Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/best-practices-use-long-acting-injectables-bipolar-disorder-part-1/12971/

Released: 11/23/2021
Valid until: 11/23/2022
Time needed to complete: 30 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Best Practices in the Use of Long-Acting Injectables in Bipolar Disorder – Part 1

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Best Practices in the Use of Long-Acting Injectables in Bipolar Disorder – Part 1” is jointly provided by Novus Medical Education and Medical Education Resources and is supported by an independent educational grant from Otsuka America Pharmaceutical, Inc.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the Learning Objectives.

Dr. McIntyre:
Hello, and thank you for joining us for our webcast titled: Best Practices in the Use of Long-Acting Injectables in Bipolar Disorder. I am Roger McIntyre, the Professor of Psychiatry and Pharmacology at the University of Toronto, and I'm delighted to be sharing this topic with my friend and colleague, Martha Sajatovic from Case Western University. Martha, introduce yourself.

Dr. Sajatovic:
Thank you. Really great to be here with you today, Roger. I'm Dr. Martha Sajatovic. I'm a Professor of Psychiatry and Neurology at Case Western Reserve University School of Medicine from Cleveland, Ohio.

Dr. McIntyre:
You know, Martha, one of the aspects about this program, which I find so interesting is that when we look at bipolar disorder, we know that it's common, we know it's severe and debilitating. And much of the debilitating aspect of bipolar is a consequence of the longitudinal course, more specifically relapse, recurrence, and functional impairment.

In today's program, we're going to speak to not just a conceptual framework of bipolar disorder specifically looking at progression of the illness both clinically and perhaps neurobiologically. But we're also going to do, Martha and I together, is we're going to be speaking to the rationale for considering a long-acting injectable in a person affected by bipolar disorder, especially where in the algorithm to initiate the treatment. I think the evidence is suggesting earlier rather than later provides the best hope for success for many people.

We're going to be talking also about working with patients. And of course, this is a time when we want patient engagement, we want shared decision-making, and what are some of the best practices around shared decision-making with people who might be a candidate for this modality of therapy.

Throughout this conversation, Martha and I are going to keep it pretty informal. And we're going to really roll up our sleeves a little bit and really speak to some of the key aspects that we as clinicians are faced with our patients and some of the learnings we've had in having discussions and implementing long-acting injectables in our patients.

So Martha, I’ll be able to start off with this whole topic of progression. And it's interesting because when I think about bipolar disorder in my practice, over 20 years now, my experience would cohere with the published evidence that most people with bipolar disorder have a propensity to relapse. The evidence would say, more than 95% of people will experience a relapse or recurrence at some time in their life. But we've also learned is that episodes seem to beget episodes. In other words, episodes, when you have more, then you tend to

have a greater risk for more episodes.

Among other things, there's been a whole literature looking at what are the factors that increased risk of relapse? We're going to say a lot about non-adherence. But there's other factors as well, such as comorbidity, drugs and alcohol, you'll speak to that. I've been particularly interested in obesity and its role in increasing the risk of relapse in bipolar.

But maybe just to stick with the concept of progression, there is a line of evidence in our field that would suggest that at the neurobiological level, some people maybe not all, but some people seem to be progressing. And maybe progressing is not the right word, maybe it's regressing is the right word. Insofar as if you look, for example, at brain structure. Brain structure begins to change across time in the wrong direction. And we know, for example, from some lines of research that those brain changes subserve changes in cognition. And that's been seen as well.

So as we talk about bipolar, we're talking about humans affected. We want to preserve human capital to the best we can, obviously alleviate the stress. And for us, we don't just want to treat bipolar, we want to also prevent the progression of bipolar.

Dr. Sajatovic:
Yes, I would agree with that. And I think in the context of the biological changes, that sort of negative footprint that a relapse episode has, you can think about all of the social ramifications and consequences. Let's say you have a hospitalization, everything that's acquired to kind of get back in your life, so you can see that it really does become kind of a wholesale - wholescale.

Dr. McIntyre:
Yeah, absolutely.

Dr. Sajatovic:
So that's important to consider. And the more we can minimize the impact of that, I think the more we can do for our patients.

Dr. McIntyre:
I agree with that. And I think that one of the maybe implicit aspects about progression is that maybe response to some of our treatments may be different at the first or second or third episode, when compared to example for the fifth or the tenth episode.

And I vividly recall some results in the psychosocial world where it was shown that, for example, cognitive behavioral therapy, a very effective treatment for many people with bipolar disorder targeting, for example, subsyndromal, depressive symptoms may not be as effective after seven or eight or ten episodes versus two to three episodes.

So for me, that's not just a clarion call to try and prevent episodes, but it's also a clarion call to be thinking about our treatments from the point of view, how good are these treatments are preventing relapse and recurrence?

Dr. Sajatovic:
I think that's an excellent point, Roger. When I have discussions with my patients and their families, sometimes I refer to what's been described by others as the Humpty Dumpty syndrome, right. So if you have a relapse, and it's a very –

Dr. McIntyre:
Yeah.

Dr. Sajatovic:
-complicated, especially a protracted kind of episodes, if you just go back to the treatment, let's say there was a medication that worked for you, it may not automatically work as well as it did previously. So the ideal plan is to try to avoid Humpty falling off the wall in the first place.

Dr. McIntyre:
So given what we've talked about, with respect to not just the theoretical, but the clinical implications of relapse and recurrence and progression, what are some of the modifiable factors in trying to really change this in a positive way? One of those factors is medication adherence.

Dr. Sajatovic:
Absolutely. So it is a topic that's near and dear to my heart.

Dr. McIntyre:
Sure is.

Dr. Sajatovic:
A big chunk of my career –

Dr. McIntyre:
Yep.

Dr. Sajatovic:
-studying medication adherence, and different types of serious mental illnesses in bipolar disorder in particular.

So if you look at the medication adherence literature, one thing that's out there is a threshold. You know, kind of almost like the good-enough mother, what's the good-enough medication adherence? Research literature typically takes a cutoff point of 80% or more, that if you take that much, you're considered adherent. Although adherence is not a all-or-none thing. Very often people will take some of their medications. That tends to be more than norm. If you look at folks with bipolar disorder, non-adherence rates in the research literature are generally anywhere between 20 and 50%.

But you know, let's think about what we as clinicians can do. So, suboptimal adherence is the norm. There are a variety of circumstances that can lead to non-adherence. So for example, when the clinician prescribes a medication, initially, the patient may not take it, or let's say they start their medication, they may not refill medications or in may not refill them in a timely pattern. They may discontinue a medication before completing a full course, guilty for being on antibiotics, right?

Dr. McIntyre:
Yeah, absolutely. I'm guilty, as well.

Dr. Sajatovic:
So we can all relate to this, right?

Dr. McIntyre:
Yeah.

Dr. Sajatovic:
Taking more or less of a medication than prescribed. Some of that might be tolerability or other concerns. Taking a dose at the wrong time. But one thing that's really common is that people just plain forget.

Dr. McIntyre:
Sure.

Dr. Sajatovic:
Especially if you have to take a medication on a daily basis. And for some of our medication treatments, people are on medications a couple of times or more per day. So we also know that the consequences of poor adherence can be really significant. We talked about hospitalizations and relapse. We talk about the biological effects on the brain. Unfortunately, in the worst cases, you can have people starting to have more risky behaviors, substance use or misuse, incarceration, in the worst case is suicide. So what seems like it could be something that happens sort of variably, can lead to, unfortunately, sometimes irreversible consequences.

So let's talk a little bit about, you know, what clinicians can do to help their patients navigate what I see is kind of a shared journey of medication taking. You know, ideally, the decision of what to prescribe and how it will be prescribed would be a shared decision between your patient and you. But we have to think about all of those determinants around poor adherence. So, you know, patient factors. Roger, you mentioned cognitive deficits, which is a hallmark of many serious mental illnesses –

Dr. McIntyre:
Absolutely.

Dr. Sajatovic:
-that could make adherence challenging. The environment. You know, maybe a person may not be able to have a standard routine, let's say they're a shift worker, it's hard to tie medication-taking into your life. There may be social environmental patterns. So families can sometimes be supportive of medication-taking, other times not so. There's a pharmacologic delivery system. So you know, I mentioned that there's some medications that you need to take more than once a day. There are others that could be, you know, we think about formulation like long-acting injectables, where the spacing of the administration can be spaced out much further. That can bring its own challenges –

Dr. McIntyre:
Right.

Dr. Sajatovic:
-of you know, how you're going to be regular with your medications. Medication response is a big deal. So, does this medication work

for me to help control my symptoms? Does it cause more side effects? What is the balance between benefit and burden for me as somebody with lived experience?

But the other the other thing that I think it's important to mention is, when a medication is prescribed, that discussion about medication adherence needs to happen right away.

Dr. McIntyre:
Yep.

Dr. Sajatovic:
And we need to be able to normalize missing some doses. Right? So how does a clinician assess for adherence? Right?

Dr. McIntyre:
Yep.

Dr. Sajatovic:
The research literature says that prescribing clinicians are not stellar at dichotomizing people into this one is adherent or this one's not. You know, we all think, just like we're all above average, right?

Dr. McIntyre:
Yeah, right.

Dr. Sajatovic:
Our patients all are adherent, but we know that that's not what, you know, not what happens in the real world.

So there are a number of tools that we can use to help us to identify medication adherence. There is a host of adherence rating scales. And most of the adherence rating scales include elements of medication taking, you know, did you actually take your medicine? Or how many times did you take it in the last X many days? As well as some assessment of attitudes or beliefs about medications. Because that will give you as a clinician some indication of what are the concerns you need to address. And how likely is it that your person might miss medication from time to time?

If I was going to say, you know, what would be my recommendations for clinicians to try to assess medication adherence? What I'd say is that there's no single perfect method. You know, use all your available information and combine that. You know, what is the patient telling you? Do they have family members that are involved in care? Are they in the session? You know, we can use self-report. And symptom flare-up might be a thing for you to ask about. So when a person has a resurgence of symptoms, you know, what is that in the context of? And this is where normalizing missing some doses can be really important to let your patient be candid with you and feel trusting enough that I can say - that they can say to you, you know, ‘This is not really working for me,’ or ‘I'm having side effects.’ Assessments need to be done repeatedly. And adherence definitely is a process rather than an event.

Dr. McIntyre:
That's a really important point, Martha. You know, I think for me, one of the pivots in my career has been really more and more practicing shared decision-making. And shared decision-making is not simply about recognizing a patient's agency and their own sort of self-efficacy. It's also about engagement and engaging in the process. The literature has shown that when patients participate in shared decision-making, not only do they tend to be more adherent, but in some circumstances, the health outcomes are improved. And I would say that that's a pivot for me professionally, to really engage the patients and their families more, layout the dashboard, we talk about oral treatments and bipolar, psychosocial treatments, where appropriate neurostimulation and where appropriate long-acting injectable, can give them really understandable digestible information and make that a shared process.

Dr. Sajatovic:
I couldn't agree more. You know, having an individual understand what their options are, and then pick the choice that's most acceptable to them is likely to get that by and that you need, you know. They’re in the session with you, you know, maybe 20 minutes, 30 minutes, 40 minutes, probably tops.

Dr. McIntyre:
Yep. Yep.

Dr. Sajatovic:
And the rest of the time they're, you know, they're them and their medication and they're making a decision. Even if you're going to go the route with long-acting injectable medication, that person still has to come back to the clinic or whatever treatment setting they are to get a medication. So reducing the frequency of medication administration does not take out that shared decision-making element.

Dr. McIntyre:
So human nature is with you throughout the entire journey, regardless of treatment.

Dr. Sajatovic:
We can't escape ourselves, right?

Dr. McIntyre:
You know, one factor just comes to mind sort of just as you're speaking, Martha, is our own biases as clinicians. And one of the observations I've had - this wasn't philosophical or ideological or anything of that sort - is that I had a bias that long-acting injectable in bipolar was only for that patient late stage, very tertiary, non-adherent. I didn't even consider the fact that maybe a patient prefers this treatment option, who may not be that person. It may be a person earlier in the illness course. May be a person who needs your definition of the 80% plus adherence and they said, 'Hey, I'd rather make one decision a month rather than 30 decisions a month.' That was my bias encroaching into the decision-making with the patient. Something I learned from just day-to-day practice.

Dr. Sajatovic:
And that's true, you know, clinicians need to look at their own biases and understand what they are. Do you think that this is infantilizing your patient –

Dr. McIntyre:
Right. Right.

Dr. Sajatovic:
- or coercion. You know, whereas one way to think about it is if you are - you prescribe an anti-psychotic, whether it's an oral or an LAI, if you're prescribing, you want that person to take their medicine every day.

Dr. McIntyre:
Of course. Of course.

Dr. Sajatovic:
And so, if we think about it, you know, make it as easy as possible.

Dr. McIntyre:
Yep, absolutely.

Dr. Sajatovic:
We all have enough other things to worry about.

Dr. McIntyre:
So, Martha, again what we say and just, you know, in day-to-day practice seeing patients, what are some of your tips on how we can just bring this up conversationally with patients?

Dr. Sajatovic:
Yeah, so I think, you know, questions about medication-taking and people's attitudes, your patient in particular's attitude is important. So an example of some questions are saying, 'Do you feel like taking medication as prescribed fits in very easily with your daily routine?' Or, 'Are there roadblocks in your routine?' Let's say, 'You're a shift worker, you have to get up really early in the morning, get your kids off to school, and then go do something yourself, does your medication-taking fall by the wayside? Is there something we can do to either change your routine, change the timing, go with a different route of medication?' But those questions can help you bring that shared decision-making to the forefront?

Dr. McIntyre:
Yep.

Dr. Sajatovic:
Is it easy to remember to take my medication at the right time? We talked a fair bit about cognitive impairment that is part and parcel of having bipolar disorder.

Dr. McIntyre:
Yep.

Dr. Sajatovic:
And it may be that, you know, people just have a hard time remembering to take medication, so you want to reduce that burden to the

greatest extent that you can.

LAI formulations have been developed in part to improve treatment adherence. And we know that there are a variety of LAIs that are available currently. And the dosing schedule can range from weeks to months. That can definitely improve outcomes –

Dr. McIntyre:
Yep.

Dr. Sajatovic:
-when you remove that burden of having to remember.

Dr. McIntyre:
That's right. Yeah, absolutely. And that's been my experience as well. And again, part of the engagement process, literacy enhancement, really get the patients involved in this. But I certainly found in my experience, that the opportunity to give patients, again, that empowerment, they take the medication with an LAI, it can be less frequently, they don't need to take it every day. For many patients, as you hinted at, that has a risk because they're forgetting maybe they want to take it a month later. But I find that taken together, the calculus has been, for most patients, it actually facilitates their adherence. And they have a sense of like greater control and a sense of agency over their life, what they're doing. And they don't - many patients have said to me, 'You know, Dr. McIntyre, I don't think the medication controls me as much,' when they take LAIs. So these types of testimonials have really affected me. And that's why when I meet with anyone who has bipolar, even as a first-episode mania, we're discussing the dashboard, I put LAIs on that dashboard. And, of course, the patient is non-adherent, multi-episode later stage, absolutely that person as well. But I've really tried to keep a check on my own biases on this issue.

Dr. Sajatovic:
I think that's true. So I was involved in a team that did an expert panel assessment of the appropriate use of LAIs. We had just over 40 experts who did this online survey. And most experts, almost 80%, agree that they were only somewhat confident that they could assess adherence. So I think it's important to understand that, you know, you can't predict or know for certain if somebody in your office, if that person is adherent or not adherent or somewhere in between which is usually the case. But what I thought was particularly interesting in this survey of these who were experts who had facility with using LAIs, with using a variety of oral medications for people with serious mental illness is that the survey results suggested that we should be considering and using these compounds earlier. So again, if you're already prescribing an anti-psychotic, that should be one of the discussed treatment options.

Dr. McIntyre:
Makes good sense.

Dr. Sajatovic:
So we have a variety of compounds now. Fortunately, there has been a proliferation of available treatments, you know, with a variety of dosing durations, different regimens, so clinicians certainly have a –

Dr. McIntyre:
Yep.

Dr. Sajatovic:
-wealth of treatments to look at. There are a couple LAIs that are FDA approved for bipolar disorder, risperidone microspheres, aripiprazole monohydrate. You know, again, just with as with any bipolar treatment, the recommendation of what to use is really going to be driven by patient preference, patient lifestyle, you know, what do you think would be the best option for your patients and ideally using a shared decision approach?

Dr. McIntyre:
Yep. Yeah, that's a really nice point, Martha. And I think that when we begin to look at the literature, in general, with the long-acting injectables, that there was a couple of summary statements. First, for me, it's clear that conventional long-acting injectables in bipolar, they've been studied for decades, not FDA approved as you alluded to, but they do increase the risk of depression in bipolar disorder. So what we want is treatments that can be stabilizing, but not be depressogenic in bipolar. You mentioned the two, risperidone and aripiprazole, LAIs of the second generation class. And we know from separate lines of research that in bipolar, when we look at, for example, epidemiologic evidence, there is a lower risk of hospitalizations with LAIs versus oral. And this is a - really an observation made only with lithium, actually. So that's a very strong proxy of the long-term stability of these are the preventing that severity of relapse and recurrence.

Dr. Sajatovic:

What I'd like to do in the clinical setting is kind of compare and contrast, you know, what are the pros and cons of each. So it's not that, you know, oral is all bad, or LAI is all good.

Dr. McIntyre:
Right.

Dr. Sajatovic:
But you know, there are a mix, and what is the best thing for you -

Dr. McIntyre:
Yep.

Dr. Sajatovic:
-you know, having to take a medication less frequently. If there's a medication dose that's missed, the clinic staff will know that right away, and there may be an opportunity to get the individual into the clinic so that we don't have those unfortunate situations where there is a complication related to poor adherence.

Dr. McIntyre:
So really nice points, Martha, and obviously, the COVID-19 pandemic has really laid bare the importance of telehealth. It's brought it forward. I think we live in a telehealth, e-health, m-health world now. So given what we've been talking about adherence and long-term management of bipolar disorder, collaborative care, how do you sort of think this through vis-a-vis in this virtual world we're increasingly living in?

Dr. Sajatovic:
Yeah, so I would say one of the small silver linings to COVID is that both clinicians and patients feel more comfortable with telehealth perhaps in a way it's opening the door for people being more sharing and more candid. You know, they're sitting there with the patient, they're not worried about checking in and sitting in the waiting room, they're in their home or wherever they are.

Dr. McIntyre:
Yeah. Yep.

Dr. Sajatovic:
And you can see their environment, right? So you have an opportunity to maybe do a finer tuned adherence assessment. It is an opportunity maybe to have your visits a little bit more frequently, if you like. You also will have the opportunity typically to collaborate with primary care, right? So this is - most of us have electronic record.

Dr. McIntyre:
Yep.

Dr. Sajatovic:
Medical records now, and this is an opportunity to note that you've discussed adherence issues or staying on track with medication. So it really becomes a team effort. And I think that is important as we as we go forward into an era that is going to include telehealth increasingly.

Dr. McIntyre:
So Martha, we've been covering a wide swath of territory here today, what would be some of your key messages and takeaway for our participants?

Dr. Sajatovic:
Yeah, well, first of all, most experts will acknowledge that adherence cannot be reliably determined in a standard treatment setting. So we would love to think that all of our patients are 100% adherence, 100% of the time. The data does not support that.

Dr. McIntyre:
Okay.

Dr. Sajatovic:
So if we kind of accept that adherence is going to be suboptimal, and that is normal.

We know that there are some risk factors for poor adherence. So if you - if a patient has one or multiple of those risk factors, that might be an opportunity to kind of really have the discussion about adherence with them.

People with limited support, with reduced health literacy, those with comorbidity might be at higher risk.

Dr. McIntyre:
Good point.

Dr. Sajatovic:
Consider their attitudes toward medication. That might be something that's modifiable, hopefully, over time. Consider LAIs early in the course of illness so that we can hopefully minimize or perhaps avoid some of those very costly and consequential relapses. The patient-clinician communication is critical for getting buy-in and acceptance of LAIs, and you know, all that kind of holistic elements of treatments and self-management.

And then collaborating with primary care physicians will be helpful in treating the whole patient rather than just their bipolar disorder.

Dr. McIntyre:
Martha, wonderful points. And maybe just to put a fine point on a couple of things for me is, I'm always reminded of the chronicity, the debilitating aspect of bipolar, which is largely a function of the long-term course, relapse and recurrence. And if we want to reduce relapse and recurrence, which we do, that can really reduce the debilitating aspect of bipolar disorder.

And to put a fine point, which you mentioned around modifiable factors. So some factors in life, we can't modify but many factors we're talking about, we can modify. And you've spoken to and you've enumerated many of them. And for me, the issue around shared decision-making, and really giving patients full scope of the treatment options that are available, not just at the very late stage, but early in that initial discussion about bipolar disorder, offering psychoeducation. Because I think for patients, this empowers them, but also, in fact, puts them in a position to, as you said, have better literacy, but also in fact, positively changed the trajectory of their illness, is what we're all hoping for, for people who are affected with bipolar disorder.

So Martha, what a pleasure. Thanks for joining me for this conversation today. And I hope for all of our participants, this has been a very helpful and enjoyable, instructive session.

Dr. Sajatovic:
Likewise, Roger, thank you.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Novus Medical Education and Medical Education Resources and is supported by an independent educational grant from Otsuka America Pharmaceutical, Inc.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.