

Long-Acting Injectable Antipsychotics and Continuity of Treatment, a Pharmacist-Led Initiative

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Conflict of Interest

- The speaker has no conflicts of interest to disclose.



Learning Objectives

1. Recognize the differences in dosing of various Long-acting Antipsychotic Injectables (LAIs) and identify most common mistakes with LAI administration.
2. Outline pharmacist-led initiatives which facilitate transition of care to outpatient for patients on LAIs.

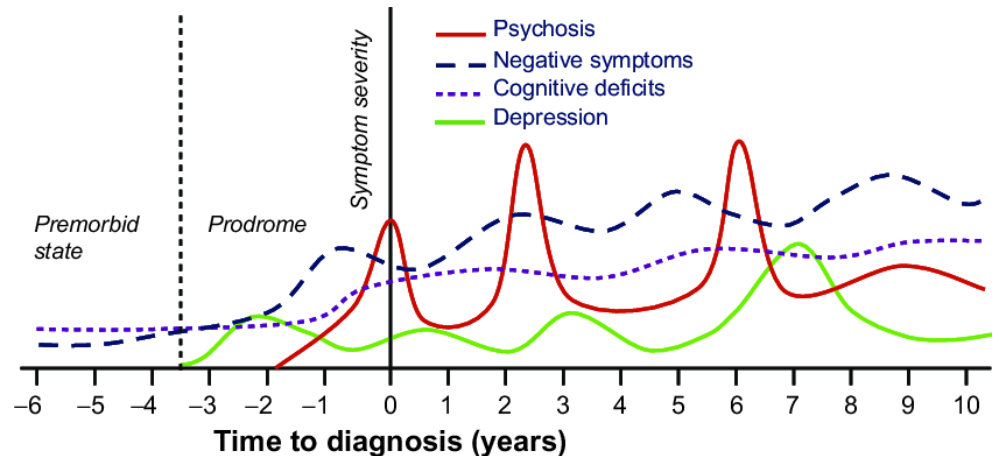


Outline

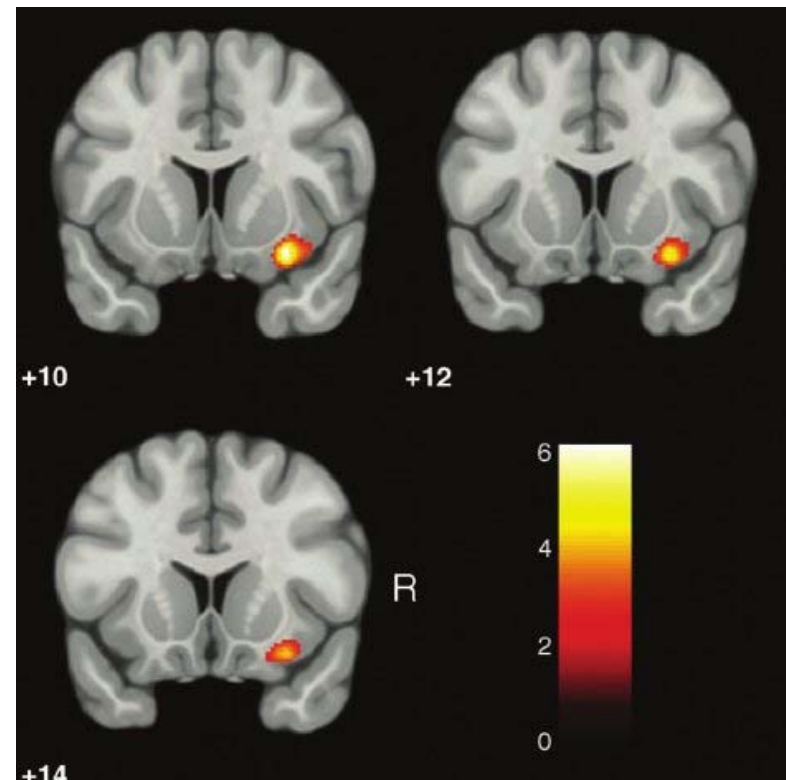
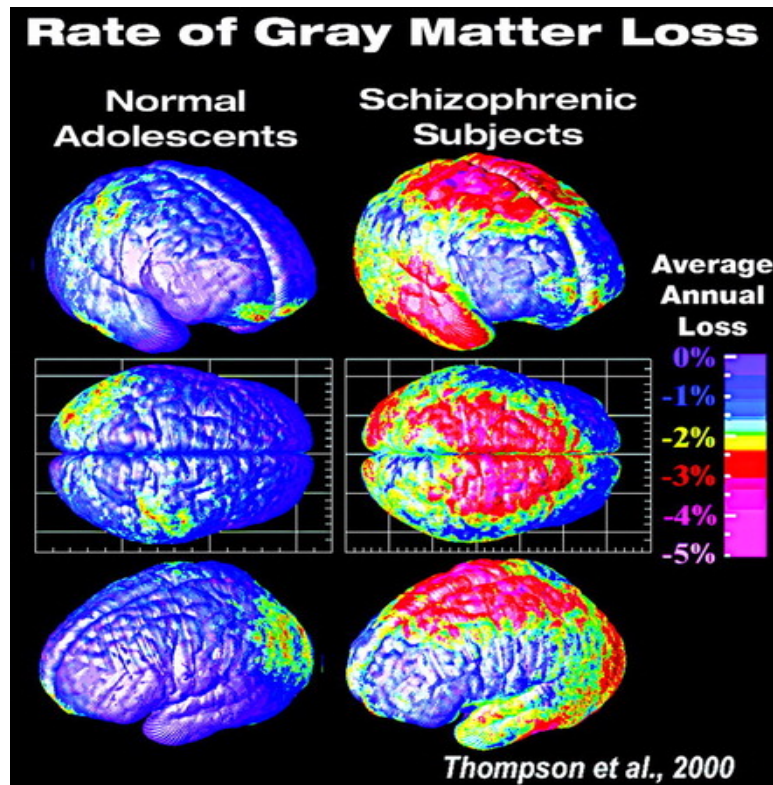
- Overview of treatment of schizophrenia with antipsychotic medications
- History of long-acting antipsychotic injections (LAI)
- Challenges with mental health treatments
- From diagnosis to successful implementation of LAIs
- Barriers to LAI implementation
- Review of dosing and administration of FDA-approved LAIs
- Common mistakes with LAIs
- Role of pharmacists and pharmacy technicians in patient safety with LAIs
- Transition of care in patients on LAIs
- Final remarks and future directions

Schizophrenia: Treatment and Prognosis

- Debilitating and chronic disorder
- Accompanied by psychosis, cognitive and social deficits (positive and negative symptoms)
- Strikes in young adulthood
- Antipsychotics reduce the risk of relapse by 2-3 times
- Non-adherence to antipsychotic treatment is frequently observed (26.5%-58.8%)
- 75% relapse within 12-18 months after discontinuing their medications



Brain Mass Loss in Schizophrenia and Bipolar Disorder



Proc. Natl. Acad. Sci. USA 2001 98 11650

The earliest deficits were found in parietal brain regions

Revista Brasileira de Psiquiatria. 2015;00

Reduction in gray matter volume in the right posterior insular cortex of patients with BD-I

Antipsychotics in Treatment of Schizophrenia

First Generation Antipsychotics: (Higher extrapyramidal side effects)

- Chlorpromazine (Thorazine)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)
- Loxapine (Loxitane)
- Perphenazine (Trilafon)
- Pimozide (Orap)
- Thiothixene (Navane)
- Trifluoperazine (Stelazine)

Second Generation Antipsychotics: (Higher metabolic side effects)

- Aripiprazole (Abilify)
- Asenapine (Saphris)
- Clozapine (Clozaril)
- Iloperidone (Fanapt)
- Lumateperone (Caplyta)
- Lurasidone (Latuda)
- Olanzapine (Zyprexa)
- Paliperidone (Invega)
- Risperidone (Risperdal)
- Quetiapine (Seroquel)
- Ziprasidone (Geodon)

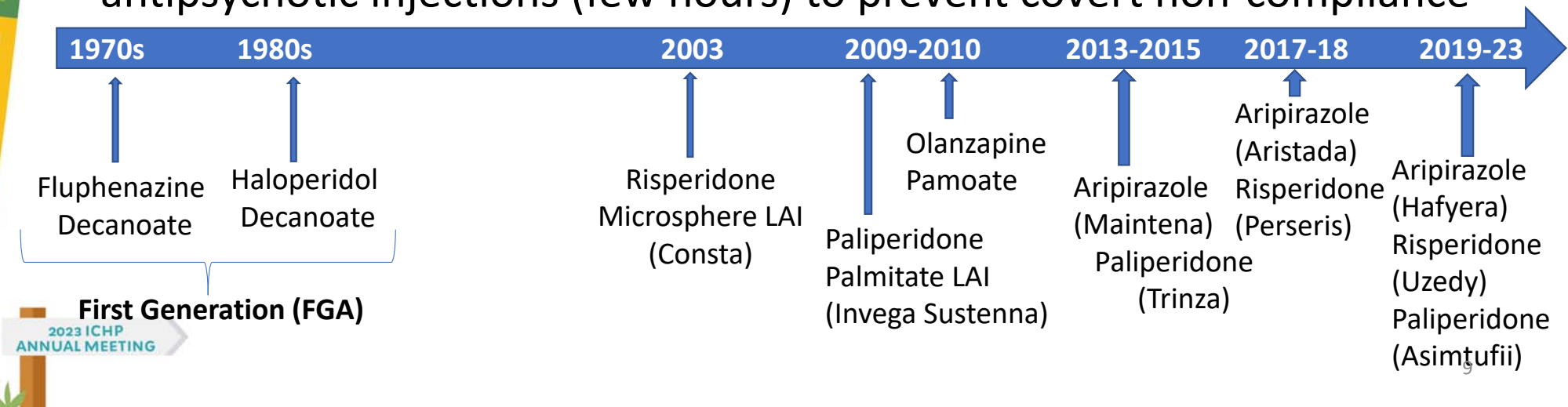


Safety Information and Side Effects with Antipsychotics

- Increased mortality in elderly patients with dementia-related psychosis
- Cerebrovascular adverse effects
- Neuroleptic malignant Syndrome (NMS)
- QT prolongation
- Tardive Dyskinesia (TD)
- Orthostatic hypotension
- Neutropenia
- Hyperprolactinemia
- Metabolic changes

History of Antipsychotic Long-acting Injections in the Treatment of Mental Health Disorders

- Injectable forms of antipsychotics used for management of acute psychosis (haloperidol and fluphenazine I.M.).
- First LAI: Fluphenazine enanthate (1966) and decanoate (1968)
- LAIs were developed to have longer half-lives (few days) than regular antipsychotic injections (few hours) to prevent covert non-compliance



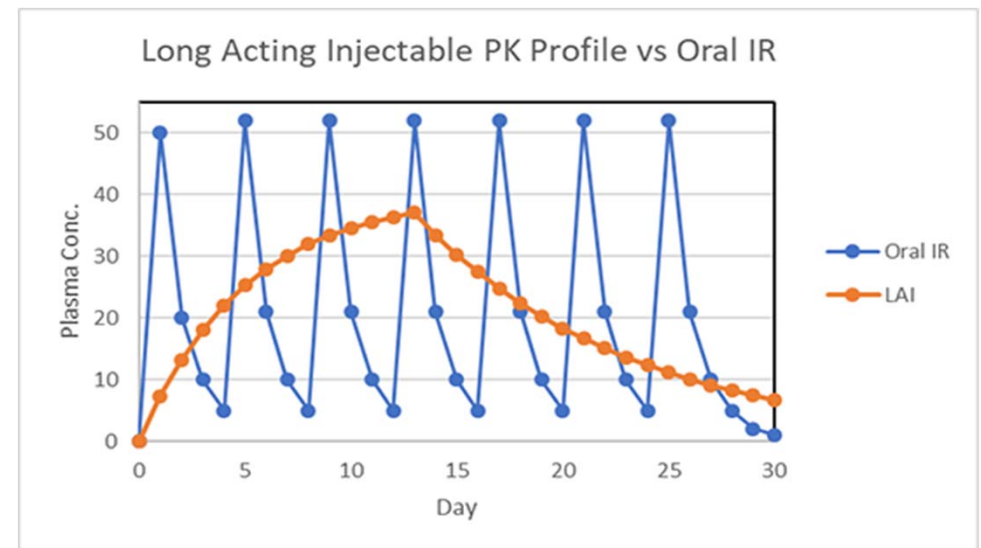
Long Acting Injections vs. Oral Antipsychotics:

Advantages (LAIs):

- Longer duration of efficacy (Half-life)
- No first-pass metabolism
- Less side effects
- Better compliance (less frequent dosing and no cheeking)
- More regular clinical check-ups

Disadvantages (LAIs):


- Long half-life (Longer time to eliminate)
- Less flexibility with dose adjustment
- Cost and insurance coverage
- Storage and administration
- Pain with administration
- Perception of stigma





Challenges With Treatment of Mental Health Disorders

- Patient insight and nature of disease
- Public and professional awareness
- Compliance
- Cost
- Stigma
- Inadequate professional services
- Poverty, crime, and homelessness
- HIPAA (adult patients)



From Diagnosis to the Successful Implementation of a LAIs in Young Adults With Schizophrenia

- What is the average age of onset of schizophrenia?
- What percentage of patients are on two or more oral antipsychotics before LAI initiations?
- What percent of newly diagnosed patients receive LAIs?

Kane et al. J Clin Psychiatry. 2023 Apr 19; 84(3)

From Diagnosis to the Successful Implementation of a LAIs in Young Adults With Schizophrenia

- What is the average age of onset of schizophrenia?
 - Male: Late adolescent to early 20s
 - Female: 20s to early 30s
- What percentage of patients are on two or more oral antipsychotics before LAI initiations?
 - About 60%
- What percent of newly diagnosed patients receive LAIs?
 - 4% (only 1% met successful implementation)



Barriers to LAI Implementation:

- Doubts regarding the benefit of LAIs
- Questions regarding their prescribing to a broader population of patients
- When to initiate LAIs
- Concerns around safety of LAIs
- Educating healthcare providers, patients, and caretakers
- Cost

Kane et al. CNS Drugs (2021) 35:1189–1205

FDA Approved First Generation Long-acting Antipsychotic Injections

LAI	Fluphenazine Decanoate	Haloperidol Decanoate
Trade Name	Prolixin Dec.	Haldol Dec.
Vehicle	Sesame oil	Sesame oil
Admin route Site of Injection Storage	SQ or IM Deltoid or Gluteal muscle Room temperature (RT)	Deep IM Deltoid or Gluteal RT
Typical Initial Dose	2.5-12.5 mg	10-20X last oral dose (Max 100mg/dose)
Typical maintenance Dose And Frequency	25 mg Q4W	10-15X last oral dose (50-200mg Q4W)
Oral dose overlap after first injection	Decrease oral dose by half Then discontinue with 2 nd injection	Taper and Discontinue after 2-3 injections

Second Generation Long Acting Injectable (SG-LAIs)

- **Olanzapine LAI:**
 - Relprevv (2009)
- **Aripiprazole LAI:**
 - Maintena (2013)
 - Aristada (2017)
 - Initio (2018)
 - Asimtufii (2023)
- **Paliperidone LAI:**
 - Sustenna (2009)
 - Trinza (2015)
 - Hafyera (2021)
- **Risperidone LAI:**
 - Consta (2003)
 - Perseris (2018)
 - Uzedy (2023)

LAI	Paliperidone Palmitate	Paliperidone Palmitate	Paliperidone Palmitate
Trade Name	Invega Sustenna	Invega Trinza	Invega Hafyera
Indication (FDA)	Schizophrenia & Schizoaffective Disorder (Adults)	Schizophrenia (Adults) Must be treated with Invega Sustenna for at least 4 months	Schizophrenia (Adults) Must be treated with Invega Sustenna for at least 4 months or Trinza 3
Vehicle	Water	Water	Water
Admin route Site of Injection Storage	Slow IM injection Deltoid or Gluteal Muscle Room temp (RT)	Slow IM injection Deltoid or Gluteal Muscle RT	Deep IM injection Only Gluteal Muscle RT
Typical Initial Dose	234mg on Day 1 and 156mg 4-8 Days later	Depending on last dose of monthly Invega Sustenna dose (4M)	Depending on last dose of monthly Invega Sustenna dose (4M) or Trinza (3M)
Typical Maintenance Dose and Frequency	39, 78, 117, 156, and 234mg Q4W after second dose	273-819mg Q3 months	1092mg or 1560mg Q6 Months
Oral dose overlap after first injection	Not required	Not required	Not required

LAI	Risperidone microspheres	Risperidone	Risperidone
Trade Name	Risperdal Consta	Perseris	Uzedy
Indication (FDA)	Schizophrenia & Bipolar I Disorder (Adults)	Schizophrenia (Adults)	Schizophrenia (Adults)
Vehicle	Water	Water	Polymer
Admin route Site of Injection Storage	Deep IM injection Deltoid or Gluteal Muscle Refrigerated or 7 days at RT	SQ Abdomen or upper arm Refrigerated or 30 days at RT	SQ Abdomen or upper arm Refrigerated or 90 days at RT
Typical Initial Dose	25mg 12.5mg in impaired hepatic/renal	90-120mg	50, 75, 100, 125, 150, 200, and 250mg
Typical Maintenance Dose and Frequency	25-50 mg q2W	90-120mg q Month	50, 75, 100, 125mg q M 100, 150, 200, 250mg q2M
Oral dose overlap after first injection	3W oral overlap	Not required	Not required

LAI	Aripiprazole Monohydrate	Aripiprazole Lauroxil	Aripiprazole Monohydrate	Olanzapine Pamoate
Trade Name	Abilify Maintena	Aristada and Aristada Initio	Abilify Asimtufii	Zyprexa Relprevv
Indication (FDA)	Schizophrenia and Bipolar I in Adults	Schizophrenia Adults	Schizophrenia and Bipolar I in Adults	Schizophrenia Adults
Vehicle	Water	Water	Water	Water
Admin Route Site of Injection Storage	Slow IM injection Deltoid or Gluteal Muscle, Room Temp	IM injection Deltoid (441mg) Gluteal Muscle (All), RT	Deep IM injection Only Gluteal Muscle Room temp.	Deep IM injection Only Gluteal Muscle Room temp.
Typical Initial Dose	400mg IM 300mg (2D6 poor metabolizer)	441, 662, 882mg, 1064mg plus 675mg (Initio) and 30mg PO	960 mg or 720mg (2D6 poor metabolizer)	210 or 300mg q2W or 405mg q4W
Typical Maintenance Dose and Frequency	400mg, 300mg QM 200mg QM 2D6+3A4inhibitors	441, 662, 882mg qM 882mg q6W or 1064mg q2 months	960 mg or 720mg q2M	150, 210, 300mg q2W or 300, 405mg q4W
Oral dose overlap after first shot	Continue oral dose for 2W	Without Initio: Oral overlap for 21 days	Continue oral dose for 2W	Not required



Common Mistakes with LAIs

- Dosing errors
- Preparation errors
- Administration errors
- Storage and Handling issues
- Errors associated with transition of care



Role of Pharmacist in Improving Patient Safety with LAIs:

- Monitoring, prescribing, and dosing of LAIs
- Reconciling medication history
- Providing training for medical team members (Providers and RNs)
- Educating patients and their caregivers
- Creating policies to ensure medication safety (Pharmacy admin team)
- Updating pharmacy team members regarding policies and procedures
- Facilitating the transition of care



Role of Pharmacy Technicians with LAIs

- Handling of LAIs according to manufacturer recommendations
- Assisting with medication reconciliation
- Managing inventory and maintaining the stock
- Educating RNs on proper methods of injection and preparation of LAIs
- Facilitating Transitions of Care



Polling Question 1 Case:

ET is a clinical pharmacist working in a behavioral hospital. He gets a call from a psychiatrist discussing an adult patient on risperidone 2mg PO BID. Patient has been complaining that medication makes his stomach upset and he also keeps forgetting to take the medication. This has contributed to poor compliance. Provider states that risperidone works well for controlling patient's psychosis. What is the best suggestion ET can provide?



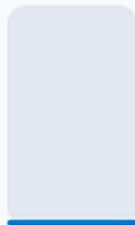
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1. What is the best suggestion ET can provide?

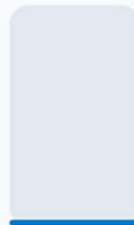


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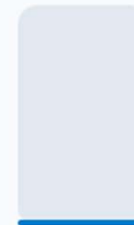
Switching to another antipsychotic medication

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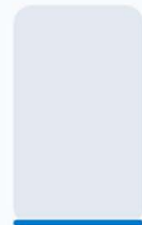
Advising to take risperidone tablet with food

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Considering using risperidone LAI

0%



Recommending antacids



Polling Question 2 Case:

JH is a pharmacy technician, who works at a psychiatric facility. She delivers risperidone LAI to a unit and notices that the nurse was under the impression that all LAIs should be given I.M. What do you think about the RN's statement?



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2. What do you think about the RN's statement?

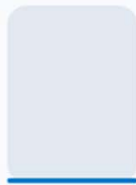
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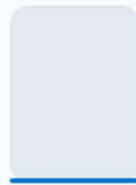
She is correct. All LAIs are given I.M.

0%



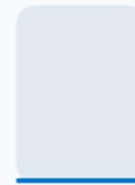
Most of the LAIs are given I.M, but some are SC injections

0%



The RN can administer LAIs either as I.M or SC, depending on patient preference

0%



The RN can give the injection to a deltoid or gluteal muscle depending on patient weight or BMI



Transitions of Care

- **Goal:** Increasing medication compliance with LAIs and lowering rate of relapse
- Providing continuity of care by filling the gaps prior to patient discharge (educating patients and their caregivers, requesting prior authorization)
- Communicating with case managers, social workers, and providers regarding the timing and location for the next injection
- Patient support programs (provided by pharmaceutical companies)
- Meds to bed programs and specialty pharmacy (link inpatient to outpatient)

Pharmacist Authority to Administer Long-Acting Antipsychotics

Based on data collected by NASPA (updated Dec 2021)



S fyt sf of sh j k X y j U m f w fh ~ F x x t h r f y t s x % S F X U F . % 5 7 6



Polling Question 3 Case:

LE is an inpatient pharmacist, who is about to verify the second injection from the initiation doses of paliperidone LAI. She notices that psychiatrist ordered paliperidone 156mg as onetime dose to be given today (four days later after patient received the first injection). Patient is going to be discharged the next day. What actions need to be taken to improve continuity of treatment?



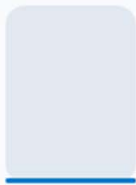
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3. What actions need to be taken to improve continuity of treatment?



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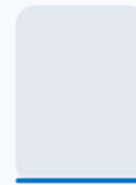
Verifying with prescriber regarding approval of prior authorization

0%



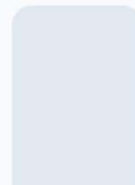
Reminding provider to enter a monthly injection order prior to discharge

0%



Confirming administration of the second injection for successful initiation

0%



All of the above



Polling Question 4 Case:

KT works with the pharmacy team at a behavioral hospital. She notices that the dose of a scheduled LAI is still not given to a patient. The medication was delivered to the unit during the last shift. Patient is going to be discharged from the hospital soon. What actions should she take to ensure patient safety and continuity of treatment?



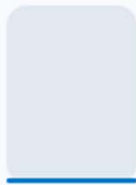
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4. What actions should she take to ensure patient safety and continuity of treatment?

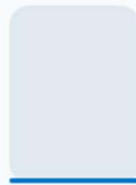
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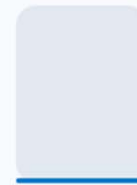
Assessing the medication integrity and quality before RN tries to administer it again

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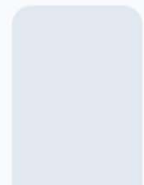
Notifying RN and pharmacist that the medication not administered

0%



Checking MAR for any documentation on med administration

0%



All of the above



Final Remarks and Future Directions

- Calling for a national registry program for LAIs to enhance medication safety and efficacy
- Advocating for early utilization of LAIs
- Encouraging policy makers and health insurance providers to support LAIs as a preferred treatment approach in schizophrenia
- Educating a wide range of health care professionals on LAIs and various aspects of mental health
- Raising public awareness and engagement for mental health disorders such as Schizophrenia and Bipolar disorder



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Questions?

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Nobody has responded yet.
Hang tight! Responses are coming in.

References:

- 1-Weiden et al. Psychiatric Annals, 2011;41(5):271–278
- 2-Brissos et al. Ther Adv Psychopharmacology, 2014;4(5): 198
- 3- Yasui-Furukori, Drug Design, Development and Therapy, 2012:6
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- 5-Kane et al. J Clin Psychiatry 2023;84(3):14544
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- 7-Medication Package inserts for FGA and SGA (FDA)
- 8-Kishimoto et al. Lancet Psychiatry 2021;8(5):387-404
- 9-Abraham et al. Research in social and admin pharmacy 2017;13(5):1004