The Long and Short of Long-Acting Injectable Medications

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March 24th, 2022

Disclosure

- Relevant Financial Conflicts of Interest
  - **CE Presenter, Omeid Vadipour:**
    - None
  - **CE mentor, Anthony May:**
    - None
- Off-Label Uses of Medications
  - None

Learning Objectives

- **Pharmacists**
  - Review and discuss indications, dosing, pharmacokinetics, and administration pearls for available long-acting injectable antipsychotics (LAI's), buprenorphine (Sublocade™), and naltrexone (Vivitrol™)
  - Describe what to do when patients miss doses of LAI's, buprenorphine, and naltrexone
  - Demonstrate understanding of differences in dosing and administration between different LAI's
  - Design a treatment plan for patients utilizing LAI's, buprenorphine, or naltrexone
- **Technicians**
  - Differentiate between the types of LAI's, and dosing schedule for each one
  - Discuss the benefits of LAI's, buprenorphine, and naltrexone on patient care
  - List the different LAI's

Abbreviations

- LAI = long-acting injectable
- BLS = basic life support
- ACPE = American Council on Pharmaceutical Education or Accreditation Council for Pharmacy Education
- RCT’s = randomized controlled trials
- NNT = number needed to treat
- CNS = central nervous system
- EPS = extrapyramidal symptoms
- NMS = neuroleptic malignant syndrome
- CYP = cytochrome
- REMS = risk evaluation and mitigation strategies

Long-acting injectable medications

- LAI medications include antipsychotics, buprenorphine, and naltrexone injections that are given to patients to treat conditions such as schizophrenia, bipolar disorder, and substance use disorders
- LAI antipsychotics share a major warning for increased risk of death in elderly patients with dementia-related psychosis
- Patients need to trial an oral regimen prior to switching to an antipsychotic LAI
- Common side effects of LAI antipsychotics include
  - EPS, NMS, prolonged QT interval, Torsades de Pointes, sedation, hyperprolactinemia, leukopenia, neutropenia, and metabolic syndrome
- The Pharmacy Practice Act states that pharmacists can administer intramuscular long-acting injectable medications in a clinic or community setting once they have been trained to do so
  - Training includes BLS certification and an ACPE accredited training program for administering LAI's

Citrome, L. *CNS Spectrums* 26, no. 2 (April 2021): 118–29.
Kane, JM., et al. *JAMA Psychiatry*. 2020;77(12):1217-1224.
Kishimoto, T., et al. *The Lancet.* Psychiatry 8, no. 5 (May 2021): 387–404.
Muench, J., and Hamer, A. *American Family Physician* 81, no. 5 (March 1, 2010): 617–22.
Utah State Legislature. Chapter 17b Pharmacy Practice Act. 2020.
Utah Division of Administrative Rules. Pharmacy Practice Act Rule. December 12, 2017.

Why use LAI's?

- Pros
  - Can help for adherence monitoring
  - Patient does not need to take a daily medication
  - Patient will regularly interact with medical staff/team
  - More stable plasma concentrations
  - Lower risk of hospitalization and relapse when compared to oral antipsychotics
  - Increases time to first psychiatric hospitalization
- Cons
  - Some require oral overlaps that may be complicated for a patient
  - Lack of dose flexibility
  - Patients may not say they receive these when performing medication reconciliation
  - Injection site reactions
  - Medications are often expensive
  - REMS programs

Kane, JM., et al. *JAMA Psychiatry*. 2020;77(12):1217-1224.
Kishimoto, T., et al. *The Lancet*. Psychiatry 8, no. 5 (May 2021): 387–404.

Comparison to oral antipsychotics

- Systematic review and meta-analysis covering RCT's, cohort studies, and pre-post studies
- Primary outcome: Rates of hospitalization, or relapse with LAI's versus oral antipsychotics
- Data reviewed from 1971 to 2020
- 32 RCT's, 65 cohort studies, and 40 pre-post studies
- 397,000 patients
- LAI antipsychotics were associated with lower risks of hospitalization or relapse when compared to oral antipsychotics in all study types reviewed

Kishimoto, T., et al. *The Lancet*. Psychiatry 8, no. 5 (May 2021): 387–404.

Comparison to usual treatment

- RCT
- Primary outcome: Time to first psychiatric hospitalization in patient with early-phase schizophrenia
- Data reviewed from December 2014 to March 2019
- Intervention: Aripiprazole LAI
- Comparator: Clinicians choice of treatment
- Results: Use of LAI's significantly delayed time to first hospitalization in patients with early-phase schizophrenia when compared to usual treatment
  - NNT: 7

Kane, JM., et al. *JAMA Psychiatry*. 2020;77(12):1217-1224.

Available LAI's

First generation antipsychotics	Second generation antipsychotics	Misc.
Haloperidol decanoate	Aripiprazole monohydrate (Abilify Maintena™)	Buprenorphine (Sublocade™)
Fluphenazine decanoate	Aripiprazole lauroxil (Aristada™, Aristada Initio™)	Naltrexone (Vivitrol™)
	Olanzapine pamoate (Zyprexa Relprevv™)	
	Paliperidone palmitate (Invega Sustenna™, Invega Trinza™, Invega Hafyera™)	
	Risperidone (Risperdal Consta™, Perseris™)	

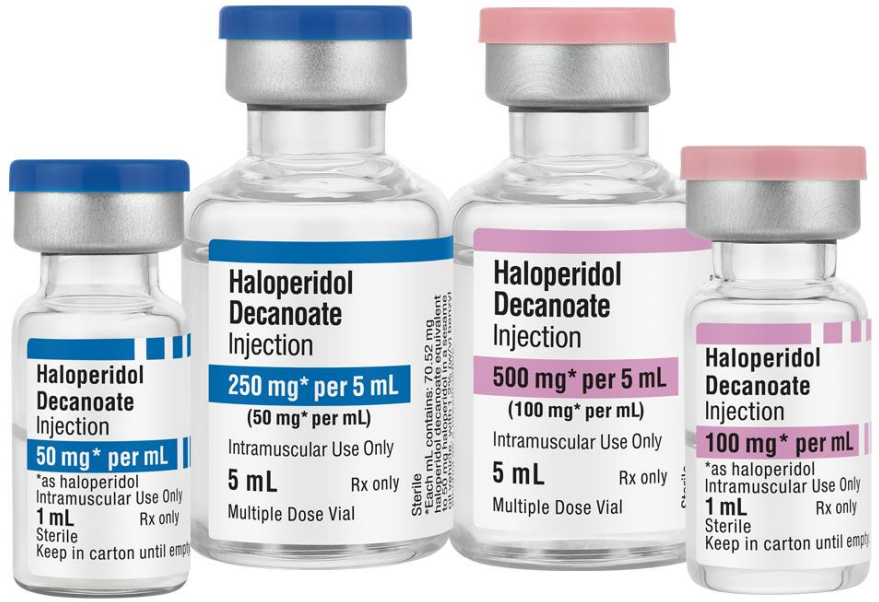
Audience Response Question

Which of the following is NOT a long acting injectable medication?

a) Haloperidol decanoate
b) Haloperidol lactate
c) Fluphenazine decanoate
d) Invega Sustenna™

Haloperidol decanoate

- Indication
  - Treatment of schizophrenia
- Pharmacokinetics
  - Time to peak: 6 days
  - Time to steady state: 3 to 4 months



Haloperidol Decanoate. Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; June 2011.
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.
Fresenius Kabi USA: Haloperidol Decanoate Injection Product Details. Accessed February 3, 2022. http://products.fresenius-kabi.us/product-52.html.

Haloperidol decanoate dosing

Initial dose	Maintenance dose	Maximum dose	Dosing interval	Oral overlap	Notes
10 to 20 times the oral total daily dose	Variable, usually 10-15 times previous oral total daily dose	450 mg	Every 4 weeks	Following first dose of LAI, taper oral dose by 25% in weekly intervals during the second or third month after starting decanoate treatment	If initial dose required >100 mg then administer the dose in 2 injections with a maximum of 100 mg for first injection and give remaining dose 3 to 7 days later
20 times the oral total daily dose	Reduce dose by ~25% each month during the second and third months, then continue adjusting based on patient tolerability	450 mg	Every 4 weeks	None	If initial dose required >100 mg then administer the dose in 2 injections with a maximum of 100 mg for first injection and give remaining dose 3 to 7 days later

Haloperidol Decanoate. Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; June 2011.
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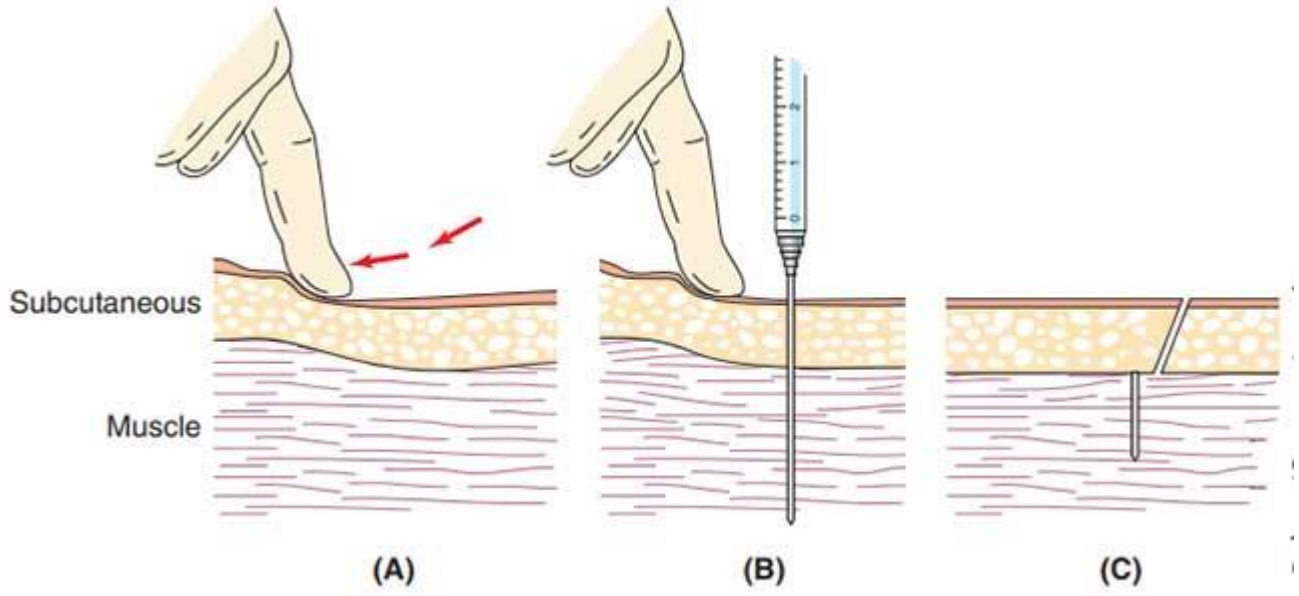
Ereshefsky, L., et al. *Psychopharmacology Bulletin* 26, no. 1 (1990): 108–14.
McEvoy, J. *The Journal of Clinical Psychiatry* 67 Suppl 5 (2006): 15–18.

Haloperidol decanoate administration

- Intramuscular gluteal muscle injection only
- Utilize Z-track technique



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Haloperidol decanoate missed doses

- Patient at steady state and <6 weeks since last dose
  - Administer next dose as soon as possible
- Patient not at steady state and 6 to 12 weeks since last dose
  - Administer next dose as soon as possible, utilize oral therapy if symptoms occur
- >13 weeks since last injection
  - Stabilize patient with oral antipsychotic, restart haloperidol decanoate when able

Haloperidol Decanoate. Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; June 2011.
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Haloperidol decanoate safety

- Contraindications
  - Parkinson’s disease, severe CNS depression
- Major drug interactions
  - CYP3A4 inducers, inhibitors, and substrates
  - CYP2D6 inducers, inhibitors, and substrates

Haloperidol Decanoate. Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; June 2011.

Fluphenazine decanoate

- Indication
  - Treatment of schizophrenia
- Pharmacokinetics
  - Time to peak: 8 to 10 hours
  - Time to steady state: 2 to 3 months

Fluphenazine Decanoate. Package Insert. APP Pharmaceuticals LLC; September 2010.
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.
Altamura, A., et al. *Drugs* 63, no. 5 (2003): 493–512.
McGuff Medical Products. “Fluphenazine Decanoate, 25mg/ML, MDV, 5mL Vial.” Accessed February 4, 2022. https://www.mcguffmedical.com/fluphenazine-decanoate-25mgml-mdv-5ml-vial.

Fluphenazine decanoate dosing

Initial dose	Maintenance dose	Maximum dose	Dosing interval	Oral overlap
12.5 to 25 mg	6.25 to 25 mg • If doses >50 mg are needed, titrate dose up in 12.5 mg increments • 12.5 mg of fluphenazine decanoate every 3 weeks is approximately equal to 10 mg daily of oral fluphenazine	100 mg	Every 2 weeks • Once a patient is at steady state, the effects of a single injection may last 4 to 6 weeks	Taper oral fluphenazine (or other antipsychotic) dose down by half after initial injection, and consider complete discontinuation of oral therapy after second injection

Fluphenazine Decanoate. Package Insert. APP Pharmaceuticals LLC; September 2010.
Kreyenbuhl, J., et al. *Schizophrenia Bulletin* 36, no. 1 (January 2010): 94–103.
McEvoy, J. *The Journal of Clinical Psychiatry* 67 Suppl 5 (2006): 15–18.

Fluphenazine decanoate administration

- Intramuscular deltoid or gluteal muscle injection
  - Experts prefer gluteal administration, but deltoid administration has also been studied and is appropriate
- Utilize Z-track technique

McEvoy, J. *The Journal of Clinical Psychiatry* 67 Suppl 5 (2006): 15–18.
Baweja, R., et al. *Current Drug Targets* 13, no. 4 (April 2012): 555–60.
Yasuhara, Y., et al. *The Journal of Medical Investigation: JMI* 59, no. 1–2 (2012): 213–19.
Gillespie, M., Toner, A., *British Journal of Nursing (Mark Allen Publishing)* 22, no. 8 (May 25, 2013): 464, 466–69.

Fluphenazine decanoate missed doses

- Patient at steady state and <6 weeks from last dose
  - Administer next dose as soon as possible
- Patient not at steady state, or 6 to 24 weeks since last dose
  - Administer next dose as soon as possible, with oral overlap if patient has a recurrence of symptoms
  - Patient should monitor for adverse effects within the first 24 hours from injection for adverse effects
- >24 weeks since last dose
  - Stabilize patient on oral antipsychotic, and reinitiate fluphenazine decanoate when able

Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Fluphenazine decanoate safety

- Contraindications
  - Patients with subcortical brain damage, severe CNS depression, hepatic impairment, or taking large doses of hypnotics
  - Children <12 years of age
- Major drug interactions
  - CYP2D6 inhibitors
  - CNS depressants

Fluphenazine Decanoate. Package Insert. APP Pharmaceuticals LLC; September 2010.

Aripiprazole monohydrate (Abilify Maintena™)

- Indication
  - Treatment of bipolar disorder and schizophrenia
    - Not studied in patients under the age of 18
- Pharmacokinetics
  - Time to peak: 4 days (deltoid), 5 to 7 days (gluteal)
  - Time to steady state: 5 to 8 months

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.
Abilify Maintena Full Prescribing Information, Dosage & Side Effects | MIMS Hong Kong. Accessed February 3, 2022. https://www.mims.com/hongkong/drug/info/abilify%20maintena?type=full.

Aripiprazole monohydrate (Abilify Maintena™) dosing

Initial dose	Maintenance dose	Dosing interval	Oral overlap
400 mg	400 mg Can reduce dose to 300 mg once monthly if patients have adverse reactions to higher dose	Monthly	2 weeks

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.

Aripiprazole monohydrate (Abilify Maintena™) administration

- Intramuscular deltoid or gluteal muscle injection
- Reconstitute vials and syringes at room temperature

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.

Aripiprazole monohydrate (Abilify Maintena™) missed doses

- Second or third missed doses
  - >4 weeks but <5 weeks: Administer next dose as soon as possible
  - >5 weeks: Administer oral aripiprazole for 14 days with next injection
- Four or more missed doses
  - >4 weeks but <6 weeks: Administer next dose as soon as possible
  - >6 weeks: Administer oral aripiprazole for 14 days with next injection

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Aripiprazole monohydrate (Abilify Maintena™) safety

- Warnings
  - May increase risk of suicidal thoughts and behavior in children, adolescents and young adults under the age of 24
  - Can cause cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.

Aripiprazole monohydrate (Abilify Maintena™) drug interactions

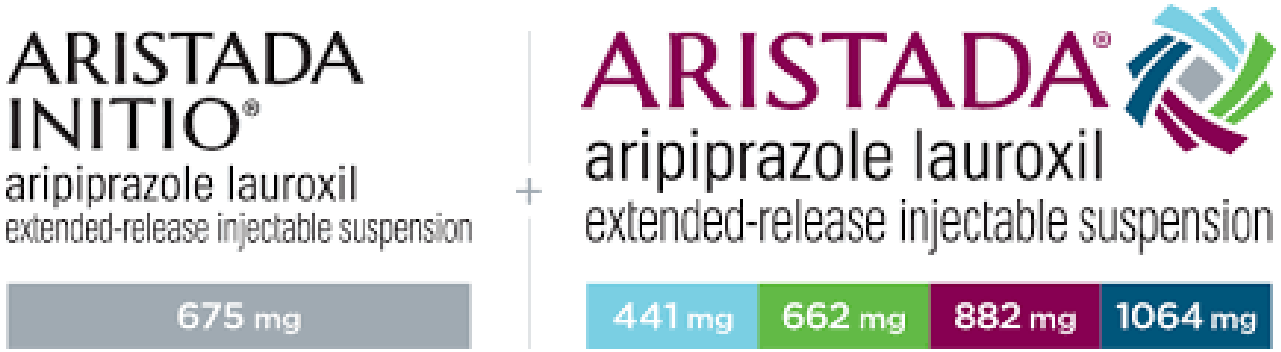
Concomitant medication	Dose changes
CYP2D6 poor metabolizers	
Known poor metabolizers	300 mg
Known poor metabolizers taking CYP3A4 inhibitors	200 mg*
Patients taking 400 mg	
Strong CYP2D6 or CYP3A4 inhibitors	300 mg
CYP2D6 and CYP3A4 inhibitors	200 mg*
CYP3A4 inducers	Avoid use
Patients taking 300 mg	
Strong CYP2D6 or CYP3A4 inhibitors	200 mg*
CYP2D6 and CYP3A4 inhibitors	160 mg*
CYP3A4 inducers	Avoid use

*These doses should only be obtained by using 300 mg or 400 mg vials, not prefilled syringes

Abilify Maintena (aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™)

- Indication
  - Treatment of schizophrenia
  - Aristada Initio™ is only used as a single dose to initiate or re-initiate Aristada™ treatment
- Pharmacokinetics
  - Time to peak
    - Aristada™: 16 to 35 days
    - Aristada Initio™: 16 to 35 days
  - Time to steady state:
    - Aristada™: 9 to 10 months
    - Aristada Initio™: 2 to 3 months



Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; October 2015.
Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
AristadaHCP.com. "ARISTADA INITIO® (Aripiprazole Lauroxil) and ARISTADA® (Aripiprazole Lauroxil) | HCP." Accessed February 4, 2022. https://www.aristadahcp.com/home.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™) dosing

LAI	Initial oral dose	Initial dose*	Maintenance dose	Dosing interval	Oral overlap
Aristada™	10 mg daily	441 mg Aristada™ monthly	Same as initial dose	Monthly to every two months	3 weeks
	15 mg daily	662 mg Aristada™ monthly 882 mg Aristada™ every six weeks 1064 mg Aristada™ every two months			
	20 mg daily	882 mg Aristada™ monthly			
Aristada Initio™	N/A	675 mg	N/A	Once	One time 30 mg aripiprazole dose

*Initial dose of Aristada™ is based on oral dose of aripiprazole

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™) administration

- Intramuscular deltoid administration is only appropriate for 441 mg doses of Aristada™ and Aristada Initio™
- Intramuscular gluteal administration is appropriate for Aristada Initio™, 662 mg, 882 mg, and 1064 mg doses of Aristada™
- Prior to administration, tap the syringe at least 10 times and shake vigorously for 30 seconds to ensure a uniform suspension
  - Repeat shaking step if syringe is not used within 15 minutes

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™) missed doses

If dose is missed, administer next dose as soon as possible

Dose	Length of time since last injection		
	No oral supplementation required	7 days of oral supplementation	21 days of oral supplementation
441 mg	≤6 weeks	>6 weeks and ≤7 weeks	>7 weeks
662 mg	≤8 weeks	>8 weeks and ≤12 weeks	>12 weeks
882 mg	≤8 weeks	>8 weeks and ≤12 weeks	>12 weeks
882 mg (every 6 weeks)	≤8 weeks	>8 weeks and ≤12 weeks	>12 weeks
1064 mg	≤10 weeks	>10 weeks and ≤12 weeks	>12 weeks
OR			
Aristada Initio™	6 to 10 weeks	6 to 12 weeks	7 to >12 weeks
	Not required	Single dose	Single dose, with a single 30 mg dose of oral aripiprazole

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; October 2015.
Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™) safety

- Warnings
  - Can cause cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; October 2015.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.

Aripiprazole lauroxil (Aristada™ & Aristada Initio™) drug interactions

Concomitant medication	Dose changes
Strong CYP3A4 or CYP2D6 inhibitor	Reduce the dose to next lowest strength No adjustment necessary for patients taking 441 mg
CYP2D6 poor metabolizer	Reduce the dose to next lowest strength No adjustment necessary for patients taking 441 mg
Strong CYP3A4 and CYP2D6 inhibitor	Avoid use for patients at 662 mg or 882 mg doses No adjustment necessary for patients taking 441 mg
CYP3A4 inducers	Increase 441 mg dose to 662 mg dose No adjustment necessary for patients taking 662 mg or 882 mg doses
Antihypertensives	Avoid Aristada Initio™
Benzodiazepines	Avoid Aristada Initio™

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; October 2015.
Aristada Initio (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.

Aristada™ vs Abilify Maintena™

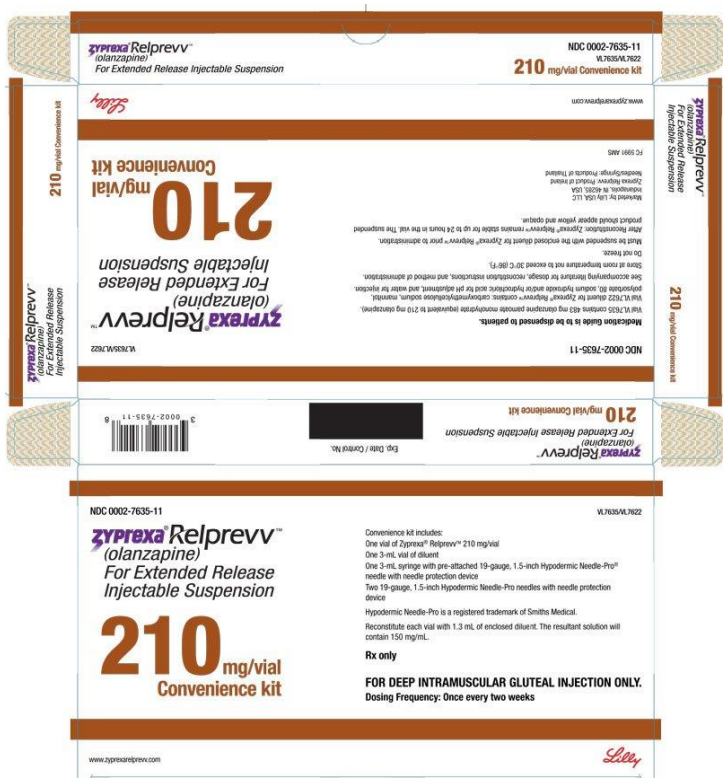
	Abilify Maintena™	Aristada™
Administration	Intramuscular deltoid or gluteal muscle injection	Depends on dosage • 441 mg dose: intramuscular injection • All other doses: gluteal injection
Time to peak	4 to 7 days	16 to 35 days
Dosing schedule	Monthly	Monthly to every two months
Oral overlap	14 days	21 days, or single dose of Aristada™ Initio (with one time 30 mg oral dose)

No data has shown a clinical difference in efficacy between the two formulations

Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; October 2015.
Aristada (Aripiprazole Lauroxil). Package Insert. Alkermes Inc; 2018.
Abilify Maintena (Aripiprazole). Package Insert. Otsuka Pharmaceutical Co; January 2016

Olanzapine pamoate (Zyprexa Relprevv™)

- Indication
  - Treatment of schizophrenia
- Pharmacokinetics
  - Time to peak: 7 days
  - Time to steady state: 5 months



Zyprexa Relprevv (olanzapine). Package Insert. Eli Lilly and Company; 2009.
drugsdepot.com. “Zyprexa Relprevv 405 Mg 1 By Lilly Eli & Co.” Accessed February 5, 2022. https://www.drugsdepot.com/store.php/drugsdepot/pd9643909/zyprexa-relprevv-405-mg-1-by-lilly-eli-amp-co.

Olanzapine pamoate (Zyprexa Relprevv™) dosing

Initial oral dose	Initial dose*	Maintenance dose	Dosing interval	Oral overlap
10 mg daily	210 mg every 2 weeks 405 mg every 4 weeks	150 mg every 2 weeks 300 mg every 4 weeks	2 to 4 weeks	None
15 mg daily	300 mg every 2 weeks	210 mg every 2 weeks 405 mg every 4 weeks		
20 mg daily	300 mg every 2 weeks	300 mg every 2 weeks		

*Initial dose is based on target oral olanzapine dose, and is continued for 8 weeks before going to maintenance dose

Zyprexa Relprevv (olanzapine). Package Insert. Eli Lilly and Company; 2009.

Olanzapine pamoate (Zyprexa Relprevv™) administration

- Intramuscular gluteal muscle injection only
- Must ensure vial is appropriately reconstituted with no remaining powder clumps before administration
- Once needle has been inserted into muscle, aspiration should be maintained for several seconds to ensure no blood is drawn into the syringe
  - If blood aspirates into the syringe, the syringe should be discarded and new drug should be prepared for administration
- Once injection is administered, patient must be monitored for 3 hours and accompanied by someone to their destination when leaving

Zyprexa Relprevv (olanzapine). Package Insert. Eli Lilly and Company; 2009.

Olanzapine pamoate (Zyprexa Relprevv™) missed doses

- Patient not at steady state
  - Give recommended loading dose for 8 weeks
- Patient at steady state and ≤2 months since last dose
  - Give next dose as soon as possible
- Patient at steady state and >2 months since last dose
  - Give recommended loading dose for 8 weeks

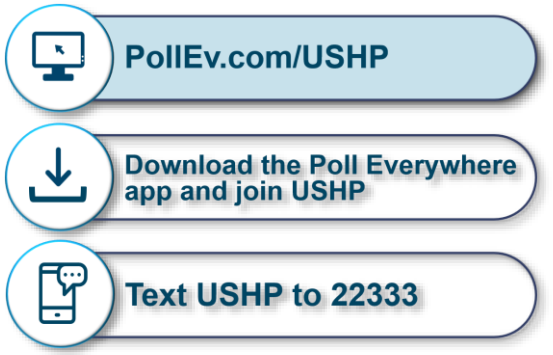
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Olanzapine pamoate (Zyprexa Relprevv™) safety

- Contraindications
  - None
- Warnings
  - Post-injection delirium/sedation syndrome
    - FDA REMS program is active, but currently on hold as of March 2020
  - Can cause cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis
- Major drug interactions
  - CYP1A2 inducers and inhibitors
  - CNS depressants
  - Antihypertensive agents

Zyprexa Relprevv (olanzapine). Package Insert. Eli Lilly and Company; 2009.

Audience Response Question



SM presents to your clinic to initiate therapy with an LAI antipsychotic. She is well controlled taking olanzapine 20 mg daily. Which of the following should you consider prior to administering the olanzapine LAI (Zyprexa Relprevv™) injection?

a) Does the patient have someone to accompany her when she leaves?
b) What other medications does the patient take?
c) Make sure the patient has at least 3 hours to remain in the clinic after the injection
d) All of the above

Paliperidone palmitate (Invega Sustenna™, Invega Trinza™, Invega Hafyera™)

- Indication
  - Treatment of schizophrenia
    - Invega Sustenna™ is also indicated to treat schizoaffective disorder
- Pharmacokinetics
  - Time to peak:
    - Invega Sustenna™: 13 days
    - Invega Trinza™: 30 to 33 days
    - Invega Hafyera™: 29 to 32 days
  - Time to steady state:
    - Invega Sustenna™: 4 to 9 months
    - Invega Trinza™: 14 to 24 months
    - Invega Hafyera™: 24 to 27 months

Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009
Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015
Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021
Invega LAI Portfolio. "Official Consumer Website | INVEGA™ (Paliperidone Palmitate) LAI Portfolio," July 27, 2020. https://www.janssenschizophreniainjections.com/.

Paliperidone palmitate (Invega Sustenna™) dosing

LAI	Indication	Initial dose		Maintenance dose	Maximum dose	Dosing interval	Oral overlap
		Day 1	Day 8				
Invega Sustenna™	Schizophrenia	234 mg	156 mg	39 to 234 mg	234 mg	Monthly	None
	Schizoaffective disorder	234 mg	156 mg	78 to 234 mg	234 mg	Monthly	None

Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009

Paliperidone palmitate (Invega Trinza™) dosing

LAI	Invega Sustenna™ dose	Initial dose	Maintenance dose	Dosing interval	Oral overlap
Invega Trinza™*	78 mg	273 mg	Same as initial dose	Every 3 months	None
	117 mg	410 mg			
	156 mg	546 mg			
	234 mg	819 mg			

*Can start after patient is stable on Invega Sustenna™ for at least 4 months

Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015

Paliperidone palmitate (Invega Hafyera™) dosing

LAI	Switching from…	Initial dose	Maintenance dose	Dosing interval	Oral overlap
Invega Hafyera™	Invega Sustenna™(a)		Same as initial dose	Every 6 months	None
	156 mg	1092 mg			
	234 mg	1560 mg			
	Invega Trinza™(b)		Same as initial dose	Every 6 months	None
	546 mg	1092 mg			
	819 mg	1560 mg			

a. Can start after patient is stable on Invega Sustenna™ for at least 4 months
b. Can start after patient is stable on Invega Trinza™ for at least one 3 month cycle

Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021

Paliperidone palmitate (Invega Sustenna™) administration

- Intramuscular deltoid injection only for initiation dose
- Maintenance doses can be given in the deltoid or gluteal muscle
- Shake syringe for at least 10 seconds prior to injection

Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009

Paliperidone palmitate (Invega Trinza™) administration

- Intramuscular deltoid or gluteal muscle injection
- Shake syringe (with tip pointing upwards) for at least 15 seconds prior to administration
- Administer within 5 minutes of shaking

Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015

Paliperidone palmitate (Invega Hafyera™) administration

- Intramuscular gluteal muscle injection only
- Shake syringe (with tip pointing upwards) very quickly for at least 15 seconds, rest briefly, then shake again for 15 seconds
  - Solution should look uniform, thick and milky white
- Administer within 5 minutes of shaking
- Inject over 30 seconds

Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021

Paliperidone palmitate (Invega Sustenna™) missed doses

Missed dose	Length of time since last injection	Dose to administer
Second initiation dose	<4 weeks	156 mg as soon as possible, followed by a third 117 mg dose 5 weeks after first dose
	4 to 7 weeks	Two doses of 156 mg one week apart
	>7 weeks	Restart recommended initiation dose
Maintenance dose	4-6 weeks	Administer regular maintenance dose as soon as possible
	6 weeks to six months	Administer regular maintenance dose twice one week apart
	>6 months	Restart recommended initiation dose

Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Paliperidone palmitate (Invega Trinza™) missed doses

Length of time since last dose	Previous dose	Dose to administer
3.5 to 4 months	273 mg to 819 mg	Administer previous dose as soon as possible
4-9 months	273 mg	Invega Sustenna™ 78 mg twice, one week apart, followed by 273 mg Invega Trinza™ one month after second Invega Sustenna™ Dose
	410 mg	Invega Sustenna™ 117 mg twice, one week apart, followed by 410 mg Invega Trinza™ one month after second Invega Sustenna™ Dose
	546 mg	Invega Sustenna™ 156 mg twice, one week apart, followed by 546 mg Invega Trinza™ one month after second Invega Sustenna™ Dose
	819 mg	Invega Sustenna™ 156 mg twice, one week apart followed by 819 mg Invega Trinza™ one month after second Invega Sustenna™ Dose
>9 months	273 mg to 819 mg	Re-initiate treatment with Invega Sustenna™ and reinitiate Invega Trinza™ after patient stable for 4 months

Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Paliperidone palmitate (Invega Hafyera™) missed doses

Length of time since last dose	Previous dose	Dose to administer
6 months and 3 weeks to 8 months	1092 mg	Invega Sustenna™ 156 mg once, followed by Invega Hafyera 1092 mg one month later
	1560 mg	Invega Sustenna™ 234 mg once, followed by Invega Hafyera 1560 mg one month later
8 to 11 months	1092 mg	Invega Sustenna™ 156 mg twice, one week apart, followed by Invega Hafyera 1092 mg one month after second Invega Sustenna™ dose
	1560 mg	Invega Sustenna™ 156 mg twice, one week apart, followed by Invega Hafyera 1560 mg one month after second Invega Sustenna™ dose
>11 months	1092 mg 1560 mg	Re-initiate treatment with Invega Sustenna™ and reinitiate Invega Hafyera™ after patient stable for 4 months

Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021
Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

Paliperidone palmitate (Invega Sustenna™, Invega Trinza™, Invega Hafyera™) safety

- Contraindications
  - Creatinine clearance < 50 mL/min
- Warnings
  - Can cause cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis
- Major drug interactions
  - CYP3A4 inducers
  - CNS active medications
  - Medications that can cause orthostatic hypotension

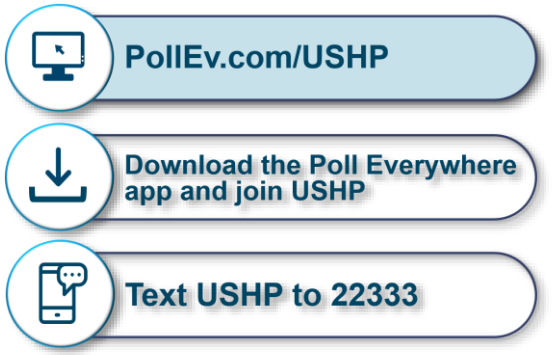
Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009
Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015
Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021

Paliperidone palmitate (Invega Sustenna™, Invega Trinza™, Invega Hafyera™) renal dose adjustments

CrCl (mL/min)	Invega Sustenna™	Invega Trinza™	Invega Hafyera™
>90 mL/min	No adjustment necessary	No adjustment necessary	No adjustment necessary
≥80 to 90 mL/min	No adjustment necessary	No adjustment necessary	Use not recommended
50 to 80 mL/min	Initiate with 156 mg on day 1, followed by 117 mg one week later Maintenance dose: 78 mg	Stabilize patient with Invega Sustenna™, then dose as previously reviewed	Use not recommended
<50 mL/min	Use not recommended	Use not recommended	Use not recommended

Invega Sustenna (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2009
Invega Trinza (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2015
Invega Hafyera (Paliperidone Palmitate). Package Insert. Janssen Pharmaceuticals, Inc; 2021

Audience Response Question



Which of the following paliperidone formulations can only be administered in the gluteal muscle?

a) Invega Hafyera™
b) Invega Sustenna™
c) Invega Trinza™

Risperidone (Risperdal Consta™)

- Indication
  - Treatment of schizophrenia and bipolar 1 disorder
- Pharmacokinetics
  - Time to peak: 8 to 24 hours
  - Time to steady state: 15 to 30 days

Risperdal Constra (Risperidone). Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; August 2010.
Janssen CarePath. “Risperdal Consta - Overview,” December 6, 2018. https://www.janssencarepath.com/hcp/risperdal-consta.

USHP

Risperidone (Risperdal Consta™) dosing

Indication	Initial dose	Maintenance dose	Maximum dose	Dosing interval	Oral overlap
Schizophrenia	25 mg	25 to 50 mg	50 mg	Every 2 weeks	3 weeks
Bipolar 1 disorder	25 mg	25 to 50 mg	50 mg	Every 2 weeks	3 weeks

Risperdal Constra (Risperidone). Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; August 2010.

Risperidone (Risperdal Consta™) administration

- Intramuscular deltoid or gluteal muscle injection
- Shake vial vigorously once diluent is added to suspend microspheres
- Administer within two minutes of shaking
  - Resuspend by shaking if necessary

Risperdal Constra (Risperidone). Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; August 2010.

Risperidone (Risperdal Consta™) missed doses

- Patient not at steady state and <2 weeks since last dose
  - Give next dose as soon as possible with 3 weeks of oral overlap
- Patient at steady state and ≤6 weeks since last dose
  - Give next dose as soon as possible with no oral overlap
- Patient at steady state and >6 weeks since last dose
  - Give next dose as soon as possible with 3 weeks of oral overlap

Carpenter, Jasmine, and Kong K. Wong. *Current Psychiatry* 17, no. 7 (July 2018): 10–12, 14–19, 56.

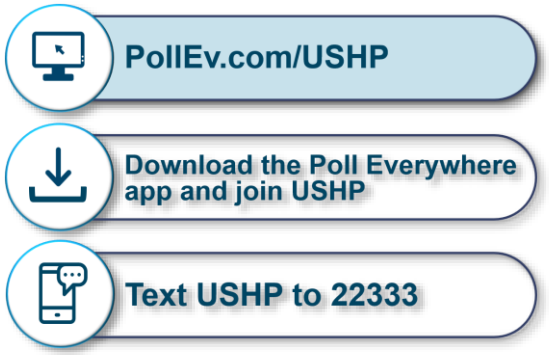
Risperidone (Risperdal Consta™) safety

- Warnings
  - Can cause cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis
- Major drug interactions
  - CYP3A4 inducers
  - CYP2D6 inhibitors

Risperdal Constra (Risperidone). Package Insert. Ortho-McNeil-Janssen Pharmaceuticals, Inc; August 2010.

Audience Response Question

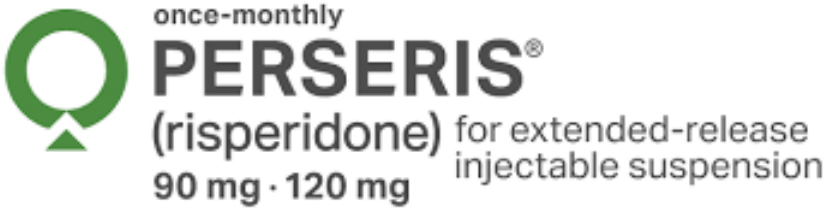
JD presents to your pharmacy distressed that he missed his last dose of his risperidone LAI. He received his last dose of Risperdal Consta™ five weeks ago, and has been consistently receiving injections for the past year. How would you reinitiate his LAI therapy?



a) Give next dose as soon as possible with three weeks of oral overlap
b) Give next dose as soon as possible with no oral overlap
c) Give next dose as soon as possible with six weeks of oral overlap

Risperidone (Perseris™)

- Indication
  - Treatment of schizophrenia



- Pharmacokinetics
  - Time to peak: 4 to 6 hours to first peak, 10 to 14 days to second peak
  - Time to steady state: 45 to 55 days

Perseris (Risperidone). Package Insert. Indivior Inc; December 2019
Patient Information about PERSERIS® (Risperidone).” Accessed February 6, 2022. https://www.perseris.com/

Risperidone (Perseris™) dosing

Oral risperidone dose	Initial dose	Maintenance dose	Dosing interval	Oral overlap
3 mg daily	90 mg	Same as initial dose	Monthly	None
4 mg daily	120 mg	Same as initial dose	Monthly	None

Perseris (Risperidone). Package Insert. Indivior Inc; December 2019

Risperidone (Perseris™) administration

- Abdominal subcutaneous injection only
- Allow medication to come to room temperature prior to preparation

Perseris (Risperidone). Package Insert. Indivior Inc; December 2019

Risperidone (Perseris™) missed doses

- Administer missed doses as soon as possible

Perseris (Risperidone). Package Insert. Indivior Inc; December 2019

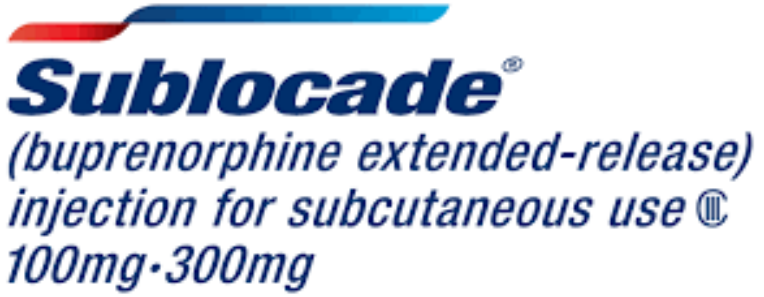
Risperidone (Perseris™) safety

- Major drug interactions
  - CYP3A4 inducers
  - CYP2D6 inhibitors

Perseris (Risperidone). Package Insert. Indivior Inc; December 2019

Buprenorphine (Sublocade™)

- Indication
  - Treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days
- Pharmacokinetics
  - Time to peak: 24 hours
  - Time to steady state: 4 to 6 months



Sublocade (Buprenorphine Extended-Release). Package Insert. Indivior Inc; June 2021.
Patient Information for SUBLOCADE® (Buprenorphine Extended-Release) Injection, for Subcutaneous Use (CIII).” Accessed February 8, 2022. https://www.sublocade.com/.

Buprenorphine (Sublocade™) dosing

Transmucosal buprenorphine dose	Initial doses		Maintenance dose	Dosing interval	Oral overlap
	First dose	Second dose			
8 to 18 mg daily	300 mg	100 mg[a]	100 mg	Monthly[b]	None
20 to 24 mg daily	300 mg	300 mg	100 mg		

a) For patients still experiencing cravings or withdrawal symptoms, this dose can be increased to 300 mg
b) For patients taking 100 mg once monthly, there may be instances (such as extended-travel) that a single 300 mg dose may be given to cover a two month period

Sublocade (Buprenorphine Extended-Release). Package Insert. Indivior Inc; June 2021.

Buprenorphine (Sublocade™) administration

- Abdominal subcutaneous injection only
- Allow medication to come to room temperature before administration
- In the event the depot must be removed, it can be surgically removed under local anesthesia within 14 days of injection

Sublocade (Buprenorphine Extended-Release). Package Insert. Indivior Inc; June 2021.

Buprenorphine (Sublocade™) missed doses

- Administer next dose as soon as possible
  - Occasional delays in dosing up to 2 weeks are not expected to have a clinically significant impact on treatment effect

Sublocade (Buprenorphine Extended-Release). Package Insert. Indivior Inc; June 2021.

Buprenorphine (Sublocade™) safety

- Warnings
  - REMS program for risk of serious harm or death if medication is administered intravenously
    - FDA REMS program is active, but currently on hold as of March 2020
  - Can only be supplied directly to a healthcare provider for administration by a healthcare provider
- Major drug interactions
  - Benzodiazepines
  - CYP3A4 inhibitors and inducers
  - HIV medications
  - Muscle relaxants
  - Serotonergic medications
  - Diuretics
  - Anticholinergic drugs
- Main side effects
  - Respiratory and CNS depression, neonatal opioid withdrawal syndrome, adrenal insufficiency, opioid withdrawal, hepatitis, jaundice, orthostatic hypotension, prolong QT interval, elevation of cerebrospinal fluid pressure

Sublocade (Buprenorphine Extended-Release). Package Insert. Indivior Inc; June 2021.

Naltrexone (Vivitrol™)

- Indication
  - Treatment of alcohol dependence
  - Prevention of relapse to opioid dependence
- Pharmacokinetics
  - Time to peak: 2 hours to first peak, 2 to 3 days to second peak
  - Time to steady state: 25 to 50 days

Vivitrol®
(naltrexone for extended-release injectable suspension)

Vivitrol (Naltrexone for Extended-Release Injectable Suspension). Package Insert. Alkermes Inc; October 2010.
ALK-VIV. "VIVITROL® (Naltrexone for Extended-Release Injectable Suspension)." Accessed February 8, 2022. http://ssshare.it/zO4b.

USHP

Naltrexone (Vivitrol™) dosing

Initial dose	Maintenance dose	Dosing interval	Oral overlap
380 mg	380 mg	Monthly	None

Vivitrol (Naltrexone for Extended-Release Injectable Suspension). Package Insert. Alkermes Inc; October 2010.

Naltrexone (Vivitrol™) administration

- Intramuscular gluteal injection
- Allow medication to reach room temperature before administration

Vivitrol (Naltrexone for Extended-Release Injectable Suspension). Package Insert. Alkermes Inc; October 2010.

Naltrexone (Vivitrol™) missed doses

- Administer next dose as soon as possible

Vivitrol (Naltrexone for Extended-Release Injectable Suspension). Package Insert. Alkermes Inc; October 2010.

Naltrexone (Vivitrol™) safety

- Contraindications
  - Patients with hepatitis or liver failure
  - Patients taking opioid analgesics, or physiological opioid dependence
  - Patients in acute opioid withdrawal
- Warnings
  - Patients should be opioid free at time of dose initiation
- Major drug interactions
  - Opioid medications
- Main side effects
  - Hepatotoxicity, can precipitate opioid withdrawal or overdose, eosinophilic pneumonia, depression, suicidality

Vivitrol (Naltrexone for Extended-Release Injectable Suspension). Package Insert. Alkermes Inc; October 2010.

Summary

Drug	Oral overlap	Administration	Notes
Haloperidol decanoate	Yes	Gluteal (Z-track)	Split dosing for >100 mg initial dose
Fluphenazine decanoate	Yes	Deltoid or gluteal (Z-track)	Not indicated for age <12
Aripiprazole monohydrate (Abilify Maintena™)	Yes	Deltoid or gluteal	Use vials for reduced doses
Aripiprazole lauroxil (Aristada™, Aristada Initio™)	Yes	Deltoid only for 441 mg Aristada™ Gluteal for all other doses	Aristada Initio™ reduces oral overlap to one does
Olanzapine pamoate (Zyprexa Relprevv™)	No	Gluteal	3 hours of monitoring post-injection
Paliperidone palmitate (Invega Sustenna™, Invega Trinza™, Invega Hafyera™)	No	Deltoid only for Invega Sustenna™ initiation dose Gluteal only for Invega Hafyera™ Deltoid or gluteal for all other doses	Renal dose adjustments
Risperidone (Risperdal Consta™)	Yes	Deltoid or gluteal	Indicated for schizophrenia and bipolar 1 disorder
Risperidone (Perseris™)	No	Abdomen	Subcutaneous injection
Buprenorphine (Sublocade™)	No	Abdomen	Subcutaneous injection Depot can be surgically removed within 14 days
Naltrexone (Vivitrol™)	No	Gluteal	Opioid antagonist

Audience Response Question

Which of the following does not require an oral overlap?

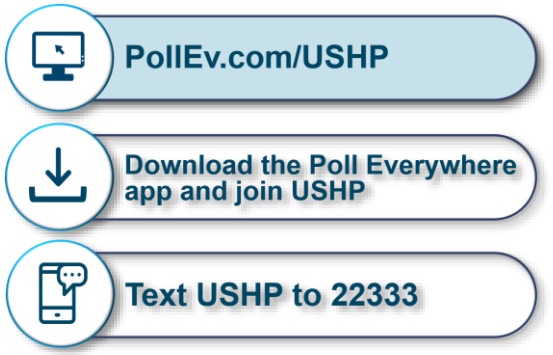
a) Aripiprazole monohydrate (Abilify Maintena™)
b) Fluphenazine decanoate
c) Risperidone (Risperdal Consta™)
d) Olanzapine pamoate (Zyprexa Relprevv™)

Audience Response Question

Which of the following LAI's is administered every three months?

a) Aripiprazole monohydrate (Abilify Maintena™)
b) Paliperidone palmitate (Invega Trinza™)
c) Risperidone (Risperdal Consta™)
d) Olanzapine pamoate (Zyprexa Relprevv™)

Audience Response Question



Which of the following is true?

a) LAI antipsychotics decrease time to first psychiatric hospitalization
b) LAI antipsychotics increase time to first psychiatric hospitalization
c) LAI antipsychotics are often inexpensive