# IMPROVING UTILIZATION OF LONG-ACTING MEDICATIONS:

# Toward Standardized Measures



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# **EXECUTIVE SUMMARY**

People living with serious mental illnesses or substance use disorders face considerable barriers to accessing and adhering to effective treatments; those barriers significantly impact clinical outcomes. Robust evidence demonstrates that treatment with long-acting medications (LAMs) substantially reduces treatment nonadherence, dropout, relapse rates, hospitalizations and overall health care costs. Despite this, LAM utilization remains low across health care settings, spotlighting a critical need for standardized, widely adopted measures and benchmarks to enhance the appropriate use of LAMs.

This report addresses the LAM utilization gap. The Medical Director Institute (MDI) of the National Council for Mental Wellbeing brought together experts in psychiatry, addiction medicine and health care quality measurement to develop actionable, standardized measures to drive increased use of LAMs. The panel specifically targeted three domains: psychotic and bipolar disorders, opioid use disorder (OUD) and alcohol use disorder (AUD).

#### Measures

We propose two core measures for each domain: initiation and continuation. Initiation measures indicate whether patients receive at least one dose of an LAM, representing a foundational step toward broader implementation. Continuation measures track sustained usage, defined as receiving two or more administrations consecutively within an established period, reflecting consistent treatment. This approach provides nuanced insights into different stages of medication uptake and retention, highlighting distinct barriers that health care systems and providers must address.

We chose to use single initiation and continuation measures for antipsychotic LAM (AP-LAM) used in psychotic and bipolar disorders because:

- Antipsychotics are first-line medication choices for both groups of disorders and practice guidelines.
- An increasing number of people with bipolar disorder are receiving antipsychotics as their primary mood stabilizer.
- There's robust evidence for improved outcomes with LAM usage for both bipolar and psychotic disorders.
- It's common for different clinicians seeing the same patient to have a different diagnosis
   schizophrenia, schizoaffective disorder or bipolar disorder but to still prescribe an antipsychotic medication as part of the regimen.

We also believe the simplicity of a single measure relevant to several diagnoses' specific measures will increase the use of utilization measures. We chose separate measures for OUD and AUD because the change in diagnosis is much more likely to be accompanied by a change in medication.

# **Calculating LAM utilization rates**

The principles MDI used to develop the guidelines for calculating LAM utilization rates emphasize relevance, feasibility and alignment with current research and standards. The measures used minimize provider burden by using readily available data, such as medical and pharmacy claims. Consistency in data specifications and methodology with established performance measures, like those from the National Quality Forum, ensure comparability and ease of implementation. Additionally, these measures prioritize simplicity and clarity, facilitating consistent and efficient data aggregation across a variety of health care settings.

Calculating denominators for LAM utilization rates involved identifying populations based on specific diagnostic criteria relevant to psychotic disorders, OUD and AUD. For a population to be included, there must be multiple episodes of diagnosis separated by defined intervals for accurate population representation. To maintain the clinical applicability and precision of the measures, we excluded patients with advanced illness or those receiving hospice care.

The numerators focus explicitly on actual medication administration. For initiation measures, patients qualify by receiving at least one administration of an LAM within a specified period. Continuation numerators require at least two sequential administrations, providing insight into adherence to and continuity of treatment. These clear criteria enable health care organizations to accurately assess their performance in initiating and maintaining patients' effective long-acting treatments.

### **Recommendations**

For AP-LAMs, MDI recommends a national benchmark of 30% initial utilization, aiming for incremental annual increases toward 50% by 2030, ultimately reaching 70%. International and regional U.S. data demonstrate the feasibility of these benchmarks; current utilization rates are already significantly higher in areas where obstacles to health care delivery have been effectively addressed. We propose a continuation measure of at least 85% of patients initiating AP-LAM continuing with subsequent administration.

Current utilization rates for OUD-LAMs, including buprenorphine and naltrexone formulations, are exceptionally low despite their proven ability to improve retention and reduce overdose risks. We propose a modest initial benchmark of 10% for OUD-LAM initiation, reflecting the urgent

need for increased adoption. The continuation benchmark is 9% of patients who receive an initial administration receiving subsequent doses.

Extended-release naltrexone, the sole available LAM for AUD, is severely underused despite strong evidence of its ability to enhance treatment adherence and reduce alcohol consumption. The proposed initiation benchmark for AUD-LAM is set at 10%, given current low prescribing rates, with continuation measures targeting at least 10% adherence for subsequent doses.

Several obstacles contribute to LAM underutilization across provider, patient and system domains. Providers have misconceptions about patient adherence to and tolerance for LAMs, often viewing them as last-resort interventions. Patient obstacles include stigma, misinformation about side effects, anosognosia, concerns about autonomy and discomfort with injection-based therapies. System-level barriers include insurance and reimbursement complexities, logistical constraints and fragmented health care delivery systems.

Strategically addressing these barriers requires comprehensive initiatives that involve improved provider education, enhanced patient communication, structural adjustments in health care delivery and policy reforms. We recommend integrating clinical decision-support tools within electronic health records, broadening continuing medical education, promoting specialty pharmacy partnerships, deploying multidisciplinary teams that include pharmacists, nurses, therapists and peer support specialists, and addressing reimbursement and access to services for administration.

Establishing and achieving these standardized benchmarks is both necessary and achievable, as demonstrated by higher utilization rates in some locations and populations. Increased LAM utilization promises significant clinical, economic and societal benefits, including reduced relapse and hospitalization rates, decreased health care costs, improved patient stability and enhanced overall health outcomes. By systematically measuring initiation and continuation, health care providers and systems gain valuable insights that help them target interventions effectively, ultimately transforming behavioral health treatment to benefit patients, providers and society at large.

# INTRODUCTION

People living with serious mental illness or a substance use disorder face significant challenges in accessing and adhering to effective treatments. Decades of research have demonstrated the life-changing potential of long-acting medications (LAMs) to prevent relapse, reduce hospitalizations and improve long-term outcomes. Nonetheless, they remain underused, with persistent gaps between evidence-based practice and real-world implementation.

However, in other specialties, technologies to increase dosing intervals are the standard of care. For example, we see this in gynecology (e.g., some IUDs and other birth control devices), endocrinology (e.g., diabetic pumps, bone density medications), and allergy and immunology (e.g., long-acting injections for immune-modulating medications).

At the core of this treatment gap is a lack of standardized and widely adopted measures to track the appropriate use of LAMs. Without clear, agreed-upon benchmarks, health care systems and providers lack data-driven tools to identify opportunities for improvement, target interventions and demonstrate the value of these transformative treatments. Standardized measurement is necessary for implementing performance incentives to reward improvement. Since utilization of LAMs is associated with improved outcomes, increasing utilization should be incentivized. That can only be done once standardized measures of utilization are available.

This report represents a collaborative effort to address the lack of standards. In January 2025, the Medical Director Institute (MDI) of the National Council for Mental Wellbeing convened a panel of leading experts in psychiatry, addiction medicine and health care quality measurement, and people with lived experience of mental illnesses and substance use disorders. Their objective was to develop a set of standardized measures and benchmarks to drive better utilization of LAMs for psychotic disorders, opioid use disorder and alcohol use disorder.

When people with these conditions receive uninterrupted treatment, they are far less likely to experience the devastating consequences of relapse, including worsening symptoms, hospitalization, incarceration and premature death. By establishing consistent, evidence-based measures, the MDI aims to empower health care systems, providers and policymakers to prioritize access to these life-saving treatments and improve outcomes for some of our most vulnerable populations.

Through the widespread adoption of these standardized measures, we can transform the landscape of mental health and addiction treatment. This new approach to LAMs moves the field away from its focus on individual patients and providers as solely responsible for adherence, and toward evidence-informed practice- and system-level measures of use. It bridges the gap between the science and reality of care delivery.

This report describes the process the MDI used to develop specific metrics to measure LAM utilization in health care organizations and delivery systems.

To provide a comprehensive analysis, we begin our report with a background discussion on barriers to medication adherence and the prevalence and consequences of medication nonadherence in people with serious mental illnesses and substance use disorders. We highlight how LAMs have emerged as a solution for addressing these challenges, particularly in conditions such as schizophrenia, bipolar disorder, opioid use disorder and alcohol use disorder. This section also reviews existing research on the benefits and limitations of LAMs, emphasizing their role in improving patient outcomes and reducing health care costs.

The report then outlines proposed methodologies for measuring LAM utilization rates, including considerations for defining appropriate metrics and identifying inclusion and exclusion criteria for various patient populations. It summarizes current research on measuring LAM utilization and proposes new benchmark rates.

Finally, we discuss policy and practice recommendations for increasing LAM utilization and provide insights into navigating factors that limit access. The report explores how system-level and provider-level changes such as improved provider training, revised formulary policies and enhanced patient education can facilitate broader use of these effective pharmacotherapies. By addressing both the measurement and implementation challenges, we aim to inform strategies for optimizing the use of LAMs in behavioral health care.

#### **BOX 1. A NOTE ON TERMINOLOGY**

In this paper, we use the term "long-acting medications" rather than "long-acting injectables." "Injectables" emphasizes the administration method over the main goal and benefit of receiving extended dosages of medication, and using "long-acting injectables" often arouses a negative reaction before any discussion of benefits has occurred.

# PROBLEM STATEMENT

Medication nonadherence is a significant challenge in the treatment of schizophrenia, opioid use disorder (OUD) and alcohol use disorder (AUD). For patients with schizophrenia and other psychotic disorders, nonadherence to oral antipsychotics is a major cause of relapse and rehospitalization (Lieslehto et al., 2022). For those with AUD or OUD, nonadherence contributes to recurrent substance use. Patients experiencing deterioration in their cognitive, psychological and overall functioning because of nonadherence also often experience challenges such as unemployment, housing insecurity, contact with the criminal justice system, alienation from family and other social supports, and physical illness.

Core diagnostic features of psychosis, such as lack of insight into their illness and cognitive impairment, directly affect an individual's ability to adhere to oral medications. Co-occurring substance use disorders (SUDs), which are common, often aggravate adherence concerns, increasing the likelihood of relapse and poor clinical outcomes. Long-acting medications (LAMs) can address these barriers by ensuring sustained therapeutic levels, ultimately reducing relapse rates, improving patient stability and even lowering mortality.

LAMs are superior to oral antipsychotic medication in relation to hospitalization and relapse (Kishimoto et al., 2021), time to treatment discontinuation (Rubio et al., 2021), ability to stay in the workforce (Solmi et al., 2022) and even medical outcomes (Taipale et al., 2020). The administration of LAMs is documented broadly across patient records, eliminating questions about whether a medication is ineffective because of nonadherence. The evidence is clear and convincing: The ethical and scientific imperative for early LAM intervention aligns with best practices in other medical fields, where preventive and continuous care is a cornerstone of treatment.

Well-established literature in peer-reviewed journals identifies the obstacles leading to underutilization of LAMs (Bosanac & Castle, 2015; Mason & Heyser, 2021). Despite proven benefits in improving medication adherence, reducing relapse rates and enhancing overall patient outcomes, these medications are prescribed at much lower rates than their potential would suggest (Bosanac & Castle, 2015; Zagorski, 2023). This underuse is a missed opportunity to improve the lives of people with serious mental illness and substance use disorders.

# LAMs as a tool for addressing nonadherence

Research supports the benefits of LAMs for improving medication adherence. LAMs can help address adherence by ensuring consistent medication levels and reducing the burden of taking pills daily. However, studies also indicate that only 10%–30% of eligible patients receive antipsychotic LAMs (AP-LAMs) (Bosanac & Castle, 2015; Bareis et al., 2022; Zagorski, 2023). The use of LAMs to treat OUD and AUD presents a promising and underused approach to improving treatment adherence, retention and outcomes — one that also reduces concerns about diversion of controlled substances.

While research on LAMs for SUDs is not as extensive as for psychotic disorders, there are clear parallels in the challenges around use. Years of prescriber and patient education have not significantly increased LAM use. There is some consensus on how to identify specific patients who would likely benefit from an LAM formulation based on clinical evaluation, but standard, routine measurement of LAM use in people receiving antipsychotics does not occur. We need performance measures that apply broadly across a range of health care providers and payers so conventional organizational quality improvement methods can be applied to LAM utilization.

# Impact of nonadherence

Nonadherence to oral medications for behavioral health conditions has clinical and economic impacts for patients and health care systems. This section reviews data that underscores the need to improve medication adherence through expanded use of LAMs.

#### COMMON REASONS FOR NONADHERENCE TO ORAL MEDICATIONS

Patient nonadherence to oral medications can stem from a wide range of factors that can be broadly categorized into patient-, medication-, provider- and system-related obstacles. They are summarized in Table 1.

Table 1. Common Obstacles to Oral Medication Adherence Specific to Antipsychotic, OUD and AUD Medications

| Level      | Antipsychotic Medications  | OUD Medications  | AUD Medications   |
|------------|--|--|---|
| Patient    | <ul> <li>Low perceived benefit</li> <li>Negative attitudes toward medication</li> <li>Lack of insight into illness</li> <li>SUD comorbidity</li> </ul>   | <ul> <li>Mental illness comorbidity</li> <li>Low readiness or motivation<br/>to sustain abstinence</li> <li>Fear of withdrawal being<br/>triggered if dose is missed</li> </ul>  | <ul> <li>Mental illness comorbidity</li> <li>Low readiness or motivation to sustain abstinence</li> <li>Greater drinking severity</li> </ul>          |
| Medication | Complex regimens/multiple daily dosing     Formulation issues  | Lack of immediate reinforcing effects  | Low perceived need  |
| Provider   | Limited provider willingness to accommodate the cognitive impairment and negative symptoms associated with psychotic and bipolar disorder when proving psychoeducation.                              | <ul> <li>Limited screening for OUD</li> <li>Lack of prescribers and addiction specialists trained in medications for OUD</li> <li>Poor integration of medications for OUD in practice</li> <li>Provider stigma toward patients using medication for OUD</li> </ul> | <ul> <li>Limited screening for alcohol use</li> <li>Limited outpatient treatment options</li> <li>Provider stigma toward patients with AUD</li> </ul> |
| System     | <ul> <li>Limited medication<br/>availability in community<br/>settings</li> <li>Financial constraints</li> <li>Insurance coverage gaps and<br/>delays</li> <li>Inadequate clinic capacity</li> </ul> | <ul> <li>High out-of-pocket costs</li> <li>Regulatory and statutory restrictions</li> <li>Data-sharing restrictions</li> <li>Pharmacy dispensing limits</li> </ul>   | <ul> <li>Financial constraints</li> <li>Limited social services integration</li> <li>Insurance barriers</li> <li>Limited follow-up systems</li> </ul> |

Compiled from sources: De Las Cuevas et al., 2017; Dunn et al., 2013; El Abdellati et al., 2020; García et al., 2016; Madras et al., 2020; Magura et al., 2014; Perez-Macia et al., 2021; Sajatovic et al., 2021; Semahegn et al., 2020; Velligan et al., 2017; Zacker et al., 2024

#### Table 2. Barriers to Oral Medication Adherence for OUD and AUD LAMS Patients

| Patient    | <ul> <li>Cognitive impairment — executive function, planning, memory deficits</li> <li>Stigma-related concerns</li> <li>Low perceived benefit</li> <li>Negative attitudes toward medication</li> <li>Lack of insight into illness</li> <li>Decreased self-efficacy</li> <li>Chaotic lifestyles and unstable routines</li> <li>Lack of social supports</li> <li>Lack of a safe place to store medications</li> <li>Competing priorities</li> </ul> |
|------------|---|
| Medication | <ul> <li>Adverse effects/side effects</li> <li>Daily dosing burden</li> </ul>   |
| Provider   | <ul> <li>Limited psychoeducation provided to patient</li> <li>Limited information provided to patient</li> <li>Poor shared decision-making</li> <li>Limited patient-provider trust (i.e., weak therapeutic alliance)</li> <li>Limited use of adherence monitoring and interventions</li> <li>Time constraints</li> <li>Limited provider training in LAMs</li> <li>Inability to absorb upfront costs of buy-and-bill model</li> </ul>              |
| System     | <ul> <li>Limited medication availability in community settings</li> <li>Limited transportation to clinic appointments, pharmacy visits</li> <li>Limited follow-up systems</li> <li>Limited social services integration</li> <li>Financial constraints</li> <li>Insurance coverage gaps and delays</li> <li>High out-of-pocket costs</li> </ul>  |

# PREVALENCE AND IMPACT OF NONADHERENCE TO ORAL ANTIPSYCHOTICS

Studies have found nonadherence rates for oral antipsychotics ranging from 40%-60% (Jeste et al., 2002; Valenstein et al., 2006). A systematic review of 103 studies estimated the overall nonadherence rate for all types of psychotics to be much lower (25%), but still considerably higher than typical nonadherence rates for other chronic conditions (Lieslehto et al., 2022).

Nonadherence to oral antipsychotic medications in the U.S. imposes significant financial and clinical burdens for patients, health care systems and populations. Research highlights increased hospitalization rates, higher direct costs and systemic inefficiencies linked to gaps in treatment. Nonadherence to oral antipsychotics shifts costs from predictable pharmacy expenses to volatile hospitalization and emergency care costs, straining patients as well as health systems. Population-wide interventions to improve adherence could reduce hospitalizations and generate substantial savings, particularly in public insurance programs like Medicaid and Medicare (Zacker et al., 2024).

- Individual-level costs: Nonadherent patients face 2.5 times higher risk of psychiatric hospitalization than adherent patients, often requiring longer hospital stays and incurring higher annual hospitalization costs (Offord et al., 2013). Adherent patients' higher pharmacy costs (Martin et al., 2022; Offord et al., 2013) are offset by lower medical expenses because of reduced relapses and hospitalizations (Dilla et al., 2013). Suboptimal adherence correlates with worse clinical outcomes, including relapse, suicide risk and functional impairment which indirectly increase personal financial strain through lost productivity and disability (Forma et al., 2020).
- Health care system costs: Hospitalization costs dominate the economic burden of nonadherence. Nonadherent patients incur up to 50% higher annual inpatient costs (Dilla et al., 2013; Martin et al., 2022). Early nonadherence (i.e., within 90 days of treatment initiation) predicts long-term discontinuation, worsening resource utilization over time (Zacker et al., 2024).
- Population-level burdens: An estimated 36.6% of schizophrenia-related hospital admissions are attributable to antipsychotic nonadherence, costing the U.S. health system \$106 million annually. A state-level analysis of California's Medicaid program, Medi-Cal, showed nonadherence contributes to 12.3% of acute inpatient stays, which indicates a savings potential from improving adherence (Dilla et al., 2013).

# PREVALENCE AND IMPACT OF NONADHERENCE TO ORAL MEDICATIONS FOR OUD AND AUD

For OUD and AUD, nonadherence is the norm rather than the exception, posing significant barriers to achieving long-term recovery.

Research indicates that nonadherence to oral medications for OUD imposes significant costs and burdens for patients, health care systems and populations. Nonadherent patients face elevated health risks, including higher likelihood of overdose, complications from illicit drug use and untreated comorbidities (Leider et al., 2011). Medication adherence reduces inpatient addiction treatment and acute care usage by as much as 25% while also boosting outpatient engagement. Fragmented care and limited access to medications for OUD (MOUDs) perpetuate high-costs. System-wide savings could be achieved through interventions to improve adherence, such as expanded access to medications (Gopaldas et al., 2023).

Nonadherence to oral medications for AUD imposes similar costs and burdens. It is associated with higher return-to-use rates and higher rates of emergency department visits and hospitalizations requiring intensified interventions.

# LAMs for treatment of psychotic disorders and schizophrenia

Every day, psychiatric providers diagnose and treat psychosis, a syndrome that encompasses several different disease states. After ruling out medical or substance use-related causes, the first line of treatment is antipsychotic medications, no matter the underlying diagnosis. Key challenges and considerations in AP-LAM implementation include diagnostic accuracy and stability over time. Psychiatric diagnoses vary throughout the lifespan but have the highest rate of stability from adolescence onward (Blázquez et al., 2019).

There are reasonable concerns about ensuring that LAMs are used appropriately, particularly in younger populations or in cases where diagnostic uncertainty exists. At the same time, there is also growing recognition of the importance of using LAMs early, including in off-label contexts such as with adolescent patients experiencing early-onset psychosis (Emsley, 2022).

Clinicians should more broadly consider LAM treatment for patients with early-phase illness. LAM use by patients with early-phase schizophrenia can significantly delay time to hospitalization, a personally and economically important outcome (Kane et al. 2020). Clinicians must also consider strategies to maximize treatment adherence and access, which will better support vulnerable populations, including people experiencing housing insecurity.

Recurrent episodes of psychosis in schizophrenia are associated with significant structural and functional negative brain alterations, such as changes in inflammatory markers, brain volume,

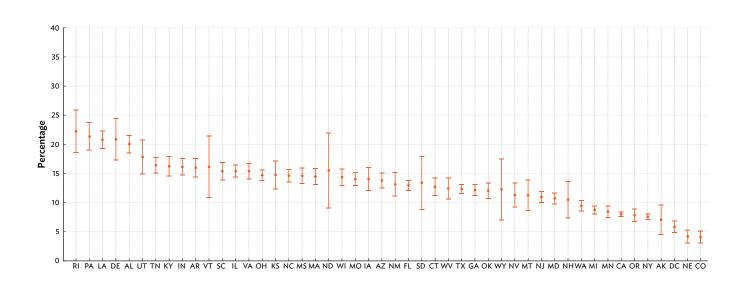
cognitive ability and treatment resistance (Thompson et al., 2001). Early LAM usage to treat schizophrenia is critical to preventing that decline, thereby improving long-term outcomes (Nasrallah, 2007; Alvarez-Jiménez et al., 2011; Taipale et al., 2022). Because LAMs offer a way to ensure consistent medication adherence, they reduce the risk of relapse, preventing negative changes and deterioration in brain structure and function, and improving long-term outcomes (Marcus, 2015).

But LAMs are particularly underused in the early phase of illness, when each relapse is most consequential. Analyses from commercial claims data found that only 10% of early-phase patients were on LAMs (Rubio et al., 2023). The approach to LAMs in schizophrenia should mirror that of cardiologists treating myocardial infarctions — for whom immediate and continuous intervention is standard practice to prevent further illness progression (Emsley et al., 2008, 2012, 2013; Subotnik et al., 2015; Nasrallah, 2017).

The ethical and scientific imperative for early LAM intervention aligns with best practices in other medical fields, where preventive and continuous care is a cornerstone of treatment. The evidence strongly supports the critical role of LAMs in preventing long-term deterioration in schizophrenia, making their early and continuous use an essential best practice in psychiatric care. While LAMs offer substantial benefits, balancing their use with potential metabolic side effects remains a consideration, particularly in adolescents. Careful monitoring and personalized treatment planning are essential to optimize benefits while minimizing risks.

Analyzing 2011-2012 Medicaid data, Bareis et al. (2022) explore the extensive variation in prescribing patterns of LAMs among adults with schizophrenia spectrum disorders in the U.S. There was significant variability across states (see Figure 1), with usage ranging from as low as 4% in Colorado to as high as 22% in Rhode Island. This five-fold difference highlights substantial inconsistencies in practices across the nation.





Source: Bareis et al., 2022

Several factors contributed to the variation, including:

- Uncertainty in professional decision-making
- Provider preferences
- Access to providers
- State-specific regulations
- Variations in health insurance benefits
- Pharmacy benefit management policies
- Patient preferences
- Number of psychiatrists per capita

These findings underscore the need for standardized measures and targeted interventions to optimize usage of AP-LAMs.

# BOX 2. AVAILABLE LAMS, THEIR INDICATIONS AND COMMON ACCEPTED USE OUTSIDE INDICATIONS

Several AP-LAM formulations are currently available.

Table 3. Selected Long-acting Medications

| Drug                                      | Dosing Interval       |
|---|-----------------------|
| First Generation                          |                       |
| Haloperidol decanoate                     | Every 3-4 weeks       |
| Fluphenazine decanoate                    | Every 2-4 weeks       |
| Second Generation                         |                       |
| Abilify Maintena® (aripiprazole)          | Every 4 weeks         |
| Abilify Asimtufii® (aripiprazole)         | Every 8 weeks         |
| Aristada® (aripiprazole lauroxil)         | Every 4, 6 or 8 weeks |
| Zyprexa Relprevv® (olanzapine)            | Every 2-4 weeks       |
| Invega Sustenna® (paliperidone palmitate) | Every 4 weeks         |
| Invega Trinza® (paliperidone palmitate)   | Every 12 weeks        |
| Invega Hafyera™ (paliperidone palmitate)  | Every 6 months        |
| Erzofri® (paliperidone palmitate)         | Every 4 weeks         |
| Risperdal Consta® / Rykindo (risperidone) | Every 2 weeks         |
| Perseris® (risperidone SC)                | Every 4 weeks         |
| Uzedy® (risperidone SC)                   | Every 4 or 8 weeks    |

**First-generation AP-LAMs (1960-1999):** The development of AP-LAMs began in the 1960s with fluphenazine enanthate (1966) and fluphenazine decanoate (1968) (Brissos et al., 2014; Crocq, 2015). These early formulations were designed to maintain stable drug levels in patients who struggled with adherence to oral medications. Haloperidol decanoate followed, becoming available in Europe in 1981 and the U.S. in 1986. While these first-generation antipsychotics were effective in reducing relapse rates, they were often associated with significant motor side effects, such as extrapyramidal symptoms and tardive dyskinesia (Hu, 2024).

**Second-generation AP-LAMs (2000-present):** Second-generation antipsychotics saw a shift toward better tolerability and broader therapeutic goals. Risperidone microspheres (Risperdal Consta), approved in 2003, were the first (Crocq, 2015; VandenBerg, 2022). Newer formulations include aripiprazole, olanzapine, paliperidone and additional risperidone products. These medications are designed to improve adherence by offering longer dosing intervals and minimizing side effects. They aim to alleviate psychosis, thought disorganization and behavioral dysregulation and to address negative symptoms and cognitive deficits, which are critical for a positive long-term prognosis.

There are two primary differences between newer and older formulations:

Dosing intervals: First-generation AP-LAMs typically require administration every one to four weeks. In contrast, newer ones offer extended dosing intervals ranging from every two weeks to six months, enhancing convenience and adherence (VandenBerg, 2022). They also aim for more consistent plasma levels, reducing excessive as well as insufficient drug exposure. The first-generation AP-LAMs, limited by their propensity to cause motor side effects, required the use of additional medications like anticholinergics. Second-generation AP-LAMs have a better side effect profile, but they are associated with metabolic issues such as weight gain and diabetes risk. Second-generation AP-LAMs have also been associated with lower mortality rates than their first-generation counterparts (Hu, 2024).

See <u>Guide to Long-acting Medications</u> from the National Council for a comprehensive overview of LAMs and considerations for selection and prescribing.

# LAMs for treatment of Bipolar Disorder

The use of LAMs is an effective strategy to improve major clinical outcomes in people with bipolar disorder. A meta-analysis of six mirror-image studies (Bartoli, 2023) that compared relevant clinical outcomes between the 12 months before (pretreatment period) and 12 months after (posttreatment period) the initiation of a LAM treatment in adults with Bipolar disorder found that LAM treatment is associated with a significant reduction in days spent in hospital and number of hospitalizations. In addition, studies consistently estimated a significant reduction of hypo-/manic relapses after LAM treatment initiation, while the effect of LAMs for depressive episodes was less clear. Finally, LAM treatment initiation was associated with a lower number of emergency department visits in the year after LAM initiation.

# LAMs for treatment of OUD

There are three medications for the treatment of OUD: buprenorphine and naltrexone, which are available in long-acting formulations, and methadone. Underprescribing of oral medications and LAMs is a major challenge, influenced by a lack of provider knowledge, historical treatment approaches rooted in nonmedical fields, and philosophical resistance.

The use of LAMs in the treatment of OUD presents a promising and underused approach to improving outcomes. While research on LAMs for OUDs is less extensive than research on LAMs for psychotic disorders, we can see clear parallels in the challenges of nonadherence and poor retention. In the treatment of OUD, cycles of nonadherence are the norm rather than the exception. Given that adherence is closely linked to improved outcomes, including reduced mortality, strategies to improve it are essential.

The Cascade of Care model is a public health framework for measuring retention and outcomes in chronic, relapsing conditions such as HIV, tuberculosis and OUD. The framework helps monitor patient flow through health care systems, identify process breakdowns, track individual patient progress and population-level outcomes, set benchmarks across populations and treatment settings, and guide quality improvement efforts.

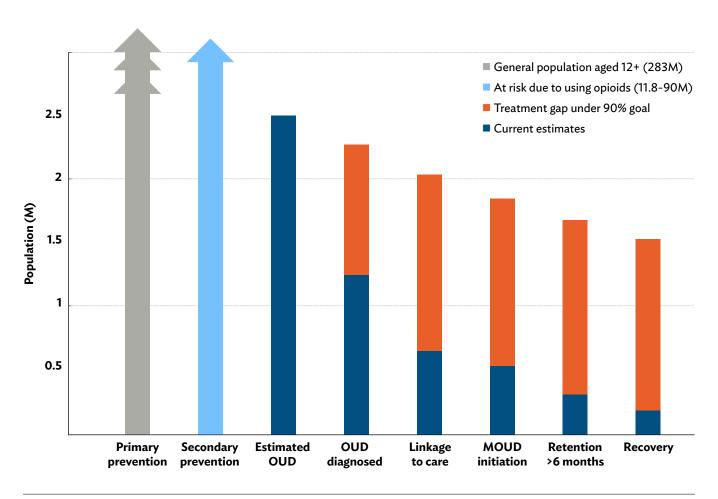
An OUD Cascade of Care (see Figure 2) establishes population estimates for primary and secondary prevention and prevalence of OUD. It also sets goals for diagnosis, linkage, medication initiation, retention in care and recovery for those with OUD. Poor retention rates are a critical challenge; data shows that treatment retention declines significantly over time (Fishman et al., 2020, 2024; Krawczyk et al., 2021). The research reveals significant gaps in the care cascade:

- Only 20%-25% of individuals with OUD receive any treatment in a given year.
- Fewer than 35% of those in care receive evidence-based medication treatment.

- Early dropout rates (within first few months) are high.
- About 38% of patients remain in treatment at six months.
- Just 26% remain at 12 months and 17% at 24 months.

The first few months of treatment are a critical window for stabilizing patients. Those who achieved 90 or more days of abstinence early in treatment had significantly better long-term retention and outcomes (Williams et al., 2019, 2022, 2024).

Figure 2. Assessing the Scope of an OUD Cascade of Care in the U.S.



Source: Williams et al., 2022

Patients using LAMs have shown better adherence to treatment than those using oral formulations. However, several barriers hinder the widespread adoption of OUD-LAMs, including the requirement for specialty pharmacies, risk evaluation and mitigation strategies, and underlying

challenges in accessing controlled substances. Applying the cascade framework to OUD-LAM utilization highlights the importance of tracking adherence, calculating utilization rates, establishing usage benchmarks and identifying strategies to improve long-term engagement.

# LAMs for treatment of AUD

The trajectory of recovery in AUD differs from that of OUD, with AUD patients often experiencing more fluctuations between abstinence and relapse. Brief relapses in alcohol use may have a less severe impact on long-term recovery than the potentially catastrophic consequences of opioid relapse, yet poor adherence and retention still lead to significant costs. Nonadherent AUD patients have higher rates of emergency department visits, hospitalizations and outpatient care. Heavy alcohol use independently predicts nonadherence to other chronic disease medications, such as those for diabetes and hypertension, further compounding costs (Grodensky et al., 2012).

There are three medications for the treatment of AUD: disulfiram (Antabuse), naltrexone (Vivitrol) and acamprosate (Campral). These medications are indicated to support abstinence and reduce heavy drinking in patients with AUD. A meta-analysis found that higher adherence to AUD medications is directly connected to improved outcomes (Swift et al., 2011). On the whole, medications to treat AUD are underprescribed. As with OUD, this is related to a lack of provider knowledge, historical treatment approaches rooted in nonmedical fields, and philosophical resistance.

Only naltrexone is available in a long-acting formulation; injectable naloxone was introduced in 2006. Naltrexone (oral or injectable) is prescribed to fewer than 10% of patients who could benefit from it (Mason & Heyser, 2021). This low usage persists despite evidence showing the medication can significantly reduce alcohol consumption and improve abstinence rates. Extended-release naltrexone has demonstrated superior adherence compared to oral AUD medications, leading to better long-term treatment success (Hartung et al., 2014). Other research indicates that extended-release naltrexone reduces health care utilization by 13%-25% compared to oral medications (Mark et al., 2010). This suggests that the true efficacy of these treatments may be underestimated because of the poor adherence often observed in real-world settings.

AUD-LAMs offer a promising approach to improving treatment adherence and enhancing treatment effectiveness. LAM formulations reduce the need for daily medication administration, addressing a key challenge in maintaining consistent treatment engagement. Optimizing the real-world impact of AUD-LAMs requires addressing key barriers, including provider awareness, patient acceptance and structural challenges in health care systems. While LAMs hold significant potential to improve outcomes in AUD, their successful integration into treatment models depends on ensuring broader accessibility and acceptance among clinicians and patients.

# Factors contributing to underutilization

Several factors contribute to the range and variation in the use of LAMs in behavioral health care. These can be broadly categorized into provider-related factors, patient preferences, and cost and logistical issues.

#### PROVIDER PERCEPTIONS AND PREFERENCES

Health care provider perceptions and preferences play a significant role in the underuse of LAMs. Most significantly, many patients are never offered LAMs as a treatment option. Providers with less experience and current knowledge in use of LAMs offer several justifications for this. Many overestimate adherence to oral medications and therefore do not consider their patients appropriate candidates. Others view LAMs as a treatment of last resort, only considering them when other interventions fail (Wehring et al., 2011). Still others may hesitate to prescribe LAMs out of concerns about tolerability, having concerns that patients feel the shots are too painful or intrusive, or difficulty in managing side effects. Although research indicates LAMs have less risk, these providers assume LAMs are associated with greater side-effect risks that cannot be ameliorated quickly given the dose's duration.

Additionally, some providers perceive injections as less acceptable to patients than other forms of administering medication. They have concerns that patients may find the shots intolerably painful or intrusive. Constraints in the clinical environment that impede provider-patient communication and limit shared decision-making can lead to misunderstandings about treatment goals and priorities. Finally, the cost of LAMs, which can be higher than oral alternatives, may also deter prescribing despite the efficacy of LAMs.

#### PATIENT ATTITUDES AND CONCERNS

Patient-related factors significantly contribute to lack of utilization of LAMs. These include patients' beliefs and attitudes toward medications, concerns about side effects and perceived lack of need (see Figure 3) (Jimmy & Jose, 2011). Patients may also experience stigma associated with mental health conditions or substance use disorders, leading to reluctance to accept LAMs (Mackey, 2020).

Figure 3. Common Reasons Patients Refuse AP-LAMs

| A. T.                    |   | ======================================= | 7   |   |
|--|---|---|---|---|
| Perception of<br>the injection<br>as painful or<br>intrusive | General lack of<br>knowledge about<br>the benefits to<br>them | Sense of coerciveness                   | Mistrust<br>of medical<br>professionals<br>due to illness | Mistrust of medical professionals due to history/recent experiences |

Source: Jimmy & Jose, 2011

Patient preferences play a crucial role in underutilization of AP-LAMs. There is a common misconception among patients that AP-LAMs are more potent than their equivalent oral formulations. This may lead to a belief that they are at risk of more serious side effects and, with it, a reluctance to initiate AP-LAMs. Other factors such as low health literacy, cognitive impairment and comorbid conditions can also impede adherence. Patient preferences for autonomy in medication management, along with past negative experiences with intramuscular injections for acute stabilization, can further influence their willingness to use AP-LAMs. Factors such as a lack of social support and financial constraints can also play a role. Some patients may find the injection process uncomfortable or anxiety-inducing (Lindenmayer et al., 2020). The concept of shared decision-making between patients and clinicians is crucial in getting individuals to agree to and subsequently adhere to any treatment with LAMs.

#### **COST AND LOGISTICS**

Cost and logistical issues present another barrier to LAM usage. Patients may find LAMs more expensive than oral medications. Insurance coverage and reimbursement for procedures and medications can vary and affect patients' ability to access LAMs consistently. The need for regular clinic visits for administration can be challenging. Limited access to health care facilities for regular LAM administration, especially in rural areas, can also hinder use. Inadequate coordination between various health care providers and a lack of integrated care models can result in fragmented treatment approaches, potentially compromising use of LAMs.

Administering LAMs in clinical settings presents several operational challenges. Medication storage is one key concern; LAMs often require refrigeration or temperature-controlled environments with specialized storage units and protocols for medication integrity. There are also space constraints and regulatory guidelines for storing controlled substances. Not all clinics have dedicated spaces

that comply with the "tiled room requirement" for reconstituting or administering certain LAMs. Additionally, certain LAMs require adherence to risk evaluation and mitigation strategies, which means yet more administrative burdens on clinics and providers.

Other clinical challenges include the need for staff training to administer injections — an investment to ensure proper technique, minimize patient discomfort and prevent adverse events. Ordering and stocking medications can be complicated by supply chain issues, formulary restrictions and reimbursement policies that delay or limit availability. Accurate recordkeeping is critical for tracking doses, monitoring adherence and meeting regulatory standards — but inconsistent electronic health record integration and manual documentation processes can create inefficiencies that increase the risk of errors. Finally, policies that dictate whether medications are dispensed directly to the patient or sent to the clinic for administration can create confusion and yet more administrative burdens for providers.

Accurately measuring and addressing the underuse of LAMs is crucial for improving care quality and outcomes for patients with SMI and SUD. This paper explores methods to quantify use and assess underutilization, as well as strategies to increase appropriate use of LAMs.

# CALCULATING UTILIZATION RATES: OVERVIEW OF SPECIFICATIONS

By increasing the use of long-acting medications (LAMs), we can improve outcomes for treatment of opioid use disorder (OUD), alcohol use disorder (AUD) and conditions treated with antipsychotics. But so far, efforts have focused primarily on provider education and technical assistance around benefits and how to increase use. Those efforts have not resulted in substantial improvement.

Benchmarking is substantially more likely to yield results: As the adage says, "What gets measured gets done." Improved performance depends on consistent, standardized measurement of specific outcomes over time. Benchmarking serves as feedback on individual prescriber and organizational performance in relation to specific outcome goals.

LAM initiation and sustained use over time both need to increase. Most studies of LAM utilization report the number of individuals receiving any LAM (single use or more). However, the smaller number that look at sustained LAM usage over time show a surprisingly large decrease in use following the initial dose.

Therefore, for each of the three categories of LAM we address in this report, we propose two measures:

- Initiation whether the patient received any LAM
- Continuation whether the patient received any subsequent administrations following the first dose in the measurement period

We have not proposed a new measure of overall adherence throughout the measurement period, because ongoing adherence measures already have well-defined specifications. Those include measures of medication- or drug class-specific medication possession rate and proportion of days covered, commonly with a cut point of 80%.

### Measures

Measures need to be relevant, feasible and grounded in up-to-date research. To guide the choice of specifications, we agreed to:

- Limit the required data for the measures of pharmacy claims and treatment service, to minimize provider burden and simplify data aggregation.
- Remain consistent with other performance measure methodology, when possible. In particular, the group adopted the coding of National Quality Forum measure 1879 (NQF)

1879), "Adherence to Antipsychotic Medications for Individuals With Schizophrenia," (HEDIS SAA) for determining:

- » Applicable age range (18-64)
- » Types of encounters and treatment settings
- » Advanced-illness and medically frail populations to exclude
- Also, the qualifying diagnosis must occur on one inpatient claim or two claims of any type for the person to be included in the measure.
- Base the measures on the patient receiving either a single administration or two or more administrations of LAM during the measurement period to make the calculation requirements as simple as possible.

The preferred observation period is 12 months from the first LAM administration. In situations where the observation period must be a calendar year for the continued use measures, we propose the NQF 1879/HEDIS SAA method of excluding instances where the first episode of qualifying medication usage occurs in the 90 days of the measurement period.

### Initiation and continuation utilization measures: AP-LAM

See Appendix A for full details.

#### **DENOMINATORS**

As noted before, psychosis is a psychiatric syndrome, just as hypertension is a medical syndrome. Hypertension is caused by numerous different disease states, but the first-line treatment always includes an antihypertensive.

In psychiatric practice, there is less diagnostic consistency across providers in identifying underlying disease states. Chart diagnosis between schizophrenia, schizoaffective disorder and bipolar disorder with psychotic features frequently fluctuates. A patient may receive two or more diagnoses at different times from the same provider or from different providers — often without significant change to treatment regimen.

Still, antipsychotics should be the first-line treatment. Antipsychotics have U.S. Food and Drug Administration (FDA) indicators and are well-established, research-proven, effective treatments for bipolar disorder (including acute manic episodes, depressive episodes and episodes with psychotic features). Second-generation antipsychotics, in large measure, have supplanted traditional mood stabilizers as treatments of choice in current practice in the United States (Rhee et al., 2020).

Given this, we chose to include the diagnoses listed in Table 4, which all represent psychotic disorders, as the denominator for both initial and continued AP-LAM utilization. This is defined as at least two episodes of a diagnosis at least 14 days apart during the measurement period.

Table 4. Included Diagnoses for Initial and Continued AP-LAM

| Diagnosis  | ICD-10-CM           |
|--|---------------------|
| Schizophrenia  | F20.9               |
| Delusional disorder  | F22                 |
| Schizoaffective disorder, bipolar type                       | F25.0               |
| Schizoaffective disorder, depressive type                    | F25.1               |
| Other specified schizophrenia spectrum or psychotic disorder | F28                 |
| Unspecified schizophrenia spectrum or psychotic disorder     | F28                 |
| Bipolar disorders  | F <sub>31</sub> .XX |

#### Other considerations

The qualifying diagnosis must occur on one inpatient claim or two claims of any type for the person to be included in the measure.

A patient-centered approach requires selecting only patients who have shown a willingness to accept treatment with any medication as candidates for LAM. Therefore, we established an inclusion criterion based on medication use: Patients must have filled at least two separate prescriptions for antipsychotic medication during the measurement period, excluding the final 90 days.

We used the same coding and classification of antipsychotic medications as NQF 1879/HEDIS SAA.

#### **Denominator exclusions**

Using criteria from the SAA HEDIS exclusion list, we excluded people with a diagnosis of dementia or psychotic disorders due to another medical condition or frailty and advanced illness, as well as people receiving hospice service, residing in skilled nursing facilities and other places of service.

Additionally, because clozapine monotherapy is the only preferred evidence-based treatment for treatment-resistant psychosis that has FDA approval, people with a PDC greater than 0.8 for clozapine were excluded from the denominator.

#### **INCLUSION CRITERIA FOR NUMERATORS**

The numerator for the initiation of AP-LAM measure includes any person in the denominator population with one or more administrations of any AP-LAM in the measurement period.

The numerator for the continuation of AP-LAM measure includes any person in the denominator population with two or more administrations of any AP-LAM. The administrations must be separated by two weeks, with the second dose administered within duration of action plus 14 days of the first administration in the measurement period.

### Initiation and continuation utilization measures: OUD-LAM

See Appendix B for full details.

#### **DENOMINATORS**

Table 5 summarizes the diagnoses included in the denominator of both initial and continued OUD-LAM utilization measures when there are at least two episodes of diagnosis at least 14 days apart.

Table 5. Included Diagnoses for Initial and Continued OUD-LAM

| Diagnosis   | ICD-10-CM                                |
|---|--|
| All opioid abuse disorders except in remission  | F11.1X except F11.11                     |
| All opioid dependence disorders except in remission   | F11.2X except F11.21                     |
| Diagnosis of opioid abuse or dependence in remission and an OUD-LAM during the measurement period | F11.11, F11.21                           |
| All opioid poisoning disorders except by assault  | All T40.XXX except<br>T40.X3A and T40.XD |

#### Other considerations

The qualifying diagnoses must occur on one inpatient claim or two claims of any type for the person to be included in the measure.

We noted — and are concerned — that many diagnosticians and prescribers are not scrupulously precise in accurately coding the International Classification of Diseases (ICD) diagnoses of opioid abuse (F11.1XX) and dependence (F11.2XX) (also known as opioid use disorders, in DSM nomenclature) versus mere opioid use (F11.9XX). Opioid use codes only apply when the patient is taking opiate medication as prescribed or an opioid use disorder is not present.

We excluded all opioid use (F11.9XX) and opioid abuse or dependence in remission (F11.11 and F11.21) diagnoses unless the opioid abuse or dependence in remission diagnosis occurred with use of an OUD-LAM with a PDC greater than 0.8.

A patient-centered approach requires selecting only individuals who have shown a willingness to accept treatment with any medication as candidates for LAM. Therefore, we established an inclusion criterion based on medication use, requiring that individuals must have filled at least two separate prescriptions for OUD medication during the measurement period, excluding the final 90 days.

For coding and classification of overall OUD medications, three categories are used: (1) buprenorphine: Jo571, Jo574, Jo575, Jo578, Jo577, Q9992, Q9991; (2) naltrexone: J2315; and (3) methadone: S0109, G2067, G2076, G2077, G2078, G2079.

#### **Denominator exclusions**

We excluded people with a diagnosis of dementia or frailty and advanced illness (criteria from SAA exclusion list) and people receiving hospice service, residing in skilled nursing facilities, or other places of service (criteria from SAA exclusion list).

Additionally, any person on methadone with a PDC greater than 0.8 is excluded from the denominator.

#### **INCLUSION CRITERIA FOR NUMERATORS**

The numerator for the initiation of OUD-LAM measure includes any person in the denominator population with one or more administrations of any OUD-LAM in the measurement period.

The numerator for the continuation on OUD-LAM measure includes any person in the denominator with two or more consecutive administrations of any buprenorphine-XR or two or more consecutive administrations of naltrexone-XR, with the second dose administered within the duration of action plus 14 days of first administration.

# Initiation and continuation utilization measures: AUD-LAM

See Appendix C for full details.

#### **DENOMINATORS**

Table 6 summarizes the diagnoses included in the AUD-LAM initiation and continuation measures are summarized. To be included, individuals must have at least two episodes of diagnosis at least 14 days apart.

Table 6: Included Diagnoses for Initial and Continued AUD-LAM

| Diagnosis                                | ICD-10-CM            |
|--|----------------------|
| Any alcohol use disorder (no exclusions) | F10.XX               |
| Toxic effect of ethanol (no exclusions)  | T <sub>5</sub> 1.0XX |
| Toxic effect of alcohol, unspecified     | T <sub>51.9</sub>    |
| Alcohol use disorders in remission       | F10.11 and F10.21    |

#### Other considerations

The qualifying diagnoses must occur on one inpatient claim or two claims of any type for the person to be included in the measure.

The measure excludes Child-Pugh Class C cirrhosis (K74.72). We noted that naltrexone-induced hepatotoxicity is a historical concern, but the FDA removed a black-box warning in 2013. Recent studies concluded that naltrexone in patients with cirrhosis was not associated with development of drug-induced liver injury using Roussel Uclaf Causality Assessment Method scoring, and naltrexone appears to be safe in patients with compensated and decompensated cirrhosis (Thompson et al., 2024). Therefore, we only exclude individuals with diagnosis of Child-Pugh Class C cirrhosis (Arab et al., 2022).

For coding and classification of overall AUD medications, three categories are used: (1) naltrexone (Vivitrol, J2315), (2) acamprosate and (3) disulfiram.

#### **Denominator exclusions**

We excluded people with diagnosis of dementia or frailty and advanced illness (criteria from SAA exclusion list) and people receiving hospice service or residing in skilled nursing facilities and other places of service (criteria from SAA exclusion list).

#### **INCLUSION CRITERIA FOR NUMERATORS**

The numerator for the initiation of AUD-LAM measure includes any person in the denominator population with one or more administrations of any AUD-LAM in the measurement period.

The numerator for the continuation on AUD-LAM measure includes any person in the denominator with two or more consecutive administrations of naltrexone-XR, with the second administration within the duration of action plus three days of first administration.

# BENCHMARKS FOR PERFORMANCE MEASURES: RECOMMENDATIONS FOR NEW STANDARDS OF PRACTICE

The utilization measures we proposed in the previous section provide guidelines for health care organizations and delivery systems to determine their own long-acting medication (LAM) utilization rates. The next step is to consider what effective utilization rates should be — that is, to establish benchmarks. The goal is to encourage incremental, but consistent, improvement driven by national standards and aligned with implementation science principles, provider incentives and payer strategies.

Benchmarking in behavioral health is a powerful approach to quality improvement, resource optimization and enhanced patient outcomes. The evidence strongly supports its effectiveness across various settings, populations and treatment modalities. From improved clinical outcomes to enhanced decision-making and resource allocation, benchmarking provides multiple benefits that directly impact patient care.

Effective performance benchmarks have several key characteristics. First, they apply to average patient populations rather than to individualized clinical outcomes. This ensures they can be generalized and put into action across various practice settings. Second, good measures are characterized by a low organizational burden — they must be straightforward to collect, aggregate and analyze. Ease of calculation reduces resistance among providers and organizations, facilitating consistent reporting and sustained adoption. Additionally, the measures should clearly align with evidence-based practice and clinical consensus, making their value apparent and encouraging providers and payers to integrate them into routine care delivery processes. This approach supports broad implementation and ensures meaningful progress without overwhelming organizational resources or introducing unnecessary complexity.

Benchmarks should reflect a value-based care approach, focusing on incremental, population-level improvement. The distinction between therapeutic benchmarks (targeting specific clinical outcomes) and process benchmarks (focusing on usage and implementation processes) is critical. The best initiatives use process benchmarks to motivate provider adherence to established best practices without holding providers accountable for uncontrollable patient outcomes.

Three aspects of LAM utilization may merit benchmarking and performance management:

Most of the published research on LAM utilization is on initiation of LAM use. A benchmark could address the problem of a large portion of patients never being offered an LAM as a treatment option.

- Benchmarking continuation on an initiated LAM could be useful because of the high percentage of patients who are initiated on an LAM but who never receive a subsequent dose.
- It could be useful to benchmark the ultimate goal: overall adherence to treatment with an LAM. However, new measures are not needed. Current methodologies to measure ongoing overall adherence using proportion of days covered or medication possession rate methodologies are well-defined and available to address this need.

Generally, we propose two performance benchmarks each for antipsychotic (AP) LAMs, LAMs for opioid use disorder (OUD), and LAMs for alcohol use disorder (AUD): (1) an **initiation measure** of whether the patient received any use of the LAM and (2) a **continuation measure** of whether the patient received two or more continuous administrations of the LAM.

### **AP-LAM Benchmarks**

#### **INITIATION OF AP-LAM**

Most of the published peer-reviewed literature on AP-LAM utilization rates focuses on initiation rates for people with schizophrenia. The literature describes the rate of people with schizophrenia who received one or more administration of an LAM during the study period.

Research indicates significant variability in LAM usage across states, ranging from less than 5% to approximately 25%. Studies of U.S. populations indicate that for people with schizophrenia in various treatment settings who receive one or more doses of an AP-LAM, the utilization rates are 23%-33%. Meta-analyses and many other studies report rates of 25%-33%. International studies that report more broadly on individuals with psychotic disorders or a portion of any individuals receiving antipsychotic medication indicate the rate of those who received an AP-LAM to be 25%-29% (Bareis et al., 2022). In a study of 234 individuals who used antipsychotic medication for five years or less and were offered LAM, over 90% accepted administration of an initial dose (Kane et al. 2020).

Given these statistics, we recommend a national benchmark of 30% initial utilization (one or more administrations) as a starting goal, with incremental annual increases toward a goal of approximately 50% by 2030 and an ultimate goal of 70%. While a benchmark of 30% represents a substantial increase over the current U.S. average (approximately 15%), there are multiple reports of other countries achieving this level of performance.

#### **CONTINUATION OF AP-LAM**

A 15-year study from an Italian psychiatric hospital reported that people diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder who started on LAM had 88%-100% continuation of usage at three months and 60%-88% continuation at 12 months, with the range reported across six different AP-LAMs (Auxilia et al., 2023). However, a seven-year Taiwanese study of patients with bipolar disorder reported only 20% of patients taking risperidone-LAM continued the therapy for more than 90 days (Wu et al., 2016). The STAR Network Depot Study found that 75%-88% of patients diagnosed with schizophrenia or bipolar disorder, and some with other disorders, who were on LAMs remained on them after three months, and 40%-70% remained on them after 12 months (Bertolini et al., 2021). These results were observed across five different AP-LAMs. A large claims analysis of 40 million Medicaid recipients with bipolar disorder or schizophrenia found that approximately 40% did not stay on LAM longer than three months, and only about 40% persisted beyond 12 months (Greene et al., 2018).

We recommend a benchmark of 85% of patients who receive an initial dose continue to two or more administrations of AP-LAM within a one month measurement period. This would be 25.5% of the eligible measured cohort (i.e., the 30% initial utilization target).

Since this is a newly developed measure, the benchmark should be revisited after it has been piloted in several populations.

#### **Pilot Results**

Members of the expert panel with access to and expertise with pharmacy claims databases were able to provide pilot results using proposed methodology and benchmarks.

#### MO HealthNet (Missouri Medicaid) with 1.2 million participants found for 2024

|  | Count  | Percent | Benchmark |
|--|--------|---------|-----------|
| Denominator (Members With Specified Diagnoses) | 43,033 | NA      |           |
| Numerator 1 (Initiation AP-LAM Measure)        | 7,200  | 16.7%   | 30%       |
| Numerator 2 (Continuation AP-LAM Usage)        | 6,428  | 14.9%   |           |
| % of AP-LAM Users Continuation Measure         | NA     | 89.3%   | 85%       |

#### MarketScan Commercial Claims data set yielded:

|  | Count  | Percent | Benchmark |
|--|--------|---------|-----------|
| Denominator (Members With Specified Diagnoses) | 64,565 | NA      |           |
| Numerator 1 (Initiation AP-LAM Usage)          | 2,779  | 4.3%    | 30%       |
| Numerator 2 (Continued AP-LAM Usage)           | 2,424  | 3.8%    |           |
| % of AP-LAM Users Continuation Measure         | NA     | 87.2%   | 85%       |

#### **OUD-LAM Benchmarks**

The percentage of people with OUD receiving buprenorphine treatment has increased substantially, from 2.7% in 2011 to 16.2% in 2020 (Heidbreder et al., 2023). However, buprenorphine-XR has only been available since 2018, and use of OUD-LAMs (buprenorphine and naltrexone) remains very low. Evidence for the efficacy of these medications is emerging. Wider adoption of and data collection related to medications for OUD are necessary next steps.

#### INITIATION OF OUD-LAM

We were unable to find any published research on the portion of people with OUD receiving one or more doses of OUD-LAMs. Given the substantial mortality data associated with untreated OUD, it is essential that providers offer these treatments. Our recommendation is to encourage systemwide adoption by establishing benchmarks for incremental increases in their use. We consider **an initiation benchmark of 10%** reasonable, given the extremely low current utilization rates.

#### **CONTINUATION OF OUD-LAM**

In one small study, 30% of people who started buprenorphine-XR had discontinued it at six months (Peckham et al., 2021). In a separate study, 47 of the 100 participants who received treatment with buprenorphine-XR were retained in treatment at 96 weeks; the median retention time was 90 weeks (Farrell et al., 2024). A retrospective cohort study of adults with OUD who were prescribed buprenorphine-XR in a low-barrier addiction medicine specialty clinic found that six-month treatment retention was greater in the treatment group than the comparison group (70.3% vs. 36.5%, p < 0.001) (Heil et al., 2024). An integrated analysis of three Phase 3 buprenorphine-XR

studies reported that 95%-100% of those receiving a first administration also received a second (Rutrick et al., 2023).

For continuation to a second administration, we chose a benchmark of 80% of those getting an initial administration — or 8% of the total cohort — given the extremely low current utilization rates and good retention following initial dose.

#### **AUD-LAM Benchmarks**

For AUD, the current utilization of naltrexone-XR remains very low. Given that, along with the evidence that medication-assisted treatment overall is severely underutilized, wider adoption of and data collection related to medications for AUD are necessary. We propose the following benchmarks based on the limited available evidence.

#### **INITIATION OF AUD-LAM**

Although naltrexone-XR has been available since 2006, we were able to locate only one publication that cited research on rates of administration of one or more doses among people with AUD or in a portion of people receiving oral medications for treatment of AUD. A claims analysis of 5,141 people receiving AUD medication reported that only 4.1% received it as an LAM (Bryson et al., 2011).

Given the substantial mortality data associated with untreated AUD, it is essential that providers offer AUD-LAM treatments. Our recommendation includes establishing benchmarks for incremental increases in their use to encourage system-wide adoption. We consider **an initial target benchmark of 10% for AUD-LAM** reasonable, given the extremely low current usage rates.

#### **CONTINUATION OF AUD-LAM**

There are few studies reporting continuation of naltrexone-XR. One small retrospective claims study showed that the average duration of therapy was three months. Among the 40% of patients who received three or more months of treatment with naltrexone-XR, 58% had gaps in treatment (Jan et al., 2011). In another study, approximately 40% of patients on naltrexone-XR filled a second prescription, as opposed to 30% of oral naltrexone patients, 25% of acamprosate patients and 20% of disulfiram patients. The naltrexone-XR group also had the highest level of continuation (15%) after the full six months of follow-up (Bryson et al., 2011). In a small chart review study of 15 people with severe AUD, participants received a mean of 4.5 injections (range 2-7) (Smith-Bernardin et al., 2018).

We consider an initial target benchmark of 6% of the total cohort for continuation to two or more administrations of AUD-LAM reasonable, given the extremely low current usage rates.

# IMPLEMENTING NEW STANDARDS OF PRACTICE

Ideally, as benchmarks are put in place, individual provider expertise, expectations and experiences will expand, and organizational systems will adapt to support practitioners.

In practice, a multitude of factors may arise and influence benchmarking of long-acting medication (LAM) usage. These include opportunities and challenges that are likely to emerge at the microand macro-levels of service delivery systems.

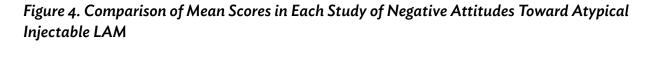
Utilization benchmarks can expand provider expertise by reinforcing the clinical evidence for the advantages of LAMs over other antipsychotics. Through repeated exposure to this evidence, providers can refine their expectations and experiences with LAMs, ultimately leading to improved patient care.

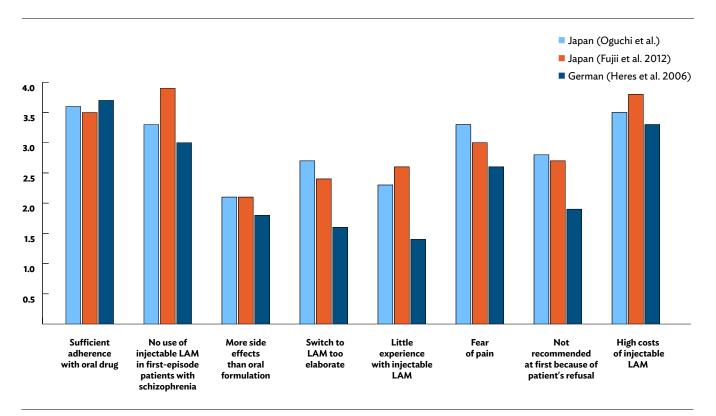
All clinicians have a professional responsibility to ensure that their practice is within the usual community standard of care. Benchmarking clearly defines the range of community practice and allows prescribing clinicians to see and consider where their individual practice falls within the standard protocol observed in similar clinical settings. Clinicians also have a professional responsibility to be self-regulating and to hold each other accountable for practicing within the usual community standard of care. Benchmarking provides the professional community a powerful tool for the collaborative discussions through which we hold ourselves accountable to practicing within the usual community standard of care.

# **Provider-level factors**

Although medical training covers the safety, efficacy and mortality benefits of LAMs, provider knowledge and awareness of the evidence base remains inconsistent (Velligan et al., 2021). Providers' decisions to offer and initiate LAMs are often influenced by their attitudes (see Figure 4), including concerns about patient receptivity and feasibility.

As initiatives promoting LAM adoption become more widespread, these impediments can be reduced. Observing positive patient outcomes firsthand can help providers challenge the misconceptions that once hindered LAM utilization. Benchmarks improve provider knowledge as they help reshape attitudes, fostering greater adoption of evidence-based practices.





Source: Oguchi et al., 2024

Additionally, benchmarks can serve as an implicit incentive for providers by emphasizing the broader impact of care. Participation in benchmarking fosters a shared sense of mission, extending beyond individual performance to collective patient outcomes. Since medical professionals are often motivated by peer comparisons, benchmarks create an opportunity for providers to align their practices with established best practices and performance expectations (Niles & Olin, 2021; Reese et al., 2014).

Despite the benefits of benchmarks, resistance may arise because of concerns about diminished clinical autonomy and disruptions to established practice norms. Providers may struggle to incorporate shared decision-making and care coordination within the constraints of limited time and ancillary support. Some may attempt to mitigate perceived or actual penalties associated with failing to meet benchmarks through passive or overt resistance. Additionally, there may be concerns about the feasibility of ensuring LAM adherence despite incentives to increase prescribing rates.

### ALIGNMENT WITH EXISTING PRACTICE GUIDELINES

To successfully increase LAM usage, providers must be supported in aligning their prescribing practices with existing clinical guidelines. National and international organizations, such as the American Psychiatric Association and the U.K.'s National Institute for Health and Care Excellence, provide clear recommendations regarding the use of LAMs for people with schizophrenia and other severe mental illnesses. However, providers might not consistently reference or integrate these guidelines into daily practice because of competing demands and variations in clinical training.

One key support would be to integrate LAM recommendations into electronic health record decision-support tools. When embedded within prescribing workflows, these tools could prompt clinicians to consider LAMs for eligible patients, reinforcing guideline-based care. Additionally, continuing medical education opportunities should emphasize LAM benefits to address persistent gaps in provider awareness and counter biases favoring oral medications. Organizations such as professional societies, hospitals, clinics, medical schools and payers can further promote alignment by establishing standardized treatment algorithms that reflect best practices and streamline decision-making in a variety of clinical settings.

### **MULTIDISCIPLINARY COLLABORATION**

A multidisciplinary approach is essential to increase provider confidence in prescribing LAMs and ensure successful patient engagement. While psychiatrists and primary care physicians often make prescribing decisions, behavioral health professionals in a variety of roles contribute to LAM uptake and adherence.

Providers must be both reassuring and confident when discussing LAMs with patients and families, particularly with those who are unfamiliar with the treatment. Many individuals and their caregivers harbor misconceptions about LAMs, including concerns about injections being painful, inconvenient or stigmatizing. A provider's ability to clearly communicate the benefits — such as improved symptom stability, medication safety, reduced relapse risk and fewer daily medications to take— can significantly influence patient acceptance. Training in motivational interviewing and shared decision-making techniques can equip providers with strategies to address concerns, build trust and empower patients in their treatment choices.

Pharmacists, particularly those who specialize in behavioral health, play a crucial role in educating patients and providers. They can clarify differences between LAM formulations, provide guidance on potential side effects and address logistical concerns related to medication access. Pharmacist-led educational sessions within clinical teams can enhance providers' knowledge and comfort with prescribing LAMs, fostering a more collaborative approach to medication management.

Nurses and peer support specialists also serve as key advocates for LAM use. Nurses, who often administer the injections, are well-positioned to reinforce treatment adherence through patient

education and ongoing engagement. Counselors provide individual and group-level education and activities that promote adherence. Peer support specialists, who have lived experience with mental health and substance use challenges, can offer a unique perspective that helps patients feel understood and supported in their decision to try an LAM. By sharing their personal journeys and highlighting the benefits of treatment continuity, peer support specialists can address fears and misconceptions in a way that resonates deeply with patients.

Table 7. Key Obstacles and Facilitators Related to LAM Utilization (Carroll, 2024)

| Implementation<br>Factors   | Obstacles   | Facilitators   |
|-----------------------------|---|--|
| Patient                     | <ul> <li>Fear of injections and side effects</li> <li>Stigma or negative perceptions about injectables</li> <li>Lack of awareness or education about LAMs</li> </ul>  | <ul> <li>Patient education and shared decision-making</li> <li>Positive peer testimonials and support groups</li> <li>Simplified consent and informational materials</li> </ul>                            |
| Provider                    | <ul> <li>Limited knowledge or training on<br/>LAMs, including reconstitution and<br/>administration techniques</li> <li>Time constraints and competing<br/>priorities</li> <li>Reluctance to change established<br/>prescribing patterns</li> </ul> | <ul> <li>Provider training and education programs</li> <li>Integration of LAMs into clinical guidelines and protocols</li> <li>Peer support and clinical champions</li> </ul>                              |
| Organizational              | <ul> <li>Limited formulary availability</li> <li>Inadequate staffing or infrastructure for administration and follow-up</li> <li>Poor integration within clinical workflows</li> </ul>  | <ul> <li>Improved access to medication formularies</li> <li>Workflow optimization and administrative support</li> <li>Organizational culture supporting innovation and evidence-based practices</li> </ul> |
| System/Policy               | <ul> <li>Cost and reimbursement</li> <li>Restrictive policy or insurance prior authorizations</li> <li>Fragmented care delivery systems</li> </ul>  | <ul> <li>Policy advocacy for better coverage and reimbursement</li> <li>Streamlined authorization processes</li> <li>Coordinated, integrated care delivery systems</li> </ul>                              |
| Community/Social<br>Context | <ul> <li>Community stigma regarding mental<br/>illness and medication use</li> <li>Social isolation of people who require<br/>care</li> </ul>   | <ul> <li>Community education and stigmareduction campaigns</li> <li>Community-based supports and outreach efforts</li> </ul>   |

# **System-level factors**

The previously mentioned provider-level factors reflect the need to explore and address system-level realities that may impact the effectiveness of benchmarks to improve LAM usage. While providers are the pathway through which patients receive LAMs, multiple steps must occur before and after the decision to use LAMs for successful, sustained administration.

A 2021 initiative underscored the complexity of increasing LAM utilization. The Multilevel Facilitation of Long-acting Antipsychotic Medication Program (MAP) aimed to address underutilization through structured assessments, motivational interventions and provider education. The initiative offered brief, targeted training to equip providers with practical considerations and communication strategies for better engagement with patients and families. Given that providers' assumptions about patient willingness to use LAMs remain a key obstacle to use, successful benchmarking efforts should focus on improving provider confidence to facilitate informed consent. MAP also used organizational champions and peer specialists to support implementation, ultimately leading to increased LAM prescribing. However, the study identified significant resource needs, emphasizing the necessity of adequate support structures to meet benchmark expectations (Velligan et al., 2021).

While the MAP study identified some key components of a successful strategy to increase LAM usage, it is important to add that each clinical setting presents unique opportunities and challenges. For example, independent outpatient clinics operate within different constraints than hospitals, influencing providers' ability to pursue benchmarked goals. Recognizing these distinctions allows for the development of realistic, setting-specific expectations that account for variations in practice settings and tailor strategies for care coordination and provider and patient support accordingly.

Regardless of setting, once shared decision-making results in a prescription, reliable access to LAMs via a streamlined process remains a central concern. Availability varies based on payer sources and health care center relationships with pharmaceutical companies. While some facilities maintain ample supplies of branded and generic LAMs, others face significant access limitations beyond the allowances of individual health plans. Practical considerations — such as determining who administers the medication and where — add layers of complexity. Engaging key stakeholders, including pharmacists, nurses, peer support specialists and therapists, is essential to streamlining processes and improving overall LAM accessibility. Their experience and expertise should be incorporated into strategic planning and clinical practice augmentation efforts before launching initiatives.

Beyond individual providers and health care facilities, system-wide factors also influence the success and sustainability of proposed practice standards. Large health care organizations and payer systems have the capacity to track usage and outcomes; however, fidelity to utilization

enhancement strategies varies across institutions. Ensuring continuity of care as patients transition between different treatment settings presents a challenge in accurately measuring long-term outcomes.

Guideline adoption is most effective when paired with outcome tracking. Health care systems should implement quality improvement initiatives that measure LAM prescribing rates, patient adherence and clinical outcomes. Regular feedback reports can help providers compare their practices to those of their peers and identify opportunities for improvement. This process fosters accountability as it reassures providers that LAM use is evidence-based and aligned with the highest standards of care.

While increased LAM utilization is expected to generate cost savings through reduced hospitalizations and improved patient stability, achieving these benefits requires upfront investments in the scaffolding needed to reach benchmarks. Resource acquisition and allocation present a challenge that requires strategic alignment among key stakeholders. Prioritizing investments in care coordination and provider support is essential to ensure that benchmarks translate into meaningful improvements in patient outcomes.

Ultimately, a successful benchmarking strategy must balance provider engagement, system-wide coordination and sustainable implementation. By addressing individual and institutional challenges, the health care system can move toward broader adoption of LAMs, leading to improved patient care and long-term cost-effectiveness.

### **BOX 3: PARTNERSHIPS WITH PHARMACIES**

Strong partnerships between health care providers and pharmacies can significantly improve LAM access and administration. Many specialty behavioral health pharmacies — and an increasing number of traditional retail pharmacies — have expertise in handling LAM prescriptions, ensuring medication availability and addressing prior authorization requirements.

One of the primary obstacles to LAM utilization is the complexity of medication procurement and insurance coverage. Pharmacies can streamline this process by assisting with benefits verification, navigating payer restrictions and expediting medication approvals. By reducing administrative burdens on providers, these partnerships help ensure that once a patient agrees to an LAM, the prescription process is smooth and timely.

Additionally, pharmacies can provide direct support in coordinating medication administration. In most states, pharmacists themselves can administer injections, offering a convenient option for patients who lack access to clinic-based administration. The pharmacist administering the injection also has a care opportunity: They can assess the patient and send the provider information regarding medication tolerance, psychiatric status, significant adverse effects and the need for evaluation by the provider prior to a scheduled appointment. For clinics with limited infrastructure for on-site LAM administration, collaborating with pharmacies that provide mobile or travel-based injection services can further enhance patient adherence. Some specialty behavioral health pharmacies even provide mobile LAM injections to unhoused patients with serious mental illness, for whom LAMs may be the only pathway out of chronic homelessness.

Integrating specialty pharmacy resources into clinical workflows also fosters improved communication between providers and pharmacists. Regular case reviews, consultation services and shared access to medication adherence data enable clinicians to make informed decisions and intervene promptly if challenges arise. Through these collaborative efforts, health care teams can maximize LAM utilization and ensure patients receive the full benefits of long-acting treatment options.

# CONCLUSION

Developing and adopting standardized measures and benchmarks for the utilization of long-acting medications (LAMs) represents a pivotal step forward in addressing the significant gap between evidence-based practices and real-world implementation. This paper proposes two critical measures each for the use of antipsychotic (AP)-LAMs, opioid use disorder (OUD)-LAMs and alcohol use disorder (AUD)-LAMs: initiation (whether a patient has started treatment with an LAM) and continuation (measuring sustained use beyond initial administration). Each measure serves a distinct yet complementary purpose, providing essential insights into treatment adoption and continuity.

The rationale for a dual-threshold approach is clear. Initiation is a foundational step toward transforming the treatment landscape, especially given the current low rates of LAM utilization across the behavioral health care system. The initiation measure establishes a baseline from which progress can be evaluated. Continuation, the second threshold, is equally critical, as sustained medication adherence is essential for achieving long-term therapeutic outcomes. This measure directly informs health care systems, organizations and providers about continuity in care, highlighting potential gaps in transitional processes. For instance, a health care organization observing high initiation but low continuation rates would identify problems related specifically to ongoing patient management, rather than initial medication acceptance.

Differentiating between initiation and continuation measures allows health care systems to isolate distinct barriers affecting each phase. Barriers to initiation often stem from provider attitudes, misconceptions and broad-based issues such as logistical challenges or inadequate provider training. In contrast, continuation barriers typically involve patient-specific factors, including perceptions of medication effectiveness, side effects, personal preferences and socioeconomic constraints. By delineating these two states, targeted interventions can be developed more precisely, addressing challenges specific to each.

The proposed benchmarks are demonstrably achievable. Evidence from other countries and select U.S. regions shows significantly higher LAM utilization rates than the current average U.S. rate (15%), confirming the feasibility of the proposed benchmarks. These regions have successfully implemented systemic changes that address the critical system-, provider- and patient-related barriers identified in this paper, validating the measures' applicability and practicality.

Higher utilization rates of LAMs confer broad and substantial benefits across multiple dimensions. Patients experience significantly improved health outcomes, reduced relapse rates and enhanced overall stability. Providers benefit from greater clarity and structured guidance, which simplify complex treatment decisions and promote confidence in evidence-based practices. Health care systems realize reductions in emergency and acute care utilization, enhancing efficiency and cost-

effectiveness. Society benefits from reduced health care expenditures and improved public health outcomes, especially within vulnerable populations.

Ultimately, the implementation of these standardized measures and benchmarks represents not just an incremental improvement, but a transformative shift toward a more effective, patient-centered approach to mental health and substance use disorder treatment. By addressing the distinct yet interconnected phases of medication initiation and continuation, health care systems can meaningfully improve clinical outcomes, organizational efficiency and patient satisfaction. The evidence clearly supports the feasibility and necessity of this approach. The benefits to patients, providers, health care systems and society at large make the commitment to achieving these benchmarks both compelling and essential.

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### **APPENDIX A: AP-LAM MEASURES**

# **AP-LAM** utilization data specifications

**Description:** The percentage of individuals living with serious mental illness (schizophrenia, schizoaffective disorders or bipolar disorders) who are using an antipsychotic long-acting injectable medication (AP-LAM) for treatment. Two rates are reported:

- **1.** AP-LAM initiation: percentage of individuals who received any AP-LAM during the measurement period.
- 2. AP-LAM continuation: percentage of individuals who received an AP-LAM at least twice during the measurement period.

### SUMMARY INFORMATION

**Intended use:** Health plan or provider group performance measurement

Data sources needed: Pharmacy and medical claims

**Denominator:** Individuals age 18 or older who had both of the following during the measurement period:

- At least two encounters that resulted in a diagnosis of a serious mental illness
- At least two prescriptions, filled at least 14 days apart, for an antipsychotic medication

**Exclusions:** Individuals who at any time during the measurement period had one of the following:

- Dementia or dementia-related disorders
- Frailty and advanced illness
- Hospice services
- Skilled nursing facility (SNF) or long-term care (LTC) residence
- Death

**Numerator:** Individuals who have received a long-acting injectable antipsychotic OR at least two AP-LAM injections at least 14 days apart during the measurement period

### **DETAILED SPECIFICATIONS**

### Eligible population (denominator)

Age: Individuals age 18 years or older at the beginning of the performance period

**Event or diagnosis** — at least one of the following:

- At least one encounter\* with a diagnosis of schizophrenia, delusional disorder, schizoaffective disorders, other psychotic disorder not due to a substance or known physiological condition, or bipolar disorders with psychotic features (see Schizophrenia Value Set) in an acute inpatient setting during the performance period
- At least two encounters\* with a diagnosis of schizophrenia, delusional disorder, schizoaffective disorders, other psychotic disorder not due to a substance or known physiological condition, or bipolar disorders with psychotic features (see Schizophrenia Value Set), with different dates of service in an outpatient setting, emergency department setting or nonacute inpatient setting during the performance period

### Table A1: Schizophrenia Value Set

| Diagnosis  | ICD-10-CM |
|--|-----------|
| Paranoid schizophrenia                                       | F20.0     |
| Disorganized schizophrenia                                   | F20.1     |
| Catatonic schizophrenia                                      | F20.2     |
| Undifferentiated schizophrenia                               | F20.3     |
| Residual schizophrenia                                       | F20.5     |
| Other schizophrenia  | F20.89    |
| Schizophrenia unspecified                                    | F20.9     |
| Delusional disorders   | F22       |
| Schizoaffective disorder, bipolar type                       | F25.0     |
| Schizoaffective disorder, depressive type                    | F25.1     |
| Other schizoaffective disorders                              | F25.8     |
| Schizoaffective disorder, unspecified                        | F25.9     |
| Other specified schizophrenia spectrum or psychotic disorder | F28       |
| Bipolar disorders  | F31       |

<sup>\*</sup>See detailed definition of encounter and place of service criteria.

**Medication usage** — Filled at least two prescriptions at least 14 days apart during the performance period for any combination of the qualifying oral antipsychotic medications listed under "Oral antipsychotic medications" or the AP-LAMs listed under "Long-acting injectable antipsychotic medications"

**Oral antipsychotic medications:** The following are the oral antipsychotic medications for the denominator, listed by class. The route of administration includes all oral formulations of these medications.

### Typical antipsychotic medications:

| Chlorpromazine | Molindone    | Thiothixene |  |
|----------------|--------------|-------------|--|
| E              | <b>D</b> 1 . | T . (1      |  |

| ■ FI | uphenazine | Perpl | nenazine | Irifluoperazine |
|------|------------|-------|----------|-----------------|
|      |            |       |          |                 |

| Haloperidol | Prochlorperazine |
|-------------|------------------|
|-------------|------------------|

Loxapine Thioridazine

### **Atypical antipsychotic medications:**

| Aripiprazole | Iloperidone | Quetiapine |
|--------------|-------------|------------|
|--------------|-------------|------------|

| Asenapine   | Lumateperone | Risperidone |
|-------------|--------------|-------------|
| , isenapine | Lamateperone | Maperiadric |

| Brexpiprazole | Lurasidone | Ziprasidone |
|---------------|------------|-------------|

- Cariprazine Olanzapine
- ClozapinePaliperidone

### **Antipsychotic combinations:**

- Perphenazine/amitriptyline
- Xanomeline/trospium

**AP-LAMs:** The following are the AP-LAMs for the denominator, by class. The route of administration includes all injectable and intramuscular formulations of the medications listed in Table A2. Since the days' supply variable is not reliable for long-acting injections in administrative data, it is estimated as the typical duration between administrations (listed below) for the AP-LAMs billed under Medicare Part D and Medicare Part B.

Table A2: AP-LAM by class for the denominator

| Drug Name  | Duration<br>(typical) | HCPCS<br>J-code |
|--|-----------------------|-----------------|
| Injection, aripiprazole lauroxil (Aristada Initio)                     | 28 days               | J1943           |
| Injection, aripiprazole lauroxil (Aristada)                            | 28 days               | J1944           |
| Injection, aripiprazole, extended release (Abilify Maintena)           | 28 days               | J0401           |
| Injection, aripiprazole, extended release (Abilify Asimtufii)          | 56 days               | J0402           |
| Injection, fluphenazine decanoate, up to 25 mg                         | 28 days               | J2680           |
| Injection, haloperidol decanoate, 50 mg                                | 28 days               | J1631           |
| Injection, olanzapine, long-acting (Zyprexa Relprevv)                  | 14 days               | J2358           |
| Injection, paliperidone palmitate extended release (Invega Sustenna)   | 35 days               | J2426           |
| Injection, paliperidone palmitate extended release (Invega<br>Trinza)  | 104 days              | J2427           |
| Injection, paliperidone palmitate extended release (Invega<br>Hafyera) | 201 days              | J2427           |
| Injection, risperidone (Risperdal Consta)                              | 14 days               | J2794           |
| Injection, risperidone (Rykindo)                                       | 14 days               | J2801           |
| Injection, risperidone (Perseris)                                      | 30 days               | J2798           |
| Injection, risperidone (Uzedy)   | 28 days               | J2799           |

### **Exclusions**

Exclude members who met any of the following during the measurement year:

- **Dementia diagnosis** Do not include laboratory claims (claims with POS Code 81).
- Hospice services Members who use hospice services or elect to use a hospice benefit any time during the measurement year. Organizations that use the Monthly Membership Detail Data File to identify these members must use only the run date of the file to determine if the member elected to use a hospice benefit during the measurement year.
- **Death** Members who die any time during the measurement year.
- Reside in skilled nursing facility (SNF) or long-term care (LTC) Medicare members age 66 and older as of Dec. 31 of the measurement year who meet either of the following:
  - » Enrolled in an Institutional SNF (I-SNF) any time during the measurement year.

- » Living long-term in an institution any time during the measurement year as identified by the LTI flag in the Monthly Membership Detail Data File. Use the run date of the file to determine if a member had an LTI flag during the measurement year.
- **Frailty and advanced illness** Members must meet both frailty and advanced illness criteria to be excluded:
  - » Frailty: At least two indications of frailty with different dates of service during the measurement year. Do not include laboratory claims (claims with POS Code 81).
  - » Advanced illness: Either of the following during the measurement year or the year prior to the measurement year:
    - Advanced illness on at least two different dates of service. Do not include laboratory claims (claims with POS Code 81).
    - Dispensed dementia medication (Dementia Medications List).
  - Members age 81 and older as of Dec. 31 of the measurement year (all product lines) with at least two indications of frailty, with different dates of service during the measurement year. Do not include laboratory claims (claims with POS Code 81).
- **Clozapine** members with any clozapine fill history during the measurement period.
- See <u>exclusion value sets</u>.

### **Numerator**

- **Measurement period** Rolling 12-month look-back preferred
  - » If not feasible, use observation period NQF 1879/HEDIS SAA, with 90-day exclusion. This defines the measurement period as Jan. 1 through Dec. 31. It requires no more than one gap in enrollment of up to 45 days during the measurement year.
- **Initiation numerator** At least one AP-LAM administration during the measurement period
- AP-LAM sustained usage measure Two consecutive AP-LAM administrations of any AP-LAM or combination of different AP-LAMs, with second administration at least 10 days after
- HEDIS definition for psychotic disorder diagnoses
- HEDIS value sets

# APPENDIX B: OUD-LAM MEASURES

# **OUD-LAM** utilization data specifications

**Description:** The percentage of individuals living with opioid use disorder (OUD) who are using a long-acting injectable medication (OUD-LAM) for treatment. Two rates are reported:

- OUD-LAM initiation: percentage of individuals who received any long-acting injectable medication for OUD treatment during the measurement period
- 2. OUD-LAM continuation: percentage of individuals who received at least two long-acting injectables for OUD treatment during the measurement period

### SUMMARY INFORMATION

**Intended use:** Health plan or provider group performance measurement

Data sources needed: Pharmacy and medical claims

**Denominator:** Individuals age 18-64 who had any of the following during the measurement period:

- A diagnosis of OUD
- An acute inpatient or residential treatment stay with principal diagnosis of OUD
- A withdrawal management visit with principal diagnosis of OUD
- Any emergency department visit with principal diagnosis of OUD or opioid poisoning
- Two or more oral buprenorphine/naloxone or buprenorphine pharmacotherapy events

**Exclusions:** Individuals who at any time during the measurement period had one of the following:

- Dementia
- Hospice services
- Frailty and advanced illness
- Skilled nursing facility (SNF) or long-term care (LTC) residence
- Death
- Adherence to OUD oral therapy

**Numerator:** Individuals who have received either an OUD-LAM treatment OR at least two OUD-LAM injections during the measurement period

### **DETAILED SPECIFICATIONS**

### **Eligible population (denominator)**

- Age Individuals age 18-64 at the beginning of the performance period
- Event or diagnosis
  - » Diagnosis of OUD or related overdose diagnosis on any event during the measurement period
  - » Acute inpatient or residential treatment stay or withdrawal management visit with principal diagnosis of OUD
    - See inpatient or residential value set codes
  - » Any emergency department visit with principal diagnosis of OUD
  - » Filled at least two oral OUD prescriptions, with a negative medication history of at least 31 days prior to first fill date (see <u>Med list</u>)

### **Exclusions**

Exclude members who met any of the following during the measurement year:

- Diagnosis for dementia
- **Frailty and advanced illness** Members must meet both frailty and advanced illness criteria to be excluded:
  - » Frailty: At least two indications of frailty with different dates of service during the measurement year. Do not include laboratory claims (claims with POS Code 81).
  - » Advanced Illness: Either of the following during the measurement year or the year prior to the measurement year:
    - Advanced illness on at least two different dates of service. Do not include laboratory claims (claims with POS Code 81).
    - Dispensed dementia medication (Dementia Medications List).
- Hospice services Members who use hospice services or elect to use a hospice benefit any time during the measurement year. Organizations that use the Monthly Membership

Detail Data File to identify these members must use only the run date of the file to determine if the member elected to use a hospice benefit during the measurement year.

- Reside in LTC or SNF and meet either of the following:
  - » Enrolled in an Institutional SNF (I-SNF) any time during the measurement year.
  - » Living long-term in an institution any time during the measurement year, as identified by the LTI flag in the Monthly Membership Detail Data File. Use the run date of the file to determine if a member had an LTI flag during the measurement year.
- **Death** Members who die any time during the measurement year.
- See <u>exclusion value sets</u>.

### Numerator

- **Measurement period** rolling 12-month look back preferred
- OUD-LAM initiation measure At least one OUD-LAM administration during the measurement period
- **OUD-LAM continuation measure** Two consecutive OUD-LAM administrations with second administration within 14 days plus or minus the first administration date

### Table B1: OUD-LAM list

| Drug Name   | HCPCS-J<br>Code |
|---|-----------------|
| Buprenorphine implant, 74.2 mg  | G2070           |
| Injection, buprenorphine extended-release (Brixadi), greater than 7 days and up to 28 days of therapy | J0574           |
| Injection, buprenorphine extended-release (Brixadi), less than or equal to 7 days of therapy          | J0577           |
| Injection, buprenorphine extended-release (Sublocade), greater than 100 mg                            | Jo578           |
| Injection, buprenorphine extended-release (Sublocade), less than or equal to 100 mg                   | Q9991           |
| Injection, naltrexone, depot form, 1 mg   | Q9992           |

# APPENDIX C: AUD-LAM MEASURES

# **AUD-LAM** utilization data specifications

**Description:** The percentage of individuals living with alcohol use disorder (AUD) who are using a long-acting injectable medication (AUD-LAM) for treatment. Two rates are reported:

- **1.** AUD-LAM initiation: Percentage of individuals who received any long-acting injectable medication for AUD treatment during the measurement period
- 2. AUD-LAM continuation: Percentage of individuals who received at least two long-acting injectables for AUD treatment during the measurement period

### SUMMARY INFORMATION

**Intended use:** Health plan or provider group performance measurement

Data sources needed: Pharmacy and medical claims

**Denominator:** Individuals 18 years of age or older who had any of the following during the measurement period:

- Diagnosis of AUD
- An acute inpatient or residential treatment stay with principal diagnosis of AUD
- A withdrawal management visit with principal diagnosis of AUD
- Any emergency department visit with principal diagnosis of AUD or alcohol poisoning
- An acamprosate or Antabuse pharmacotherapy event

**Exclusions:** Individuals who at any time during the measurement period had one of the following:

- Child-Pugh Class C cirrhosis
- Dementia
- Frailty and advanced illness
- Hospice services
- Skilled nursing facility (SNF) or long-term care (LTC) resident
- Death

**Numerator:** Individuals who have received either any AUD-LAM treatment OR at least two longacting AUD injections during the measurement period

### **DETAILED SPECIFICATIONS**

### **Eligible population (denominator)**

- Age Individuals aged 18-64 years of age at the beginning of the performance period
- Event or diagnosis
  - » Diagnosis of alcohol disorder (**Alcohol Use Disorder**) or related overdose diagnosis on any event during the measurement period:
    - ICD-10 Code F10
    - ICD-10 Code T51X
  - » An acute inpatient or residential treatment stay or withdrawal management visit with principal diagnosis of alcohol use disorder
    - See <u>inpatient or residential value set codes</u>
  - » Any emergency department visit with principal diagnosis of alcohol use disorder
  - » An oral AUD pharmacotherapy event with a negative medication history of at least 120 days
    - See value set definitions.

### **Exclusions**

Exclude members who met any of the following during the measurement year:

- Diagnosis for Child-Pugh Class C cirrhosis with presence of Diagnosis Code K74.72 on any event
- Diagnosis for dementia
- Frailty and advanced illness Members must meet both frailty and advanced illness criteria to be excluded:
  - » Frailty: At least two indications of frailty with different dates of service during the measurement year. Do not include laboratory claims (claims with POS Code 81).

- » Advanced Illness: Either of the following during the measurement year or the year prior to the measurement year:
  - Advanced illness on at least two different dates of service. Do not include laboratory claims (claims with POS Code 81).
  - Dispensed dementia medication.
- Hospice services Members who use hospice services or elect to use a hospice benefit any time during the measurement year. Organizations that use the Monthly Membership Detail Data File to identify these members must use only the run date of the file to determine if the member elected to use a hospice benefit during the measurement year.
- **Reside in LTC or SNF** and meet either of the following:
  - » Enrolled in an Institutional SNF (I-SNF) any time during the measurement year.
  - » Living long-term in an institution any time during the measurement year as identified by the LTI flag in the Monthly Membership Detail Data File. Use the run date of the file to determine if a member had an LTI flag during the measurement year.
- **Death** Members who die any time during the measurement year.
- See exclusion value sets.

### **Numerator**

- Measurement period rolling 12-month look back preferred
- AUD-LAM Initiation Measure at least one AUD-LAM administration during the measurement period
- **AUD-LAM Continuation Measure** Two consecutive AUD-LAM administrations with second administration within 14 days plus or minus first administration date

### Table C1: AUD-LAM list

| Drug Name   | Indication | Code  |
|---|------------|-------|
| Injection, naltrexone extended release (Vivitrol) | AUD, OUD   | J2315 |

# APPENDIX D: SECOND-GENERATION LAMS

Table A: Selected Long-acting Antipsychotic Medications

| Class             | Drug<br>(links to<br>package<br>inserts) | Dosing<br>Interval    | Initiating Dosing / Oral Supplementation Requirements   | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages  | Strategies with<br>Delayed/ Missed<br>Dosing   |
|-------------------|--|-----------------------|---|---|---|--|
| First Generation  | haloperidol<br>decanoate                 | Every 3 to 4<br>weeks | Day 1: 50 mg Day 8: (Monthly Dose — 50 mg) Monthly Dose = Total oral Daily Dose x 10 Initiate q4 week interval from Day 8 Optimally, oral supplementation 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 secondgeneration antipsychotics.  Lower cost than secondgeneration LAMs. | Risk of: Tardive Dyskinesia (TD), EPS, Neuroleptic Malignant Syndrome (NMS) and prolactinemia. Individuals may associate this medication with haloperidol HCl intramuscular experience, risk of neuroleptic induced negative syndrome. May require anti- EPS treatment. |  |
|                   | fluphenazine<br>decanoate                | Every 2 to 4<br>weeks | Day 1: Oral dose x 1.25. Alternatively, may initiate 25 mg IM q2 weeks and titrate/taper based on treatment response and tolerability.  Optimally, oral supplementation for 3 to 5 weeks  | Can more rapidly titrate or taper due to shorter half-life, and short onset to peak plasma levels (2 to 5 days).  Less metabolic syndrome risk than secondgeneration agents.              | q2 weeks, risk of:<br>TD, EPS, NMS and<br>prolactinemia.<br>May require anti-<br>EPS medications.   |  |
| Second Generation | Abilify<br>Maintena®<br>(aripiprazole)   | Every 4 weeks         | 400 mg then q4<br>weeks; 300 mg<br>if slow CYP2D6<br>metabolizer.<br>Requires 2 weeks<br>of overlap with oral<br>aripiprazole.  | Very low risk of prolactinemia.  Less metabolic risk than other secondgeneration antipsychotics, but more than first-generation agents.   | Fixed dosing with low dose flexibility.  Risks: akathisia, metabolic syndrome, Type 2 Diabetes, dyslipidemia, obesity, hypertension, EPS/TD.  High cost.  | For second or third injection: >5 weeks delayed, reload and oral supplement x2 weeks. If fourth dose or thereafter and >6 weeks delayed, reload and oral supplement x2 weeks |

| Class             | Drug<br>(links to<br>package<br>inserts) | Dosing<br>Interval    | Initiating Dosing / Oral Supplementation Requirements   | Medication-<br>Specific Benefits   | Medication-<br>Specific<br>Disadvantages   | Strategies with<br>Delayed/ Missed<br>Dosing  |
|-------------------|--|-----------------------|---|--|--|---|
| uo                | Abilify<br>Asimtufii®<br>(aripiprazole)  | Every 8 weeks         | Requires 2 weeks of overlap with oral aripiprazole.   | q8 weeks  Very low risk of prolactinemia.  Less metabolic risk than other secondgeneration antipsychotics, but more than first-generation agents.  | Risk of akathisia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD. High cost. | If more than 8 weeks, but less than 14 weeks, have elapsed since the last injection, administer the next dose as soon as possible. The once-every-2- month schedule should be resumed. If more than 14 weeks have elapsed since the last injection, restart concomitant oral aripiprazole for 14 days with the next administered injection. |
| Second Generation | Aristada® (aripiprazole lauroxil)        | Every 4, 6 or 8 weeks | Dosing and oral dose equivalents: 1064 mg q8 weeks = Abilify 15 mg PO daily 882 mg q6 weeks = Abilify 15 mg PO daily 882 mg IM q4 weeks > Abilify 20 mg PO daily 662 mg IM q4 weeks = Abilify 15 mg PO daily 441 mg q4 weeks = Abilify 10 mg PO daily Requires 3 weeks of overlap with oral aripiprazole or single administration of Astrida Intio. | Low risk of prolactinemia.  Less metabolic risk than other secondgeneration agents, but more than first-generation aripiprazole preparation with dose adjustment options (vs. Maintena).  Dosing interval flexibility. | Risk of akathisia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD. High cost. | 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 882 mg or 662 mg dosing: if 8 to 12 weeks since last dose, oral supplement for 7 days.  If missed >12 weeks, reload.  For 441 mg dosing, see package insert.    |

| Class             | Drug<br>(links to<br>package<br>inserts)          | Dosing<br>Interval            | Initiating Dosing / Oral Supplementation Requirements  | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages   | Strategies with<br>Delayed/ Missed<br>Dosing   |
|-------------------|---|-------------------------------|--|---|--|--|
| Second Generation | Aristada<br>Initio®<br>(aripiprazole<br>lauroxil) | Single initial administration | After establishing tolerability with oral aripiprazole, administer 675 mg injection of Aristada Initio (which corresponds to 459 mg of aripiprazole) and one 30 mg dose of oral aripiprazole.  The first Aristada injection (441 mg, 662 mg, 882 mg or 1064 mg) may be administered on the same day as Aristada Initio or up to 10 days after. | Low risk of prolactinemia.  Less metabolic risk than other secondgeneration agents, but more than first-generation aripiprazole preparation.  Allows prompter use of extended dose intervals. | Risk of akathisia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD. High cost. | When a dose of Aristada is missed/delayed more than 6 to 12 weeks (depending on the dose of Aristada missed) a single dose of Aristada Initio may be used to supplement or re-initiate the standing Aristada dose.  See product insert for detailed recommendations. |

| Class             | Drug<br>(links to<br>package<br>inserts)           | Dosing<br>Interval | Initiating Dosing / Oral Supplementation Requirements  | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages  | Strategies with<br>Delayed/ Missed<br>Dosing   |
|-------------------|--|--------------------|--|---|---|--|
| Second Generation | Zyprexa<br>Relprevv®<br>(olanzapine)               | Every 2-4<br>weeks | Target Oral Dose  — 10 mg/day first 8 weeks: 210 mg/2 weeks or 405 mg/4 weeks Maintenance Dose: 150 mg/2 weeks or 300 mg/4 weeks  Target Oral Dose  — 15 mg/day First 8 weeks: 300 mg/2 weeks  Maintenance Dose: 210 mg/2 weeks or 405 mg/4 weeks  Target Oral Dose  — 20 mg/day first 8 weeks: 300 mg/2 weeks  Maintenance Dose: 300 mg/2 weeks  Maintenance Dose: 300 mg/2 weeks  Oral supplementation generally not necessary | q2-4 weeks LAM option for patients who respond better to olanzapine than other antipsychotics.  | Requires monitoring post-injection for 3 hours due to black box warning for post-injection delirium/sedation syndrome.  Risk of prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD.  High cost. | Typically given by a health care professional in an emergency setting, so patients are unlikely to miss a dose.  |
|                   | Invega<br>Sustenna®<br>(paliperidone<br>palmitate) | Every 4 weeks      | Day 1: 234 mg IM;<br>Day 8: 156 mg IM;<br>then q4 weeks<br>maintenance dose<br>from Day 8.<br>Oral<br>supplementation<br>not necessary.  | 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 234 mg follow package insert.  If >6 months delay, reload according to package insert. |

| Class             | Drug<br>(links to<br>package<br>inserts)          | Dosing<br>Interval           | Initiating Dosing / Oral Supplementation Requirements  | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages  | Strategies with<br>Delayed/ Missed<br>Dosing   |
|-------------------|---|------------------------------|--|---|---|--|
|                   | Invega<br>Trinza®<br>(paliperidone<br>palmitate)  | Every 12 weeks<br>(3 months) | Transition only from paliperidone palmitate (Invega Sustenna) (stable dose for 4 months). Invega Sustenna to Invega Trinza conversion:  78 mg = 234 mg;  117 mg =410 mg;  156 mg = 546 mg  234 mg = 819 mg  Oral supplementation not necessary.  | 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 to 4 months, administer last dose of Trinza.  If miss 4 to 9 months, use reinitiation regimen with Sustenna as per package insert.  If > 9 months, reload with Sustenna and follow insert. |
| Second Generation | Invega<br>Hafyera™<br>(paliperidone<br>palmitate) | Every 6 months               | Can transition patients after 4 months Invega Sustenna or 3-month cycle of Invega Trinza 2 options for transition: From Invega Sustenna after 5 months stabilization on either 156 mg or 234 mg/month. From Invega Trinza after 1 dose of either 546 mg or 819 mg q3 months. Oral supplementation not necessary. | Longest interval between LAM doses available (every 6 months).  May reduce risk of jail or prison due to psychotic relapse when lost 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. Restart Invega Sustenna with next 2 doses at 234 mg initiation dose if 4 weeks late or more.  |

| Class             | Drug<br>(links to<br>package<br>inserts)         | Dosing<br>Interval | Initiating Dosing / Oral Supplementation Requirements   | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages  | Strategies with<br>Delayed/ Missed<br>Dosing  |
|-------------------|--|--------------------|---|---|---|---|
| Second Generation | Erzofri® (paliperidone palmitate)                | Every 4 weeks      | 351 mg initial dose, then 39 mg to 234 mg q4 weeks.  Recommended monthly dosage for treatment of schizophrenia is 117 mg. Some patients may benefit from lower or higher monthly doses within the additional available strengths (39 mg, 78 mg, 156 mg, 234 mg).  Oral supplementation not necessary. | No oral dose supplementation is needed after loading doses, q4 week interval.  Excreted by the kidney, which is advantageous for people with liver disease. | Second oncemonthly paliperidone palmitate formulation approved July 2024. No advantage in efficacy or safety demonstrated. High cost.   | If delayed less than 2 weeks (4-6 weeks since last injection), resume monthly dosing at previously stabilized dose.  If more than 6 weeks to 6 months since last injection, resume the same dose (unless stabilized at 234 mg, then administer 156 mg), as soon as possible; then second injection 1 week later; then resume monthly. |
|                   | Risperdal<br>Consta®<br>Rykindo<br>(risperidone) | Every 2 weeks      | Oral dose conversion oral risperidone to Consta:  mg: 3-5 = 37.5  mg: >5=50 >8  mg=N/A  Requires at least 3 weeks of overlap with oral risperidone, optimally at least 5 weeks  | Less EPS/<br>TD/ NMS/<br>antipsychotic-<br>induced negative<br>syndrome<br>risk than first-<br>generation agents.   | q2 weeks, low<br>therapeutic ceiling<br>vs. Sustenna<br>high risk of<br>prolactinemia,<br>metabolic risk, EPS.<br>Requires<br>refrigeration.**<br>High cost (varies by<br>state formulary). | If missed<br>dose during<br>maintenance<br>for more than 2<br>weeks, consider<br>oral supplement<br>6 weeks after<br>restarted injection<br>for duration of<br>missed dose.   |

| Class             | Drug<br>(links to<br>package<br>inserts) | Dosing<br>Interval    | Initiating Dosing / Oral Supplementation Requirements   | Medication-<br>Specific Benefits  | Medication-<br>Specific<br>Disadvantages  | Strategies with<br>Delayed/ Missed<br>Dosing  |
|-------------------|--|-----------------------|---|---|---|---|
| Second Generation | Perseris® (risperidone SC)               | Every 4 weeks         | Can administer the low or high dose (90 mg or 120 mg) without any oral supplementation if the patient was previously exposed to either risperidone or paliperidone. Otherwise, give patient 2 mg of risperidone or 3 mg of paliperidone orally for 2 days to rule out any allergic reaction.  Oral supplementation not necessary. | 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.                |
|                   | Uzedy®<br>(risperidone<br>SC)            | Every 4 or 8<br>weeks | For q4 week dosing, 50:2 mg Uzedy:oral risperidone. For q8 week dosing, 100:2 mg Uzedy:oral risperidone. Oral supplementation not necessary.  | 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. Prefilled syringe. | Risk of prolactinemia, metabolic syndrome, DM2, dyslipidemia, obesity, HTN, EPS/TD.  Patients may feel a nodule under the skin.  High cost.   | Give SC dose<br>whenever patient<br>returns whether<br>acutely psychotic<br>or stable with no<br>acute psychosis. |

|   |  | Indication   |  |  |
|---|--|--|--|--|
|   | Alcohol Use Disorder<br>or<br>Prevent relapse to opioid<br>use disorder after opioid<br>detoxification | id Moderate to severe opioid use disorder  |  |  |
| Drug (links to package inserts)                       | <u>Vivitrol®</u> (naltrexone)  | Sublocade® (buprenorphine)   | Brixadi® (buprenorphine)   |  |
| Dosing Interval                                       | Every 4 weeks  | Every 4 weeks  | Either weekly or Every 4 weeks (different formulations)                |  |
| Initiating Dosing / Oral Supplementation Requirements | 380 mg every 4 weeks as gluteal IM injection.  Oral supplementation not necessary                      | Requires withdrawal symptoms to be controlled by oral buprenorphine for at least 7 days prior to initiation. | Requires test dose if patient not currently taking oral buprenorphine. |  |
| Medication-<br>specific Benefits                      | q4 weeks vs. daily oral<br>naltrexone  | q4 weeks vs daily oral<br>buprenorphine  | q4 weeks vs. daily oral<br>buprenorphine                               |  |
| Medication-specific<br>Disadvantages                  | Must stop using opioids prior to initiation (minimum 7 to 10 days).  Requires refrigeration.**         | Requires refrigeration.**  |  |  |

### \*\*Refrigeration Requirements:

- **Risperdal Consta:** The entire dose pack should be stored in the refrigerator (36° to 46°F; 2° to 8°C) and protected from light. If refrigeration is unavailable, Risperdal Consta can be stored at temperatures not exceeding 77°F (25°C) for no more than seven days prior to administration. Do not expose unrefrigerated product to temperatures above 77°F (25°C).
- **Vivitrol:** The entire dose pack should be stored in the refrigerator (2 °C to 8 °C, 36 °F to 46 °F). Unrefrigerated, Vivitrol can be stored at temperatures not exceeding 77°F (25°C) for no more than seven days prior to administration. Do not expose the product to temperatures above 77°F (25°C). Vivitrol should not be frozen.
- **Sublocade:** Store refrigerated at 35.6°F to 46.4°F (2°C to 8°C). Once outside the refrigerator this product may be stored in its original packaging at room temperature, 59°F to 86°F (15°C to 30°C), for up to 12 weeks prior to administration. Discard Sublocade if left at room temperature for longer than 12 weeks.

Training Resources: The American Association of Psychiatric Pharmacists offers a complimentary training program on LAMs focused on appropriate patient selection, LAM preparation, administration techniques and engaging patients. The program includes six webinars and tools such as an LAM pocket guide containing information on each available antipsychotic LAM and an LAM administrative toolkit.

# THE UNDERUTILIZATION OF LONG-ACTING MEDICATIONS

The Medical Director Institute of the National Council for Mental Wellbeing convened an expert panel to develop a national technical report focused on measuring the underuse of long-acting injectable medications for psychosis, opioid use disorder and alcohol use disorder. Although extensive research has demonstrated the clinical benefits of long-acting medications and identified barriers to their use, utilization rates remain low. At the time, there were no standardized, population-level performance measures to assess underutilization, limiting the ability of health care systems, payers and regulators to monitor progress or implement quality improvement initiatives.

The meeting took place in Washington, D.C., Jan. 14-16, 2025.

# **Acknowledgments**

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