This transcript was lightly edited for readability.

Introductory Remarks

Moderator, PhD, RTI International

Thank you for joining us today for the CMS Medicare Drug Price Negotiation Town Hall. I am **[MODERATOR]** from RTI International. I will be the facilitator for the Town Hall today.

If you would like to listen to this town hall in Spanish, please follow the directions for accessing the Spanish line on the screen. We also will have sign language interpretation throughout the Town Hall. To start us off, I will share a brief introductory video from Steph Carlton, CMS Chief of Staff and Deputy Administrator.

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.

Moderator, PhD, RTI International

Thank you. There are several CMS representatives joining the Town Hall today to hear from today's speakers. Please welcome **[CMS STAFF]** from CMS.

00:03:03

Welcome and Overview

CMS Staff

Thanks, **[MODERATOR]**. Hello. I'm **[CMS STAFF]**, part of the leadership team here at CMS, and I'm greeting you here today on behalf of CMS staff and leaders who are listening to the livestream. We really appreciate the time and input shared by the individuals who are joining us today as speakers, as well as everyone who is listening and watching the livestream this afternoon. We are looking forward to the second session of the Town Hall, and with that, I'm going to turn it back to **[MODERATOR]**. Thank you all so much.

Moderator, PhD, RTI International

Thank you, **[CMS STAFF]**. The Town Hall today has a morning and an afternoon session. For this afternoon's session, we will hear from speakers on seven drugs in the order you see listed here. The goal of the Town Hall is to provide an opportunity for clinicians, researchers, and other interested parties to share input focused on the clinical considerations related to the drugs selected for the second cycle of negotiations.

CMS will use the information shared during the Town Hall meeting to better understand clinicians' experiences prescribing and/or managing treatment with the selected drugs or therapeutic alternatives and clinicians' considerations that drive treatment choice between the selected drugs and therapeutic alternatives.

In addition to this Town Hall meeting, CMS hosted 15 patient private, patient-focused roundtable events, one for each selected drug, each of which was open to patients, patient advocacy organizations, and caregivers. CMS will use the information shared during the roundtable events to better understand patients' experiences with the conditions and disease treated by the selected drugs and patients' experiences with the selected drugs themselves.

The information shared during both the Town Hall meeting and the roundtable events will also inform CMS' identification of therapeutic alternatives, key outcomes, and adjustment of the starting point to develop the initial offer in negotiating with manufacturers of selected drugs. The speakers at today's Town Hall meeting include clinicians, researchers, patients, caregivers, and patient advocates. The number of speakers for each selected drug varies based on how many speakers registered to speak for each of those drugs.

This meeting is being live-streamed. Participation is voluntary, and speakers acknowledged and agreed by participating in the meeting that any information provided, including individually identifiable information and personally identifiable information, will be made public during the meeting through a livestream broadcast. Clinicians should be mindful of their obligations under HIPAA [Health Insurance Portability and Accountability Act of 1996] and other privacy laws.

CMS intends to make a redacted version of the transcript for the meeting available in May. Speakers were asked to disclose any potential conflicts of interest, or COI, with the drug they are speaking about. As I introduce each speaker, I will note, and you will see on the slide, any disclosed potential COI. To accommodate as many speakers as possible, each speaker will be limited to four minutes for their remarks. There will be time for a brief follow-up after each set of speakers, and I appreciate everyone sticking to these time limits so that we're able to hear from everyone.

The first five speakers will share remarks about semaglutide, or Ozempic, Rybelsus and Wegovy, which are commonly used to treat type 2 diabetes, type 2 diabetes and cardiovascular disease, type 2 diabetes and chronic kidney disease, and obesity/overweight conditions with cardiovascular disease. The first speaker is **[Speaker 1]**. This speaker disclosed a potential conflict of interest as shown on the slide. [Note: There were six speakers instead of five as noted in introduction.]

00:07:00

Speaker Remarks for Ozempic, Rybelsus, Wegovy

Speaker 1 (registered as a healthcare provider)

Declared Conflicts of Interest	
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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

Good afternoon. My name is **[Speaker 1]**. I'm a board-certified internist and primary care physician at **[REDACTED]** Hospital and instructor of medicine and drug policy researcher at **[REDACTED]**, and a former fellow at the Program on Regulation, Therapeutics and Law, or PORTAL. Thanks for the opportunity to join this Town Hall. I just want to clarify that the views expressed here today are my own, and not those of any organization or the federal government.

Recently, one of my patients with diabetes, let's call him Jack, came to the clinic. Jack has a Medicare Advantage Plan. While reviewing his medication list, we talked about his Lantus glargine insulin, metformin, and I asked him about Ozempic, which we had started recently. 'How are you tolerating this injection?' I asked. He replied, 'When I went to CVS, it was $500.' Pin drop silence. I bit my lip, squinted my eyes, nodded gently, looked him right in the eye, and shook my head. Jack and his wife live on a fixed income, $2,500 per month from Social Security. He continued, 'I don't mind $35 of insulin, but $500 is way too much. They want to make money from retired people. I paid taxes for 30 years, and what do I get from this?' I empathized with him, and I told him I would try my best to help. Ozempic had the potential to help him lose weight and lower his blood sugar, and we had unsuccessfully tried Jardiance, because of it, due to a side effect. His remaining options were more insulin, both short- and long-acting, tirzepatide, just as expensive and would have likely lowered his A1C a little bit further, or to apply for a patient assistance program for semaglutide. He really wanted to try semaglutide first, so we spent ten minutes during my lunch break completing the paperwork for the patient assistance program. There are patients with Medicare who cannot afford Ozempic and the high out-of-pocket cost, particularly in the deductible phase of Medicare Part D, are too high.

In contrast, my patients with Medicaid here in Massachusetts, MassHealth, do not face these challenges. They pay less than $4 out of pocket for the same exact Ozempic. CMS should consider the five following principles when negotiating for drug prices for semaglutide.

Number one, public funding played a role in the discovery of semaglutide. The basic science behind GLP-1s [glucagon-like peptide] and its role in insulin secretion, which was co-discovered by Dr. **[REDACTED]** here at **[REDACTED]**, was done so with NIH support. Number two, the semaglutide patents, most semaglutide patents are for the device, and not for the drug. An analysis by Dr. **[REDACTED]** and my colleagues showed that 21 of the 25 patents listed in the FDA Orange Book for Ozempic focus on the delivery device, not semaglutide itself, and this will further delay generic competition. Number three, manufacturing costs are quite low, less the estimated cost to produce an injectable semaglutide is about $3.40 for a month, and about $2 for oral semaglutide, and that's from research by Dr. **[REDACTED]**and colleagues. Number four, semaglutide prices internationally are around $90 or less. A one-month supply of Ozempic is $83 in France, $87 in Australia, and while, and about $69 for oral semaglutide in Japan. That's based on a KFF-Peterson Health Analysis. And finally, negotiated prices during round one remained high. I applaud CMS' efforts for taking this first important step as a proof of concept. And an analysis by Dr. **[REDACTED]** and Dr. **[REDACTED]** showed that negotiating prices for the first ten drugs were about three to five times higher than France or Australia, except for insulin.

My patient Jack, and millions of others, are counting on Medicare to deliver significant savings at the pharmacy counter. And negotiating lower drug prices that translate to lower out-of-pocket costs will make an enormous difference in their lives. Thank you so much.

00:11:24

Moderator, PhD, RTI International

Thank you. The second speaker is **[Speaker 2]**. This speaker has indicated that there is no conflict of interest.

00:11:33

Speaker 2 (registered as a healthcare provider)

Declared Conflicts of Interest	
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Hello, good morning. MyMy name is **[Speaker 2]**. I am an endocrinologist and obesity specialist in **[REDACTED]**, and I will also say that these are my views, and not of any organization or the government.

I'm here today as a physician to urge Medicare to expand coverage to semaglutide, better known as Ozempic, Rybelsus, and Wegovy, for the treatment of obesity and type 2 diabetes. These medications are not just glucose control and weight loss, they are disease-modifying therapies that reduce the risk of heart attacks, strokes, and death, even in people without diabetes, and this has been demonstrated. One trial in 2023 that was published in the *New England Journal of Medicine* of over 17,000 people showed that Wegovy, or semaglutide, 2.4 milligrams, was able to reduce major cardiovascular events by 20% in individuals with obesity in established heart disease, even without diabetes. In people with type 2 diabetes, the SUSTAIN [Trial to Evaluate Cardiovascular and Other Long- term Outcomes with Semaglutide in Subjects with Type 2 Diabetes] 6 trial and PIONEER [Peptide InnOvatioN for Early diabEtes tReatment] 6 trial for Ozempic and Rybelsus, respectively, showed cardiovascular benefit in individuals with diabetes, specifically. There's other studies showing improvement in chronic pain, obstructive sleep apnea, metabolic dysfunction-associated steatotic liver disease, and they are just an incredible disease modifying treatment. Rybelsus is an oral GLP receptor agonist and is important because there are many older individuals who require oral medications because they have needle phobias or difficulties using injectables due to cognitive impairment or arthritis, and it offers the same therapeutic class and proven benefit in a more accessible form. Obesity is now recognized as a chronic disease, yet Medicare still does not cover these treatments for weight management because of legislation written in 2003.

Before this, we didn't have any of this data. We didn't have the STEP [Semaglutide Treatment Effect in People with Obesity] 1 trial, published in 2021 showing that with Wegovy, you could lose 15% of your body weight, and many more achieving more than 20%. And with this improvement, you can improve blood sugars, blood pressure, sleep apnea, mobility, chronic pain, and quality of life, especially in the Medicare population. I see this in my practice every day. I care for older adults with obesity and type 2 diabetes who are on multiple medications living with these complications, living with heart failure, with neuropathy, with cardiovascular disease, and many are not able to take other obesity medications. And semaglutide may be the safest, most effective option, but it is not affordable without Medicare coverage. These medications are cost-effective, they reduce long-term complications, like insulin dependence, hospitalizations, and dialysis. And covering semaglutide isn't just clinically right, it's fiscally smart.

And finally, this is an equity issue. Many private insurers and state Medicaid plans now cover Wegovy, but Medicare beneficiaries who are older, sicker, and more vulnerable are left behind. I urge Medicare to modernize its policies and cover all FDA-approved forms of semaglutide, including oral Rybelsus, to improve care, reduce disparities, and save lives. Thank you for letting me speak today.

00:14:53

Moderator, PhD, RTI International

Thank you. The third speaker is **[Speaker 3]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

00:15:04

Speaker 3 (registered as a representative of a patient advocacy organization)

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Thank you for the opportunity to speak today on behalf of the Obesity Action Coalition. OAC is the leading national nonprofit dedicated to improving the lives of individuals living with obesity through awareness, education, advocacy, and support. Our mission is rooted in ensuring that everyone living with obesity is treated with respect and has access to effective and evidence-based care.

One of the most pressing concerns we hear from our more than 85,000 members across the country is the lack of coverage and affordable access to FDA-approved obesity medications, especially GLP-1 therapies like semaglutide. The brand name product Wegovy is approved for the treatment of obesity and cardiovascular disease risk reduction, as previously mentioned, in those living with obesity. However, the CVD indication is the only indication with coverage under CMS today.

These treatments can be truly transformative, helping people improve their mobility, reduce pain, manage chronic additions, and regain quality of life. But for too many patients, the cost is simply out of reach. We hear heartbreaking stories weekly. An OAC member battling several chronic conditions was recently denied coverage under Medicare despite needing obesity management to improve their health. Another member, 73 years old and on a fixed income, told us he could manage a couple hundred dollars a month, but not over a thousand, the current out-of-pocket price without coverage.

OAC's most recent membership survey found that 42% of people with obesity identify lack of pharmacy benefit coverage as a top barrier to treatment. High copays and deductibles are compounding this problem with many patients forced to make impossible choices between their health and financial stability. We cannot ignore this problem any longer. Affordability is not optional, it is essential. Obesity is a chronic progressive disease like diabetes, heart disease, or cancer. It requires long-term, consistent management. Yet the newest and most effective obesity medications remain inaccessible to those who need them most, because they are either excluded from coverage, approved for narrow indications, or simply priced beyond reach.

We strongly support CMS' Drug Price Negotiation process to address affordability, and CMS' continued consideration to reinterpret the Medicare Part D exclusion and allow coverage of obesity

medications. No one should be denied treatment simply because they can't afford it. Obesity care must be evidence-based and financially accessible for all. Thank you so much.

00:18:00

Moderator, PhD, RTI International

Thank you for your insights. The fourth speaker is **[Speaker 4]**. This speaker has indicated that there is no conflict of interest.

00:18:22

Speaker 4 (registered as a healthcare provider)

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Good morning, CMS. Thank you for giving me the opportunity to speak on Ozempic this morning. I am Dr. **[Speaker 4]**, a practicing rheumatologist in **[REDACTED]** California, also a **[REDACTED]** of the Arthritis Foundation, as well as the Alliance for Patient Access.

As a rheumatologist, I'm keenly aware of the impact obesity has on patients with arthritis. Arthritis is the leading cause of disability in the United States, and osteoarthritis is the most common type of arthritis. Over 70% of osteoarthritis cases can be directly linked to obesity. Studies have shown that a mere 5-10% loss in weight can reduce pain in these patients by over 50%. Weight loss has been shown to decrease progression of disease. In addition to chronic pain, and disability, ultimately, osteoarthritis leads to costly joint replacement. All of this would be avoidable if the incidence of obesity declined in the U.S. through use of semaglutides.

In addition, several studies in unrelated diseases, like rheumatoid arthritis, have shown that obesity not only complicates their treatment, but worsens their prognosis. In my own clinic, I see countless patients with RA [rheumatoid arthritis] who are obese, and because of their RA, are unable to get significant exercise to lose weight. These patients then develop osteoarthritis and often decline joint replacements, since it would mean that they would have to discontinue their life-saving biologics. Thus, their conditions deteriorate, and eventually, their RA meds become less effective.

Conversely, I have other patients with psoriatic arthritis, who, because of their obesity, and obesity-related NASH [nonalcoholic steatohepatitis], are unable to take some disease-modifying medications, and therefore get further joint destruction. As the impact obesity has continued to plague seniors in the United States, we have limited choice in therapeutic alternatives in the past. Historically, fenfluramine and phentermine, or fen-phen, was used in this patient population.

However, this was shown to lead to pulmonary hypertension and heart valve disease, which could sometimes be fatal. Despite this, recent innovations, including Ozempic, have shown that the appropriate pharmacological treatment of obesity is possible, and can dramatically improve patients' outcomes.

In addition, these treatments have already shown effectiveness in diabetes, heart disease, as well as ongoing studies in Alzheimer's, sleep apnea, etc. Beyond pharmaceutical options, patients living with obesity and associated comorbid conditions have limited options. Until recently, this consisted of surgical intervention in lieu of pharmaceutical therapy. However, endoscopic sleeve gastroplasty may provide a viable option; however, coverage by health plans has been lacking. When considering costs to a health care system, this cannot be overstated. Ensuring providers, prescribers, and pharmacies can continue to offer all these therapies to patients across disease states is of utmost importance. Thank you for the opportunity to provide comment, and I'm happy to answer any questions. Thank you.

00:21:33

Moderator, PhD, RTI International

Thank you. Thank you for your insights. The fifth speaker is **[Speaker 5]**. The speaker has indicated that there is no conflict of interest.

00:21:45

Speaker 5 (registered as a representative of a patient advocacy organization)

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Thank you. Thank you for the opportunity to share the perspective of the liver disease community. I'm **[Speaker 5]**, **[REDACTED]** of the Community Liver Alliance, which advocates on behalf of patients, clinicians, and researchers working to combat liver disease across the U.S.

Liver disease is a growing, often overlooked, public health crisis. It ranks among the top ten cause of death in the U.S. and is the second leading cause of years of life lost in Americans ages 25 to 49, yet still remains vastly underdiagnosed, especially in older adults, rural areas, and communities of color. The most common, MASH [metabolic dysfunction-associated steatohepatitis] and MASLD [metabolic dysfunction-associated steatotic liver disease], as obesity-related diseases, the most common liver disease today, metabolic dysfunction-associated steatotic liver disease, or MASLD, and its more severe form, MASH, is directly linked to obesity, type 2 diabetes, and cardiovascular

disease. These conditions affect more than one in three adults, and are fueling rising rates of cirrhosis, liver cancer, and transplants. But despite this, patients have long faced a treatment void. The recent FDA approval of Madrigal Pharmaceuticals' Rezdiffra marks a breakthrough, but it's just the beginning. We need access to multiple therapies that address different stages of disease and patient needs.

Semaglutide's promise for MASH, the GLP-1 receptor agonist, like semaglutide, offers significant promise in liver care. Though approved for diabetes and obesity, semaglutide is now cited in the 2023 American Association for the Study of Liver Disease guidelines for MASH and listed in the DrugDex Part D compendium, meeting CMS criteria for relevant off-label use. Providers increasingly use semaglutide to treat patients with overlapping obesity, diabetes, and liver diseases. These drugs not only reduce liver inflammation and fibrosis but also improve metabolic markers and weight, critical to preventing disease progression.

I have a couple of real-world impact statements from both a patient and a provider. I'd like to read to you an excerpt from a patient. 'My enzymes dropped, my A1C is down, I've lost weight, I finally feel hopeful again.' Patients also reported decreased cravings for alcohol, an unexpected but important benefit for those with co-occurring behavioral health challenges. And from one hepatologist, she mentioned, 'For the first time, I can intervene early in MASH with therapies that target the root cause.' So, these GLP-1 therapies are delivering whole-person benefits, affecting physical and behavioral health together. These results translate to fewer hospitalizations, reduced transplant demand, and lower long-term health care costs, especially for the Medicaid population. Limiting access to semaglutide now due to early price setting would jeopardize future research for expanded indications.

CMS must consider not just current approval status, but clinical utility and real-world value. And the burden of liver disease is highest in the Medicaid, Medicare-aged adults, rural communities, and minority populations. Those who often have the least access to specialty care. If innovation therapies aren't accessible through Medicare Part D, these patients will be left behind again. Semaglutide has the potential to close a critical treatment gap. It must be considered part of the solution for liver- and obesity-related diseases. And we know that Senator John Fetterman recently credited GLP-1s for improving his mental clarity, health, and confidence, saying it made him feel a decade younger. We have sources for this public statement. And another public statement was made by Elon Musk, praising GLP-1s, saying nothing would do more to improve health, lifespan, and quality of life for Americans.

So, on behalf of the liver community, we urge CMS to ensure price negotiation decisions protect patients' access and support innovation, not just for today's approvals, but for the future of public health. Thank you.

00:26:25

Moderator, PhD, RTI International

Thank you. The sixth speaker is **[Speaker 6]**. This speaker has indicated that there is no conflict of interest.

00:26:41

Speaker 6 (registered as a healthcare provider)

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Hi. Good morning, everyone. I am a physician who works as a primary care physician. I also do clinical research in these medications, GLPs. My name is Dr. **[Speaker 6]**. I'm a primary care physician in California. I also do clinical research, and I've been doing research on this GLP class for over six years. And the other speakers have already made excellent points that I don't want to duplicate. I wanted to mention just a few other points. One is, again, I want to emphasize the long-term benefit of semaglutides in all of its forms, oral and injectable. But I think what hasn't been mentioned is how it helps us as physicians with our limited time. I'm sorry, is there?

With our limited time we have very little chance to... Sorry there's, I'm going to pause and then pause. Something with my audio. So I...

00:28:10

Moderator, PhD, RTI International

[Speaker 6], you need to turn off the livestream, because there's a delay, and so we're hearing the livestream and your comments at the same time.

00:28:18

Speaker 6 (registered as a healthcare provider)

How do I turn off the livestream? Is that any better?

00:28:33

Moderator, PhD, RTI International

Yes. Go ahead.

00:28:42

Speaker 6 (registered as a healthcare provider)

Can you hear me better now?

00:28:44

Moderator, PhD, RTI International

Yes, we can.

00:28:52

Speaker 6 (registered as a healthcare provider)

Okay, great. So again, sorry about that. Dr. **[Speaker 6]**, primary care physician, researcher, have been doing GLP research for over five years, five or six years now. Excellent points have already been made. I wanted to make a few other points. One, primary care physicians really need this drug because the Medicare population has so many diseases that can be treated with one drug. We've heard about the importance of treating obesity, we all know the importance of treating diabetes, we all know that treating liver disease is very important. But when you give a primary care physician ten minutes to speak about all of this and try to address every single one, we have now a wonderful drug that can do all of that, that a primary care physician can talk about that, give one drug, and treat everything. Otherwise, that would be three, four, five visits. So, I think that needs to be emphasized.

I think the other thing that needs to be emphasized is the data that is coming in about how many conditions this drug may be able to treat. As a researcher, you've heard about how rheumatologic diseases may improve, autoimmune skin diseases may improve, and neurologists have seen a decrease of severity of autoimmune neurologic conditions. So, I think it's extremely important for us to be able to have this drug as clinicians to help our Medicare population. Thank you.

00:30:34

Moderator, PhD, RTI International

Thank you. Thank you all for sharing your experience and perspectives about Ozempic, Rybelsus, and Wegovy. I have one follow-up question for you all. Can you talk more about the main benefits or main drawbacks of Ozempic, Rybelsus, and Wegovy based on your experience or understanding? Please raise your hand, and we will take the first respondent. We have just a minute for your brief response. **[Speaker 5]**, go ahead.

00:31:13

Speaker 5 (registered as a representative of a patient advocacy organization)

Thank you. When we think about the opportunity for liver patients to access this important therapy, we know that this is a game changer. It's not just about out the economics, but the health of communities. And we know that if access can be gained for patients, that we can create a healthier society and reduce the burden of obesity-related diseases across our nation.

00:31:46

Moderator, PhD, RTI International

All right. We have about 30 seconds if anybody else wants to follow up.

00:32:03

Speaker 5 (registered as a representative of a patient advocacy organization)

Somebody asked for the question to be repeated.

00:32:07

Moderator, PhD, RTI International

The question was, can you talk more about the main benefits or main drawbacks of Ozempic, Rybelsus and Wegovy based on your experience or understanding. Go ahead, **[Speaker 4]**. We just have a few seconds left.

00:32:30

Speaker 4 (registered as a healthcare provider)

It affects other diseases beyond obesity. Like I mentioned before, arthritis, which is a leading cause of disability. And I think also, in terms of obesity as a disease entity, I think the sooner it becomes recognized as a disease, there'll be less pushback by health plans to not cover as it is today.

00:32:57

Speaker Remarks for Janumet; Janumet XR

Moderator, PhD, RTI International

All right, thank you. We will now move on to Janumet and Janumet XR with four speakers. Janumet and Janumet XR are commonly used to treat type 2 diabetes. The first speaker is **[Speaker 1]**. The speaker has indicated that there is no conflict of interest.

00:33:23

Speaker 1 (registered as a healthcare provider)

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Can you hear me?

00:33:26

Moderator, PhD, RTI International

Yes, we can.

00:33:27

Speaker 1 (registered as a healthcare provider)

Hi, my name is **[Speaker 1]**, and I'm the **[REDACTED]** at CHI St. Alexius, and I would like to start this presentation with the line, Janumet XR, supporting safe, simple diabetic care for those who need it most.

So, introduction. Janumet XR is a prescription medicine that contains two prescription diabetes medicines, that is, sitagliptin and extended-release metformin, hydrochloride. Janumet XR can be used along with diet and exercise to lower blood sugar in adults with type 2 diabetes, and the manufacturer is Merck. It's widely prescribed to Medicare Part D enrollees. And I would like to read out one of the lines said by a patient saying, 'I like Janumet XR is just once a day. It fits better with my routine, and I don't have to worry about forgetting a second dose, like I did with regular metformin.' So, the treatment goals and outcomes to assess the improvement, or the primary goals includes, reduce HbA1c levels to individualized targets, achieve glycemic control with minimal side effects, especially hypoglycemia, and minimize risk of macrovascular and microvascular complications.

Janumet XR is preferred in patients needing combination therapy in a single pill, enhancing their adherence. And the outcomes monitored are HbA1c reductions over 3- to 6-month periods, fasting and postprandial glucose levels, adverse events including incidents, particularly hypoglycemia and GI [gastrointestinal] side effects, renal function, and cardiovascular outcomes, if applicable. So, the consideration driving treatment choice for Janumet XR includes indications used for managing type 2 diabetes when lifestyle changes alone are insufficient, and dual mechanism of action combine sitagliptin DPP-4 [dipeptidyl peptidase] inhibitor and metformin, which is a biguanide, to lower blood glucose by increasing insulin secretion and improving insulin sensitivity.

Convenience. It's a once-daily extended-release formulation, improves patient adherence, and reduces gastrointestinal side effects compared to immediate-release metformin. Renal and cardiovascular safety. Suitable for patients with moderate renal impairment and has neutral positive effects on cardiovascular health. Weight management. Weight neutral or modest weight loss benefits, making it suitable for overweight or obese patients. Patient considerations. Ideal for those needing comprehensive blood sugar control with minimal side effects and improved patient compliance. This combination therapy offers convenience, efficacy, and safety, particularly for patients with cardiovascular risk or moderate renal issues.

And the unmet medical needs addressed or not addressed. The addressed medical needs are needs for patients requiring stronger glucose control than monotherapy, simpler regimens for patients on polypharmacy, reducing hypoglycemia risk compared to sulfonylureas or insulin. And it doesn't address need for cardiovascular event reduction, need for weight loss therapy, and affordability challenges due to lack of generics.

And other key information CMS should consider is patent life still limits competition, affecting affordability. Renal considerations are critical, dosing must be adjusted or avoided in severe CKD [chronic kidney disease]. Therapeutic role, important but ideal for patients needing combination therapy without moving to injectables or more expensive, newer classes. Clinical flexibility, important for oldest, complex Medicare population. And patient perspectives, preference for fewer pills, lower risk of hypoglycemia, and minimum daily. And final thoughts for CMS consideration are, it's a simple, once-daily oral option combining two proven agents to improve adherence and glycemic control in type 2 diabetes, and it's especially beneficial for older adults and patients needing combination therapy without moving to complex regimens. Thank you.

00:37:25

Moderator, PhD, RTI International

Thank you. The second speaker is **[Speaker 2]**. This speaker has indicated that there is no conflict of interest.

00:37:34

Speaker 2 (registered as a healthcare provider)

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Hello again. Thank you for letting me speak today. And again, I have no disclosures. And these are my views. But I'm here to talk about Janumet. Specifically, this is metformin and sitagliptin, as just described. Specifically, though, the extended-release version. And I'm going to speak on behalf of my patients. Particularly, the older patients with type 2 diabetes who rely on combination medications such as this because of the single tablets and the increased adherence to therapy. They're already on a bunch of different medications. These medications, specifically metformin and sitagliptin, are effective, well-tolerated, and affordable options that many of my patients use to maintain blood sugar control without the risk of low blood sugar, and without weight gain, and those are two important, important factors in the disease process that is diabetes. They also reduce the number of pills that my patients have to take, which is no small thing in this population living with many different chronic diseases. So sitagliptin, specifically, works by enhancing the body's ability to lower blood pressure. It is weight neutral, it doesn't cause hypoglycemia, and it is safe in older adults. And there is even some formulations where it's safe to use in kidney disease with proper dosing, or at any dose, depending on which one you're using. Metformin, of course, we've had around for a very long time, and it remains the first-line therapy for type 2 diabetes because of its effectiveness, its low cost, its potential cardiovascular benefit.

A meta-analysis within the last five years looked at 700,000 individuals living with type 2 diabetes and noted that metformin reduced the risk of mortality by 56% and reduced adverse cardiovascular outcomes by 27% in those treated with metformin compared to those without. The extended-release version, specifically, it improves the ability for them to take it, it decreases those GI issues that somewhere between 10 and 30% of people experience when they first start metformin. And by combining these two medications, you're able to not only decrease their side effects, you're able to increase adherence and you're able to improve blood glucose control with one pill that they can take once a day. So, it's not just convenience, it has clinical impact. Patients are more likely to take

these meds consistently, leading to better blood sugar control and fewer complications. And we have evidence showing this. So, in a pooled analysis of multiple, randomized controlled trials, it showed that Janumet was able to improve the hemoglobin A1C by up to 2% with low rates of side effects and no weight gain. These agents are well studied in older adults, and the safety profile of sitagliptin has remained excellent over decades of use.

I also want to briefly speak on access and equity. While we have newer medications, we just spoke on semaglutide, the GLP and the SGLT2 [sodium-glucose co-transporter] inhibitors are well, they're very effective, but they're not appropriate for everyone. There are some people who cannot tolerate them for many different issues, whether it is cost or another end organ effect that they are living with. So, we need to have a larger arsenal. We need to have medications that we can choose, based on the patient themselves and their comorbidities.

Janumet is often the most clinically appropriate and affordable option, and it's important for those who manage multiple medications due to dementia, arthritis, and vision issues. Losing coverage or placing this medication in a higher cost-sharing tier would disappropriately affect the most vulnerable patients, those with the limited incomes, the complex health needs. We need to reduce their pill burden. We need to improve their adherence and avoid implications like amputations, blindness, and kidney failure in these individuals. I urge CMS to continue supporting coverage of Janumet and Janumet XR, specifically, as vital components of evidence-based, patient-centered diabetes care for Medicare beneficiaries. Thank you.

00:41:55

Moderator, PhD, RTI International

Great. Thank you. The third speaker is **[Speaker 3]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

00:42:10

Speaker 3 (registered as a healthcare provider)

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Thank you. Hi, everyone. Good afternoon, my name **[Speaker 3]**. I'm a board-certified internist at **[REDACTED]** Hospital and instructor of medicine at **[REDACTED]**, studied drug policy research and a former fellow at the Program on Regulation, Therapeutics and Law, or PORTAL. Just want to clarify, my views today are my own and not that of any other organization or the federal government.

Just want to make few quick points about Janumet. As we all know, a combination of sitagliptin and metformin and, the first point is that it is less effective than other drugs at treating diabetes on the outcomes that matter most. And in particular, both SGLT2 inhibitors and GLP-1 receptor agonists are more effective when it comes to improving cardiovascular outcomes. For some drugs, reducing all-cause mortality and reducing the progression of chronic kidney disease. I think this is really important, because when I'm making a decision to prescribe a drug or offer it to a patient with diabetes, I would prefer to prescribe the most effective drug that can help prolong their life and improve their quality of life. And this is also consistent with the clinical guidelines.

The second point to make here is that I reserve prescribing of Janumet for four specific scenarios One of which is the patient can't tolerate the side effects of other, more effective therapies that we just talked about. Two, the patient has a contraindication for prescribing other, more effective therapies. Three, the patient has been on this medication, historically, they've been on Janumet historically, they like it, they're tolerating it well as a once-a-day option, they don't have any side effects, they're affording it well, we'll just continue them on that medication. And finally, Janumet also is really a good option for patients who are not interested in an injectable medicine, who want a once-a-day, oral option.

Definitely agree with some of my colleagues who spoke earlier, that the extended-release version is much more preferred. There's a lot of pharmacoepidemiologic research that shows that daily use of medicines improves ability to take them regularly. So, I almost never prescribe the twice-a-day option. And a few additional points. [T]here's a recent survey of 1,000 registered voters that was commissioned by Arnold Ventures and conducted by Fabrizio Ward just a couple months ago that found that about 86% of Americans support Medicare to not pay more than what other countries pay for similar drugs. And as I mentioned in my previous remarks, Medicare has done a great job in this first round when it comes to proof of concept of negotiating drug prices, but the Part D drugs still, negotiated prices are still about three to five times higher than they are in France and Australia.

And one piece of information to direct the team's attention to is that, in 2021 the GAO [Government Accountability Office] wrote a report on prescription drugs that compared average U.S. prices to prices in Australia, Canada, and France. And the good news is that the report specifically lists the price of Janumet XR, the 1,050-milligram combination pill, and in Australia in 2020, the cost was $40 per package, and it was $90 per package in Ontario, Canada. So, I encourage the CMS team to keep this in mind when they're negotiating the prices. Also, if you look at Pharmacy Checker, which is an online website that tries to validate reputable, international pharmacies, and you type in Janumet XR, you'll find that there are drugs available internationally kind of in a similar range, $50-100 for a one-month supply. Thanks so much for the opportunity to share remarks.

00:46:07

Moderator, PhD, RTI International

Thank you for your insights. The fourth speaker is **[Speaker 4].** This speaker disclosed a potential conflict of interest, as shown on the slide.

00:46:19

Speaker 4 (registered as a representative of a patient advocacy organization)

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Hello. My name is **[Speaker 4]**. I am **[REDACTED]** of the National Forum for Heart Disease and Stroke Prevention, which is a coalition of patients, providers, public health, payers, purchasers, and innovators. Janumet is a key therapeutic option for patients managing type 2 diabetes, which remains one of the most significant drivers of cardiovascular disease in the U.S. The burden is especially high among older adults, many of whom rely on Medicare and are navigating multiple chronic conditions. What sets Janumet apart is its combination of sitagliptin and metformin in a single daily pill, which supports better medication adherence, a critical factor in preventing complications, such as heart disease, hypertension, and stroke. For many patients, taking one medication instead of two dramatically improves their ability to stay on track with the treatment.

In 2015 the landmark Teco's trial, published in the *New England Journal [of Medicine]*, studied over 14,000 patients with type 2 diabetes and existing cardiovascular disease. It found that sitagliptin did not increase the risk of major adverse cardiovascular events or hospitalization for heart failure. These results confirmed the cardiovascular safety of DPP-4 inhibitors like sitagliptin, offering clinicians reassurance when treating patients at high cardiovascular risk.

Despite its clinical value, Janumet's cost remains a significant barrier for many patients. When coverage is denied or cost-sharing is too high, patients are often forced to take metformin and sitagliptin as two separate pills, or worse, to skip one or both medications entirely. This fragmentation of treatment increases the likelihood of non-adherence, particularly in older adults who are managing multiple medications. The consequences of this are serious.

A 2023 population-based cohort study published in *Therapeutic Advances in Chronic Disease* found that adherence to metformin alone was associated with reduced hospitalization for myocardial infarction and stroke, clearly illustrating that staying on therapy makes a measurable difference in cardiovascular outcomes. The implication is clear. When patients can access and afford combination therapies like Janumet, they're more likely to stay adherent, avoid complications, and reduce long-term costs to taxpayers.

Our recommendations to CMS are first, promote affordable access to combination medications that simplify treatment and support medication adherence, especially for Medicare beneficiaries at risk of cardiovascular disease. Second, ensure cost-sharing structures do not penalize patients for

choosing combination therapies with adherence benefits. And third, recognize and reward therapies that deliver long-term value by preventing heart attacks, strokes, and other costly complications of poorly managed diabetes.

In closing, we urge CMS to take a holistic view of diabetes care. One to prioritize is access to medications like Janumet, which simplify treatment, improve outcomes, and reduce the burden of cardiovascular disease. By doing so, we can advance both fair access to care and efficiency in Medicare.

00:50:01

Moderator, PhD, RTI International

Thank you and thank you all for sharing your experiences and perspectives about Janumet and Janumet XR. I have one follow-up question for you all. Can you briefly address how the benefits and drawbacks of Janumet and Janumet XR compare to other medications taken to treat type 2 diabetes based on your experience or understanding? Please raise your hand to respond. We have just a minute for your brief response.

[Speaker 2], go ahead.

00:50:40

Speaker 2 (registered as a healthcare provider)

So, metformin has been around the longest, so we have the most data on it, both for efficacy and safety. And patients tolerate it. There is a large portion, 10 to 30% can have symptoms but they usually resolve. It is not the most effective. The GLP-1s, semaglutide, tirzepatide, those ones are more effective for weight loss and for blood glucose control, but Janumet is an incredible option that can improve A1Cs by over two percent and do not cause hypoglycemia.

00:51:21

Moderator, PhD, RTI International

All right, and we have a few seconds, **[Speaker 4]**, if you want to add to it.

00:51:27

Speaker 4 (registered as a representative of a patient advocacy organization)

Thank you, **[MODERATOR]**. Yeah. As C. Everett Koop told us, the best medications only work when people take them. And one of the great advantages of Janumet as a combination medication is that it is shown to improve adherence, and we know that improving medication adherence is kind of the holy grail in treatment. So, even if other options are superior in terms of clinical efficacy, if people aren't taking them, then they're of limited benefit both to the patient and to society. So, not to suggest that they are less beneficial or we should take those away, but I think it does underscore the value of Janumet.

00:52:11

Speaker Remarks for Tradjenta

Moderator, PhD, RTI International

Great! Thank you. We will now move on to Tradjenta with three speakers. Tradjenta is commonly used to treat type 2 diabetes. And the first speaker is **[Speaker 1]**. This speaker has indicated that there is no conflict of interest.

00:52:32

Speaker 1 (registered as a healthcare provider)

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Hello, everyone. My name is **[Speaker 1]**, and I'm the **[REDACTED]** at CHI St. Alexius Garrison. And let's start with the introduction of Tradjenta. So, Tradjenta, which is linagliptin, is a DPP-4 inhibitor used in the management of type 2 diabetes. It works by increasing insulin secretion and decreasing glucose production in the liver in response to meals. Unlike other DPP-4 inhibitors, Tradjenta does not require dosage adjustments in patients with renal impairment, making it a convenient option for individuals with kidney issues. It's typically used alone or in combination with other diabetes medicines like metformin to include the glycemic control.

So, the real-world experience with Tradjenta. Tradjenta has made a real difference for many patients who struggle to manage type 2 diabetes alongside other serious health issues, especially kidney disease and aging-related challenges. As a health care provider, I have spoken with individuals who finally found some stability in their treatment after switching to Tradjenta. One of the most important things I have heard is this, it's simple, and it works for me. That matters. People who are on multiple medications or who are worried about the side effects need something that won't complicate their daily lives. This ease of use and once-daily oral administration increases patients' adherence. Clinicians also value Tradjenta's low risk of hypoglycemia, particularly in older adults.

The treatment goals and assessment of outcomes. The primary treatment goals for type 2 diabetes include reducing HbA1c, maintaining glycemic control without significant hypoglycemia, minimizing long-term complications. Outcomes used to assess effectiveness. HbA1c measurements, fasting and postprandial glucose levels, adverse event profiles, cardiovascular outcomes, renal function markers. Considerations in treatment choice. Tradjenta versus alternatives. Clinicians consider several factors when they are selecting a therapy. The first one is renal safety. Tradjenta is unique among DPP-4 inhibitors for not requiring dose adjustment in renal impairment. Tolerability. It's generally well-tolerated, and once-daily oral using drug and no need for blood glucose monitoring with monotherapy and in older adults and patients with polypharmacy, benefits from simpler regimens.

Therapeutic advancement compared to other alternatives. While Tradjenta does not represent a significant therapeutic advance over other oral agents in glycemic control efficacy, it offers safety

and convenience benefits for certain populations, like unique renal dosing profile patients comparable efficacy to other DPP-4s, no superiority in cardiovascular outcomes compared to GLP- or SGLT2 inhibitors, which now offer cardiovascular and renal protection. Thus, Tradjenta is more of a therapeutic agent rather than a groundbreaking advancement.

And unmet medical needs address or not addressed. Tradjenta helps to meet the needs of patients with moderate to severe CKD who cannot use metformin, elderly patients at high risk of hypoglycemia, and those needing simpler, once-daily therapy with good safety, but it does not fully address unmet needs around cardiovascular protection, weight loss, or obesity management using insulin dependency in complex cases.

Final thoughts for CMS consideration is Tradjenta remains relevant in specific clinical populations, even if it is not the most innovative therapy on the market. Any pricing decision should reflect its safety profile and unique use case especially among older adults, and inclusion in formularies should be maintained to preserve clinical flexibility. And other relevant information for CMS is [inaudible], making cost a key factor in formulary decisions. Alternatives such as alogliptin and sitagliptin are similar but have renal dose adjustment. While Tradjenta may not be the first line agent, its tolerability, safety, and renal dysfunction, and simplicity offers sustained value, especially in vulnerable Medicare populations. Thank you.

00:56:40

Moderator, PhD, RTI International

Thank you. The second speaker is **[Speaker 2]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

[Speaker 2], are you there? Okay, we will move to the next speaker. The next speaker is **[Speaker 3]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

00:57:29

Speaker 3 (registered as a representative of a patient advocacy organization)

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Hi. I'm **[Speaker 3]**, **[REDACTED]** of The National Forum for Heart Disease and Stroke Prevention, which is a coalition of patients, providers, payers, purchasers, and innovators. Tradjenta plays an important role in managing type 2 diabetes, a leading contributor to cardiovascular disease. Adults with diabetes are twice as likely to experience heart disease or stroke, and cardiovascular

complications remain the number one cause of death in this population. That's why access to effective glucose lowering therapies with a favorable, cardiovascular safety profile is critical.

Tradjenta is especially notable, because unlike many medications in its class, it is renal-friendly. That's a crucial distinction for Medicare beneficiaries, who often have both diabetes and chronic kidney disease. The Carmelina trial, published in JAMA [*Journal of the American Medical Association*], examined over 6,900 patients with type 2 diabetes and high cardiovascular and renal risk, and it found that linagliptin did not increase the risk of major cardiovascular events, a reassuring find for treating complex patients.

In short, Tradjenta offers a safe, evidence-based option that addresses both blood sugar control and cardiovascular risk, particularly in older adults with comorbidities. Unfortunately, access to Tradjenta is not guaranteed. Many patients face significant barriers due to high out-of-pocket costs and formulary exclusions under Medicare. This forces some patients to delay or forego treatment altogether despite the clear clinical benefit. Without affordable access, patients face a higher risk of serious complications, including heart attacks, strokes, and hospitalization. These aren't just personal tragedies. They are also avoidable costs to taxpayers.

As highlighted by Taylor in 2020, the rising cost of diabetes drugs disproportionately affects low income and elderly populations, deepening health gaps between different groups of Americans and driving preventable hospitalizations. Our recommendations to CMS are three. First, ensure uninterrupted access to medications like Tradjenta for patients at elevated cardiovascular risk, particularly Medicare beneficiaries managing multiple chronic conditions. Second, address cost-related non-adherence by reducing patient cost-sharing for essential medications that prevent long-term complications. And third, incentivize access to dual-benefit therapies, those that support both diabetes and cardiovascular health when assessing formulary coverage and negotiating prices.

In closing, we urge CMS to center real patient needs, especially those of older adults in underserved communities when evaluating coverage for life-sustaining therapies like Tradjenta. A fair prevention-focused approach can improve outcomes and reduce long-term health care costs. Thank you for this opportunity.

01:00:56

Moderator, PhD, RTI International

Thank you both for sharing your experiences and perspectives about Tradjenta. I have one follow-up question. What other information or evidence do you think CMS should consider in evaluating Tradjenta? Please raise your hand to respond. We have just a minute for your brief response. **[Speaker 3]** go ahead.

01:01:20

Speaker 3 (registered as a representative of a patient advocacy organization)

I just learned yesterday, **[MODERATOR]**, from the president of the National Kidney Foundation, that renal disease, kidney failure is the fastest growing chronic disease in the United States. We all know that there's a massive cost to Medicare for dialysis and treatment of chronic kidney disease. So. The additional renal benefit within safety profile with this medication is of even added importance.

01:01:58

Speaker Remarks for Pomalyst

Moderator, PhD, RTI International

All right. Thank you very much for your insights. We will now move on to Pomalyst with one speaker. Pomalyst is commonly used to treat Kaposi sarcoma and multiple myeloma. The speaker is **[Speaker 1]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

01:02:24

Speaker 1 (registered as a healthcare provider)

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Thanks, **[MODERATOR]**. My name is **[Speaker 1]**. I'm a practicing hematologist and oncologist in Colorado. I take care of many patients with multiple myeloma. I'm speaking today on behalf of the American Society of Hematology, or ASH. I have a role where I advise ASH about its positions on health care policy. My comments today will focus on the role of pomalidomide or Pomalyst in the treatment of patients with multiple myeloma.

When a patient is diagnosed with multiple myeloma, they go through what is called induction therapy, which consists of multiple drugs given together to induce a remission. Induction therapy is then followed by administration of high-dose chemotherapy and autologous stem cell transplant. But despite this intensive and difficult therapy, the cancer myeloma nearly always returns, and when the myeloma returns, patients undergo a series of treatments one after the other. Often these treatments are successful at inducing a remission again. But then the cancer cells get smart, become resistant to the treatment, and that leads to a relapse of the myeloma. This pattern happens over and over again, and the patients get sicker and sicker, and eventually all these treatments stop working, and many patients eventually die from their myeloma.

When I was training more than 20 years ago, a time when the standard treatment for myeloma consisted of conventional chemotherapy, the median survival of patients with multiple myeloma was only about two or three years. Now, in the modern era we have multiple targeted agents and immunotherapies like pomalidomide available, and the median survival of patients with myeloma is around 10 years, or even more. So clearly, in the last couple of decades we've made incredible progress in the treatment of this disease, although we still almost never cure it.

Pomalidomide is an important component of the arsenal of weapons that has been developed to treat multiple myeloma. Like other drugs used in myeloma, it tends to work better when given in combination, so in practice we tend to give pomalidomide along with other immunotherapy drugs or targeted drugs. Like many new drugs in cancer treatment, pomalidomide is extremely expensive, with a cost of around $25,000 for a 21-day supply, or, roughly, $1,000 per tablet. Because pomalidomide is an important component of this treatment arsenal, it is critical for patients to have access to it. But because it's so expensive, many patients have difficulty affording their own copays and co-insurance for the drug. Many of my patients depend on grant support from either the manufacturer or from other charitable organizations to pay for their treatment.

And when a new year rolls around and the patients' grant assistance has expired, there is often a delay of several weeks in my experience, during which my office staff tries to help patients secure funding for their pomalidomide for the next year. And sometimes during those several weeks, or even a month or two, patients may have to do without their pomalidomide, which, of course, is not ideal. I've also had patients choose to change the scheduled administration from daily treatment to every other day treatment, just in order to save on personal expenses. Patient adherence to pomalidomide, like all medications, is critical and ensuring barriers to access pomalidomide are minimized is in the best interest of the health and welfare of our society. So, thanks for your time and hope this information has been helpful.

01:06:22

Moderator, PhD, RTI International

Thank you, **[Speaker 1]**, for sharing your experiences and perspectives. I have a follow-up question for you. Can you talk more about the main benefits or main drawbacks of Pomalyst based on your experience or understanding?

01:06:34

Speaker 1 (registered as a healthcare provider)

Yeah, the main benefit of it is that it is an effective treatment against myeloma. When a patient with myeloma relapses, it's one of the drugs that they should receive at one point or another. The sequence of treatments in relapsed myeloma can vary from patient to patient and doctor to doctor, but for sure, nearly all patients with relapsed multiple myeloma should at some point be given a trial of pomalidomide.

Its drawbacks are it, like all drugs, has side effects. That's not unique to pomalidomide. It does cause some problems with low blood counts and skin rash sometimes, but really, it's not different than other drugs that we use all the time in the treatment of cancer.

01:07:28

Speaker Remarks for Xifaxan

Moderator, PhD, RTI International

All right. Thank you very much for your time this afternoon. We will now move on to Xifaxan with three speakers. Xifaxan is commonly used to treat hepatic encephalopathy and irritable bowel syndrome with diarrhea. The first speaker is **[Speaker 1]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

01:07:57

Speaker 1 (registered as a healthcare provider)

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Thank you. I am an associate professor of clinical medicine at **[REDACTED]** in **[REDACTED]**, New York, where I also serve as the director of liver quality and inpatient liver services. I will be speaking to Xifaxan's use in the treatment of hepatic encephalopathy. I'm a transplant hepatologist with over 15 years of experience caring for patients with cirrhosis and complications including overt hepatic encephalopathy, or OHE for short. OHE is brain dysfunction that occurs in patients with liver cirrhosis as a consequence of bacterial-derived neurotoxins, such as ammonia, not being removed from the bloodstream in the setting of liver dysfunction. It is manifested by a range of neurologic and psychiatric symptoms.

OHE, overt hepatic encephalopathy, is associated with poor patient survival. The median survival of patients with decompensated cirrhosis, including those who have developed OHE, is one and a half to two years in the absence of liver transplantation. The presence of OHE also markedly reduces patient quality of life, and, importantly, is a major cause of hospital admissions and readmissions among this population.

Xifaxan is a poorly absorbable antibiotic that decreases the burden of bacteria in the intestine, thereby lowering the production of ammonia, allowing for improved neurologic function in the setting of OHE, overt hepatic encephalitis. Xifaxan is the only FDA-approved therapy for OHE and has been demonstrated to reduce the risk of recurrent episodes of OHE and HE-related [hepatic encephalopathy] hospitalization in patients who have previously experienced one or more episodes of overt hepatic encephalopathy, both in clinical trials and real-world settings.

Xifaxan is remarkably safe and well-tolerated. It is an oral medication, and it is safe even in patients with advanced cirrhosis since the vast majority of Xifaxan acts within the intestine and is not absorbed into the bloodstream. Consensus practice guidelines, including those issued by the American Association for the Study of Liver Diseases, strongly recommend Xifaxan in combination with the laxative lactulose for the prevention of recurrent episodes of overt hepatic encephalopathy.

Multiple studies have demonstrated the cost-effectiveness of Xifaxan therapy for OHE, including among Medicare patients. Cost savings on Xifaxan therapy are attributed to lower rates of all-cause and overt hepatic encephalopathy-related hospitalization, which results in lower facility and

professional costs. The average cost per HE hospitalization was estimated to be approximately $50,000 in 2017. Xifaxan plus lactulose dual therapy has been shown to reduce the risk of hepatic encephalopathy-related hospitalization by 50% over a six-month period compared to lactulose by itself.

So, in summary, overt hepatic encephalopathy is a serious complication of liver cirrhosis linked to high hospitalization rates, reduced quality of life, and poor survival. Xifaxan, the only FDA-approved therapy for overt hepatic encephalopathy, is a well-tolerated, cost-effective treatment that significantly reduces recurrent episodes and hospitalizations, making it an essential medication for this population and a key component of evidence-based care recommended by our clinical guidelines.

01:11:57

Moderator, PhD, RTI International

All right. Thank you. The second speaker is **[Speaker 2]**. This speaker has indicated that there is no conflict of interest.

01:12:06

Speaker 2 (registered as an academic researcher; representative of a patient advocacy organization)

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Yeah. Hi, can you hear me okay?

01:12:08

Moderator, PhD, RTI International

Yes, we can.

01:12:09

Speaker 2 (registered as an academic researcher; representative of a patient advocacy organization)

Excellent. I'm **[Speaker 2]** from Public Citizen's Health Research Group. No financial conflicts of interest on this matter. I want to discuss today rifaximin's use for irritable bowel syndrome with diarrhea and specifically, I want to point out that we and others have a number of concerns related

to this that we think CMS should know about. And our day-to-day at Public Citizen is to educate consumers and others about concerns with regard to medicine, so we think this should be helpful in terms of coming to a fair price for this medication.

There are alternatives to rifaximin for this indication. Loperamide and bile acid sequestrants come to mind, specifically a randomized, controlled trial supporting those alternatives. We were not able to identify any studies comparing rifaximin to other medications for irritable bowel syndrome with diabetes. So, there's a dearth of head-to-head randomized control trials in order to do that. But there is a systematic review and a network meta-analysis published in 2020 by Black and colleagues that found that rifaximin was no better than placebo for the global symptoms of IBS [irritable bowel syndrome] or for abdominal pain, specifically.

All the way back to 2017, my research group at Public Citizen actually rated rifaximin as a do not use drug because we simply think that the risks do not exceed the benefits, so that should have bearing on the price for sure. Why pay for something if it really doesn't compete well and doesn't offer benefits over risks the way that you would want with the medicine. And of course, all medicines have risks. There is clinical trials data out there, evidence from the so-called targets one through three trials, comparing rifaximin to placebo and showing some slight release, improvement of symptoms, but because they were such short-term, the FDA all the way back in 2011 rejected initial approval of rifaximin, and the agency requested the manufacture to provide additional data to support the drug's effectiveness for this indication.

Thus came the target three trials, which evaluated again only for 14 days, but sequential exposure separated by 10 weeks in adults, again with IBS with diarrhea. And, after the second 14 days were repeated, the symptoms recurred. This was a fairly large trial but nearly two-thirds of the subjects actually had recurring symptoms. So, some questions about its durability of effect for sure.

Rifaximin can alter balance and bacteria in the intestine, one of the biggest concerns that we have about this. For example, in the target three trial there were high incidence of influenza and bronchitis in rifaximin compared to placebo. Concerns about developing antibiotic resistance carry with this medication and should be considered in pricing it. And there's concerns about even very serious infections like *C. diff* with this medicine. Also concerns about risk of liver damage, and it may be associated per the label with muscle pain and spasms as well. And elevated creatine phosphokyinase blood levels as well, suggesting potentially some muscle degradation that comports with the use of this. Serious allergic reactions as well.

So overall, we think if CMS wants to make this medicine available, certainly the price seems absurd. It's like over $2,000. I was looking at The Medical Letter today compared to other drugs that treat the same indication that seems absurd and ridiculous. International reference pricing and manufacturing, accounting, and stuff certainly would be important to negotiating a fair price, but overall, we feel that this drug just isn't worth very much, the willingness to pay for the health care system and certainly for consumers, is not very high, and that should be considered too. So, happy to take questions. Thank you very much.

01:16:54

Moderator, PhD, RTI International

Thank you. The third speaker is **[Speaker 3]**. This speaker has indicated that there is no conflict of interest.

01:17:03

Speaker 3 (registered as a representative of a patient advocacy organization)

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Hi. Good afternoon. My name is **[Speaker 3]**, and I'm **[REDACTED]** of Transplant Recipients International Organization, a survivor of end-stage liver disease, inoperable liver cancer, and, thanks to the gift of life, a liver transplant recipient. Today I speak to you as a patient, a sister of a transplant recipient who walked this road last year, and for every voice that cannot be here today.

I didn't know that I didn't know. That is a silent thief. In cirrhosis, scar tissue forces blood to bypass the liver, ammonia that should be detoxifying races to the brain, hijacking our thoughts. That is hepatic encephalopathy, HE, the silent thief of minds. I lived a nightmare with end-stage liver disease. First step one was lactulose. It helped sometimes. Too often, it didn't. I had to wear adult diapers, because I couldn't make it to the bathroom in time. Picture a 49-year-old professional reduced to a five-year-old's judgment. I surrendered my car keys for two years. ER [emergency room] visit were sometimes up to twice a week until I slipped into a coma waking up unable to know my name, where I was, my daughter's name, my family. It was terrifying for my family and my daughter.

My doctor prescribed Xifaxan, and at the pharmacy the cost was $800, and I had commercial insurance. And my aunt begged for a couple pills, and we got three days of pills for three days of clarity. She talked to the transplant center and two weeks of calls before the medication arrived. All this while my mind was slipping. No one offered a simple copay card. Even with discounts, that cost would have crushed us just like it crushes families today.

No one with HE should have to choose between clear thinking and bankruptcy. And what I hear every week, in five years I mentored over 400 liver patients, lactulose helps some, not all. Every delayed dose can spike ammonia, then equals confusion which causes people to call 911. Yet metabolically, we are unique, yet we all hit the same paywall. We all suffer trying to get the medicine.

And I'm going to ask three urgent asks for you. Affordability, a cap out-of-pocket cost at $50 a month for every beneficiary or immediate access, a guaranteed 14-day bridge fill, a negotiated price while prior authorization grinds on. And transparency, place patient assistance, one click, one link away on the drug's homepage, and staff a live phone line for Medicare and Medicaid patients, because those are not normally on the front page. It's always a copay cards. And for HE patients, a

fair price isn't a comfort upgrade. It's the guardrail that keeps our minds, our dignity, and our lives intact. Thank you for listening and for acting.

01:20:39

Moderator, PhD, RTI International

Thank you. We appreciate your honesty and candor. The fourth speaker is **[Speaker 4]**. This speaker has indicated that there is no conflict of interest.

01:20:55

Speaker 4 (registered as a patient)

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Hello. Can you hear me?

01:20:57

Moderator, PhD, RTI International

Yes, we can.

01:20:59

Speaker 4 (registered as a patient)

Okay. Hello. My name is **[Speaker 4]**, and I'm a patient living with mass-related cirrhosis and hepatic encephalopathy since 2009. I also run a support group for 4,000 members living with hepatic encephalopathy. Hepatic encephalopathy is a brain dysfunction caused by liver disease where the liver fails to filter toxins from the blood leading to cognitive deficits. As ammonia builds up in the body, those deficits worsen resulting in reduced attention span and concentration, with difficulty focusing on tasks of following conversations, sleep disturbances, including insomnia, hyperinsomnia, or changes in sleep patterns, mild mood or personality changes, such as increased irritability, anxiety and depression, and subtle cognitive impairment, including difficulties with logical thinking, memory, problem-solving.

And as the condition progresses, more severe symptoms may appear, including flapping hands, tremor, confusion, agitation, disorientation, and even coma and death. Currently, there's only two medications available for HE, lactulose and Xifaxan. Lactulose, which is a commonly prescribed

medication helps many patients, but still some individuals continue to experience breakthrough symptoms, at which point Xifaxan is often prescribed to aid in these breakthrough symptoms.

Lactulose has unpleasant side effects, causing the body to expel ammonia through the bowels. While it's beneficial for some patients, others are unable to tolerate it due to the adverse side effects. I am one such patient. In 2019, I was paralyzed and between the HE and the Xifaxan, it has allowed me to have dignity, and to be able to be involved in my community and to be able to think clearly. As a result, I would often lose control of my bowels in public on lactulose, which was embarrassing and distressing. After five years, on being on Xifaxan, I'm now able to drive again and spend quality time with my terminally ill mother and sister throughout their passing. Being able to do this was a significant improvement from my previous mental decline.

I run a support group, as I said, for 4,000 members, and I've witnessed firsthand the incredible impact of Xifaxan. However, Medicare frequently challenges its use, requiring patients to demonstrate that lactulose alone is insufficient. I recall a heart wrenching experience with a terminal patient whose family begged for help after their insurance denied Xifaxan coverage, watching their father struggle with liver disease and cognitive decline, was devastating. Fortunately, we were able to collaborate with a hepatologist and secure two bottles of sample medication. The son drove for four hours to get their father the medication that he needed. He died two weeks later, but during that period he was cognitive and was able to be present in mind with his family. I'm sorry, I'm stuttering. There will always be those patients like myself, for whom Xifaxan is my only hope for living an active life, where I am mentally present and able to live a life with dignity and value. Please ensure that this effective and important medicine is always available to the patient living with hepatic encephalopathy. Thank you.

01:25:07

Moderator, PhD, RTI International

Thank you very much for your willingness to share your story. Thank you all for sharing your experience and perspectives about Xifaxan. I have one follow-up question for you. What other information or evidence do you think CMS should consider in evaluating Xifaxan? Please raise your hand to respond. We have just a minute for your brief response. **[Speaker 1]**, go ahead.

01:25:33

Speaker 1 (registered as a healthcare provider)

Yes, thank you. I briefly touched upon this, but I believe a deep dive into the cost-effectiveness of Xifaxan, specifically for the treatment of overt hepatic encephalopathy, would be warranted, particularly as it pertains to hospitalization costs and hospital-associated expenses that are incurred by patients with overt hepatic encephalopathy, including in the Medicare population. I think it's also worthwhile to mention that quality of life can be improved as hepatic encephalopathy is treated with Xifaxan, and so I would focus on these aspects of effective therapy for hepatic encephalopathy in making further determinations. Thank you.

01:26:29

Speaker Remarks for Xtandi

Moderator, PhD, RTI International

All right, thank you all. We will now move on to Xtandi, with one speaker. Xtandi is commonly used to treat prostate cancer. The speaker is **[Speaker 1]**. This speaker disclosed a potential conflict of interest, as shown on the slide.

[Speaker 1], are you there? There we go.

01:27:10

Speaker 1 (registered as a representative of a patient advocacy organization)

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Can you hear me? I can't get my video to work here.

01:27:12

Moderator, PhD, RTI International

Yes, we can.

01:27:14

Speaker 1 (registered as a representative of a patient advocacy organization)

Okay, I'll just start without video. Okay, good afternoon. My name is **[Speaker 1]**, and I'm the **[REDACTED]** for Extramural Discovery Science for the American Cancer Society. I'm also a practicing medical oncologist. I'm representing both American Cancer Society and the American Cancer Society Cancer Action Network, which is what we call ACS CAN. We advocate on behalf of cancer patients, caregivers, families, and survivors. I'm pleased to be here today to share the views of a subset of cancer patients who use the oncology drug Xtandi, as well as patients who take the other four cancer medications on the Medicare negotiation list.

Cancer patients rely on oncology medicines to treat both their cancers and to prevent recurrence. So as an oncologist, I've seen firsthand what a difference the effect of treatments can make in the lives of patients. And failure to take those medications can be devastating. For example, while not on the list of drugs discussed today, I did have a patient opt out of taking Lynparza because of high

out-of-pocket costs. She had the perfect cancer type where this drug would have worked to prevent relapse, but she didn't take it due to cost. And her cancer came back. She's now back on a highly toxic multiagent chemotherapy. She has side effects, and she has a low quality of life.

So, affordability of oncology therapies remains a serious obstacle for many cancer patients. A major factor in cancer is age, so Medicare coverage of cancer therapies is critical. Yet even with Medicare coverage, beneficiaries who need access to innovative cancer drugs may find their out-of-pocket costs running into the thousands of dollars each year. Administered thoughtfully, Medicare Negotiation Program can help lower the cost for cancer patients.

Equally important to affordability is access to future oncology therapies, so it's critical that, along with lowering prices, the development of new therapies and access to these treatments not be impeded in any way. So, ACS CAN did a survey of cancer patients, and I'm pleased to share with you today some of the personal experiences cancer patients have had with Xtandi and the three other cancer drugs on the negotiation list. Working with Magnolia Innovation, ACS CAN conducted a survey of 126 cancer patients taking the four cancer drugs on the negotiation list to generate the patient experience information that CMS is looking for. Individuals surveyed have a diagnosis of cancer, have Medicare as their primary health care coverage, and have been prescribed one of the cancer medications on the negotiation list for treatment of their cancer within the last 18 months.

I'll start with Xtandi. For patients taking Xtandi, the most important factors in considering this medication as a therapy were impact on survival, lack of side effects, and their provider's recommendation based on clinical guidelines. In terms of their overall experience taking the medication, 92%, 33 of 36, patients say that Xtandi has been very important to their cancer care and treatment, and one-third, 12 of 36, say it was the only effective therapy for managing their cancer. Only one in four, nine of the 36 Xtandi patients, say that there were alternative therapies that could have been considered. Ninety-seven percent of the cancer patients we surveyed said Xtandi made their daily life much better; 94% say that Xtandi had a very positive impact on their mental or emotional well-being; 21 patients tried other therapies first and about half of those were required to do so before Xtandi would be covered.

Patients taking the other cancer therapies on the negotiation list had similar experiences. For instance, patients taking Calquence shared that the five most important factors for their use of the medications were lack of side effects in 74%, quality of life in 67%, impact on survival in 60%, ease of administering the medication in 48%, and coverage by insurance in 41%. The overarching findings about patient experience from our survey work that I want to share with you include patient access to needed therapies is a key consideration. Patients surveyed identified several types of delays and barriers to access including utility management by payers, for example, step therapy and prior authorization, pharmacy dispensing delays, and cost-sharing. These insurance utilization management techniques are creating at least temporary barriers. Twenty-five percent of the Xtandi patients, more than any drug selected and surveyed, reported delays due to step therapy and prior authorization. Additionally, one-third of Xtandi patients were required to ensure step therapy prior to receiving Xtandi.

ACS CAN was pleased by the recent CMS memo indicating that you will be monitoring the use of UM [utilization management] by plans as well as the formulary placement to ensure these do not become barriers. Patients surveyed reported overall that life was much better while on these therapies, based on patient responses. Nearly 86% of patients reported that their specific selected therapy had significant positive impact on their emotional and well-being. Insurance coverage and/or insurance costs were rated as two of the top five important factors for all of the selected drugs included in the research. Part D cost-sharing...

01:33:17

Moderator, PhD, RTI International

Pardon the interruption. You've actually answered my follow-up question. So, I'm going to give you another few seconds to wrap up, but no more than about 15, 20 more seconds.

01:33:28

Speaker 1 (registered as a representative of a patient advocacy organization)

Thank you so much. Part D cost-sharing is another area of concern for patients. While only a small number of patients identified cost-sharing as a factor in treatment delays, at least one patient taking each of the four drugs reported skipping doses, taking a partial dose, or not picking up their prescription due to cost. Despite the new maximum patient out-of-pocket, Part D patients will still need protection from high cost-sharing. As one patient said related to cost-sharing and access, we need strong support from CMS. Thank you.

01:33:59

Moderator, PhD, RTI International

All right, thank you. I will now turn over the host role to my colleague from NORC, **[SECONDARY MODERATOR]**, for the final drug of the afternoon.

01:34:14

Speaker Remarks for Vraylar

Secondary Moderator, NORC

Thanks, **[MODERATOR]**. Good afternoon. My name is **[SECONDARY MODERATOR]**, and I'm from NORC at the **[REDACTED]**. As **[MODERATOR]** mentioned, our next and last drug of the day is Vraylar, and we will have three speakers. Vraylar is commonly used to treat bipolar 1 disorder, acute treatment of manic or mixed episodes, bipolar 1 disorder, treatment of depressive episodes, major depressive disorder, and schizophrenia. We will move on to our speakers now. Our first speaker will be **[Speaker 1]**, a health care provider. He has declared no conflicts of interest. **[Speaker 1]**?

01:35:07

Speaker 1 (registered as a healthcare provider)

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Okay, and thank you very much, **[SECONDARY MODERATOR]**. My name is **[Speaker 1]**. I'm a clinic professor of psychiatry at the University **[REDACTED]**, here in **[REDACTED]** California, and I've been practicing for about 35 years. My main area of specialty are the three conditions that Vraylar treats, schizophrenia, bipolar disorder, and depression when it's not responding to your primary antidepressant.

As many of us know, these three conditions that Vraylar's indicated for, are three of the conditions that cause some of the greatest morbidity for people within the United States and really worldwide. High economic cost for these three conditions. Since the big challenge we have with these conditions is keeping people on medicines. We've had medicines for these conditions for well over 50 years. However, once somebody gets better, because these are brain illnesses, the likelihood of maybe decreasing dosages, becoming partially compliant is very common. One of the biggest factors that also leads to that is side effects to many of the medications that treat schizophrenia, bipolar disorder, and major depression. They may work, but they have pretty significant side effects. Some include weight gain. They can cause diabetes. They can cause neuromuscular side effects. So, you can imagine somebody's getting a little bit better, they a brain illness where they already may be a little ambivalent about taking a treatment, and now they have a side effect that comes on top of that. [A] recipe for stopping their medicine, leading to rehospitalization, possibly homelessness, incarceration, significantly increased caretaker burden for that family that has to help support their loved one.

So, when Vraylar came out in 2015, this was a time that we were developing compounds that worked at least as well, hopefully better, but significantly lower side effects, so it was the right mix that our hope was we would have better outcomes and keep people well. Well, that has certainly been the case with a medicine like Vraylar.

The other real nice feature, we want to simplify dosing for people that have chronic mental illness. And that has been the case with Vraylar. It's a once-a-day dose. You can imagine somebody with a mental illness having to take a medicine twice a day, three times a day. And it's quite the average number of medicines people with these three conditions are on is three medicines. Make it simple for the patient caretaker who supports that. And that has been the case with Vraylar.

Over these ten years, we have a lot of also good outcome data looking at quality of life. Are people able to live on their own, return to work, develop relationships? And that has been the case with medicines like Vraylar. We also know that these illnesses can affect your cognition. We have very good data showing Vraylar can help improve cognition in individuals who have these severe illnesses.

So, with the tenure experience of Vraylar, it's been a very nice fit for myself as a psychiatrist. If you look at my practitioners, my colleagues in primary care medicine and in other areas, it is also an area of growing use in those areas. About 90% of depression treatment in the United States is in the primary care setting. So, this is a medicine that they've been able to introduce in their treatments because of ease of use, once a day, good efficacy, and good tolerance. So, yeah, it's really win-win across the board to have access to a medicine like this that is clearly linked to better outcomes. Thank you very much.

01:39:40

Secondary Moderator, NORC

Thank you. Our next speaker is **[Speaker 2]**. This speaker has indicated a potential conflict of interest. **[Speaker 2]**?

01:39:51

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

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Thank you. Thank you for the opportunity to participate. My name is **[Speaker 2]**. I'm the **[REDACTED]** with the Alliance for Aging Research, a patient advocacy organization.

Vraylar is an oral medication approved by the FDA for the treatment of schizophrenia, acute treatment of bipolar 1 depression, and/or manic or mixed episodes associated with bipolar 1 disorder, and as an adjunctive therapy for major depressive disorder. This means it is used in addition to an antidepressant to help treat depression.

Vraylar is a second-generation antipsychotic or atypical antipsychotic. It works by rebalancing dopamine and serotonin to improve thinking, mood, and behavior. Research consistently points to a noticeable overlap between schizophrenia and bipolar disorder, meaning that a significant percentage of individuals diagnosed with one condition also meet the criteria for the other.

According to the Mayo Clinic, studies performed to date have not demonstrated geriatric-specific problems that would limit the usefulness of Vraylar in older adults. However, older patients are more likely to have age-related kidney, liver, or heart problems, which may require caution and an adjustment in the dose for patients receiving Vraylar.

For people living with bipolar disordered depression of schizophrenia, Vraylar has made meaningful differences. Patients often describe experiencing more stable moods and clear headspace with many reporting that both manic and depressive symptoms become easier to manage. Vraylar works for treatment-resistant depression in many patients who have failed on other medications. Compared to other antipsychotic medications, Vraylar tends to cause less sedation.

Some individuals notice improvements quickly, even within the first week describing boosts in mood, motivation, and overall, energy. Vraylar helps to temper both the manic-depressive episodes

with bipolar 1 and the highs and lows of schizophrenia. Vraylar has a long half-life, which allows for once-daily dosing, as we mentioned is a great convenience.

The price of Vraylar can be prohibitive, thus why we're here, making it difficult for some patients to stay on therapy consistently, and consistent dosage is essential with these types of drugs. It's important that the effort to reduce price barriers to Vraylar does not unintentionally reduce future patient access in other ways. A June 2024 report by Manatt Health highlighted some of the unintended consequences of the Medicare Drug Price Negotiation Program provisions that shift cost to Medicare part D plans. Plans are incentivized to cut these losses by excluding negotiated drugs from formularies and tightening utilization management strategies through prior authorization and step therapy that will delay or eliminate access.

CMS has in the past warned prescription drug plan sponsors to place drugs selected for non-formulary tiers without clinical justification. I urge CMS to use its authority to crack down on this process. Further, a survey conducted in January 2025 by the National Community Pharmacists Association indicates that approximately 61% of independent pharmacists are strongly considering not stocking one or more drugs with prices negotiated under Medicare Part D because of cash flow problems and payment delays related to IRA implementation.

CMS should require that drugs for which CMS has established a maximum fair price, be given preferred formulary status without utilization management. We urge CMS to improve plan transparency, so beneficiaries can easily see when drugs have utilization management restrictions. We further call upon CMS to enforce minimum payment rates to pharmacies to prevent sponsors from diverting patients away from community pharmacies. Consider pre-funding program costs and requiring Part D plans and PBMs [pharmacy benefit managers] to reimburse pharmacies no less than the maximum fair price.

And finally, we urge CMS to improve its appeals and grievance processes to reduce the burden of challenging a plan's coverage decision. It is essential that price negotiations for Vraylar and other drugs truly improves access for patients who rely on this medication as it brings down prices. Thanks again for the opportunity to participate in this important process.

01:44:02

Secondary Moderator, NORC

Thank you, **[Speaker 2]**. Our next and third speaker will be **[Speaker 3]**. **[Speaker 3]** has indicated that she has a potential conflict of interest. **[Speaker 3]**?

01:44:14

Speaker 3 (registered as a representative of a patient advocacy organization)

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Thank you. My name is **[Speaker 3]**, and I am the **[REDACTED]** at the Alliance for Aging Research. The Alliance is the leading nonprofit organization dedicated to changing the narrative to achieve healthy aging and equitable access to care. For many of the millions of Americans who live with serious mental health conditions like bipolar 1 disorder, schizophrenia, or major depressive disorder, medications such as Vraylar can play a critical role in improving quality of life.

Vraylar is a once-daily oral atypical antipsychotic that treats the full spectrum of bipolar 1 disorder, and also the conditions I mentioned earlier. Older adults living with mood or psychotic disorders are often managing multiple health conditions at once, making treatment complexity a real concern. Vraylar has a well-characterized safety profile, and requires only once-daily dosing, which improves adherence and reduces the risks associated with polypharmacy in the older adult population.

A growing body of real-world evidence supports the importance of continued access to mental health medications like Vraylar. For instance, studies show that people living with bipolar 1 disorder often experience symptom relapse when medications are delayed or withheld, due to utilization management processes. These disruptions are not only harmful to patients' health, they also result in avoidable hospitalizations, increased health care costs, and added stress on caregivers.

The Alliance is deeply concerned about the increasing use of utilization management by PBMs and Part D plans since the passage of the Inflation Reduction Act. A study published in the *Journal of Managed Care and Specialty Pharmacy* analyzed 17,418 patients prescribed Vraylar and cariprazine and other generic versions and found that 1,554 or 8.9% had their initial prescription rejected due to formulary-related reasons, such as non-coverage, prior authorization requirements, or step therapy mandates. Among these rejections, 46.5% were due to the product or service not being covered, and 38.5% required prior authorization. The consequences of these reductions were significant. Patients whose initial cariprazine claims were rejected experienced 22% more all-cause hospitalizations and 24% more mental health-related hospitalizations compared to those whose claims were approved. Additionally, 76.8% of patients with rejected claims never received their medication, and 34.7% did not receive any antipsychotic thereafter. For those who eventually accessed their treatment, the average delay was approximately six months.

I want to encourage CMS to ensure that any savings achieved by the Negotiation Program translate to lower out-of-pocket costs for beneficiaries, and do not allow utilization management to impede access to care for older adults on Vraylar. Lastly, CMS must invest more in the Medicare Prescription Payment Plan to ensure that beneficiaries with severe mental health conditions, especially those who rely on high-cost medications like Vraylar, can access and afford the treatments they need. This program allows beneficiaries to spread their out-of-pocket costs for prescription drugs over the course of the year, rather than facing unaffordable upfront payments of the pharmacy. Unfortunately, many older adults still do not know about this program or are facing significant burden while trying to enroll. For people managing serious mental illness, financial

barriers that can lead to skip doses or treatment interruptions can have devastating consequences for health and stability. Thank you so much for the opportunity to speak.

01:47:44

Secondary Moderator, NORC

Thank you, **[Speaker 3]**. We have a follow-up question from CMS. The question is, can you briefly address the benefits and drawbacks of Vraylar compared to other medications taken to treat the conditions Vraylar is indicated for? Please raise your hand, and you will have a minute to answer the question. **[Speaker 1]**?

01:48:14

Speaker 1 (registered as a healthcare provider)

Yeah, **[SECONDARY MODERATOR]**. So, the benefits and drawbacks as compared to other medicines that are indicated for the conditions that Vraylar is, first and foremost in my mind, is its very nice safety profile – low risk of weight gain, low risk of metabolic disturbance, such as glucose elevation, cholesterol, triglyceride changes, which are very common and with this class of second-generation agents. It also has a very low risk of movement disorders. So, that's one area.

Its efficacy is similar to some other compounds that have come forward in the last 12, 14 years, but safety does seem to stand out a little bit. And then, second, it's once-a-day dosing. That's a very important profile. Often the initial dose, it could be the final dose with this agent. You can titrate it up, but it's once-a-day, so it really makes it easy for our colleagues who don't have the training during their residency in mental health in depth, such as primary care clinicians, where this medicine is becoming widely used. Very easy to introduce. So, those are two big advantages manages that come up in my mind.

01:49:49

Secondary Moderator, NORC

Thank you.

01:49:58

Moderator, PhD, RTI International

All right. That brings us to the end of this afternoon's Town Hall session. I would like to thank all our speakers for joining us today and providing important input for the Medicare Drug Price Negotiation Program. We also extend our thanks to everyone who tuned in throughout the day to hear these valuable insights. You can find additional information and news about the Negotiation Program on the CMS website listed on this slide. If you have questions, please contact CMS using the email listed on the slide. Thank you again and have a wonderful afternoon.

=== 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