Needs Assessment Sample: **Long-acting Injectable Antipsychotics Agents in the Management of Schizophrenia**

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Educational Objectives and Agenda

Educational Objectives

After participating in the activity, the learners are expected to be better able to:

1. Describe the role of long-acting injectable antipsychotic agents in the management of schizophrenia.
1. Cite current data on approved long-acting injectable antipsychotic agents for the treatment of patients with schizophrenia.
2. Identify patients with schizophrenia who may derive benefit from treatment with an available long-acting injectable antipsychotic agent.

Agenda

15 min - Welcome, Introduction, Pre-Polling
After welcoming participants, the faculty expert will briefly review the topics that will be covered during the activity and briefly explain the CaseBook educational format, describing integrated patient scenarios to illustrate appropriate selection and treatment of schizophrenia patients. The audience will also be polled on their knowledge and competence in the management of schizophrenia in an era of increasing LAI antipsychotic medications.
30 min - The Role Of Long-Acting Injectable Antipsychotic Agents In The Management Of Schizophrenia
This segment will start with a review of the options, benefits, and risks of LAI antipsychotics for treating schizophrenia. This will encompass a review of the efficacy and safety data followed by coverage of respective delivery systems and dosing schedules of approved therapies for the treatment of schizophrenia. The advantages and significance of using LAI antipsychotics to increase adherence through inherently controlled monitoring and reduced administration will be emphasized.
30 min - Casebook Session: Selecting the Patient and Optimal LAI Antipsychotic for Management of Schizophrenia

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In the CaseBook session, an expert speaker will review case studies illustrating how LAI antipsychotics can improve patient outcomes, reduce relapses, and reduce hospitalizations In schizophrenic patients. Featured cases from the CaseBook: An adult patient with tardive dyskinesia who has taken oral risperidone for 6 years and has been repeatedly hospitalized for severe schizophrenia. An adult schizophrenic patient on medicaid. The patient desires treatment, but has family that has doubts about using any type of antipsychotic medication. A 51 years old schizophrenia patient with a history of violent behavior and a criminal record. An adult schizophrenia patient with a history of alcoholism who has been experiencing sedation while receiving clozapine.
In the final segment, the faculty expert will summarize the key objectives and take-home points discussed during the activity. Before closing the event, the presenter will address questions submitted from the online audience (live webcast). The audience will also be polled on changes in knowledge and competence.

Examples of Practice Aid downloadable point-of-care tools for this proposed activity may include the following:

New and emerging LAI antipsychotics

- Delivery systems
- Dosing schedules
- Efficacy and safety

Factors to consider when deciding to administer LAI antipsychotics

- Risk of non-adherence (eg, history of non-adherence, severe symptoms, comorbid substance use, cognitive impairment, ambivalence or negative attitudes towards medications)
- Relapse risk and severity

Benefits of LAI antipsychotics

- Increased adherence
- Less frequent dosing
- Ability to inherently monitor adherence
- Reduced risk of overdose
- Stable drug levels with avoidance of first-pass metabolism (ie, better relationship between dose and blood level of drug)
- Lower and less frequent peak plasma levels, leading to reduced side effects
- Reduced relapse frequency and rehospitalization rates
- Increased patient-centered care interactions with staff

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Faculty Considerations

Potential Chair and Faculty Members include, but are not limited to:

The faculty will be selected based on expertise, research, and published data. Faculty selection will also take into account the ability of particular experts to stimulate interactivity in the learning experience through their presentation style. All final decisions regarding activity faculty will be made by Medical Learning Institute.

Potential faculty members include, but are not limited to:

Michael W. Jann, PharmD, FCCP, BCPP
Professor of Pharmacotherapy
University of North Texas System College of Pharmacy
University of North Texas Health Science Center
Fort Worth, Texas

Leslie Citrome, MD, MPH
Clinical Professor of Psychiatry & Behavioral Sciences
New York Medical College
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Professor of Psychiatry and Molecular Medicine
Hofstra North Shore-LIJ School of Medicine
Hempstead, New York
Medical Director, Recognition and Prevention Program
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Maurizio Fava, MD
Director, Division of Clinical Research of the MGH Research Institute
Executive Vice Chair, Department of Psychiatry
Executive Director, MGH Clinical Trials Network & Institute (CTNI)
Associate Dean for Clinical & Translational Research, Slater Family Professor of Psychiatry, Harvard Medical School
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David C. Henderson, MD
Professor of Psychiatry
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APPENDIX

Summary of Gaps and Needs with Related Educational Objectives for the Proposed Intervention

A. Summary of Current Science

Schizophrenia is a chronic medical condition with periods of remission and relapses occurring over a patient's lifetime. Continuous antipsychotic medications are the foundational approach to management of patients with schizophrenia[1-3]. However, the successful treatment of schizophrenia requires patient adherence to medication. Studies indicate that treatment non-adherence leads to increased risk of relapse, hospitalization, and suicide.[4] Non-adherence with medication is a major problem and particularly challenging in schizophrenia due to the illness's association with social isolation, stigma, substance misuse, depression, and cognitive impairment.[5]

Long-acting injectable (LAI) antipsychotics were developed in part to address non-adherence.[3,6] LAI antipsychotics provide significant benefits over oral short-acting medications. Clinical data indicate that LAI antipsychotics can reduce relapse frequency and rehospitalization rates and increased interactions between patients and staff.[7,8] Additional significant benefits of LAI antipsychotics include the ability to monitor adherence and the ability to provide greater control of drug levels which reduces the risk for overdose. This is made possible in part due to avoidance of first-pass metabolism (ie, better relationship between dose and blood level of drug) associated with oral formulations.

LAI antipsychotic formulations involve physician-administered injections with dosing intervals of greater than 1 month.[3,9,10] By comparison, *oral* dosing must be self-administered typically daily. The less-frequent dosing of LAIs improves patient adherence in patients and correlates with improved patient outcomes.[9]

Significantly, the lower serum levels associated with LAI antipsychotics demonstrably improve patient medication tolerance and acceptance.[8] Safety profiles of LAIs are are comparable to their oral counterparts in terms of safety and tolerability, if injection site reactions are not taken into account.[3] LAI antipsychotics are recommended by clinical guidelines as a treatment option when non-adherence is a concern, for frequent and recurrent relapse, or for patient preference.[11,12]

Long-acting antipsychotic formulations are available include 2 first-generation antipsychotics (haloperidol decanoate and fluphenazine decanoate), and four second-generation (atypical) antipsychotics (risperidone microspheres, olanzapine pamoate, paliperidone palmitate, an intramuscular depot formulation of aripiprazole, and aripiprazole lauroxil).[3,13,14] A formulation of paliperidone palmitate is the first LAI agent to extend the dosing administration beyond the

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typical monthly time period to 3 months.[3] Aripiprazole lauroxil represents the newest LAI antipsychotic. and can be administered once-monthly, every 6 weeks, or every 2 months.[15,16] A phase III clinical trial with aripiprazole lauroxil was conducted in patients with schizophrenia (N = 623) who had an acute exacerbation of symptoms at baseline. Patients were randomized 1:1:1 into three groups: AL 441 mg (aripiprazole 300 mg equivalent), AL 882 mg (aripiprazole 600 mg equivalent), and placebo (IntralipidÒ, fat emulsion). Each dose was injected into the gluteal muscle every 4 weeks for the duration of the 12-week study. Aripiprazole lauroxil was shown to be efficacious in patients with acute symptoms of schizophrenia and was associated with a low risk of changes in metabolic parameters, similar to placebo over the 12-week study.[17]

Different choices of formulations can make the difference in finding the right intervention for the individual patient. There are also novel LAI antipsychotics under development. RBP-7000 represents the first second-generation antipsychotic to be available as a subcutaneously administered long-acting injectable.[18] It has a safety profile reportedly similar to that of oral risperidone that demonstrably.[19] Risperidone In Situ Microparticles® (ISM®) is a new long-acting intramuscular formulation for monthly administration currently in phase 3 of development.[20] BB0817 is a risperidone implant that met its primary endpoint in a 6-month study of the safety, tolerability, and pharmacokinetics of transferring patients diagnosed with schizophrenia or schizoaffective disorder and stabilized on oral risperidone.[21-23]

B. Optimal/Desired State of Practice

Physicians who care for patients with schizophrenia must be aware of the latest advances in LAI antipsychotics and the optimal incorporation of these therapies into clinical practice.

C. Gaps Based on Current Practice

Our research suggests that the management of schizophrenia is suboptimal. Many physicians are unaware of clinical evidence for LAI antipsychotics and the appropriate use of these agents. Recent expert analysis of needs and treatment opportunities to optimize schizophrenia treatment concluded that early timely intervention and relapse prevention are particularly essential for effective management of schizophrenia.[24]

D. Underlying Unmet Needs

Clinicians managing patients with schizophrenia need to improve their knowledge of LAI antipsychotics.

Clinicians managing patients with schizophrenia need to improve their competence in Incorporating LAI antipsychotics into patient-centered treatment plans.

E. Educational Objectives

To address the gaps and unmet needs related to treatment of schizophrenia, we are proposing the development of a unique infographic-based educational activity (please see the section of the proposal titled “Educational Rationale, Design, and Features” for further details) with the following educational objectives and goals:

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Proposed educational objectives (*as a result of participating in this activity, the learners are expected to be better able to)*:	**Relevant outcome level*** (*this learning objective will measure a change in*)**:** **ABMS, IOM, & National Quality Strategy (NQS)**	**competencies & domains** (*the proposed activity based on these learning objectives will address the following competencies*)**:**
1. Describe the role of long-acting injectable antipsychotic agents in the management of schizophrenia.	Knowledge (Level 3)	**ABMS:** ☒ Patient care ☒ Medical knowledge ☒ Interpersonal & communication skills **IOM:** ☒ Provide patient-centered care ☒ Work in interdisciplinary teams ☒ Employ evidence-based practice **NQS:** ☒ Making Care Safer ☒ Patient and Family Engagement ☒ Communication and Care Coordination ☒ Prevention and Treatment Practices
2. Cite current data on approved long-acting injectable antipsychotic agents for the treatment of patients with schizophrenia.	Knowledge (Level 4)	
3. Identify patients with schizophrenia who may derive benefit from treatment with an available long-acting injectable antipsychotic agent.	Competence (Level 4)	

*Moore DE Jr et al. *J Cont Educ Health Prof.* 2009;29(1):1-15. Please see the section of the proposal titled "Outcomes Measurement" for an overview of the methodology and outcomes that will be reported.

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F. Details of Underlying Unmet Needs & Proposed Educational Objectives

The following sources were used in this gap analysis and needs assessment (specific details relevant for each educational objective are reported below):

1. Review of published evidence in schizophrenia
1. Expert perspectives on the advances and challenges in the management of schizophrenia
2. Advanced outcomes/survey data from prior CME/CE activities focused on the management of schizophrenia
3. Questions and comments submitted by learners participating in prior CME/CE activities focused on the management of schizophrenia

Educational Need 1: Greater understanding of the therapeutic benefits of LAI antipsychotic medicationss.
Educational Objective 1: Describe the role of long-acting injectable antipsychotic agents in the management of schizophrenia.

Relapse can be exceptionally distressing for patients with schizophrenia. Reductions in relapse recurrence can exert a significantly positive impact on the outlook and quality of life for these patients.[25] The most common cause of relapse in treated schizophrenia is poor adherence to oral medication and this is increasingly controllable by using the proper long-acting antipsychotic.[26] LAI antipsychotics require administration every month or three months. Studies indicate that early intervention is essential for the effective management of schizophrenia.[24] Medication with the appropriate therapeutic agent that increases the likelihood for adherence combined with psychosocial therapy has the greatest potential of achieving prolonged relapse-free periods with the lowest risk of adverse events. Psychiatrists and general practitioners must be made aware of the benefits of using long-acting injectable antipsychotics to control adherence and the importance of early treatment to reduce relapses and obtain optimal management of patients with schizophrenia.

A wide variety of patient-specific factors may contribute to non-adherence including denial of illness, cognitive impairment, stigma associated with taking medication, substance abuse, access to health care/poverty, and insurance status. Lack of social support may also affect adherence, necessitating the assistance of health care professionals such as social workers.[9] The discontinuation rate for oral antipsychotics in schizophrenia ranges from 26% to 44%, and up to two-thirds of patients are at least partially non-adherent.[9,25] Many barriers to adherence may be simply circumvented by administering long-acting antipsychotics.

Despite the positive impact of non-adherence on patients with schizophrenia, studies suggest that physicians do not apply strategies to overcome this barrier. For example, although LAI antipsychotics are recommended by clinical guidelines and have been demonstrated to improve

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patient adherence and relapse rates, studies have shown that they are underutilized.[25,27-32] Barriers to LAI use in current practice include clinicians' lack of knowledge and negative attitudes about LAIs, resource issues, and cost.[27]

Psychiatrists must be aware of the side effects associated with specific LAI antipsychotic formulations. Adverse drug reactions can also contribute to non-adherence according to patients.[9,25] A cross-sectional survey of patients with schizophrenia found that medication non-adherence was significantly associated with the occurrence of side effects.[33] The second-generation LAI antipsychotics have reduced risk of extrapyramidal symptoms but do have long-term risks of weight gain with development of the metabolic syndrome.[3] However, a meta-analysis of clinical trials comparing LAI aripiprazole monohydrate 400 mg to oral aripiprazole determined that the LAI aripiprazole monohydrate was equally effective to oral aripiprazole with a low risk of discontinuation due to adverse events.[34]

Moreover, communication between patients and physicians may be inadequate, even though a better therapeutic relationship is associated with better adherence to medication among patients with schizophrenia.[35] Dr. John M. Kane, MD, Vice President for Behavioral Health Services of the North Shore - Long Island Jewish Health System and Chairman of Psychiatry at The Zucker Hillside Hospital in Glen Oaks, New York, Dr. Kane emphasizes that patients are more likely to be adherent to the management plan if they have a clear understanding of the illness and treatment expectations: "*it is important for the patient to understand why a particular treatment is appropriate and what side effects are associated with it. Clinicians must also provide psychoeducation to address misperceptions about and stigmas associated with the illness*.".[36] A survey of attitudes of patients, relatives, and psychiatrists revealed that two-thirds of patients did not receive information about LAIs.[31] Also, a disconnect has been identified between physician and patient assessment of adherence in schizophrenia thus underscoring the issue of inadequate patient communication.[32]

Analyses of surveys that included the target audience have revealed a lack of competence among physicians regarding approaches to improving medication adherence in patients with schizophrenia. For example:[37]

- 50% could not identify paliperidone as an antipsychotic agent available in a formulation that can be *administered 4 times a year*.
- 73% were unaware that aripiprazole lauroxil allows for multiple doses and intervals that can improve PANSS scores compared with placebo.
- 70% did not know that patients receiving olanzapine pamoate should be monitored for 3 hours after injection for the presence of post-injection delirium sedation syndrome.
- Only 47% indicated that they consider LAI antipsychotics for the treatment of patients with schizophrenia.
- Only 40% revealed that they always educate patients with schizophrenia about their illness, treatment expectations, and potential side effects.
- Strikingly, only 3% indicated that they were "very confident" in their ability to overcome barriers to achieving optimal outcomes in patients with schizophrenia, including non-adherence.

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Moreover, questions submitted by participants of previous educational activities further underscore inadequacies in treatment selection:[37]

- *What is the best first- then second-line therapy?*
- *Many patients with schizophrenia on multiple medications for control also have substance abuse that interferes with their treatment. How do you manage these patients?*
- *What is typically considered the drug of choice when starting therapy for schizophrenia?*
- *What is your stepwise approach in terms of pharmacotherapy?*
- *How do you manage patients who continue to have residual positive symptoms despite highest tolerated dose of best choice medication?*
- *What is your approach to treatment-resistant schizophrenia in patients who do not respond to maximum doses of one antipsychotic?*

Psychiatrists and general practitioners need to have an increased awareness of the therapeutic value, importance, and urgency of using LAI antipsychotics so they can make optimal treatment selection for the individualized patient with schizophrenia towards achieving optimal outcomes.

Educational Need 2: Improvement in professional knowledge of efficacy and expected adverse events of respective long-acting injectable antipsychotic treatment options.
Educational Objective 2: Cite current data on approved long-acting injectable antipsychotic agents for the treatment of patients with schizophrenia.

Antipsychotic medications have revolutionized the potential treatment of schizophrenia, but practicing physicians must be made aware of the efficacy data to be able to make appropriate treatment decisions. All of these medications block dopamine (especially D2) receptors in the brain, while the newer atypical agents also affect serotonin signaling. Data indicate that these medications are not more effective than traditional agents (eg, haloperidol, droperidol, fluphenazine) in the treatment-resistant patient with the possible exception would be clozapine, which may be more effective, but has the added risk of agranulocytosis.[38]

Data from surveys that included psychiatrists support the need for education on the clinical evidence for LAIs in schizophrenia. For instance:[37]

- 68% were unaware that the 3-month formulation of paliperidone palmitate is associated with a statistically significant difference from in delaying time to relapse relative to placebo.
- More than one-half (58%) of participants did not know that significant efficacy was observed with the 441-mg dose of aripiprazole lauroxil as early as 1 week, and improvements continued over 3 months.

Furthermore, questions submitted to faculty by participants indicate unmet educational needs:[37]

- *Are there any discernable differences in efficacy among the 3 most widely prescribed long-acting atypicals?*
- *Are there studies comparing no pharmacologic treatment and patients only being in therapeutic milieu?*
- *What new agents are currently being developed for schizophrenia patients?*

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Physicians must be made aware of the efficacy and safety data for the latest LAI antipsychotics to increase physician confidence and awareness of these powerful therapeutic options for managing and controlling schizophrenia

Educational Need 3: Improvement in professional ability to incorporate long-acting injectable antipsychotic agents into patient-centered treatment plans
Educational Objective 3: Identify patients with schizophrenia who may derive benefit from treatment with an available long-acting injectable antipsychotic agent.

The long-acting injectable second-generation antipsychotics are primarily indicated for the treatment of patients with schizophrenia.[3] However, none of the guidelines have clearly defined a recommended a defined threshold for the initiation of LAIs.[11] To address this issue, Kishimoto et. al defined and described three criteria to determine strength of indication:

1. Strong indication: hospitalization because of non-adherence AND at least *two* previous hospitalizations because of non-adherence.
1. Moderately strong indication: same as above, but *one* previous hospitalization due to non-adherence.
2. Moderate indication:

Of 305 reviewed charts from 279 unique patients, 27.2% were judged to have an indication for an LAI (n = 76), but only 32.9% of these (n = 25) were discharged on an LAI. This analysis indicates physicians LAI prescription overall was underutilized on the basis of their defined criteria.

Schizophrenics that have a history of violent behavior present a unique population with a strong indication for LAIs. A review of retrospective, population studies, case series, and post hoc analyses of randomized controlled trials reveals that treatment non-adherence with subsequent relapse can increase risk of violent acts.[39] *Adherence is one of few modifiable factors for adjusting the risk of violence.* Psychiatrists and general practitioners must be made aware of the value in using LAI antipsychotics in court-ordered commitment treatment both for the benefit of the patient and for the benefit of society at large.

When asked, physicians learners expressed a need for additional education topics addressing following:[37]:[37]

- Matching schizophrenia patients with the correct treatment
- Use of more than one antipsychotic agent
- More clinical details on how this impacts clinical care (ie, more clinical scenarios)
- Relating and integrating pharmacologic receptor data details into clinical phenomena

Psychiatrists need to be able to identify patients that will derived the most benefit from properly selected LAI antipsychotic medications based on the characteristics of the individual patients with consideration of adherence history, medical hospitalization history, drug-reimbursement policies, attitudes towards medication, and other comorbidities to achieve optimal outcomes. Ultimately, non-adherence remains an ongoing problem in the treatment of patients with schizophrenia, but significant evidence-based data has demonstrated that LAI antipsychotic

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medication can be safely used to reduce relapses and hospitalizations. Psychiatrists and general practitioners must be made aware of the latest positive therapeutic opportunities for addressing the major problem of non-adherence in treating schizophrenia.

In summary, the different elements of this needs assessment demonstrate significant gaps and unmet needs and further education is needed to approach best practice standards.

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