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Setting Treatment Goals in Ulcerative Colitis: Real-Patient Provider Discussion

Narrator:
At the intersection of science and clinical experience in IBD, this is *Gut Reactions*. Settle in, as our host, Dr. David Rubin, brings leading gastroenterologists together for one-on-one conversations. This podcast is brought to you by AbbVie.

Dr. David Rubin:
Welcome to the *Gut Reactions* podcast. I'm your host, Dr. David Rubin, Chief of the section of Gastroenterology, Hepatology, and Nutrition, and Director of the Inflammatory Bowel Disease Center at the University of Chicago. Today, we are fortunate to be joined by Adam, my patient with moderately to severely active ulcerative colitis, who also has experience working with the Crohn's and Colitis Foundation. In this episode, we're going to explore the treatment journey for patients with ulcerative colitis.

Ulcerative colitis, commonly referred to as UC, is a chronic immune condition characterized by inflammation within the large intestine, which means the colon and the rectum. The diagnostic process for ulcerative colitis entails a comprehensive review of physical symptoms, a detailed medical history, and an array of tests which may include blood tests, testing of stool samples, and procedures such as colonoscopies with biopsies.

Diagnosing ulcerative colitis is indeed a complex process and there is no single definitive test to confirm its presence. This complexity is heightened due to the overlapping symptoms with other conditions. That necessitates a thorough approach. Additionally, it's worth noting that the average time to confirm a UC diagnosis can vary depending on individual cases. For some people, it can take a few months and for others up to several years.

Adam, can you provide a brief overview of your history with ulcerative colitis, including how it presented, what your symptoms were, and your overall experience trying to get a diagnosis?

Adam:
Absolutely. First off, thanks for having me, Dr. Rubin. I really appreciate it. I'm honored to be here. Yeah, so I was diagnosed when I was nine years old. And my first symptoms really were urgency and increased frequency to need to use the bathroom as well as blood in the stool and all of that. And so, I was taken to my primary care, who is a great doctor. And she got me plugged in with the hospital here pretty quick. And we were able to turn around a diagnosis relatively quickly, which I know isn't always the case with a lot of patients.

Dr. David Rubin:
One of the things I often ask my patients about, and I see adult patients with these problems, is when do you think it actually started? Do you recall having symptoms for a while before you brought it to the attention of your parents, or was it pretty obvious?

Adam:
I think it was pretty obvious. I know I was having the issues, I was diagnosed fall of 1999. And so, I know I remember having issues in the summer and whatnot. So, I know at least a few months prior to the diagnosis. But yeah, so I think it was months, not years though.

Dr. David Rubin:
How did you learn about ulcerative colitis? Did they refer you to some information or was it just what the doctor told you or where did you go?

Adam:
So, things turned around pretty quick in getting an appointment with a GI doctor here, and he's phenomenal. But the first thing we did, I

remember within the first year, year and a half, was go to a Crohn's and Colitis Foundation talk in Wisconsin Dells here. And that was kind of where we started. And the Crohn's and Colitis Foundation has a lot of resources where we began. And then our doc filled in the gaps.

Dr. David Rubin:
The Crohn's and Colitis Foundation, for those who are less familiar, is a society that actually includes both professionals who take care of people with these conditions and patients. So, it's combined there. And it's obviously a very helpful resource, especially when you're fully newly diagnosed, but as you go through that journey. So, what were you treated with initially? Do you remember?

Adam:
Yeah, I was first started on the steroids and the typical 6-MP. But right, it was again in 1999. So the first anti-TNF medications were just about hitting the market. And so I was able to get started on one of those, which helped me immensely, I think.

Dr. David Rubin:
So, the management of ulcerative colitis, as in Adam's case, often involves a stepwise approach to treatment, where the diagnosis comes with a prognosis. How severe does the disease look to the doctor who's making the diagnosis, and how sick is the individual? We're still in an era, even now, where we don't necessarily know which treatment's going to be effective. But we do know what the goal of management was. So, Adam, when you started to feel better, what symptom improved first, or do you remember how you felt and when you knew that you were actually responding to those steroids?

Adam:
Yeah, I remember just the urgency and frequency of having bowel movements really changed. And then slowly the blood in the stool also improved.

Dr. David Rubin:
We think of aminosalicylates as a common therapy, the 5-ASA treatments for moderate colitis. And then we move our way up. If a patient isn't responding to aminosalicylates, we consider the use of corticosteroids, and even, as you mentioned, six mercaptopurine. In the United States, we've really moved away from thiopurines as often. But when these treatments are used, the goal is the same, which is we want people to feel better, and then we want it to last. And recognizing that colitis can be a chronic relapsing and remitting condition.

So, when patients don't respond to these therapies, or when they have a relapse early after starting one of these treatments, it's appropriate that we move on to advanced therapies in UC, which include biological treatments, monoclonal antibodies that target a variety of different proteins, or some of our synthetic targeted small molecules like S1Ps or Janus kinase inhibitors. So Adam, in your journey, tell us about what therapy worked or what didn't and how you made your way all the way to me.

Adam:
Yeah, so I think I was just thinking back on all the therapies I've been on, including steroids and whatnot.

I was started on an anti-TNF medication, that I was on for a few more years and got me through high school. And then kind of as school went on and whatnot, I've been on interleukin inhibitors, a JAK inhibitor, mesalamine formulations and steroids, different type of steroids.

Dr. David Rubin:
So, which symptoms of yours came back and how did you know that that was going on?

Adam:
Yeah, I think the big things would be the urgency and frequency of using the bathroom and then bleeding would start as well. So those are the big first symptoms. Some of these meds that I've been on just never took off.

Dr. David Rubin:
Yeah, I have a lot of patients where they have been on one therapy after another that either was a primary failure or the therapy worked for a little while and they lost response, which we call secondary non-response or loss of response and that can really wear on you.

So, in fact, what we've learned has led to an approach in our space called treating to a target. And the targets of treatment are supposed to be proactively pursued as opposed to waiting for somebody to just feel better or waiting for them to not do well. And the whole point of that means that you provide a therapy to a patient with ulcerative colitis and after a defined interval of 6 to 12 weeks, you reassess to see how they're doing both symptomatically as well as more objectively. And the point of treating to a target is that if you're not getting the response you need after an appropriate trial of a therapy, you then will make an adjustment. You discuss with the patient your options. Is it a different dose?

Is it a second therapy added or are you gonna switch treatments altogether? So, there's a well-described and highly discussed consensus statement that's called STRIDE-II. This was a consensus of experts who said that the long-term target for treating ulcerative colitis is endoscopic remission.

And with STRIDE-II, we also talk about histology, which is the biopsies. But the whole point of STRIDE-II is to move us from a treatment strategy that was very reactive, waiting for the patient like Adam to call us and say,

“I'm having urgency again and what am I gonna do?” So, Adam, as far as your management has gone, and maybe you can even talk about more recently when we've been working together, can you comment on how your management has been a bit more proactive and what measures were used?

Adam:
Yeah, I think some of the, well, the big things are always the screening colonoscopies and making sure or surveillance colonoscopies, I should say, in terms of making sure disease is under control. And there are times where I felt great and have gone into a colonoscopy and the scope didn't look great. So, I think that would be one point in terms of the surveillance of the disease and then making adjustments based on that.

Dr. David Rubin:
Well, in terms of your own colitis, what have been the measures that we've used to know that you've gotten where you need to go?

Adam:
Yeah, so I think one of them is how I'm feeling and how are my symptoms, urgency specifically, frequency of using the bathroom, blood in my stool, and then doing scopes and seeing how it looks and how more recently I think having scopes that look good gives reassurance that we're doing the right thing.

Dr. David Rubin:
Stemming from this larger conversation about treatment switches, we’re going to talk next about a treatment option that may help our patients with moderate to severe UC who have failed or who have an intolerance to an anti-TNF.

Narrator:
INDICATION

RINVOQ is indicated for the treatment of adults with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers. If TNF blockers are clinically inadvisable, patients should have received at least one approved systemic therapy prior to use of RINVOQ.

Limitations of Use: RINVOQ is not recommended for use in combination with other Janus kinase (JAK) inhibitors, biological therapies for UC, or with potent immunosuppressants such as azathioprine and cyclosporine.

SAFETY CONSIDERATIONS FOR RINVOQ (upadacitinib)

Serious Infections: RINVOQ-treated patients are at increased risk of serious bacterial (including tuberculosis [TB]), fungal, viral, and opportunistic infections leading to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.

Mortality: A higher rate of all-cause mortality, including sudden cardiovascular (CV) death, was observed with a Janus kinase inhibitor (JAKi) in a study comparing another JAKi with tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients ≥50 years with ≥1 CV risk factor.

Malignancies: Malignancies have occurred in RINVOQ-treated patients. A higher rate of lymphomas and lung cancer (in current or past smokers) was observed with another JAKi when compared with TNF blockers in RA patients.

Major Adverse Cardiovascular Events: A higher rate of CV death, myocardial infarction, and stroke was observed with a JAKi in a study comparing another JAKi with TNF blockers in RA patients ≥50 years with ≥1 CV risk factor. History of smoking increases risk.

Thromboses: Deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated for inflammatory conditions with JAK inhibitors, including RINVOQ. A higher rate of thrombosis was observed with another JAKi when compared with TNF blockers in RA patients.

Hypersensitivity: RINVOQ is contraindicated in patients with hypersensitivity to RINVOQ or its excipients.

Other Serious Adverse Reactions: Hypersensitivity reactions; gastrointestinal perforations; hypoglycemia in patients with diabetes;

laboratory abnormalities; and embryo-fetal toxicity.

Please continue listening and stay tuned for additional Important Safety Information within this podcast.

Dr. David Rubin:
When I treat patients with active ulcerative colitis, I always start by saying, “I want you to feel better as soon as possible.” Do you want to share a little bit about how your life has progressed since you achieved remission?

Adam:
Yeah, and I guess now is probably a good time to say that. So, I'm a gastroenterology fellow in Milwaukee.

Prior to starting RINVOQ, the big symptoms being the fatigue that I was experiencing, the urgency of having to use the bathroom.

Dr. David Rubin:
I think that it's a reminder to everybody two things. I think one is how important it is to really understand your patient's treatment goals and match the treatment that they're receiving with those goals. But secondly, it's not a surprise to anybody listening that there's a lot of gastroenterologists who have IBD or whose family members have IBD. So, a lot of people come to this quite honestly because of their personal and family experiences. So we talk a lot about moving along in treatment choices and having a goal treatment, but also what I usually say is trust but verify, meaning when a patient says they're feeling better, especially with colitis, which is somewhat of a noisy symptomatic disease, we of course are very happy, but we want to make sure that they’re actually improved. It's remarkable to remember that some people who say that they're feeling better with colitis will have inflammation if you look with a scope or biopsies or get a stool calprotectin.

So, Adam, we talked a bit about your treatment options when I met you. Can you reflect on how we came to the decision about RINVOQ and what your experience with that therapy was?

Adam:
Going into that appointment, I kind of felt like I was at the end of the line. You had presented to me the effects of RINVOQ and despite failure on past anti-TNFs and whatnot that RINVOQ was really a good medication that you've had a lot of success with.

Dr. David Rubin:
RINVOQ has a well-studied safety profile. It's backed by over six years of safety data in IBD.

So, it doesn't come without some concerns and education that we share with our patients. During our consultation, I explained to Adam that I understood his concerns about being on a new medicine and what the safety might imply. And I wanted to address these thoroughly. So, I mentioned, RINVOQ has some side effects.

However, I emphasize the importance of weighing those risks against the benefits, of course. It's important for me that they understand that while my primary goal is to effectively manage their UC, I am equally committed to prioritizing their safety. The benefit versus risk conversation between the patient and doctor should be applied to each patient and assessed individually.

Narrator:
The most common adverse reactions in RINVOQ clinical trials were upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, headache, peripheral edema, increased blood creatine phosphokinase, increased blood cholesterol, hypersensitivity, folliculitis, abdominal pain, increased weight, influenza, fatigue, neutropenia, myalgia, influenza-like illness, elevated liver enzymes, rash, and anemia.

Dr. David Rubin:
When we evaluate a patient who has not responded appropriately or who's lost response to therapies, we want to be thoughtful about what was the reason for each of those problems. And another really important prognostic factor is, did the patient ever achieve remission with prior therapies. But in Adam's case, we knew he had done really quite well with anti-TNF earlier in his disease journey, and it made sense that we would be able to try to get him back on track. We also knew that he lost response to an anti-TNF because he developed anti-drug antibodies.

JAK inhibitors like RINVOQ can help provide effective symptom relief and can help achieve remission. So, it's a very good option to consider this in patients who have been on an anti-TNF and either didn't respond at all or who, like Adam, were on an anti-TNF and lost response.

RINVOQ was approved for ulcerative colitis in 2022. After two 8-week, multi-center, double-blind, placebo-controlled ulcerative colitis induction trials, participants on RINVOQ who achieved clinical response at Week 8 with 45 milligrams of RINVOQ were moved into the U-ACHIEVE Maintenance trial. The clinical trials had a primary endpoint of clinical remission, which in these trials means no rectal

bleeding, reduced stool frequency, and an endoscopic subscore that's less than or equal to 1 without any friability. And there were a variety of ranked secondary endpoints, which included clinical response based on an adapted Mayo Score, endoscopic improvement and histo-endoscopic mucosal improvement. That means the combination of histology and endoscopy. In the 52-week Maintenance trial, RINVOQ met its primary endpoint, demonstrating clinical remission at Week 52. 42% of the 148 patients on RINVOQ 15 milligrams and 52% of the 154 patients on RINVOQ 30 milligrams achieved clinical remission compared to only 12% of the 149 patients who received placebo. So, Adam, what were the first few weeks of treatment with RINVOQ like?

Adam:
I was going down with a buddy from med school to go see somebody else and ended up having an accident in terms of not making it to the bathroom that first day. Prior to starting RINVOQ, I was probably having one to two accidents at least every month.

And I think that was the last accident I had had or incontinence episode, I should say, I had for over a year after that initial two weeks. So, at first when I was first switched, I was like, ah here we go again. But at the same time, I was like, it's only the first dose. Let's give it a little time. I think energy really came back with RINVOQ.

Narrator:
During the 8-week, double-blind, placebo-controlled Phase 3 clinical studies of 988 patients (473 patients for U-ACHIEVE and 515 patients for U-ACCOMPLISH) with moderately to severely active UC who demonstrated prior treatment failure to oral aminosalicylates, corticosteroids, immunosuppressants, and/or biologic treatment, researchers assessed the impact of RINVOQ on fatigue, a common symptom for those with ulcerative colitis. Fatigue levels were assessed by change from baseline in FACIT-Fatigue Scale, a validated patient-reported tool.

At Week 8, 59% of patients on RINVOQ experienced clinically meaningful improvement in fatigue, as opposed to 34% of those given a placebo.

These findings suggest that RINVOQ may offer relief from fatigue, providing a potential benefit in managing the overall burden of ulcerative colitis. The effect of RINVOQ to improve fatigue after 8 weeks of induction has not been established.

Dr. David Rubin:
Certainly, that rapidity of response in your situation is really nice to hear and it's been described in the clinical trials as well. And also, the ability to avoid steroids because the drug works quickly enough. RINVOQ pivotal trials also evaluated histology by using an endpoint of histo-endoscopic mucosal improvement. And patients who achieved this rigorous endpoint demonstrated both the endoscopic improvement indicated by a Mayo endoscopic subscore of 0 or 1 without any friability and histologic improvement, which was defined as a Geboes score of 3.1 or lower. That score signifies neutrophil infiltration in less than 5% of crypts without crypt destruction and the absence of erosions, ulcerations, or granulation tissue. This is an endpoint that's of great interest in these trials. It's important to note that the relationship between histo-endoscopic mucosal improvement and disease progression or long-term outcomes was not assessed.

Narrator:
Endoscopic results are based on a full colonoscopy or flexible sigmoidoscopy, depending on the extent of disease at study entry, and histology results are based on a set of 2 biopsies.

Dr. David Rubin:
So RINVOQ also has long-term extension data. The long-term extension study evaluates as-observed data over an extended period. We're combining the results of the initial 52-week Maintenance trial with the long-term extension findings. And we thoroughly examine the two-year data in episodes one and two of this podcast. You should tune into those episodes to learn more, by the way.

So, I think it's really quite important to know that in Adam's case, we have in fact performed endoscopy, and as he referenced, he just had a scope with me recently and it looked better. So, in order to assess if we should continue Adam on RINVOQ, not only did I evaluate those endoscopy results, but in addition, histo-endoscopic improvement that was seen when we did biopsies. With that holistic assessment, the results indicated that he was doing great. And of course, then we continued the treatment. So the drug is approved for maintenance at 30 or 15 milligram.

Narrator:
The recommended dosage of RINVOQ for maintenance treatment is 15 mg once daily. A dosage of 30 mg once daily may be considered for patients with refractory, severe or extensive disease. Discontinue RINVOQ if an adequate therapeutic response is not achieved with the 30 mg dosage. Use the lowest effective dosage needed to maintain response.

Dr. David Rubin:

And Adam, what maintenance dose are you on?

Adam:
Currently 30 milligrams.

Dr. David Rubin:
And the visual evidence from his endoscopy combined with clinical remission tells us that we've achieved that level of control for him. And I really believe that this dual approach enables us to set realistic expectations. And I spend a lot of time with my patients emphasizing the goals of management. So we're all on the same page and we have the same expectations.

I saw a new patient earlier this week, who has ulcerative colitis, she had recently been diagnosed and she had not yet heard about remission. She didn't know what the goal of management was. And that is not what we want. So Adam, what was it like when you got the results from your first endoscopy after you'd been on RINVOQ?

Adam:
Yeah, I definitely got choked up and it was definitely an emotional thing.

Dr. David Rubin:
I'm so glad you're doing well. So Adam, overall, you have many years of experience living with ulcerative colitis, and now you're actually taking care of people who have IBD.

So, do you have any advice about how to approach someone who's on their way to being diagnosed or maybe newly diagnosed?

Adam:
Yeah, I think the biggest thing that I've always been taught is meet the patient where they're at. And I felt like my providers were able to, not only in their limited amount of time in an appointment, able to provide answers, reassurance, and comfort, but also directing patients to appropriate resources like the Crohn's and Colitis Foundation, like other avenues where they can get simplified information. And I think as providers just knowing those resources and utilizing our limited time in clinic with patients that we have to give reassurance and that they're not alone in this is definitely a place to start and then the relationship I think develops after that.

Dr. David Rubin:
That's really great, Adam, and I appreciate all your insights and the fact that you've joined us on this *Gut Reactions* podcast. I want to summarize for our colleagues that we've talked today about the journey people have in being diagnosed and then treated with ulcerative colitis. And Adam and I emphasized the approach that includes understanding the disease and getting the right information, a goal-based strategy emphasizing the need for symptomatic remission, as well as a treat-to-target strategy and understanding how you can be more proactive in managing folks. We talked a bit about different treatment strategies and of course educated you a bit more about RINVOQ.

If you've enjoyed this episode of *Gut Reactions* and found it educational, you can share it via the share button, email, LinkedIn, or on any of your preferred platforms. Also check out our previous episodes if you want to hear some more. Until next time, this is *Gut Reactions*.

Narrator:
Please continue listening for additional Important Safety Information.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with RINVOQ are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids. If a serious infection develops, interrupt RINVOQ until the infection is controlled.

Reported infections include:

- **Active tuberculosis (TB), which may present with pulmonary or extrapulmonary disease. Test patients for latent TB before RINVOQ use and during therapy. Consider treatment for latent TB infection prior to RINVOQ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

Carefully consider the risks and benefits of treatment with RINVOQ prior to initiating therapy in patients with chronic or recurrent

infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with RINVOQ, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

MORTALITY

In a large, randomized, postmarketing safety study comparing another Janus kinase (JAK) inhibitor with tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients ≥50 years old with at least one cardiovascular (CV) risk factor, a higher rate of all-cause mortality, including sudden CV death, was observed with the JAK inhibitor. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ.y

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with RINVOQ.

In a large, randomized, postmarketing safety study comparing another JAK inhibitor with TNF blockers in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]), lymphomas, and lung cancer (in current or past smokers) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk.

With RINVOQ, consider the benefits and risks for the individual patient prior to initiating or continuing therapy, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy when on treatment, and patients who are current or past smokers. NMSCs have been reported in patients treated with RINVOQ. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. Advise patients to limit sunlight exposure by wearing protective clothing and using sunscreen.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

In a large, randomized, postmarketing study comparing another JAK inhibitor with TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk. Discontinue RINVOQ in patients that have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ, particularly in patients who are current or past smokers and patients with other CV risk factors. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.

THROMBOSIS

Thromboses, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated for inflammatory conditions with JAK inhibitors, including RINVOQ. Many of these adverse events were serious and some resulted in death.

In a large, randomized, postmarketing study comparing another JAK inhibitor to TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of thrombosis was observed with the JAK inhibitor. Avoid RINVOQ in patients at risk. Patients with symptoms of thrombosis should discontinue RINVOQ and be promptly evaluated.

HYPERSENSITIVITY

RINVOQ is **contraindicated** in patients with known hypersensitivity to upadacitinib or any of its excipients. Serious hypersensitivity reactions, such as anaphylaxis and angioedema, were reported in patients receiving RINVOQ in clinical trials. If a clinically significant hypersensitivity reaction occurs, discontinue RINVOQ and institute appropriate therapy.

GASTROINTESTINAL PERFORATIONS

Gastrointestinal (GI) perforations have been reported in clinical trials with RINVOQ. Monitor RINVOQ-treated patients who may be at risk for GI perforation (e.g., patients with a history of diverticulitis and patients taking NSAIDs or corticosteroids). Promptly evaluate patients presenting with new onset abdominal pain for early identification of GI perforation.

HYPOGLYCEMIA IN PATIENTS WITH DIABETES

Hypoglycemia, including severe hypoglycemia, has been reported following initiation of RINVOQ and other JAK inhibitors in patients with diabetes. During treatment with RINVOQ, consider increased monitoring of blood glucose as clinically indicated in patients with diabetes. Advise patients with diabetes to notify their healthcare provider if they develop signs or symptoms of hypoglycemia.

LABORATORY ABNORMALITIES

Neutropenia

Treatment with RINVOQ was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] <1000 cells/mm^3). Treatment with RINVOQ is not recommended in patients with an ANC <1000 cells/mm^3. Evaluate neutrophil counts at baseline and thereafter according to routine patient management.

Lymphopenia

Absolute lymphocyte counts (ALC) <500 cells/mm^3 were reported in RINVOQ-treated patients. Treatment with RINVOQ is not recommended in patients with an ALC <500 cells/mm^3. Evaluate at baseline and thereafter according to routine patient management.

Anemia

Decreases in hemoglobin levels to <8 g/dL were reported in RINVOQ-treated patients. Treatment should not be initiated or should be interrupted in patients with hemoglobin levels <8 g/dL. Evaluate at baseline and thereafter according to routine patient management.

Lipids

Treatment with RINVOQ was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Manage patients according to clinical guidelines for the management of hyperlipidemia. Evaluate patients 12 weeks after initiation of treatment and thereafter according to the clinical guidelines for hyperlipidemia.

Liver enzyme elevations

Treatment with RINVOQ was associated with increased incidence of liver enzyme elevation compared to placebo. Evaluate at baseline and thereafter according to routine patient management. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. If increases in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are observed during routine patient management and drug-induced liver injury is suspected, RINVOQ should be interrupted until this diagnosis is excluded.

EMBRYO-FETAL TOXICITY

Based on findings in animal studies, RINVOQ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with RINVOQ and for 4 weeks after the final dose. Verify pregnancy status of females of reproductive potential prior to starting treatment with RINVOQ.

VACCINATION

Avoid use of live vaccines during, or immediately prior to, RINVOQ therapy. Prior to initiating RINVOQ, patients should be brought up to date on all immunizations, including prophylactic varicella zoster or herpes zoster vaccinations, in agreement with current immunization guidelines.

MEDICATION RESIDUE IN STOOL

Reports of medication residue in stool or ostomy output have occurred in patients taking RINVOQ. Most reports described anatomic or functional GI conditions with shortened GI transit times. Instruct patients to contact their healthcare provider if medication residue is observed repeatedly. Monitor patients clinically and consider alternative treatment if there is an inadequate therapeutic response.

LACTATION

There are no data on the presence of RINVOQ in human milk, the effects on the breastfed infant, or the effects on milk production. Available data in animals have shown the excretion of RINVOQ in milk. Advise patients that breastfeeding is not recommended during treatment with RINVOQ and for 6 days after the last dose.

HEPATIC IMPAIRMENT

RINVOQ is not recommended for use in patients with severe hepatic impairment.

ADVERSE REACTIONS

The most common adverse reactions in RINVOQ clinical trials were upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, headache, peripheral edema, increased blood creatine phosphokinase, hypersensitivity, folliculitis, abdominal pain, increased weight, influenza, fatigue, neutropenia, myalgia, influenza-like illness, elevated liver enzymes,

rash, and anemia.

Inform patients that retinal detachment has been reported in clinical trials with RINVOQ. Advise patients to immediately inform their healthcare provider if they develop any sudden changes in vision while receiving RINVOQ.

Dosage Forms and Strengths: RINVOQ is available in 15 mg, 30 mg, and 45 mg extended-release tablets.

Visit rxabbvie.com/pdf/rinvoq_pi.pdf for Prescribing Information, including BOXED WARNING, for RINVOQ.