



Long-Acting Injectable Medication Products

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Disclosures

Dr. Waters is a consultant with Johnson & Johnson. She will discuss all drugs without bias. All financial interests with ineligible companies (as noted) have been mitigated.

Learning Objectives

- Compare and contrast among different long-acting injectable (LAI) medications currently available for the treatment of schizophrenia, bipolar disorder and substance use disorders including:
 - Dosing
 - Generic and brand names
 - Adverse effects
 - Administration schedule
 - Overlap with oral medications
 - FDA-approved indications

Long-acting
Injectable
Antipsychotics



Currently Available LAI Antipsychotics	
Generic Name	Brand Name
First-generation antipsychotics	
Fluphenazine decanoate	Prolixin Decanoate
Haloperidol decanoate	Haldol Decanoate
Second-generation antipsychotics	
Aripiprazole lauroxil	Aristada Aristada Initio
Aripiprazole monohydrate	Abilify Maintena Abilify Asimtufii
Olanzapine pamoate	Zyprexa Relprevv
Paliperidone palmitate	Invega Sustenna Invega Trinza Invega Hafyera Erzofri
Risperidone	Risperdal Consta Uzedy

Establishing Tolerability

- Tolerability to oral formulation should be established prior to administration of LAI antipsychotic (**safety**)
- Best practice to also establish **efficacy** prior to LAI initiation

Oral Overlap with LAI Antipsychotics

- Some LAI antipsychotics require that patient continue treatment with oral antipsychotic for a specified time
 - LAI may not immediately be at therapeutic level



Oral Antipsychotic Overlap Requirements

LAI Antipsychotic		Oral Overlap Required?	Duration of Required Overlap
Generic	Brand		
Fluphenazine decanoate	Prolixin decanoate	Yes	Not definitively established
Haloperidol decanoate	Haldol decanoate	Yes	Not definitively established
Aripiprazole lauroxil	Aristada®, Aristada Initio®	Yes*	21 days*
Aripiprazole monohydrate	Abilify Maintena®	Yes	14 days [†]
	Abilify Asimtufii®	Yes	14 days
Olanzapine pamoate	Zyprexa Relprevv®	No	
Paliperidone palmitate	Invega Sustenna®, Invega Trinza®, Invega Hafyera®, Erzofri®	No	
Risperidone	Risperdal Consta®	Yes	21 days
	Uzedy®	No	

*Requires oral overlap only if Aristada Initio® is not administered along with Aristada®

[†]Unless using 1-day Abilify Maintena initiation strategy

Storage Requirements

- All risperidone-based products require refrigeration:
 - Risperdal Consta
 - Uzedly
- Must be allowed to come to room temperature prior to administration



Risperdal Consta [package insert]. Janssen Pharmaceuticals; 2007; Uzedly [package insert]. Teva Neuroscience, Inc.; 2023.

First-Generation LAI Antipsychotics: Dosing and Clinical Pearls

FGA LAI Dosing

FGA LAI Dosing (IM)				
Medication	Loading Dose?	Initial Dose	Target Dose	Frequency
Fluphenazine decanoate	No	1.25 x daily oral dose	6.25-50 mg (Max 100 mg)	2-4 weeks
Haloperidol decanoate	Yes	10-20 x daily oral dose *1st injection max 100 mg* For initiation doses > 100 mg, must split the dose: 100 mg on day 1 then the remainder any day from day 4-8	10-15 x daily oral dose (May administer >100 mg per injection, max 450 mg)	4 weeks

Fluphenazine decanoate [package insert]. APP Pharmaceuticals, LLC; 2012; Haldol decanoate [package insert]. Janssen Pharmaceuticals; 2005

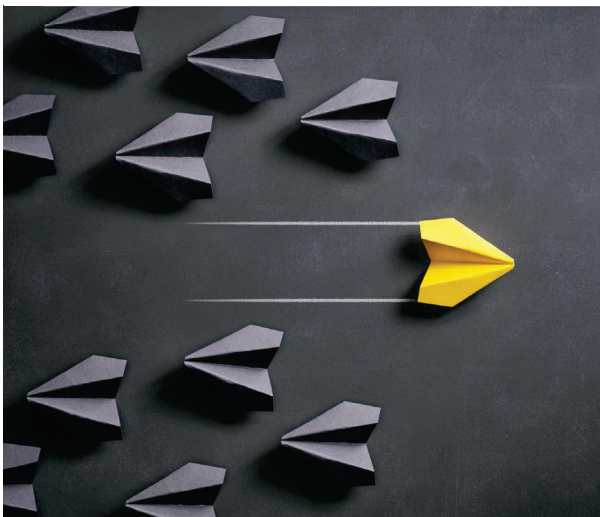
FGA LAI Clinical Pearls

- Both fluphenazine and haloperidol are **high-potency** antipsychotics
 - More likely to experience extrapyramidal symptoms (EPS) including acute dystonic reactions
 - Most patients will continue treatment with an oral anticholinergic (i.e. benztropine) to prevent EPS
- Both medications are intramuscular injections
- Both are in a **sesame seed oil base**
 - May consider Z-track injection technique
 - Oil-based injections may be more painful than water-based

Fluphenazine decanoate [package insert]. APP Pharmaceuticals, LLC; 2012; Haldol decanoate [package insert]. Janssen Pharmaceuticals; 2005

Second-Generation LAI Antipsychotics: Dosing and Clinical Pearls

Different Aripiprazole LAI Formulations



- Aripiprazole monohydrate vs. aripiprazole lauroxil
 - Activity of aripiprazole monohydrate mostly from parent drug
 - Aripiprazole lauroxil = prodrug (*N*-lauroyloxymethyl aripiprazole)
- **Not interchangeable**

Aripiprazole Monohydrate LAI Dosing

- Dose of LAI not based on oral aripiprazole dose

Medication	Dose	Frequency	Dose Adjustments	Administration Method	Continue oral?
Abilify Maintena	400 mg	Monthly	300 mg if experiencing ADEs	IM (deltoid or gluteal)	14 days unless following 1-day initiation method (next slide)
Abilify Asimtufii	960 mg	Q 2 months (56 days)	720 mg if experiencing ADEs	IM (gluteal)	14 days

Abilify Maintena [package insert]. Otsuka America Pharmaceutical, Inc.; 2002; Abilify Asimtufii [package insert]. Otsuka Pharmaceutical Co., Ltd; 2023

Abilify Maintena Initiation Methods

1. 1-day initiation:

- 2 separate injections of 400 mg IM AND one oral dose of aripiprazole 20 mg all on day 1

2. 14-day initiation:

- 1 injection of 400 mg IM on day 1 then 14 consecutive days of concurrent oral aripiprazole (10-20mg)

Abilify Maintena [package insert]. Otsuka America Pharmaceutical, Inc.; 2002

Aripiprazole Lauroxil LAI Dosing

Aristada Initio + Aristada

Day	Dose
Day 1	30 mg oral aripiprazole + Aristada Initio® 675 mg
Any day from day 1 to day 10	First dose of Aristada based on oral aripiprazole dose*
No overlap with oral aripiprazole	

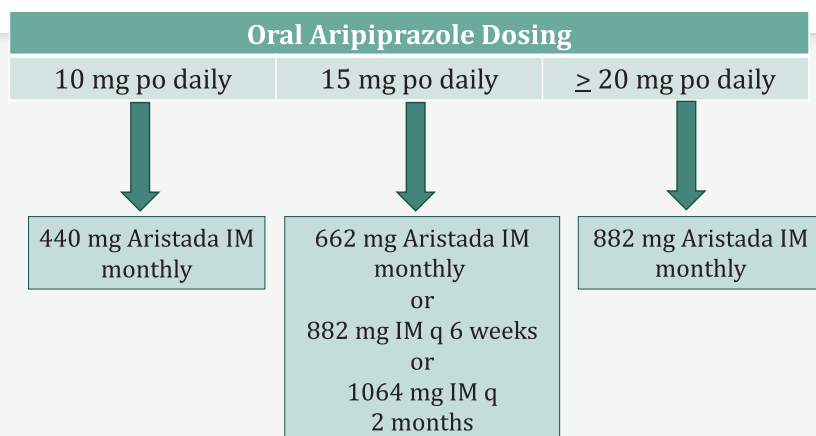
Aristada only

Day	Dose
Day 1	First dose of Aristada based on oral aripiprazole dose*
Day 1 to 21	Continue oral aripiprazole

*Dose conversion on next slide

Aristada [package insert]. Alkermes, Inc.; 2015; Aristada Initio [package insert]. Alkermes, Inc.; 2020

Aripiprazole Lauroxil LAI Dosing



Aristada [package insert]. Alkermes, Inc.; 2015; Aristada Initio [package insert]. Alkermes, Inc.; 2020

Olanzapine Pamoate LAI Dosing & Considerations

- Zyprexa Relprevv can only be administered in a registered healthcare facility with ready access to emergency response services
 - **Risk of post-injection delirium/sedation syndrome: risk for severe sedation (including coma) or delirium after each injection**
 - Requires direct monitoring for ≥ 3 hours after each dose
- Only available through restricted distribution program
 - REMS: Olanzapine Pamoate Patient Care Program
- Dosed every 2 weeks or every 4 weeks

Zyprexa Relprevv [package insert]. Eli Lilly and Company; 2009

Audience Question 1

A patient with bipolar disorder has been treated with aripiprazole 25mg po daily for several months. The provider would like to initiate LAI aripiprazole and prefers the medication with the longest dosing frequency so that the patient can receive injections less often. The patient also prefers if they did not have to take oral aripiprazole at all after receiving their injection. Which of the following is true?

- A. Aristada could be administered every 2 months for this patient.
- B. The dosing frequency for Aristada and Abilify Maintena would be the same for this patient.
- C. The patient could receive Aristada every 2 months as long as they also receive Aristada Initio on day 1.
- D. The patient could be treated with Abilify Asimtufii every 2 months without any oral overlap.

Audience Question 1

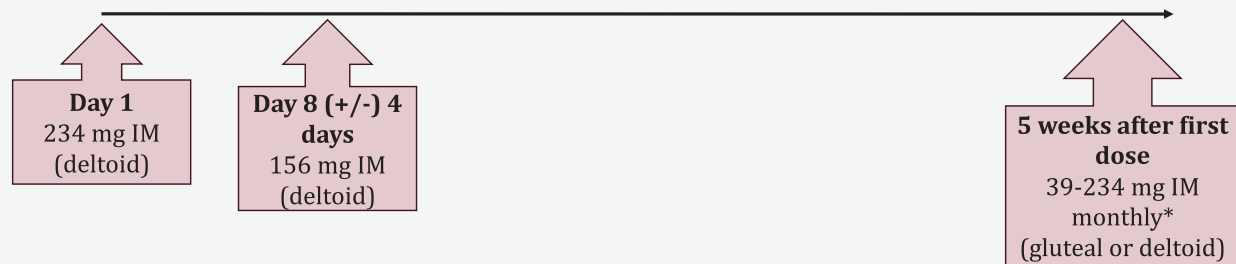
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Paliperidone Palmitate LAI Dosing

- “Invega” pathway: 3 formulations:
 - Every 1 month (Invega Sustenna)
 - Every 3 months (Invega Trinza)
 - Every 6 months (Invega Hafyera)
- **All patients must start with Invega Sustenna**
 - If patients receives ≥ 4 monthly injections (with last 2 doses being the same strength) can transition to Invega Trinza or Invega Hafyera

Paliperidone Palmitate LAI Initiation Dosing



Invega Sustenna [package insert]. Janssen Pharmaceuticals, Inc.; 2009; Invega Trinza [package insert]. Janssen Pharmaceuticals, 2015; Inc.; Invega Hafyera [package insert]. Janssen Pharmaceuticals, Inc.; 2021

*Dose conversion on next slide

Paliperidone Palmitate LAI Initiation Dosing

- Paliperidone = active metabolite of risperidone
- Most patients convert from oral risperidone (instead of oral paliperidone)

Daily Oral Paliperidone Dose (mg)	Daily Oral Risperidone Dose (mg)	Monthly IM Paliperidone Palmitate Dose (mg)
3	1	39
3	2	78
6	3	117
9	4	156
12	6	234

Invega Sustenna [package insert]. Janssen Pharmaceuticals, Inc.; 2009; Invega Trinza [package insert]. Janssen Pharmaceuticals, 2015; Inc.; Invega Hafyera [package insert]. Janssen Pharmaceuticals, Inc.; 2021

Transitioning to Every 3- or 6-Month LAI Dosing

- Can convert directly from every 1-month formulation to EITHER every 3-month or every 6-month formulations

Every 1-Month (Invega Sustenna) Dose	Every 3-Month (Invega Trinza) Dose	Every 6-Month (Invega Hafyera) Dose
39 mg	N/A	N/A
78 mg	273 mg IM every 3 months	N/A
117 mg	410 mg IM every 3 months	N/A
156 mg	546 mg IM every 3 months	1,092 mg IM every 6 months
234 mg	819 mg IM every 3 months	1,560 mg IM every 6 months

Invega Sustenna [package insert]. Janssen Pharmaceuticals, Inc.; 2009; Invega Trinza [package insert]. Janssen Pharmaceuticals, 2015; Inc.; Invega Hafyera [package insert]. Janssen Pharmaceuticals, Inc.; 2021

Erzofri

- FDA-approved in 2024 based on Invega Sustenna clinical trial data and open-label, randomized, multiple-dose, parallel-group PK study comparing bioavailability of Erzofri and Invega Sustenna
- Different dosing protocol that does not require the 2nd dose on day 8

Indication	Initial Dose (deltoid) Day 1	Monthly Dosage (deltoid or gluteal)	Maximum Monthly Dosage
Schizophrenia	351 mg	39-234 mg	234 mg
Schizoaffective disorder	351 mg	78-234 mg	234 mg

Erzofri [package insert]. Luye Innomind Pharma Shijiazhuang Co., Ltd. 2024

Paliperidone Palmitate LAI Clinical Pearls

- Invega Sustenna and Erzofri require renal dose adjustments
- Initiation doses of both should be administered IM in deltoid muscle
 - Maintenance doses of 1-month formulations: Deltoid or gluteal
 - 3-month formulation: Deltoid or gluteal
 - 6-month formulation: Gluteal

Invega Sustenna [package insert]. Janssen Pharmaceuticals, Inc.; 2009; Invega Trinza [package insert]. Janssen Pharmaceuticals, 2015; Inc.; Invega Hafyera [package insert]. Janssen Pharmaceuticals, Inc.; 2021

Risperidone LAI Dosing

	Risperdal Consta	Uzedy
Initial Dose	25 mg	50-250 mg*
Maintenance Dose	12.5-50 mg	50-250 mg*
Frequency	Every 2 weeks	Monthly or every 2 months*
Administration Method	IM	SQ
Administration Site	Deltoid or gluteal	Abdomen, back and outer area of upper arms

Risperdal Consta [package insert]. Janssen Pharmaceuticals; 2007; 2023; Uzedy [package insert]. Teva Neuroscience, Inc.; 2023

*Dose conversion on next slide

Uzedy Dose Conversion

Daily Oral Risperidone Dose	Corresponding SQ LAI Risperidone (Uzedy) Dose	Frequency
2 mg	50 mg	Monthly
	100 mg	Every 2 months
3 mg	75 mg	Monthly
	150 mg	Every 2 months
4 mg	100 mg	Monthly
	200 mg	Every 2 months
5 mg	125 mg	Monthly
	250 mg	Every 2 months

Risperdal Consta [package insert]. Janssen Pharmaceuticals; 2007; 2023; Uzedy [package insert]. Teva Neuroscience, Inc.; 2023

LAI Risperidone Clinical Pearls

- Some LAI risperidone products do not have equivalent dosing to common oral risperidone daily doses:
 - Uzedy does not have equivalent dosing for 6 mg daily of risperidone
- FDA-approved max daily dose of oral risperidone is 6 mg
 - In practice up to 8 mg/day may be used

Risperdal Consta [package insert]. Janssen Pharmaceuticals; 2007; 2023; Uzedy [package insert]. Teva Neuroscience, Inc.; 2023

Missed Doses



- All LAI antipsychotics have specific recommendations for how to re-initiate dosing if patient misses dose(s)
- Within the medication-specific timeframe, may be able to simply resume dosing
 - Sometimes have to re-initiate or change dose

LAI Antipsychotics per FDA-Approved Indication			
	Schizophrenia	Schizoaffective Disorder	Bipolar I Disorder
Haldol decanoate	x		
Prolixin decanoate	x		
Aristada Aristada Initio	x		
Abilify Maintena Abilify Asimtufii	x		x
Zyprexa Relprevv	x		
Invega Sustenna Erzofri	x	x	
Invega Trinza Invega Hafyera	x		
Risperdal Consta	x		x
Uzedy	x		x

Audience Question 2

Which of the following patients would be eligible to receive Invega Hafyera?

- A. A patient transitioning from oral risperidone 4 mg daily to an LAI for the first time
- B. A patient who has been treated with Risperdal Consta 50 mg monthly for several years and prefers an extended dosing frequency
- C. A patient treated with oral paliperidone who is only accepting of injections into the deltoid muscle
- D. A patient who has been treated with Invega Sustenna for 6 months and has received 156 mg monthly for the last 3 months

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Long-acting Injectable SUD Medications



Naltrexone LAI (Vivitrol)

- Approved for alcohol use disorder (AUD) and opioid use disorder (OUD)
- 380 mg IM monthly in gluteal muscle
- **Patients must be opioid-free for 7-10 days prior to administration**
 - Pretreatment with oral naltrexone not required

Naltrexone LAI (Vivitrol)



Consider recommending
naloxone



Requires refrigeration



REMS program due to risk of
severe injection site reactions

Buprenorphine ER LAI Products & Dosing

- Buprenorphine LAI products require induction (≥ 1 dose of ≥ 4 mg) with SL buprenorphine prior to initiation if not already established on treatment:
- All products are administered SQ
 - Buttock, thigh, abdomen, or back of upper arm
- Sublocade requires refrigeration

Medication	Dose	
Sublocade	300 mg SQ monthly x 2 months THEN: 100 mg SQ monthly* (may be increased to 300 mg monthly)	
Brixadi: Available in weekly and monthly formulations (not interchangeable, cannot combine)		
Daily dose of SL buprenorphine	Brixadi (weekly)	Brixadi (monthly)
≤ 6 mg	8 mg	x
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

*May be increased to 300 mg monthly if clinically indicated

Buprenorphine LAI Clinical Pearls

- Consider recommending naloxone
- Caution in patients taking other CNS/respiratory depressants (i.e. benzodiazepines)
- Sublocade and Brixadi both have boxed warning and REMS program:
 - **Risk of serious harm or death from IV self-administration**
 - Healthcare settings and pharmacies that order and dispense must be certified
 - Can only be dispensed directly to healthcare provider for administration (**not to patient**)
 - Pharmacies cannot distribute, transfer, loan, or sell drug

LAI Medications for SUDs per FDA-Approved Indication

	Alcohol Use Disorder	Opioid Use Disorder
Vivitrol	x	x
Sublocade		x
Brixadi		x

Audience Question 3

A patient with polysubstance use disorder (alcohol, cocaine, opioids) presents to receive LAI naltrexone (Vivitrol). Which of the following is the best course of action?

Medications:

Acamprosate 666 mg po TID

Gabapentin 300 mg po TID

Methadone 80 mg po daily

Sertraline 100 mg po daily

- A. Administer Vivitrol 380 mg IM today.
- B. Do not administer Vivitrol today because patient is being treated with methadone.
- C. Do not administer Vivitrol today because of patient's active cocaine use disorder.
- D. Do not administer Vivitrol today because patient is on multiple sedating medications.

Audience Question 3

A patient with polysubstance use disorder (alcohol, cocaine, opioids) presents to receive LAI naltrexone (Vivitrol). Which of the following is the best course of action?

Medications:

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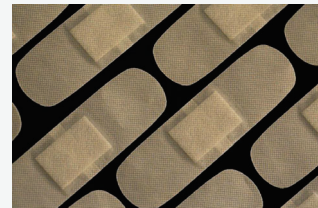
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Injection-Related Adverse Effects



Types of Injection-Site Reactions

- Pain
- Tenderness
- Swelling
- Bleeding
- Infection
- Erythema
- Hematoma (bruising)
- Leakage
- Induration



Incidence of Injection-Site Reactions: Antipsychotics		
Generic Name	Brand Name	Incidence of Injection-Site Reactions
Fluphenazine decanoate	Prolixin Decanoate	Unknown
Haloperidol decanoate	Haldol Decanoate	<1%
Aripiprazole lauroxil	Aristada Aristada Initio	4-5%
Aripiprazole monohydrate	Abilify Maintena	5-19%
	Abilify Asimtufii	~19%
Olanzapine pamoate	Zyprexa Relprevv	2-4%
Paliperidone palmitate	Invega Sustenna	Up to 12%
	Invega Trinza	5-9%
	Invega Hafyera	11-13%
	Erzofri	>5%
Risperidone	Risperdal Consta	1%
	Uzedy	5-21%

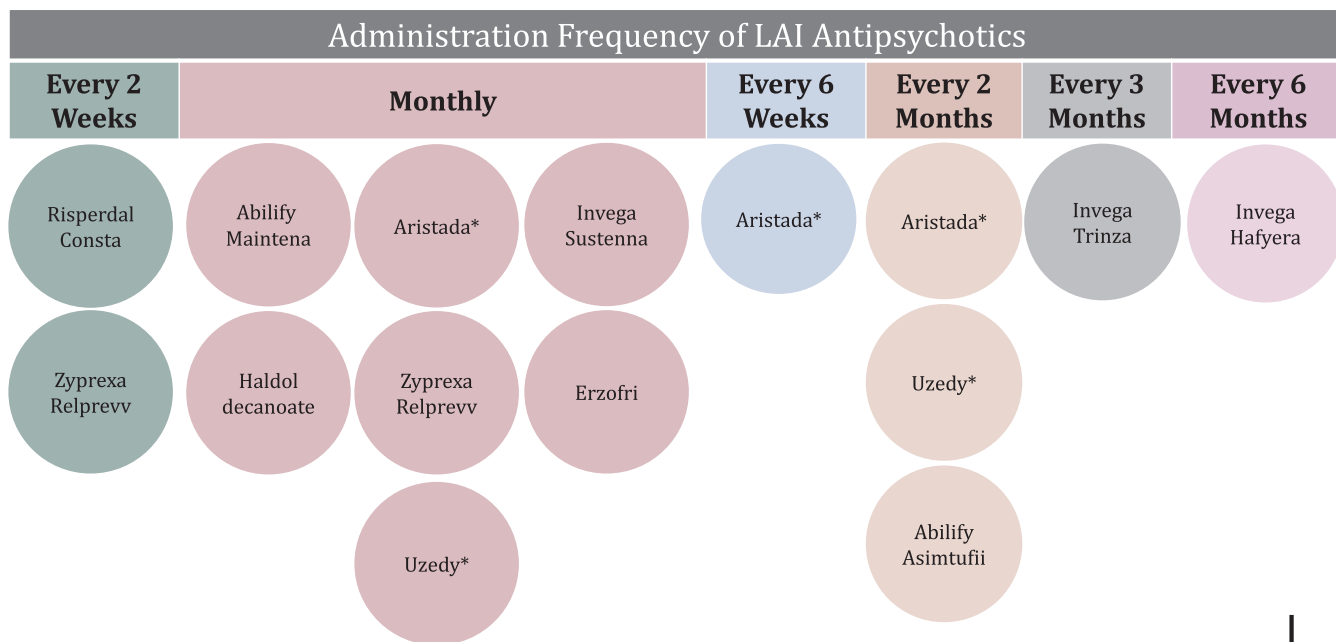
Incidence of Injection-Site Reactions: SUD Medications		
Generic Name	Brand Name	Incidence of Injection-Site Reactions
Naltrexone	Vivitrol	Overall: 65% Injection site pain: 13% Induration: 30% Pruritis: 8% Rash: 6%
Buprenorphine	Sublocade	16%
	Brixadi	20%

Management of Injection-Site Reactions

- Recommendations for **pharmacist:**
 - Change injection site with each administration
 - Consider topical anesthetic
- Recommendations for **patient:**
 - Report any reaction that does not resolve in 2 weeks
 - Cold compress
 - OTC analgesic for pain
 - OTC antihistamine for itching

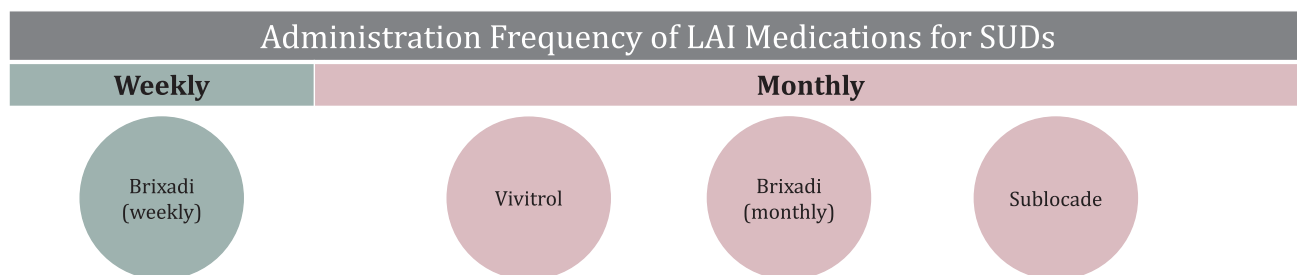
Cole B. *Pharmacy Times*. 2019;1

Summary



*Dosing frequency dependent on dose of oral antipsychotic

Note: Fluphenazine decanoate not pictured, can be administered every 2-4 weeks



Summary

- Multiple LAI medications are available for the treatment of schizophrenia, bipolar disorder, and substance use disorders
- Administration frequency can range from weekly to every 6 months
- Some LAI medication dosing is dependent on the dose of the oral medication patient was receiving prior to initiation
- Patients may need to continue oral medication for a specified period depending on the medication administered



Long-Acting Injectable Medication Products

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