Guide to

LONG-ACTING MEDICATIONS

for Clinicians and Organizations

NATIONAL COUNCIL
for Mental Wellbeing

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NATIONAL COUNCIL *for* Mental Wellbeing

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INTRODUCTION: CALL TO ACTION

This Guide to Long-acting Medications (LAMs) is a call to action for psychiatrists, other clinicians and mental health and substance use treatment organizations to increase the use of LAMs (more sensitive language as injectables may arouse a negative reaction), which are also known as long-acting antipsychotic medications (LAAs) and long-acting injectables (LAIs). Drawing upon clinical guidance developed by the American Association of Community Psychiatrists (AACP) and research evidence from the National Institute for Mental Health (NAMI) and others, the National Council for Mental Wellbeing believes that all community mental health and substance use treatment clinicians should provide LAMs as a first-line treatment option to patients and encourages its members to increase and support the safe and effective use of LAMs. Currently, LAMs are most often utilized as a strategy to address medication nonadherence; however, research supports the use of LAMs as first tier medications, not just as a second or third tier approach.

Although targeted to psychiatrists and other clinicians, these recommendations require that organizations play an active role in establishing systems to support staff, patients and families with information and education about the safe and effective use of LAMs and the infrastructure, policies and procedures needed to deliver this method of treatment. It is further recommended that organizations establish a continuous quality improvement (CQI) process to make necessary improvements that will increase patient understanding of and access to LAMs. Collecting, analyzing and using data is critical to monitoring progress and guiding the change process.

WHAT THE SCIENCE TELLS US

The idea that early treatment leads to better outcomes is standard in medicine, just as early detection offers better prognosis. The longer an illness is left unchecked and unmanaged, the more complex and difficult treatment becomes. Although research is still clarifying the neurodevelopmental aspects of schizophrenia, there is enough science to demonstrate the neurodegeneration effects of each psychotic episode on the brain tissue of a person with schizophrenia. To avoid further neurodegeneration, some experts have urged psychiatrists to approach treatment of psychosis in much the same way they would treat a heart attack – as something that must be prevented from recurring (Nasrallah, 2017).

According to Henry A. Nasrallah, M.D., there is enough data to show that timely intervention with LAIs reliably prevents relapse in most patients, thereby averting progressive neurodegeneration and subsequent disability in people who develop schizophrenia. "The additional damaging effects of the second episode is what leads to clinical deterioration and can start the process of treatment resistance. But if no psychotic episodes are allowed to recur after the first episode, many patients can return to their baseline functioning, such as participating in school or work activities. Prompt treatment of the first episode of psychosis and starting the patient on a LAI can protect the brain from another destructive round of neuroinflammation and oxidative stress," (Nasrallah 2021).

To successfully prevent relapse, clinicians should focus on the modifiable or preventable risk factors that lead to poor outcomes, such as longer duration of untreated psychosis, early nonresponse to antipsychotic medications, multiple relapses and nonadherence to medications (Carbon, 2014). Research has consistently found a link between poor adherence and relapse (Morken, 2008). A major advantage of LAMs over oral medication is the ability to identify nonadherence early when it can be more easily and effectively addressed. Studies have demonstrated significantly increased adherence in patients taking LAMs and significantly fewer psychotic exacerbations or relapses than in patients receiving oral medications (Subotnikl, 2015).

"The prevention of relapse in schizophrenia remains an enormous public health challenge worldwide and improvements in this area can have tremendous impact on morbidity, mortality and quality of life, as well as direct and indirect health care costs … in our view when all of the data from individual trials and meta-analyses are taken together, the findings are extremely compelling in favor of depot [long-acting injectable] drugs. However, in many countries throughout the world fewer than 20% of individuals with schizophrenia receive these medications," (Kane, 1998).

THE CASE FOR USING LONG-ACTING MEDICATIONS (LAMs)

LAMs are widely available and have research-proven clinical benefits compared to oral medications for individuals with schizophrenia, schizoaffective disorder or bipolar disorder. These include a significant delay and reduction in relapse, particularly in patients with early-phase or first-episode schizophrenia and a lower risk of discontinuation and frequency of hospitalizations compared with oral antipsychotics.

"Long-acting injections can be a valuable tool in managing schizophrenia and facilitating optimum outcome. Perhaps more data are necessary to develop a broader consensus; however, physician and patient biases and reluctance remain important targets for guidance, psychoeducation and shared decision-making. Given the personal suffering, family burden and societal costs associated with nonadherence and consequent relapse, in our opinion the potential value of LAI medication continues to be inadequately appreciated," (Kane, 1998).

Despite the evidence, LAMs are underutilized and only 15-28% of eligible patients with schizophrenia in the U.S. receive them (Sajatovic M, 2018). As a treatment option, they are often reserved for patients who are nonadherent to oral medications, have experienced multiple relapses or have expressed a preference for LAMs. However, recent evidence and guidance support recommending LAMs over oral medications to all eligible patients as a better treatment option. Using LAMs is an effective prevention strategy for future nonadherence and relapse/deterioration (Llorca, 2013) (Correll, 2016). LAMs also simplify the treatment regimen and reduce patient medication-taking burden.

ADVANTAGES OF LAM ***(Sajatovic m, 2018)***

- Prevention of future nonadherence.
- Prevention of relapse.
- Simplified the medication regimen.
- Reduced patient medication-taking burden.
- Improved medication adherence.
- Reduced side-effects.
- Allow for more accurate assessment of dosing and regularity of treatment.
- Potential to strengthen the therapeutic alliance.
- Slowing anti-psychotic clearance.

EXPANDING THE USE OF LAMs

The benefits of LAMs go far beyond their use as agents that increase medication adherence. The National Council Medical Director Institute recommends the use of LAMs for all patients as a better choice than oral medications, particularly for those in the early stages of the illness as these have the potential to address a variety of clinical and social challenges and prevent negative outcomes such as frequent relapses.

CLINICIANS SHOULD CONSIDER PRESCRIBING LAMs FOR:

Patients who may be at high risk for nonadherence to medications. Patients who experience high utilization of emergency departments, unstable living conditions, co-occurring substance use, cognitive challenges, anosognosia or limited insight.

Patients involved in transitions of care. Patients being discharged from psychiatric hospitals, residential programs or leaving jail or prison.

Patients demonstrating challenges with adherence: Past history of nonadherence to oral medications, challenges remembering to take medications as prescribed or misplacing medications.

Patients seeking to relieve the burden of medication-taking. Patients who experience frustration or challenges with regimens associated with taking pills, sometimes two to three times a day as well as the associated frequency of visits to the physician and pharmacy.

Patients experiencing first-episode psychosis. This is an optimal time to educate patients and families about LAMs as they have the potential to reduce the rate of relapse thereby mitigating further impact on the brain and functioning.

Patients who indicate using a LAM as their personal preference. This requires access to education by multiple staff, including peer coaches, and availability of informational brochures and videos.

Clinicians should have established processes for assessing nonadherence to medications. For patients who are identified as nonadherent, clinicians should work with the individual to determine if LAMs are the right option for them. In addition to the risk criteria already discussed, risk indicators can include limited insight. The decision whether to take antipsychotic medications may be a daily stressor because the individual believes they do not have a mental illness requiring medication. With LAMs, the decision to take medications, needs to be made much less frequently. The option of taking a LAM every few weeks or months removes the repetitive daily reminder of the belief that their experience is mislabeled or not fully understood, thereby strengthening both the individual's self-esteem and treatment engagement.

EXAMPLES OF BELIEFS RELATED TO LIMITED INSIGHT, MAY INCLUDE:

- I don't know what this medication is for.
- I only take medications when I feel ill.
- I should be strong enough to deal with my problems without medication.
- Medications can't be a good choice because they are not natural.

PRESCRIBER PRACTICES

USE RECOVERY-ORIENTED AND TRAUMA-INFORMED CARE

The Substance Abuse and Mental Health Services Administration (SAMHSA) defines recovery as

"a process of change through which people improve their health and wellness, live self-directed lives and strive to reach their full potential."

They describe four major dimensions that support recovery:

- **Health.** Overcoming or managing one's disease(s) or symptoms and making informed, healthy choices that support physical and emotional wellbeing.
- **Home.** Having a stable and safe place to live.
- **Purpose.** Conducting meaningful daily activities and having the independence, income and resources to participate in society.
- **Community.** Having relationships and social networks that provide support, friendship, love and hope.

Recovery is about seeing beyond a person's mental health problems, helping them recognize their strengths, abilities and interests and supporting them in achieving their own goals, aspirations and dreams. Resilience and recovery are strongly linked to social inclusion. A key role for mental health and social services is to create opportunities for individuals to take part in social, educational, training, volunteer and employment opportunities (Jacob, 2015).

From a recovery perspective, LAMs should not just be viewed as a tool for preventing relapse, but as a resource to help patients work toward their own recovery goals. The process of recovery is highly personal and occurs via many pathways. Hope and healing can only occur within a strong therapeutic relationship; therefore, clinicians should work toward empowering individuals to identify the treatment approaches that will lead to achieving their personal goals. This could be as simple as offering education and information on all treatment options, including LAMs, early in the treatment process rather than as a secondary option.

RECOVERY RESOURCES

- Wellness Recovery Action Planning (WRAP). An approach to facilitate recovery.
- Recovery Star. A tool that allows people with mental health conditions who are using services to measure their own recovery progress.

It is also important to note that the majority of people living with mental health, substance use conditions or homelessness have a history of trauma. Although trauma impacts individuals in different ways, because of the nature of adverse experiences, difficulty establishing trusting relationships is often a major challenge.

A strong therapeutic relationship is a critical component of the treatment process and promoting medication adherence. Individuals with a history of trauma and/or coercive intramuscular (IM) injection medication may be at risk for trauma-related symptoms activated by LAM administration or discussion. This can be addressed by establishing a trusting relationship, using less stigmatizing language and highlighting choice and preference for LAMs where there may have been little choice involved in IM medications for agitation. In a trauma-informed approach, one asks, "What happened to you?" rather than, "What is wrong with you?"

Before administering the first and subsequent injections, employ a trauma-informed approach by providing information, choice and empowerment. This can be achieved by:

- Offering a step-by-step description of what the process entails and what it may feel like.
- Allowing the individual to choose the spot or arm for the injection site.
- Inquiring about the person's preference regarding having a family member or other person join them in the room for support.
- Asking if there is anything else that can be done to make them feel more comfortable.

For more information on trauma-informed and recovery-oriented care, SAMHSA's Treatment Improvement Protocol and Recovery-oriented Systems of Care Resource Guide are helpful resources.

COMMUNICATE EFFECTIVELY AND EMPOWER PATIENTS

Talking to patients about LAMs does not have to be uncomfortable for the patient or practitioner. Use of approaches such as shared decision-making (SDM) and motivational interviewing (MI) can promote effective communication, collaboration, choice and empowerment.

Employ SDM and MI strategies throughout the course of care to help patients make meaningful treatment decisions, feel more empowered to make decisions about their care and experience the clinician as a recovery partner. SDM approaches may include exploring treatment options like oral antipsychotic medications, psychosocial treatment only or LAMs when clinically indicated. When sensitively guided by the clinician, this process provides an important foundation to make self-directed medication decisions about LAMs. Motivational engagement strategies like MI can be implemented when the clinician identifies clear benefits of LAMs and the person is not yet ready to accept a trial of this treatment. If there is an involved family member or a supportive person in their social network, it is important to include them in constructively assisting the patient with decision-making regarding LAMs, particularly as an important tool in support of the person's recovery goals. Although individuals might decline LAMs for months, or even years, assertive MI and SDM are often effective in evoking and increasing the person's motivation over time.

Use language that is less frightening and stigmatizing such as long-acting medications rather than "the IM," long-acting injectables or "the needle." Individuals may associate this with previous experiences with short-acting, injectable medications administered in coercive situations. Actions that may be perceived as coercive have the potential to activate a person who has a history of trauma, such as physical or sexual abuse.

USE THE REAP MODEL

- Recognize life goals.
- Explain how a LAM antipsychotic supports their life goals.
- Acknowledge patient concerns.
- Provide accurate information to patients and their families.

The Changing the Conversation Tip Sheet provides step-by-step guidance for clinicians on how to have conversations with your patients about LAMs using the REAP model.

EDUCATE AND INVOLVE PATIENTS

To make informed decisions, patients must be educated about the potential risks and benefits of oral vs. injectable medications. To improve education and involvement of patients in making decisions about treatment:

- Use SDM and MI strategies to promote effective communication, empowerment and collaboration.
- Develop a collaborative treatment plan.
- Have patient education brochures, videos, infographics and posters that reflect the patients' language and contribute to increased knowledge and decision-making.

Useful resources to share with patients include:

- A discussion guide that helps patients think through potential questions, concerns and options for long-acting medications.
- Video testimonials of patients who use LAMs.
- Culturally appropriate patient brochures included in the Selected Long-acting Antipsychotic Medications table.

INVOLVE FAMILIES AND CAREGIVERS

Family members can play an important role in the treatment planning and recovery process. Involving families, other members of the patient's support network or a peer recovery coach in care begins with finding out who, if anyone, is included in their social support network. Always seek patient consent to keep their family and caregivers fully informed about the details of their treatment and what they can do to assist. The patient or staff person should then reach out to that person to invite them to join one or more visits with the patient present. In addition to addressing mental health literacy, the identified support person will need education about the risks and benefits of long-acting medications and how they can provide support in a way that works for the patient. Culturally appropriate informational brochures on potential risks and benefits of LAMs should be available for family members. In cases when the patient will not consent to the clinician sharing treatment information with their family clinicians are still able to listen to and consider any information that family members offer. HIPAA does not require patient consent for a clinician to receive information about them volunteered by others.

INITIATING LAMS

■ Start early.

Initiate discussion about LAMs as the preferred treatment option early in the treatment process and consider a possible long-term LAM transition plan when you begin administering oral medications. Key scenarios or decision points when prescribers should consider introducing long-acting medications as a treatment option include newly diagnosed patients, patients with a recent relapse or patients transitioning from in-patient care or incarceration. A study published in the Journal of the American Medical Association (JAMA) about the use of the long-acting injectable risperidone provides more information on the clinical advantages of starting LAMs early. Second generation LAMs are usually preferred due to superior relapse protection, neuro-protection (Nasrallah, 2017) and lower mortality (Taipale, 2018).

■ Convey a clear, optimistic message.

When discussing the recommendation to choose a LAM, use the following approaches:

1. Introduce the option as a "long-acting medication" formulation. Do not start by describing it as an injection. Present the advantages compared to oral medication first:
    - » Fewer side-effects.
    - » More effective in reducing symptoms (do not say "control" symptoms).
    - » Smoother action – don't feel it "kicking in" or fading away.
    - » Decreased risk of hospitalization.
    - » Addresses the challenge of having to remember to take a daily pill.
    - » Reduces the total amount of medication taken compared to oral medication.
2. Inform the patient that the frequency of injections is once per month or less and compare this experience to taking a vitamin B-12 or Depo-Provera (for female birth control) injection and ask for questions.
3. Directly recommend starting a LAM based on your belief that it will be the most effective treatment approach.
4. Consider letting the patient know that this form of medication, "is more expensive for Medicaid/Medicare/insurer but we want you to have the best treatment available and we will work hard to get it for you."

■ Start with a trial of oral medications.

For those who are not already taking an oral antipsychotic medication, a brief trial of oral medications for one week to one month is recommended to identify severe adverse reactions, response, dosing and/or ability to tolerate the agent. Prescribers can also use this tip sheet on choosing an LAI antipsychotic agent.Start low and go slow.

■ Start low and go slow.

Consider under-dosing the LAM at the beginning, rather than risk prolonged side-effects that may lead the person to refuse further LAM administrations. Use this recommended starting dosage tip sheet.

- **Transition with oral medications.**

When starting a LAM, continue prescribing the oral antipsychotic medication the patient is already taking during the initiation period, when clinically indicated, and allow for flexible dosage adjustment to compensate for initial over- or under-dosing.

- **Maintain needed oral medications for extrapyramidal symptoms (EPS).**

Individuals prescribed oral antipsychotic and anti-EPS medications who start on a LAM may be at risk for EPS due to nonadherence of oral anti-EPS medications. Educate patients receiving LAMs about the importance of taking anti-EPS medications even if they are not taking oral antipsychotic medications. Use of a symptom rating scale is also recommended.

- **Taper EPS medications.**

Some patients who required treatment for EPS on oral medications may no longer need it after switching to a LAM. Other individuals may do well on lower anti-EPS dosing than with oral medication after transition to a LAM. Consider a slow taper of EPS medication after doing well on LAM for several months.

- **Use dosage conversion tables.**

See the Selected Long-acting Antipsychotic Medications table.

- **Improve access.**

Clinicians can improve access to LAMs by developing the capacity to administer LAMs themselves based on their trusted relationship with the patient, hiring trained nurses to administer LAMs or training their own nursing staff in the safe and effective administration of LAMs. Access can be greatly increased by providing outreach services – in-home injections. Organizations may also consider partnering with pharmacy services that can administer LAMs onsite. This can be accomplished through co-location or cooperative agreements with local pharmacies. Another option is to consult with the patient's primary care provider to see if the nursing staff can provide LAM injections for your shared patients.

MONITORING LAMs

- **Check plasma levels.**

For those who are experiencing a suboptimal response, consider checking plasma levels of antipsychotic medications. This is advantageous when therapeutic ranges are known (e.g., haloperidol) and to identify rapid metabolizers (e.g., fluphenazine, risperidone, paliperidone) which can lead to better results after adjusting dosage and/or interval accordingly.

- **Anticipate benefits from more consistent plasma levels.**

Individuals at risk of antipsychotic discontinuation syndrome due to abrupt cessation of oral antipsychotics often experience clinical benefits from a LAM. Many patients have fewer side-effects due to avoiding the higher plasma medication concentration peaks associated with oral absorption.

CONTRAINDICATIONS FOR LAMs

- Needle phobia is another consideration. This may be addressed with cognitive behavioral therapy (CBT) (Florida Center for Behavioral Health Improvements and Solutions, 2020).

ORGANIZATIONAL SUPPORTS

EDUCATE ALL STAFF

- Educate all staff on the potential benefits of LAMs and how to talk to patients and families about them. Prescribers, therapists, case managers, peer specialists and nurses should all regularly discuss medication adherence and the benefits of LAMs with their patients. The Care Transitions Network's Resource Library has tip sheets, case studies and guidance documents to education staff.
- Peer specialists who have lived experience with LAMs can be effective advocates and support for LAM utilization and education and information shared by them is particularly valuable. Strive to include peers on treatment teams.
- Train clinicians and nursing staff proper administration techniques to ensure the safety and efficacy of LAMs and minimize discomfort to patients. Review Z-Track technique, needle stick safety, proper anatomical locations and aseptic administration.
- Ensure that all staff are trained in effective communication and engagement strategies including MI and SDM.

PREVENT MISSED APPOINTMENTS

- Offer in-home administration of injections and/or transportation to injection sites.
- Involve family members/other partners in care.
- Involve peer support specialists or recovery coaches in care.
- Provide telephone reminders about appointments for LAMs.
- Provide LAM reminder cards to individuals upon administration so they know – and can track – their last LAM date and next LAM date. This minimizes the risk of early or redundant LAM administration by another provider and often increases individuals' participation in the LAM process.

ENSURE SAFETY AND EFFICACY

- Identify a safe, private space for medication administration.
- Have appropriate supplies on hand such as safety/retracting needles, gauze, alcohol, Band-Aids and gloves.
- Arrange for refrigeration if Risperdal Consta is to be used.
- Develop a system for sharps and hazardous waste disposal.

ADDRESS POTENTIAL BARRIERS

- Utilize assistance programs, provided by many pharmaceutical companies, to support patients and clinicians in navigating coverage and cost of LAMs. The Desk Guide for Obtaining Coverage is a useful resource for staff responsible for supporting patients' access to LAMs.
- Prevent negative patient perception of LAMs through education, use of sensitive language and effective communication and decision-making strategies.
- Overcome stigma associated with injections through patient and family education, brochures, posters and use of destigmatizing language.
- Improve provider knowledge of or experience with LAMs through practitioner education and organizational supports, policies and practices.
- Address staff and infrastructure barriers through updates to organizational environments, policies and procedures, including having a nurse or pharmacist handle pharmacy payment assistance needs, providing transportation to injection appointments and involving peer specialists with LAM experience on the treatment team as educators.
- Implement a tracking system or registry to ensure that patients are monitored for signs of medication nonadherence or partial adherence such as hospital admissions, emergency department (ED) visits and unexpected symptom recurrence. Ensure that flagged patients receive a recommendation for LAMs.

INSTITUTE POLICIES AND PROCEDURES

- Create a formal procedure for LAM orders to be communicated if the non-prescribing clinician or more than one clinician may be administering LAMs. Update orders through an electronic health record (EHR) when feasible.
- Create or update a bloodborne pathogen exposure policy in case of needlestick.
- Update formulary to include LAMs and clozapine.
- Create additional policies and procedures that support the safe and effective use of LAMs, such as the standard operating procedure created by Black Country Partnership NHS.

COLLECT, ANALYZE AND UTILIZE DATA

- Implement systems to continuously collect, analyze and utilize data on the rates of LAM utilization by individual clinicians.
- Clinicians, as a group, should review and discuss their individual variation in utilization of LAMs periodically.
- Collect, analyze and utilize data that demonstrates patient improvements in care such as progress toward recovery goals, reductions in utilization (such as hospitalizations, EDs), or advances in levels of care, such as AACP's Levels of Care Utilization System for Psychiatric and Addiction Services.

Table: Selected Long-acting Antipsychotic Medications

Medication name	Typical Maintenance, administration interval: Time to peak level:	Loading or initiating dosing	Oral medication supplementation indicated at the initiation of LAA	Medication -specific benefits	Medication specific disadvantages	Strategies with delayed/ missed dosing	Supplementary Materials
Paliperidone Palmitate (Sustenna)	Administration Interval: q4 weeks Peak blood levels after injection: 2 weeks	Day 1: 234mg IM Day 8: 156mg IM Then q4 weeks maintenance dose from day 8.	Not necessary to oral dose during initiation.	No oral dose supplementation is needed after loading doses, q4 week interval. Excreted by the kidney which is advantageous for people with liver disease.	Risk of: prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD risk. High cost.	If > 6 weeks delay for maintenance dose, administer maintenance dose on day 1 and 8. Exception: if maintenance dose 234mg follow package insert. If > 6 months delay, reload according to package insert.	Invega Sustenna Patient Brochure
Paliperidone Palmitate (Trinza)	Administration Interval: q12 weeks Peak blood levels after injection: 4-5 weeks	Transition only from paliperidone palmitate (Sustenna) (stable dose for 4 months). Sustenna to Trinza Conversion: mg: 78=234 mg:117=410 mg:156=546 mg:234=819	Not applicable. (Transitioned from Sustenna LAA)	q12 weeks Excreted by the kidney, which is advantageous for people with liver disease.	Slow to taper or titrate if suboptimal dose or symptom exacerbation. Risk of: prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD risk. High cost.	If delayed >3.5 -4 months, administer last dose of Trinza. If miss 4-9 months, use re-initiation regimen with Sustenna as per package insert. If > 9 months, reload with Sustenna and follow insert.	Invega Trinza Patient Brochure
Paliperidone Palmitate **(Hafyera)**	Administration interval: q6 months 1) 1,092 mg for those receiving 156mg/month of Sustenna oor 546mg q3 months of Trinza. 2) 1,560mg for patients receiving 234mg/months of Sustenna or 819 q3 months of Trinza.	2 options for transition: 1) From Invega Sustenna after 5 months stabilization on either 156 or 234mg/month. 2) From Invega Trinza after 1 dose of either 546 or 819mg q3 months.	No oral supplementation needed.	No oral tabs needed. Longest interval between LAM doses available (every 6 months). May reduce risk of jail or prison due to psychotic relapse when last to follow-up. Can be given to patients with liver failure or cirrhosis because it is excreted from the kidney.	Risk of: prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD risk. High cost. Must be given in the gluteal region only – not in the deltoid. Injection site rash or erythema.	Give the usual dose if 1-3 weeks late. Re-start Invega Sustenna with 2 initiation doses if 4 weeks late or more	Patient Brochure

Medication name	Typical Maintenance, administration interval: Time to peak level:	Loading or initiating dosing	Oral medication supplementation indicated at the initiation of LAA	Medication-specific benefits	Medication-specific disadvantages	Strategies with delayed/ missed dosing	Supplementary Materials
Aripiprazole (Maintena)	Administration Interval: q4 week Peak blood levels after injection: 5-7 days	400mg then q 4 weeks 300mg dose if slow metabolizer CYP2D6.	Yes. 1st 2 weeks.	Very low risk of prolactinemia, less metabolic risk than other second generation antipsychotics, but more than first generation agents.	Fixed dosing with low dose flexibility. Risk: akathisia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, high cost, EPS/TD.	For 2nd or 3rd Injection: >5 weeks delayed, reload and oral supplement x2 weeks. If 4th dose or thereafter, >6 weeks delayed, reload and oral supplement x2 weeks.	Patient Appointment Prep Guide
Aripiprazole (Aristada) Lauroxil	Administration Intervals: q4 weeks, q6 weeks or q8 week dosing Peak blood levels after injection: 3-5 days	Dosing and oral dose equivalents: 1064mg q8 weeks=Abilify 15mg PO daily 882mg q6 weeks =Abilify 15mg PO daily 882mg IM q4 weeks > Abilify 20mg PO daily 662mg IM q4 weeks=Abilify 15mg PO daily 441mg q4 weeks=Abilify 10mg PO daily	Yes. 1st 3 weeks.	Low risk of prolactinemia, less metabolic risk than other second-generation agents, but more than first generation, aripiprazole preparation with dose adjustment options (vs. Maintena) and dosing interval flexibility.	Risk of akathisia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, high cost, EPS/TD.	For q8 wk. dosing: Delayed 10-12 weeks from last injection, supplement with oral meds for 7 days. If >12 weeks since last injection, reload dose and oral supplement. For 882mg or 662 mg dosing: if 8-12 weeks since last dose, oral supplement for 7 days. If missed >12 weeks, reload. For 441mg dosing, see package insert.	Patient Brochure
Risperidone LAA "Consta"	Administration interval: q2 weeks Peak level after injection: 3 weeks	Oral dose conversion oral risperidone to Consta: mg: <3 =25 mg: >3-5 = 37.5 mg: >5=50 >8mg=N/A	Yes. At least 5 weeks recommended after initiation. Manufacturer recommends briefer duration.	Less EPS/TD/ NMS/ antipsychotic induced negative syndrome risk than first generation agents.	q2 weeks, low therapeutic ceiling vs. Sustenna, high risk of prolactinemia, metabolic risk, EPS. Must refrigerate. High cost (varies by state formulary).	If missed dose during maintenance for more than 2 weeks, consider oral supplement 6 weeks after restarted injection for duration of missed dose.	Patient Leaflet

Medication name	Typical Maintenance, administration interval: Time to peak level:	Loading or initiating dosing	Oral medication supplementation indicated at the initiation of LAA	Medication -specific benefits	Medication -specific disadvantages	Strategies with delayed/ missed dosing	Supplementary Materials
Olanzapine (Zyprexa)	Administration Interval: Every 2 to 4 weeks	Target Oral Dose – 10mg/day First 8 weeks: 210 mg/2 weeks or 405mg/4 weeks Maintenance Dose: 150 mg/2 weeks or 300 mg/4 weeks Target Oral Dose – 15mg/day First 8 weeks: 300 mg/2 weeks Maintenance Dose: 210 mg/2 weeks or 405 mg/4 weeks Target Oral Dose – 20mg/day First 8 weeks: 300 mg/2 weeks Maintenance Dose: 300 mg/2 weeks	Oral supplementation was not generally necessary.		Patient needs to remain in the clinic for 3 hours after administration.	Typically given by a health care professional in an emergency setting, so patients are unlikely to miss a dose.	
Sustained Release Risperidone via subcutaneous injections (SC)	q1 month available in two doses: 90 and 120mg, both monthly	Can administer the low or high dose (90 or 120mg) without any oral supplementation if the patient was previously exposed to either risperidone or paliperidone. Otherwise, give patient 2mg of risperidone or 3mg of paliperidone orally for 2 days to rule out any allergic reaction.	No oral supplementation needed.	No oral supplementation. Rapid onset of action to an early serum peak after a few hours and a later peak after a few days. Subcutaneous instead of IM.	Risk of: prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD risk. Requires lengthy mixing of the medications prior to injection. Injections given SC over abdominal area requiring lying supine. Patients may feel a nodule under the skin. High cost.	Give SC dose whenever patient returns whether acutely psychotic or stable with no acute psychosis.	Patient Leaflet

Medication name	Typical Maintenance, administration interval: Time to peak level:	Loading or initiating dosing	Oral medication supplementation indicated at the initiation of LAA	Medication-specific benefits	Medication-specific disadvantages	Strategies with delayed/ missed dosing	Supplementary Materials
Haloperidol Decanoate	Administration interval: q4 weeks Peak blood levels post-injection: 5-7 days	Day 1: 50mgl Day 8: (Monthly Dose – 50mg) Monthly Dose= Total oral Daily Dose x 10 Initiate q4 week interval from day 8	Yes. Optimally, at least 6 weeks (duration recommended based on clinical experience of authors). May taper oral dose earlier and more rapidly if EPS or other side-effects.	Q4 week dosing, lower cost, lower metabolic risk, clear oral dose conversion. Less metabolic syndrome risk than second generation antipsychotics. Lower cost.	Risk of: TD, EPS, NMS* and prolactinemia. Individuals may associate this medication with haloperidol HCl IM experience, risk of neuroleptic induced negative syndrome. May require anti-EPS tx.		Patient Leaflet Patient Leaflet (2)
Fluphenazine Decanoate	Administration Interval: q2-3 weeks Peak blood levels after injection: 2-5 days	Day 1: Oral dose x 1.25. Alternatively, may initiate 25mg IM q2 weeks and titrate/taper based on treatment response and tolerability.	Yes. Optimally, for 3-5 weeks.	Can more rapidly titrate or taper due to shorter half-life, short onset to peak plasma levels (2-5 days), lower cost. Less metabolic syndrome risk than second generation agents. Lower cost.	Q2 weeks, risk of: TD, EPS, NMS and prolactinemia. May require anti-EPS medications.		Patient Leaflet

Table adapted from table developed by the AACP

Note: Authors have no clinical experience with Olanzapine Relprevv. Use in the community is limited due to the risk of post injection delirium/sedation syndrome, required 3-hour monitoring after administration and administration location of a registered health care facility with ready access to emergency services.

TD: tardive dyskinesia, EPS: extrapyramidal signs/symptoms, NMS*: neuroleptic malignant syndrome

Prescribing clinicians must check package inserts, review scientific literature and consult guidelines while prescribing. Content from this table consists of clinician experience and consensus.

REFERENCE LIST

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