hotel room that she shared with three other girls on her team. She was having an episode of IBS. She had to play at 7 o'clock in the morning, and all she could say is, Mom, they all know they can hear me in here. They all know. She was crying, and as a mom, there was just nothing that I could do. I couldn't be there. All I could say is, I love you, baby. It's going to be okay. But it just can be very, very challenging for people to have a normal life.

00:16:10

Moderator, RTI International

Thanks, **[Participant 1]**. Others want to talk about, how does IBS-D affect daily life of yourself or people you know and love or people you advocate for?

I also want to talk about, for IBS-D, what to you all is most important that is managed or treated for IBS-D? Again, what aspects of IBS-D are most important to people to have managed or treated?

00:16:44

Participant 1 (registered as a patient and representative of a patient advocacy organization)

So again, for me, I go back to urgency, and that not knowing, just that surprise in the middle of the day. You have a meeting to attend. You got a call you have to go on. You don't know if you'll make it through. The cramping starts, and you're trying to focus on what you're trying to do.

And just being able to navigate your thought processes when you're going through an episode is very difficult. There's a lot of pain. And then, just really and truly, just the surprise attacks, I think, is probably the most, the thing that needs to be under control before you even get to the fact that you might be in the bathroom 10 times a day.

That's a whole other level of having to know where a bathroom is, because you may have to run there 10 different times in one day. Having to go back and forth to the bathroom is bad enough, but I think if I knew, I'm going to go to the bathroom at intervals, or right after I eat, or whatever the case may be, that's better than, I'm having a great day. And then, all of a sudden, I'm not. And having to cancel plans and things like that.

00:17:54

Moderator, RTI International

Okay.

00:17:55

Participant 7 (registered as a patient)

If I could piggyback off that a little bit. That pain, that unbearable fetal position pain, it literally will hit you out of left field, and it's almost as bad as me running to the bathroom. And sometimes you're in the bathroom, going to the bathroom, and still dealing with the cramps. So, it's just those two particular aspects, I think, are really difficult for anybody, even just to make it through that workday. I'm lucky that I work remotely. However, when my camera's off, I'm running somewhere else in the house, you know, but that is one of the biggest problems.

00:18:37

Participant 1 (registered as a patient and representative of a patient advocacy organization)

And to piggyback right off **[Participant 7]**, not only do you have the cramping, you're running to the bathroom. It's exhausting, like when you have a bowel movement, sometimes you end up off the toilet, on the bathroom floor, curled up in that fetal position. The pain might not be as strong. Maybe it's a dull ache, sometimes it's still strong, you never know, but sometimes it's just difficult. It's just like, I feel like my energy is just sapped out of me.

And it takes me a moment to regain. I feel like my heart's beating, and I just want to crawl up in the bed and take a long, fat nap. But then, of course, in a few minutes you're just running to the bathroom again.

00:19:19

Participant 7 (registered as a patient)

And then one other piece of that is with the diarrhea comes other things like dehydration, which actually at my worst, ended up with me in the ER [emergency room] for dehydration. So, it's just, it's a cycle.

00:19:35

Participant 1 (registered as a patient and representative of a patient advocacy organization)

It is.

00:19:36

Moderator, RTI International

Appreciate that. Any others want to share important aspects of IBS-D to be managed or treated?

Okay, **[Participant 3]**?

00:19:47

Participant 3 (registered as a representative of a patient advocacy organization and caregiver)

I just was going to mention that I think **[Participant 1]** and **[Participant 7]** have expressed so well the pain and the physical symptoms, but **[Participant 1]** also hit on a really important point on the psychological damage, the stigma, the embarrassment, not just the urgency, but you don't want to isolate yourself. But you almost, if you're sharing a room, you're traveling with the team. I mean, it affects young people as well, across the age spectrum. And so, it can create all kinds of problems in the workplace. Why are you away from your desk so much? Things like that, I think, are really important to keep in mind, too. And it restricts people's, what job can you take? Or are you open to taking? How flexible is your opportunity to work because of the episodes that you're dealing with, and all of those are factors that affect people, as well as the physical symptoms.

00:20:45

Participant 1 (registered as a patient and representative of a patient advocacy organization)

Absolutely. I know at IFFGD, they did a campaign about 'what's in your bag,' and people were just taking their pocketbooks and dumping them out, or their briefcases, and the change of clothes, the baby wipes that you always have to clean yourself up with if you have an accident. All of those things. It's really heartbreaking to know all the extra stuff that people have to sometimes carry with them every day. I know patients that have changes of clothes at the office. They have them in their car. They have them in the bathroom already, because they know that they're just going to get, sometimes have to go right into the shower to clean themselves up, so that they can get dressed for the day.

And just all of that extra planning just adds more stress to your life. I mean, life's hard enough to navigate, especially with as busy as we all are these days. So, those are all things that people have to think about when they're living with IBS-D.

00:21:50

Moderator, RTI International

All right. I also want to hear from the folks speaking for hepatic encephalopathy.

So first, thinking beyond Xifaxan and thinking about treatments, I wanted to hear from you all in your own words, how does hepatic encephalopathy affect your day-to-day life, or the day-to-day life of people you know and love and work with?

Yeah. **[Participant 5]**? Go ahead.

00:22:21

Participant 5 (registered as a patient)

So hepatic encephalopathy, it's really complex, and it affects you in so many ways in every day and aspects of your life.

When you're going through an episode of hepatic encephalopathy, you can have anything from tremors to memory loss to stuttering of speech, slurring of speech. You're confused. It robs you of your independence and your dignity in a sense. It's almost like having dementia and Alzheimer's without having that diagnosis. So, imagine you trying to live an independent life or trying to be a caregiver, a wife, or a mom, or just live life.

And you have this condition, and you don't know when it's going to hit. The wind could blow wrong, and you could get an episode. It could be too hot. You could be dehydrated, you could get sick. Anything could happen. And you get into these episodes, and if the episode is so bad, you have to go to the emergency room. You need to seek emergency help. Without it you can slip into a coma, and there is a risk of passing away from it when you go into the ER and they hear that you have liver disease or that sort of thing, and you're stuttering. You're slurring, you're trying to advocate for yourself. You're trying to get that emergency help. There is a stigma around it. A lot of people think, well, liver disease, you're an alcoholic. You did this to yourself. You must be drunk, because you're slurred. It delays that care. It puts you in this vulnerable position to be open in a room full of people, having to explain yourself, needing help and not being able to adequately help yourself, and regardless of how you got the condition, whether it's alcohol or not alcohol. When you need help and you need treatment, you need that help, and you need that treatment without anybody judging you. But it puts you in that position to be open to this. And it's something hard to explain to people that you'll be okay one day, and the next day you can't. How do you plan your life like that? How do you plan your life when you walk out that door, and sometimes you don't remember where you parked? You don't remember where you lived. You don't know your date of birth. Today is a very good day for me, but other than that, it's not something that I can plan or live my life around. And it does become very challenging, and it becomes challenging for people around you, because your personality changes and your family has a hard time understanding why you act a certain way when you don't have dementia or Alzheimer's. So, it encompasses everything, and it is very time consuming. And you get very exhausted trying to navigate it, to just be okay and not be in a hospital.

00:25:15

Moderator, RTI International

Thank you, **[Participant 5]**. I appreciate that. **[Participant 2]**, you were next. Go ahead.

00:25:20

Participant 2 (registered as a representative of a patient advocacy organization)

Sorry, **[Participant 6]**, if I'm jumping in front of you, but I think it's important just to point out, I normally would never start an introduction with the fact that I am not an alcoholic or a drug addict. But it's important to point out for liver disease, because it is a very stigmatized space. Even, I think all of us in the room can think of a scenario, even in our past, or maybe in our present, where we have thought about liver disease and understand that there is an automatic stigma related to cirrhosis, and when you hear the word cirrhosis it can be a trigger to jump to the conclusion that someone may have alcohol-related liver disease or something similar.

So that's why I stated it. It's not something I normally do or am a champion of. But I stated it specifically for this group that it is a very highly stigmatized condition for all liver patients, even rare liver disease patients. Just some background, hepatic encephalopathy itself, this is a very quick summary, but because of your limited liver function or impaired liver function, it causes a buildup of ammonia in your system.

And so, when the ammonia happens or the ammonia overload happens, it creates symptoms that are similar to intoxication, dementia, confusion. It creates caregiver resentment because some families and caregivers, like **[Participant 5]** was mentioning, can't understand what's happening, and they think you'll get over it, or there's no explanation that your doctor or maybe you can provide. Or maybe our primary care physicians aren't as educated on how to navigate hepatic encephalopathy and assume, maybe, that it's drinking, or that it's related to dementia or something.

So, getting to treatment is difficult. And the first line of treatment is usually a generic drug called, or generic formulary, called lactulose, which is a horrible, disgusting concoction that you have to drink, and most of the time. And it creates your body to produce waste or rid your body of waste very quickly. And so it creates a similar situation to our IBS-D patients, where you have to be near a bathroom all the time, and the only way that you can obviously rid your body of waste is to have diarrhea all the time, and to keep that constantly cycling out of your body, so that you're ridding yourself of the ammonia, so that you're not having as many dementia, confusion, neurological symptoms as you would normally as a patient.

So, the addition for most patients of rifaximin or Xifaxan helps to manage that diarrhea. It's a concoction or pairing that helps to manage the frequency of the necessity to be near a restroom or a toilet all the time and improves quality of life in that regard. So, I think that's really important to note, and that for caregivers again, I've got everyday patients, and I experienced it myself when I didn't remember getting from point A to point B sometimes in a car, and so many hepatic encephalopathy patients are not able to drive or liver patients because they're affected by this condition, and you don't often find out about that until you're in advanced liver disease clinics, clinic care. And often by that time, you're facing transplant. You don't have any options previous to that. So, it's difficult to get it diagnosed early, but then have the earlier options available because of pricing and access. Most of the patients that I know, including myself, who were on Xifaxan were not able to stay on due to access issues and cost.

So that was another problem. A lot of patients will, right or wrong, hoard Xifaxan so that they can bank it, so to speak, for later use, which, again, it's not best practice. But it's something that happens in the liver community. And, most hepatologists that I know have agreed that it's a very important medication, and most patients who have been on it and experienced the difference agree that it's an important medication.

00:29:41

Moderator, RTI International

And **[Participant 2]**, yeah, I'll talk about Xifaxan in a moment.

00:29:43

Participant 2 (registered as a representative of a patient advocacy organization)

Absolutely. Yeah.

00:29:44

Moderator, RTI International

At the moment, I just want to focus on how hepatic encephalopathy affects people's day- to-day lives. **[Participant 6]**, I also saw you had your name up or hand up. Sorry. How does it affect people's day-to-day lives?

00:29:55

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

So, I can tell you that when I was first diagnosed, I was going to a gastroenterologist, and they said, your ammonia level is not that high. However, when I was working, they asked me, are you taking any kind of pain pills? I was like no, because I was slurring my words. I couldn't think. I stopped driving for two years. I literally forgot my address, didn't know who I was, and would go off on tangents, thinking I knew something was happening, and it wasn't happening.

And so, for my aunt that moved in with me to help me, she was like, it's like redirecting a five-year-old because you're so focused, hyper-focused on something that's not happening. But in your mind, it is, and in your mind is going on. You know, again the bathroom.

So I had the lactulose. It was horrible, and as a patient, I didn't like taking it. And then, of course it wasn't working. So, that's when I had to switch over and do both drugs. So, I mean, it's a problem with access. I remember that they had diagnosed, they had given me the drug, but then it was going to be an exorbitant amount, and my aunt had to wheel and deal with the pharmacy to see if she could only get a couple of pills until she could get it passed through. I mean, so literally, I have an aunt, an older aunt having to try to navigate this stuff, and I had no clue what was going on. I did not understand, and I slept all the time, and that was very frustrating, because I would not get out of bed, because I couldn't think, couldn't get out of bed. Didn't want to. It just it robs you of life.

00:31:51

Moderator, RTI International

Thanks, **[Participant 6]**. And **[Participant 4]**, I need to jump to the next question, but I'll give you about 30 seconds, how hepatic encephalopathy affect people's day-to-day lives.

00:32:01

Participant 4 (registered as a patient)

Yes, for me. When I was first diagnosed, I was a mom of two young teenage sons, and for me it took away my driving ability, but also the ability to sleep and to wake, and times of where I would stay awake for two and three days, and then for three days I slept solid, 18 hours all the time, so it impacts every aspect of your life, from the top of your head to the bottom of your toes. HE [hepatic encephalopathy] affects you, and I know you're wanting to cut it short, so I'll respect that, and we'll come back to something else.

00:32:35

Moderator, RTI International

Yeah, we'll talk more. Don't worry. Thanks, **[Participant 4]**.

For hepatic encephalopathy, what aspects are most important to you to have managed or treated? Again, what aspects are most important to have managed or treated? **[Participant 4]**?

00:32:51

Participant 4 (registered as a patient)

For me, it was being able to be a part of my family's life and to be respected. I am a woman who was a supervisor and a manager of a large facility with people with developmental disabilities. And now, my family won't trust me with my nieces and nephews to watch them. I have people telling me I can't drive. They're afraid to leave their loved ones in my care, and I am teaching abuse and neglect and exploitation, and people are afraid that I'm going to make bad decisions.

I was so humiliated that my son, at the time was 14. We went to pick him up from a dance, and I was arguing with my husband, a professional woman about at midnight, running into Walmart to go buy press-on nails, because that's what I thought I needed. They get me in there. I am so argumentative and unpleasant with them. My son has refused to go shopping with me all the rest of those years. For almost seven years he wouldn't go with me because I ran into a huge pile of Campbell's. I don't even remember doing it. My husband tried getting me out. I ended up spending $350 on items I did not want. They get me into a car, and I completely pass out, knocked out sound asleep. And they could hardly wake me up. We didn't know there was anything called HE, until I went to a support group and told them about the situation. And that's where, for me, it was devastating. It was humiliating, so to not be respected by your loved ones, your professionals, your friends, and to now be thinking that you're mentally incompetent. It's devastating.

00:34:46

Moderator, RTI International

Thanks, **[Participant 4]**. **[Participant 5]**, maybe like a quick 30 seconds, and then we'll give **[Participant 6]** 30 seconds before I go to another question. But go ahead.

00:34:54

Participant 5 (registered as a patient)

Yeah, but basically, pretty much the same thing that **[Participant 4]** is saying, it's like you want your dignity back. For me, I worked in pharmacy for 20 years, rapid thinker, high thinker. That all changes, you go from that to basically not being able to be left alone, basically being treated almost like a five-year-old. Your decisions are questioned.

You have to question things. I couldn't even remember the proper temperature to cook chicken on. And basically don't know where the car is, hand-holding, being led to things. It does rob you of who you are and your dignity, and I also have a child in school, a school-aged child, and that makes it a lot more challenging to navigate that way. But basically, yeah, get your dignity. Get your life back.

00:35:50

Moderator, RTI International

Okay. Last one. **[Participant 6]**?

00:35:53

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

For me, just the HE, I fell quite a bit. And then I forget that I fall, and then I would have a bump or have something going on, because that's just a part of it. And so, just the fact of not knowing what I was doing daily and then randomly, all of a sudden, be okay, and then it hits you again. It was very hard for my daughter and just for my family, in general, because I didn't understand things. As everyone else has said. I mean, I was running a billion-dollar company that the diversity, with the minority women-owned businesses on a large construction project, and I could not drive now, so it robs you of life.

00:36:45

Moderator, RTI International

Okay. Great. Thanks, **[Participant 6]**.

All right. I want to talk, now that we've talked about the impact on people's lives, I want to talk a little bit about the different medications, and we're going to talk both broadly about Xifaxan and also other medications that are to treat indicated conditions which, I'll call these a therapeutic alternative. So, it's drugs like Xifaxan, and they help with your symptoms.

So first, for the people speaking for IBS-D, when considering potential medications for IBS-D, what matters most to patients when considering medications? **[Participant 1]**?

00:37:30

Participant 1 (registered as a patient and representative of a patient advocacy organization)

It works.

00:37:31

Moderator, RTI International

It works? Okay.

00:37:32

Participant 1 (registered as a patient and representative of a patient advocacy organization)

It works. I think for patients with IBS-D, they just want to have that control, like I said before, back in their lives. And so, they need a medication that is dependable, and that works that they know that they can at least, I mean, there's no miracle drug, right? Like it's not going to cure you by any means, even if you take it daily. It's not going to cure you. However, if you know that it does work, it makes it better. I think the, for IBS-D like **[Participant 7]** said, the pain is a huge part of it, that sort of cramping pain.

And if you think about having a stomach bug, or food poisoning, and how your stomach just like it cramps up, and then you have to run to the bathroom, and you have diarrhea. People with IBS deal with that every day. And so, that's really and truly what it's like a charley horse in your stomach, and you just want it gone.

So, I think that's sort of the main thing. You want to get your life back. So, it's the pain and the frequent episodes of diarrhea that don't come on just urgently, so that you can navigate life better.

00:38:53

Moderator, RTI International

Okay, thanks **[Participant 1]**. For others, when considering potential medications for IBS-D, what matters most to people?

00:39:00

Participant 7 (registered as a patient)

I think all of that, plus the side effects. I'm a person that I'm sensitive to medications and even small increment changes, I get side effects. So usually, if there are some side effects, it's me calling the doctor. But yeah, I think some of the other medications that were offered I was either allergic to or there were intense nausea with it, and I believe one was headache and dizziness, and I'm like, I already have to deal with running to the bathroom with diarrhea that's potentially making me dehydrated. So, if we could limit the amount of side effects we're looking at and know that it's effective, of course not going to cure it, but effective to turn this flare around. That's really the most important part for me.

00:40:03

Moderator, RTI International

And then for hepatic encephalopathy, and you all have used the initials "HE," so I'm just going to use the initials HE, if that's okay with you. I think you all use those initials, so I'm going to do that as well.

So, when considering potential medications for HE, what matters most to people? Again, when it comes to medications for HE, what matters most? **[Participant 4]**?

00:40:27

Participant 4 (registered as a patient)

Obviously that it works. But that also, it is a medication that fills in the gaps, while the other medication that does work, we are required to try that first. And almost 100% of the cases, that other medication we have to take. And there's only one other medication, and it's lactulose, and you're guaranteed to be going to the bathroom and be in front of the toilet all of the time.

So, being able to have, even if you take lactulose, you'll still have these breakthrough episodes. So, the only therapeutic medication that's available is Xifaxan, and it allows people to have their life back. And then there's people also, like for myself, who I was paralyzed in 2019 and have no bowel control and bladder control, as well as I have IBS. And so, when you have those situations, I had to come off the lactulose. There was no treatment beyond Xifaxan for me, and when I got that medication, it has significantly improved the quality of my life. It is therapeutic, it works, and it is the only medication available. There is nothing else.

00:40:03

Moderator, RTI International

[Participant 6]?

00:41:53

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

You know, when I started taking lactulose, they required us to take it, and that didn't work, and then trying to get the Xifaxan, and being able to get that, helped in so many ways. But still, I had breakthroughs where I ended up in the hospital in a coma, didn't know my daughter, and my daughter actually was like, you went in to have a paracentesis, to have a procedure, and then you don't know who I am. You don't know who anyone is for three days, and I'm in the hospital.

My brother had a transplant in May of last year. He had problems. He had to take Xifaxan because lactulose didn't work. I work with patients all the time, and there is 90% of them have to go on Xifaxan, and they struggle because it's like gold in the liver community, and a sense of trying to just get it. And a friend of mine, she had HE so bad that she passed away because of the problem of HE. And so, it's getting the medication and getting something that we can have access to is really the bottom line. Thank you.

00:43:02

Moderator, RTI International

Yeah. **[Participant 5]**?

00:43:08

Participant 5 (registered as a patient)

So also, to kind of piggyback on that, too. Yeah, the other medication that's used to treat HE is lactulose. And again, like others have said, it is a laxative, so you drink it, and the idea is for you to rid yourself of that toxin, of that waste by form of diarrhea, of it flushing out of your body about three times a day. So, that creates a lot of complications similar to like how IBS is, you have to, you can't go anywhere, you have to know where all the bathrooms [are]. It's very hard on your system, and then there's people like me who lactulose simply is not enough. And you have to, I mean, yeah, lactulose is simply not enough. And you have to add in the Xifaxan as well to have a dual treatment.

So, I kind of think of it almost in the sense of gout, if you guys are familiar with that. Well, you have one medication that when you're having a gout attack, you take that one medication to stop that attack. That's kind of like lactulose. But to prevent that build up to keep having those attacks, you're going to take a maintenance medication. Well, it's kind of like the same concept, where Xifaxan is the only medication that lessens that likelihood of these reoccurring episodes. And that's going to in turn, limit the amount of time that you're going to the hospital for emergent help and kind of help you with that.

And the other thing that people need to realize as well, too, who are not aware is, each episode that you have, and the higher and the worse the episodes get, it can cause irreversible brain damage. So, the more episodes you keep having without medications like Xifaxan, that is proven to lessen all of those. You're putting yourself at an increased risk for a permanent brain damage, and then that will lead to a whole other situation in itself.

00:45:04

Moderator, RTI International

So, lessening the recurrence of episodes is very important in a medication?

00:45:08

Participant 5 (registered as a patient)

Correct.

00:45:09

Moderator, RTI International

[Participant 2]?

00:45:11

Participant 2 (registered as a representative of a patient advocacy organization)

Thank you so much. Just briefly, thank you, **[Participant 5]**. To reiterate **[Participant 5]**'s point, there is long-term damage that can be done if you don't manage the ammonia levels within your system. It's ammonia toxicity essentially, that can cause long-term damage. But the point that I wanted to make and just reiterate is that lactulose is the generic frontline that is often provided to patients, and Xifaxan, rifaximin is the only other option that's as accepted within practice guidelines as a treatment alternative or supplemental. It is the only other option. So, that's what we have. That's what we have to work with. And it's important because of that, at the very least. Thank you.

00:46:00

Moderator, RTI International

So, we've talked a bit big picture. And for this next part, I want to drill down and talk specifically about Xifaxan for treating IBS-D and HE. And again, I'm going to start with IBS-D first. When it comes to Xifaxan, what are some of the main benefits that people experience taking Xifaxan for IBS-D? What do people like about it? **[Participant 1]**?

00:46:29

Participant 1 (registered as a patient and representative of a patient advocacy organization)

So, I think that most people like the fact that it does slow down the diarrhea, and it makes it more manageable to live day to day. With the Xifaxan, and sort of the same. You can take Imodium over the counter. You can get Imodium by prescription, or you can take a drug that is black-labeled for IBS-D, and so, something that was on the market, pulled from the market, back on the market. Highly dangerous. No one wants to take that because of the health risks. So, it's sort of the best option that you have for IBS-D.

00:47:20

Moderator, RTI International

Okay. Others? Some of the benefits of Xifaxan for IBS-D?

00:47:27

Participant 7 (registered as a patient)

I would say, in my case, because it was the IBS had contributed it to SIBO. We were looking at it as more of an antibiotic that doesn't get absorbed into your bloodstream. There are other antibiotics that will work. But again, with the side effects, Flagyl gives me open sores in my mouth and rashes, and Cipro is just, Cipro for me is just not, it's a no-go. So, that was the other option on the market for the SIBO, which was caused directly from the IBS-D. If I didn't have access to that, I mean, it took me five weeks to get it. Insurance said no. My pharmacy said, you can have it for $3,700, and I ended up ordering it from Canada, and paid $67 to have it delivered to my door, but I suffered for five more weeks with those in between. So, it really did help, and I don't know where I'd be without it.

00:48:38

Participant 1 (registered as a patient and representative of a patient advocacy organization)

So, for full transparency, I took a course of Xifaxan for SIBO, and not for my IBS-D. Most people that I talked to, the Xifaxan who take it for IBS-D, they love having it. They call it their miracle drug. For me it was a miracle drug, but it was actually for SIBO. I had done the breath tests, and they were off the charts, but my doctor at the time didn't give me any medication. And so, for seven years it just continued to get worse and worse and worse. And then I switched gastroenterologists, and she looked at my charts, and she said, why have you never been prescribed Xifaxan? And I said I don't know. I took every antidepressant and psychotic medication that you can imagine, being diagnosed as a woman with IBS-D. But nothing to treat the SIBO and the SIBO had to gotten to the point where it was like razor blades in my gut, and so, when I would take a step, it literally felt like something was slicing through my abdomen because of the bacterial overgrowth.

And again, I was unable to get the medication through my insurance, and it was denied. I couldn't afford to pay out-of-pocket. My gastroenterologist actually talked to the pharmaceutical rep that visited her clinic and said, can I get a course for this patient who is really suffering? And I was traveling a lot, and so it was very difficult for me to do my job effectively, and so she gave me a course of rifaximin, and it was instantaneous relief. When I finished that course, I have not had another, it's starting, I feel the buildup. So, I have it because I have slow motility in my small intestine, so that causes that bacterial overgrowth, and it will come back, and I will have to treat it again. But those razor blades just vanished in my gut immediately, like with one course.

00:50:41

Participant 7 (registered as a patient)

Yeah.

00:50:42

Moderator, RTI International

And just to make sure, I know, for acronym SIBO, small intestinal bacterial overgrowth, just want to make sure we all understood. Just so today's discussion makes sense for everyone.

So, we talked about the benefits of Xifaxan for IBS-D, I want to talk about some of the challenges. **[Participant 1]**, you already alluded to cost, that's one challenge. What are some of the other challenges you've had, either with the treatment itself or other parts of Xifaxan?

00:51:05

Participant 1 (registered as a patient and representative of a patient advocacy organization)

My daughter was prescribed Xifaxan, and she said it just didn't make her head feel right. I think that was more the dizziness that can be a side effect. But she was just sort of like, I just I don't feel right. And she was a volleyball player, and so precision mattered. And she played in college, and she was like, I have to be on point. She's a setter, and so she didn't continue with the medication. But I don't know if that would have went away if she continued on it or not but that was a difficulty that she had. She felt like she couldn't think.

00:51:46

Moderator, RTI International

[Inaudible] side effects. For IBS-D, any other challenges with Xifaxan?

00:51:53

Participant 7 (registered as a patient)

I think for me the biggest one was just the accessibility of it. I mean nothing beats what I was dealing with for five whole weeks trying to get it. That was actually the episode that landed me in the ER for dehydration, because I was having diarrhea upwards of at least 10 to 15 times a day. I couldn't work anymore during all of that. I had my own business. I ended up losing it, and in the state of New York, you can't apply for unemployment and get benefits if you're self-employed. So, we were trying to live a normal life, and it just was not going to happen under those conditions. So, accessibility was my key issue, as far as that goes. It did help with the symptoms. But I don't know what I would have done if I couldn't get it.

00:52:51

Moderator, RTI International

Okay, let's talk about HE, focusing specifically on Xifaxan. What are some of the benefits you've experienced for HE using Xifaxan?

Yeah, **[Participant 4]**?

00:53:11

Participant 4 (registered as a patient)

For me, it was multiple things, but the biggest was I was able to not have to rush to the restroom. I got my mental capabilities back, but because of my bowel paralysis that I have with the other medication, I could not go anywhere. I was constantly in the bathroom, or if I was in public, I lost control of my bowels in public with my family, and it was humiliating. So, with Xifaxan when they took me off, when they got me finally going on it consistently, it allowed me to not have to use the bathroom as frequently, and have the accidents that I was having, but also to have my mental capability back and to be able to articulate things. It also allowed me to develop a normal sleep and wake cycle. I'm not 100, but it's better than what it was.

I'm also more articulate, and I can write. All of those things I lost when my HE was flaring. I have been stable for almost five years. And so, it doesn't mean I don't have HE days. It just means that I'm more normal than where I had been, where it was leading towards coma, hospitalization. I haven't had any of those issues to that level in five years thanks to consistent Xifaxan use.

00:54:44

Moderator, RTI International

[Participant 5], what's some of the difference you've seen with Xifaxan for HE?

00:54:49

Participant 5 (registered as a patient)

Yeah. So, one of the biggest things is, when I first got HE and I first started on the traditional first line, lactulose. During that period of time, I still really didn't understand what was happening, and it wasn't enough for me. The lactulose was not enough for me, and my body was still having too many toxins, too many ammonias, and it was to the point where I was on the couch, and basically almost like a coma-like state. I could not get up. I could not care for myself, could not feed myself. I could not bathe myself, and I was like that for several months where I needed hands-on care, and it was just all a blur.

And then, when I got put on Xifaxan, that is what helped to change that. I was then able to get up and care for myself and feed myself. Now, the same thing goes. Nothing makes it go away a hundred percent. But it definitely improves things. It makes it so that you don't have as many of those what we call overt HE episodes where you're just like in that state where you have to go to the hospital. You're kind of like in crisis mode at that point. So, that makes it so that you're more kind of like an even field where it kind of brings that normalcy back where you can sort of still have a normal-ish life, so to speak, rather than for me being on a couch, basically in a coma-like state.

00:56:31

Moderator, RTI International

Thanks, **[Participant 5]**. **[Participant 2]**, you were next. Go ahead.

00:56:34

Participant 2 (registered as a representative of a patient advocacy organization)

Thank you. For me, I think the biggest changes were just the improvement in my overall cognition and ability to function, and after being on it for a while, the ability to parent and be a parent to my children was a big one. It wasn't ever the same, but it definitely improved significantly to the point where I was a functioning parent. Definitely fewer hospital visits and emergency room visits. That was something that had become kind of a pattern and changed really significantly with the medication. I just think that the biggest thing for me was the cognition, definitely more energy or less sleeping, more alertness, and I had a sense of hope for the first time, for sure.

00:57:24

Moderator, RTI International

Yes, I've heard cognition a few times, and it sounds like that really just improved your daily life. Being a parent, like you mentioned, and so forth.

[Participant 6]?

00:57:34

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

Hi, so I was functioning on a daily basis. That's the one thing, lactulose caused gas and bloating for me and running to the bathroom, and so Xifaxan gave me, I wasn't running to the bathroom as much. I could actually function, but I still wasn't, my liver disease was so bad that the Xifaxan I had to take that every day on time, and I had to have someone making sure I was taking it because one missed pill leads to another problem. And that's your ammonia levels will go back up and things like that.

But I was able to start understanding what people were telling me, because I was dying in trying to navigate to even get to a doctor, and then getting to the doctor, and then not understanding anything they're telling me because I didn't have access to Xifaxan, or I got access to Xifaxan. And now I can understand much better. So, I think it's a game-changer for patients navigating the system or dealing with chronic liver or gastrointestinal issues for us to even focus and function.

00:58:54

Moderator, RTI International

All right. Now, so those are some of the benefits folks with HE experience with Xifaxan. On the flip side, what are some drawbacks or challenges that you've experienced with Xifaxan? Okay, **[Participant 5]**?

00:59:13

Participant 5 (registered as a patient)

So, one of the main challenges or the drawbacks is going to be basically cost. I mean, it does involve prior authorizations and things like that, and that can be very cumbersome and very hard thing to deal with. A lot of times, you can try to speed up that process and get a prior authorization help fast track, those sorts of things. But you can't fast track money that you don't have.

So, walking into a pharmacy and them holding this medication that essentially kind of gives you your life, or your dignity, or the ability to not be in the hospital 10 times a year, and say you can have it, if you got $3,000. That's not realistic. And it's not like, okay, well, that's the drug we choose. We want that because we don't want to take X, Y, and Z. This is the only one that we can take that's going to work in that way to help keep that even field, to help you kind of be okay, and to put a price on that, I understand, everything has a price. But it just makes it, it's unobtainable, and people lose hope for it. And we're just, I consider myself a working midclass, and for something like that, you just can't do it. I've walked out of the pharmacy without that medication, and I've had my husband, who works 70 plus hours a week, just so upset that he cannot properly care for his wife, that he feels like he failed something when it has nothing to do with him, and then you have to explain to your child why mommy is sick and why mommy's going to continue to be sick because mommy doesn't have $3,000 to get one month supply of this medication. It has to, you gotta make it make sense.

01:01:06

Moderator, RTI International

Great. Thank you, **[Participant 5]**. **[Participant 6]**, finish off, then I have a different question. Go ahead, **[Participant 6]**.

01:01:12

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

I'm just going to say that the cost in general is horrible, and it's horrible for patients, not only for myself trying to get it, and not having access, or having to spend $20 to $30 a pill just to get it until we could manage to get the paperwork to send in, and I had commercial insurance. It wasn't even a Medicare or Medicaid. I had commercial insurance and still could not afford it.

And then to find the information in order to get the medicine was on a different website. And so, that's something that we should, that probably isn't on another meeting that we should talk about, it is access all day, every day, and the cost is overwhelming, and patients decide whether they're going to take it or not take it, and they ration it out.

01:02:08

Moderator, RTI International

Thanks, **[Participant 6]**. I want to talk now, going back to IBS-D. Other than Xifaxan, what are some other drugs that you've used, or medications that you've used to treat IBS-D? So, a quick list.

01:02:25

Participant 1 (registered as a patient and representative of a patient advocacy organization)

For me, the only thing I've ever taken is loperamide, because I have to stop the diarrhea. I'm prone to hemorrhoids. And if I have lots of diarrhea it does, I don't know why my sphincter reacts the way that it does, but I've had them surgically removed twice. It's not something that I will ever repeat again. They actually scarred my anal wall, so that they won't come back.

But for me it was the loperamide, and you used to be able to get them in the big bottles at Costco. Can't anymore. They blister package them, and you can't buy more than like 12 pills at a time. Because of the issues of people using it for opioid and taking 150 pills in one sitting to get high. And so now the loperamide is rationed. It's not rationed, like you can buy as much as you want of it, but you can only buy it in small quantities, and it's blister packed. So, I have to use actually a paring knife to cut the foil to get them out, and when I buy a box, I literally empty the whole box and put them in a little mini Tupperware thing, so that I don't have to go fumbling with it when I'm in an episode.

But that's the only thing. I know that there is one that has been pulled from the market because of some hard access issues. And I won't risk that personally. Mine isn't that bad when I do have my episodes. I just work from home instead of the office, and I can do that. So, the loperamide is the only thing that I've done for the diarrhea.

01:04:09

Moderator, RTI International

And for others, [inaudible] from the HE standpoint, what are some medications that… Sorry, **[Participant 7]**, you had one you wanted to mention for IBS-D, go ahead.

01:04:19

Participant 7 (registered as a patient)

Yeah. So, I've tried, at least for IBS-D, it's hyoscyamine. It's something I'm newly trying. It only works when I'm having that immediate attack with the cramps, but it does nothing for the diarrhea. Absolutely nothing. So, I mean you win some and you lose some, I guess. Separate the symptoms out, but that's been the only other one I've really had recently.

01:04:51

Moderator, RTI International

And then for HE, actually let me continue on IBS-D. I want to talk now and compare these other drugs that you've used for IBS-D and compare it to Xifaxan. So, we're comparing these therapeutic alternatives to Xifaxan. First, how do the benefits of these drugs differ from Xifaxan, like how are these other alternatives better than Xifaxan?

01:05:18

Participant 1 (registered as a patient and representative of a patient advocacy organization)

Loperamide's cheap.

01:05:19

Moderator, RTI International

So, they're cheaper. Okay.

01:05:20

Participant 1 (registered as a patient and representative of a patient advocacy organization)

The problem, though, is that it also constipates you in a heartbeat. You can't get on a regimented dose of it, especially because IBS-D is episodic. So, you're not having diarrhea every day, all day. But you do have it on some days, and when you do, it's terrible. So, you can't really take it preventatively until you're in an attack, and then you have to take it. And then all of a sudden, you're constipated, and of course I'm prone to constipation anyway. So, when I go through these months where I'm in an IBS-D mode, what ends up happening is that I constipate myself, and then I've got to use a laxative or MiraLAX or something to unconstipate myself. And then I get in this whole cycle. And your body's not controlled.

You're going from D to C to D to C, consistently, because the loperamide is, you just can't control how that works for you. And I was put on the hyoscyamine, that's actually a smooth muscle relaxant. So that helps with the pain. But it's relaxing your smooth muscles, which is just actually going to make the diarrhea worse.

And so, I think that really there isn't another alternative for the IBS-D population that's viable. There are the smooth muscle relaxers, which they don't treat the underlying problem. So, I think that's the problem that we have kind of just like the rest of the guys do, like this is it, there's no other option really.

01:07:04

Moderator, RTI International

Okay.

01:07:05

Participant 7 (registered as a patient)

I would say, Xifaxan is the only one that gets to the root of the problem as far as IBS goes.

01:07:14

Moderator, RTI International

So, when you say get to the root of problem, **[Participant 7]**, what do you mean?

01:07:16

Participant 7 (registered as a patient)

And so, most of the time, it's the bacterial growth in the small intestine that is causing, or at least that's what I've been told by physicians, that is causing so much pain. You're bloated to the point where you look pregnant. You're in a lot of pain. You're in the bathroom. It's that bacterial growth getting stuck in there and not finding its way out. And that's part of why they say Xifaxan being an antibiotic that doesn't get absorbed into the bloodstream. It stays in the gut and kind of does its job there, if that makes sense.

01:07:56

Moderator, RTI International

Yep, it does.

01:07:58

Participant 1 (registered as a patient and representative of a patient advocacy organization)

With IBS-C, there's lots of options, right? There's several medications in the market. You have choices. If one doesn't work for you, you can try something else. With IBS-D, you don't have that luxury. So, it's difficult.

01:08:13

Moderator, RTI International

Now for HE, what are some of the other drugs that you all have taken, these therapeutic alternatives to Xifaxan? Yeah, **[Participant 4]**?

01:08:30

Participant 4 (registered as a patient)

There is very little, next to nothing, but it's truly lactulose. And some doctors will prescribe MiraLAX to help with getting the bowels moving, but it does not remove the toxin. The only medications that remove the toxins is lactulose and then Xifaxan. There is another herbal medication that some doctors will give out. But it is not something that is well given out. It's called LOLA [L-ornithine L-aspartate], but those are the only things, but truly the only two prescribed medications out there is lactulose and Xifaxan. There is nothing else.

01:09:11

Moderator, RTI International

Yeah, **[Participant 5]**?

01:09:17

Participant 5 (registered as a patient)

Yeah, kind of same thing like what **[Participant 4]** said. The only other medication besides Xifaxan is lactulose. Some people can't tolerate it. I myself have to be on both, because lactulose itself is not enough. So, lactulose, when you're taking it, it's flushing your body. It's pulling your toxins. So, HE you get because of the ammonia buildup, and it goes up to your brain. And that's how you can develop that over HE. So, when you take the lactulose, it's pulling it out of your bloodstream and flushing it through your body like a laxative.

There's a couple of different problems with that. People who are intolerant to it, and if it flushes you too much, then you start to get dehydrated. Well, dehydration is also a trigger for HE, you're kind of cycling yourself. So, when you take a product like Xifaxan, Xifaxan is working directly in your gut to slow that bacterial growth that gives off that waste product for that ammonia. So, for me it's like a twofold, but for others I can see where if you can't take the lactulose or the lactulose is not enough, you would have to have that Xifaxan to kind of help keep your body in check. It's like having someone there constantly working at a factory. That person goes home and everything piles up, and you end up in a big situation.

So, I kind of think of it like that where it's working two different ways. One is like more of an emergency way, getting rid of it right now. But it's not something you can necessarily do multiple times a day on a daily basis, versus Xifaxan will kind of help keep that even tone for you.

01:11:05

Moderator, RTI International

We're already talking about it, so, **[Participant 2]**, maybe we'll talk about this. But we talked about some of the alternatives to Xifaxan for HE, the therapeutic alternatives.

How do these therapeutic alternatives work better? And also, how do they not work as well? **[Participant 2]**, do you want to take that on?

01:11:23

Participant 2 (registered as a representative of a patient advocacy organization)

Sure, I can just start by saying lactulose is so bad and so horrible that there's a song about it. So, you can go to YouTube, and you can look up the lactulose song. And you can learn all you want to know about what happens to your body when you take lactulose.

Xifaxan is literally the only thing that controls the faucet, so to speak, and helps you regulate your body. And so, the other therapeutic alternatives are not widely available or recommended, and those would be over-the-counters like Metamucil or something similar, MiraLAX, and not Metamucil, MiraLAX. And then the LOLA stuff, like **[Participant 4]** talked about. But, most people are not keen to try herbal remedies that may or may not be safe. So, we count on hopefully taking safe medications and medications that are proven to be safe so that we can do the best for our bodies. But other than that, there aren't a lot of options.

And diet and nutrition play a role in this. I think, as liver patients, we all pay very close attention to our diet, so that we're trying to limit any possibility of an ammonia overload, and so that whatever ammonia is there can be managed by lactulose or Xifaxan, but it's very difficult to do so. It's very difficult.

01:12:46

Moderator, RTI International

[Participant 6], maybe 30 seconds. I need to move to the next topic but go ahead.

01:12:51

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

I was just going to say, metabolically, it's all a little bit different. Xifaxan is the game-changer. All patients react differently. And so most patients that have liver disease, it depends on where they're at, but their bodies are going to react differently from someone that's in a stage 4 or stage 3 with cirrhosis versus end-stage liver disease is going to be different, so it can hit a person at any point during their stages. And that's one thing that's really important. It's not just for at the very end of the liver disease. It's for during the entire process, as it is for IBS-D. So, that's all I wanted to share.

01:13:36

Moderator, RTI International

Yeah, thanks **[Participant 6]**.

So, I want to talk about, for IBS-D, what would it be like if Xifaxan or other medications for this drug were not available to take? What would it be like if there were no medications for IBS-D? **[Participant 1]**? I see you're unmuted.

01:13:59

Participant 1 (registered as a patient and representative of a patient advocacy organization)

I am. I don't know if I have words for that. That would be devastating, because there's nothing else. There are so many people that are able to do things normal in life, have a job, have a sex life, just being in relationships. As a single woman, I just didn't date when I was in my episodes of IBS-D. You just put off those because you just don't want to be in the middle of a date and have to run to the bathroom. I think, for people with IBS-D, the pain is very intense, and the diarrhea is humiliating when you have accidents.

Most people with IBS-D that severe wear diapers every single day. They're not fecally incontinent, but they might as well be, because if you can't get there in time, you're not going to make it, and it's a terrible place to be. There's so many people that with severe cases of IBS-D that don't leave their home, so without this as an option for them.

There's a huge psychological component, like **[Participant 3]** had mentioned earlier. And there's a lot of people who suffer from IBS-D that get into very severe bouts of depression. There's a lot of stress and anxiety about urgency and being able to find a bathroom. But then, after years of being in this cycle, where it doesn't stop, I'm lucky that mine is very episodic, and I do have some good days that may even go into weeks when I'm lucky.

People fall into very deep bouts of depression, and I've known patients that we have lost because of that depression and feeling like they're never going to have a life.

01:16:13

Moderator, RTI International

Thanks, **[Participant 1]**. And **[Participant 3]**?

01:16:18

Participant 3 (registered as a representative of a patient advocacy organization and caregiver)

Just to **[Participant 1]**'s point as well, is that you have to also remember that a lot of people, I think, with both diseases, what you've heard today, have to go through a long period of time before they even get a diagnosis, of what exactly is going on and what is happening. So, living through these diseases and the pain and suffering that they cause to even be diagnosed and validated in a lot of ways, like you know something is wrong. But to get that diagnosis and then to find treatments that work are so important in that access that you've heard, as well. But I think it's important to also keep in mind the journey that it takes to get to the point where you have something that works for you, can be long and arduous, and take a toll on both the physical and emotional health as well.

01:17:10
Moderator, RTI International

Now for HE, if Xifaxan or other treatments were not available for HE, what would your life be like?

01:17:22
Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

I would be dead, literally, because it can cause you to die.

01:17:28
Participant 2 (registered as a representative of a patient advocacy organization)

You took the words right out of my mouth.

01:17:30
Moderator, RTI International

So, death is pretty much the answer.

01:17:33
Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

Yeah.

01:17:34
Moderator, RTI International

[Participant 5]?

01:17:37
Participant 5 (registered as a patient)

I was going to say the same thing. Yeah, death. You end up in a coma, and you end up passing away, or it's just, it's so complicated. The toxins are so high that you have no life, and then you literally have no life.

01:17:58
Moderator, RTI International

Now for IBS-D, so we do have Xifaxan and other medications, but what aspects of IBS-D is Xifaxan and other drugs unable to address? So again, what can Xifaxan and other drugs not address for IBS-D?

01:18:22
Participant 1 (registered as a patient and representative of a patient advocacy organization)

Well, there's no cure, right? And it makes it manageable, and it makes it better. But it doesn't make it go away. Just taking Xifaxan doesn't mean that you're going to be 100% healthy. I know that there are like, if you're diabetic and you take your insulin every day, and you eat well, then, you have no diabetic episodes. You can manage that with this medication, and you can live a normal life, with just taking the medication.

With IBS-D, it's episodic. It also has varying degrees of severity with each episode even, like, you may have an episode, and it's severe. And you're in bed for three days. And then you have another episode. And you're like, okay, I can power through this and actually do something today.

So, I think because of that one thing, one medication, even if you keep it in your bloodstream for IBS-D. And I've heard them say it's different for HE but if you take it, **[Participant 6]** was talking about taking it at the same time every single day, so that it's consistently in her bloodstream. With IBS-D, there's nothing on the planet that will make your IBS-D perfect, even if you manage it perfectly towards the doctor's recommendations, by label. Does that make sense? So, none of the drugs can do that, not just Xifaxan.

01:19:49

Moderator, RTI International

And then thinking about HE, what aspects of HE are drugs available in the market today unable to address for you?

Yeah, **[Participant 5]**?

01:20:04

Participant 5 (registered as a patient)

Basically, like the same thing, a cure. There's no cure for it. The cure, I guess, in a sense, would be to get a liver transplant. And those don't come by very often. So, that's the thing, is it makes it a little bit more manageable. But it doesn't ever make it go away. It will still be there to some degree and different, same thing, you have different episodes, different flares, severities, where you can manage at home. Somebody can be with you, or you need to go to the hospital or you end up in a coma, those sorts of things. But it's not going to cure it.

01:20:44

Moderator, RTI International

[Participant 6], what is Xifaxan and other drugs not able to address?

01:20:49

Participant 6 (registered as a patient, representative of a patient advocacy organization, and caregiver)

So, Xifaxan, if a patient, I'm going to talk about the broad spectrum of patients, because if a patient is on a transplant list and they don't have access to Xifaxan, and they end up in a coma in the hospital or having an episode, they are removed and put inactive on the waiting list, so they will not receive a liver at that time, so either the medicine, if they don't take it, will kill them, or if they are inactive on the waiting list, they may not even get a transplant because they were sick because they didn't have access. And so that's something that we always need to think about the broader scope of where it's landing in the patient's sight. And that's something that, it interrupts the flow of being able to get that transplant.

01:21:42

Moderator, RTI International

Great. So, we started a little early. We have about six minutes left, and I want to pause for a moment and open the door to ask you all if there's anything else that we didn't talk about today that you feel like it's important to share with CMS? Because, as I mentioned, we have some staff listening, what do you think is important for you all to share with CMS that we haven't talked about?

01:22:15

Participant 1 (registered as a patient and representative of a patient advocacy organization)

Other than to thank you for having us here. Last week I was honored to be able to talk about IBS-C, and we talked about our three main points. Really, it came down to access, which is again coming up today. For IBS-C, we talked about choices, because there are choices and there aren't any choices for any of us sitting at this table. I think that all of us, no matter what our disease state, has reiterated that we don't have choices. We wish we did. But then access, and then, of course, that it works and that it is a medication. And so, I think that Xifaxan works, it works really well, and it saves lives. We want to have access to that. And we wish there were choices. I know, CMS, that's FDA, not you guys. But we appreciate you allowing us to be here to share our stories and to let you see what goes on in our lives as patients.

01:23:11

Moderator, RTI International

We appreciate you're here, too, **[Participant 1]**. **[Participant 5]**?

01:23:16

Participant 5 (registered as a patient)

Yeah, just sort of the same thing, thankful for their time, for listening to us and considering that even though we each have our own stories, and we're individuals. And we take the medications, and we have different things that happen and different outcomes. The bottom line is that this medication works, and it's super beneficial. It is truly the difference between life and death.

I know the drug costs a lot, and there's a lot of things in factor. And when you're doing things for profit and that sort of thing, it has to make sense. But I ask them to consider our lives and our family lives and how impactful that is, and not getting the proper treatment or the proper care, yes, will ultimately lead to death. But along the way, also incurs a lot of costs, a lot of medical costs. You have a lot of hospitalizations, rehospitalizations. You could be put in care homes. You could have permanent brain damage. You could not be able to care for yourself. You need caregivers. I mean, there's a lot that goes on that can simply not be cured but be greatly improved by and managed by this medication that you can take in your home twice a day.

So that's all I ask for them to consider, is take that into consideration.

01:24:44

Moderator, RTI International

Thanks, **[Participant 5]**. Yeah, **[Participant 3]**, and then we'll finish with **[Participant 4]**. So go ahead, **[Participant 3]**.

01:24:49

Participant 3 (registered as a representative of a patient advocacy organization and caregiver)

Okay, sure, and I'll be quick. I think it's also important to keep in mind that this is an antibiotic medicine. IBS and HE were the second and third indications. It started out as a medicine for travelers' diarrhea. So, the dramatic impact that it's had on the people's lives that we've had today started out with something more acute and minor condition.

We have a real problem with antibiotic development. The pipeline is very sparse, and there are a lot of reasons why that is the case, and there may be antibiotics in the future that could help and provide even more relief. But I would just say that also needs to be a factor in consideration that you know how impact, the decisions that you make about this medicine, and really valuing the value that it's brought to these people's lives and improve access and balance that also with the need for more innovation on these diseases and in the antibiotic space in general. Thanks.

01:25:53

Moderator, RTI International

Thanks, **[Participant 3]**. And **[Participant 4]**, did you have a final thought you wanted to say?

01:25:58

Participant 4 (registered as a patient)

[Participant 3] really got what I was wanting, and it was just that we really need to focus on the research of this and hopefully coming up with better options, because there really isn't any. That was all.

01:26:12

Moderator, RTI International

Great. Thanks, **[Participant 4]**.

So, thank you all again for participating in today's group. We appreciate your time and talking with us today. Your experiences and input were really valuable and will help inform CMS' negotiations for these drugs. As I mentioned, CMS staff have been listening to this roundtable and will be able to take your perspectives back to their teams.

[CMS STAFF], just want to see if you had any final thoughts before we finish today?

01:26:39

CMS Staff

Yeah, I just want to take a minute to thank everybody on behalf of CMS and certainly on behalf of my colleagues who are on the call today and have been listening. We just want to let you know that we really appreciate you taking the time to share your experiences and your knowledge with us today. You certainly have given us a lot to think about, and we're just really grateful for the time and energy today. So, thank you.

01:27:01

Moderator, RTI International

Thank you. And we're going to put a slide up here that has an email address that I mentioned. If you have any questions following today's session, you can submit them to this mailbox, which is IRARebateAndNegotiation@cms.hhs.gov. And then put the subject line, public engagement events.

And that's all I have for you all today. Thank you all so much for your time today. I really appreciate it and hope all is well. See you soon. Bye.

=== END OF TRANSCRIPT ===

For a list of the drugs selected for the second cycle of the Medicare Drug Price Negotiation Program, click on the following link: https://www.cms.gov/files/document/factsheet-medicare-negotiation-selected-drug-list-ipay-2027.pdf

For more information on the Medicare Drug Price Negotiation Program, please click on the following link: https://www.cms.gov/priorities/medicare-prescription-drug-affordability/overview/medicare-drug-price-negotiation-program

Appendix

Participant 1: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s); a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
Yes	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 2: Registered as a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 3: Registered as a representative of a patient advocacy organization; a caregiver for an individual who has experience with the selected drug, the condition(s) treated by the selected drug, or other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
Yes	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 4: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 5: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 6: Registered as a patient who has experience with the condition(s) treated by the selected drug; a representative of a patient advocacy organization; a caregiver for an individual who has experience with the selected drug, the condition(s) treated by the selected drug, or other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 7: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., Gifts', funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest