INDICATION
ARISTADA is indicated for the treatment of schizophrenia.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ARISTADA reimbursement guide

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IMPORTANT SAFETY INFORMATION (continued)

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Reactions, Including Stroke: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
The treatment of schizophrenia is complicated and can involve multiple sites of care, provider resources, and different approaches to treatment over time. People living with schizophrenia may have complex health insurance coverage as well, with some having overlapping coverage from different payers, or gaps in coverage from one payer that are met by another.

The ARISTADA reimbursement guide is designed to help support patient access to ARISTADA® (aripiprazole lauroxil), a long-acting injectable atypical antipsychotic therapy for the treatment of schizophrenia.¹

This ARISTADA reimbursement guide provides an overview of useful information for healthcare professionals to help patients navigate key aspects of coding, coverage, and payment for treatment with ARISTADA in the following settings of care:

- Healthcare professional offices
- Community Mental Health Centers (CMHCs)
- Partial hospitalization treatment programs
- Hospital outpatient
- Hospital inpatient

**Tips for using this guide**

The ARISTADA reimbursement guide is designed to help patients gain access to treatment with ARISTADA based on the patient’s prescription drug coverage and site of care. Information is organized by payer type and site of care. For information and tips on how payers cover ARISTADA treatment, refer to the tabs in the ARISTADA coverage considerations by payer type section of this guide. For detailed information on billing for treatment with ARISTADA, refer to the appropriate tab in the Sites of care and claim forms section.

*This is not a guarantee of payment, coverage, or reimbursement. Alkermes does not provide any advice, recommendation, guarantee, or warranty relating to coverage, reimbursement, or coding for any product or service. Healthcare providers are responsible for determining coverage and reimbursement information and ensuring the accuracy and completeness of claim submissions for their patients. Coding, coverage, and reimbursement vary significantly by payer, patient, and setting of care and are subject to change. Additional information may exist. Actual coverage and reimbursement decisions are made by individual payers.*

**IMPORTANT SAFETY INFORMATION (continued)**

**Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Benefit verification tips for ARISTADA

- Schizophrenia is a severe mental illness. Some states provide category-level protections for medications used to treat severe mental illness, which may encompass unencumbered access to all antipsychotic medications
- Under Medicare Part D, antipsychotics are one of 6 “protected” drug categories where plans must cover “all or virtually all” prescription medications
- Coverage of ARISTADA (aripiprazole lauroxil) can vary. Thoroughly research a patient’s health insurance plan (or plans) and the prescription coverage of ARISTADA before it is ordered or prescribed

ARISTADA Care Support can help with the benefit verification process to provide important information that may help patients with coverage, claims, and appeals for treatment with ARISTADA.

Contact ARISTADA Care Support (1-866-ARISTADA [1-866-274-7823]) for support with patients’ benefit verification, prior authorization, and access for ARISTADA.

IMPORTANT SAFETY INFORMATION (continued)

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ARISTADA® (aripiprazole lauroxil) is a long-acting injectable atypical antipsychotic for the treatment of schizophrenia.

Factors affecting coverage

Three main considerations affect coverage and reimbursement for treatment with ARISTADA (Figure 2). These are:

Type of payer – Insurance coverage varies by type of payer as well as by site of service, patient condition, and medical history. Medicaid and Medicare are important payers for many people living with schizophrenia and many patients may have coverage under both government insurance programs (e.g., dual eligibility). Some patients may have coverage from private or commercial payers, which includes many of the plans that are available to individuals through the state health insurance marketplaces. Fully understanding the patient’s insurance coverage and benefit structure is a key step in helping to obtain treatment with ARISTADA.

Benefit category – Providers can obtain ARISTADA for their patients in different ways, depending on the patient’s insurance coverage and benefit structure—that is, whether the insurance plan covers the medication under the medical benefit or the pharmacy benefit. In some situations, a payer may cover the medication under either or both benefits. This key information can be obtained during the benefit verification process. For patients receiving ARISTADA, it is always important to check both the plan’s medical and pharmacy coverage for ARISTADA.

Place of service – Insurance coverage of provider-administered medications varies by site where the service is provided. People living with schizophrenia may rely on several different sites of care, including physician offices, CMHCs, partial hospitalizations, hospital outpatient, or hospital inpatient settings. Over time, the site of care may change, as these individuals move in and out of community-based living. It is essential to coordinate care across sites of service to support continued patient access to medication.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- Hyperglycemia/Diabetes Mellitus: Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Pathways for obtaining ARISTADA

A site of care has several options for obtaining ARISTADA, depending on preferences and payer requirements. It is important to always check with each payer prior to ordering or administering ARISTADA to verify the policies applicable to the patient.

1. Order ARISTADA and submit claim (buy and bill)
   This acquisition method allows a site of care the ability to purchase ARISTADA for administration to patients. ARISTADA Care Support can help with the benefit verification process to confirm the patient’s coverage for ARISTADA if the practice prefers to buy and bill. Contact 1-866-ARISTADA (1-866-274-7823) for support and assistance with benefit verification, prior authorization (PA), ordering, and patient access for ARISTADA.

2. Specialty Pharmacy Provider (SPP)
   This option enables an SPP to purchase ARISTADA for delivery and administration at a site of care. ARISTADA Care Support is available to assist in coordinating delivery of ARISTADA through an available SPP based on the patient’s insurance coverage and any payer-specific rules regarding use of in-network SPPs. ARISTADA Care Support can confirm shipment and/or delivery of ARISTADA to the site for the identified patient. Contact 1-866-ARISTADA (1-866-274-7823) for support and assistance with benefit verification, PA, and patient access for ARISTADA.

3. Retail pharmacy
   In certain circumstances, retail pharmacies may be able to deliver ARISTADA to a site of care for administration. Contact 1-866-ARISTADA (1-866-274-7823) for additional details or support and assistance with benefit verification, PA, and patient access for ARISTADA.

IMPORTANT SAFETY INFORMATION (continued)

- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

**Pathological Gambling and Other Compulsive Behaviors:** Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping ARISTADA if a patient develops such urges.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ARISTADA Care Support

ARISTADA Care Support provides a comprehensive suite of services to help make ARISTADA® (aripiprazole lauroxil) therapy more accessible for patients.

ARISTADA Care Support services include:

- **Access Services:** Reimbursement support and financial assistance programs to help patients access treatment
- **Hospital Services:**
  - A program to help hospitalized patients trial ARISTADA in the hospital
  - A program to help patients secure potential sites and providers for follow-up care
- **Product Support:** Samples, ordering information, and answers to questions about ARISTADA
- **Patient Support:** Educational materials, transition assistance, injection services, and appointment reminders are available for patients and caregivers who need them

Reimbursement support

Insurance coverage may pose challenges for patients. We’ll provide the most up-to-date coverage information and, if requested, help navigate access barriers. There are both phone and web options for reimbursement support.

- Live representative – Call **1-866-ARISTADA (1-866-274-7823)** to receive general coverage information, including prior authorization requirements. We can also execute a full benefit investigation upon receiving a patient’s enrollment with ARISTADA Care Support. We’ll follow up with patient-specific research, including plan-specific prior authorization requirements, usually within 24 hours

Learn more at ARISTADACareSupport.com, or call us at 1-866-ARISTADA (1-866-274-7823)

Monday through Friday, 8 AM to 8 PM EST

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**IMPORTANT SAFETY INFORMATION (continued)**

**Orthostatic Hypotension:** Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

**Falls:** Antipsychotics including ARISTADA may cause somnolence, postural hypotension, or motor and sensory instability, which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ARISTADA coverage considerations by payer type

A patient’s coverage for treatment with ARISTADA® (aripiprazole lauroxil) will vary based on the type of insurance they have and each payer’s specific policies regarding coverage and reimbursement for treatment with long-acting injectable atypical antipsychotic medications, such as ARISTADA. There are two major types of payers that provide coverage for persons living with schizophrenia: public insurance programs funded by state or federal governments (e.g., Medicaid and Medicare), and private (or commercial) insurance, which includes plans available to individuals through the health insurance marketplaces (Figure 3).

Figure 3: Insurance Coverage At A Glance

Public insurance
(Federal, state, or other tax-payer funded)

<table>
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<th>Medicaid</th>
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<tr>
<td>Coverage for low-income and other qualified populations</td>
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<th>Medicare</th>
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<td>Aged ≥65 years</td>
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<td>Aged &lt;65 years with certain disabilities</td>
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<tr>
<th>Other federal</th>
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<td>Veterans Affairs</td>
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<td>Department of Defense</td>
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<td>Tricare</td>
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<table>
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<th>Managed Medicaid</th>
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<tr>
<td>State Medicaid or Fee-for-Service Medicaid</td>
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<th>Medicare Part A</th>
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<td>(Hospital Insurance)</td>
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<th>Medicare Part B</th>
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<td>(Medical Insurance)</td>
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<th>Medicare Advantage (MA)</th>
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<tr>
<td>or Medicare Advantage-Prescription Drug (MA-PD)</td>
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<th>Medicare Part D</th>
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<tr>
<td>(Outpatient Prescription Drug Coverage)</td>
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Private insurance (commercial)

Employer

Individual, including Marketplace

This is not a guarantee of payment, coverage, or reimbursement. Alkermes does not provide any advice, recommendation, guarantee, or warranty relating to coverage, reimbursement, or coding for any product or service. Healthcare providers are responsible for determining coverage and reimbursement information and ensuring the accuracy and completeness of claim submissions for their patients. Coding, coverage, and reimbursement vary significantly by payer, patient, and setting of care and are subject to change. Additional information may exist. Actual coverage and reimbursement decisions are made by individual payers.

IMPORTANT SAFETY INFORMATION (continued)

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm^3) and follow their WBC until recovery.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicaid provides coverage for many people living with schizophrenia. It is jointly administered by each state and CMS, operated by the federal government, and covers various groups of individuals, including people with disabilities and individuals who have little income. Some states have extended coverage to nondisabled adults with limited incomes and Medicaid is expected to continue to grow as more states opt in to expand their programs under the Affordable Care Act (ACA).

Federal law requires that states cover certain benefits for Medicaid beneficiaries, but other benefits are determined at the state level. Prescription drug coverage, home and community-based services are some of the optional Medicaid benefits that are determined on a state-by-state basis.

Medicaid coverage and payment for prescription medications vary by state. Some programs or plans may have coverage restrictions on long-acting injectable antipsychotic medications such as ARISTADA® (aripiprazole lauroxil). These may include policies such as dose limitations, prior authorization (PA), step edits, or use of an in-network pharmacy. Other states may protect treatment for schizophrenia as a severe mental illness to ensure that patients have access to care and treatment options including treatment with drugs like ARISTADA.

Contact the state Medicaid office to determine what type of benefit coverage the patient has and how this may affect coverage for treatment with ARISTADA.

MANAGED MEDICAID

Depending on where a practice or place of service is located, more than 50% of Medicaid patients may receive coverage through a Managed Medicaid plan that is administered by a commercial payer, such as UnitedHealth Group, Anthem®, or Molina. States continue to expand their participation in Managed Medicaid programs.

Patients who are enrolled in Managed Medicaid plans may have different coverage for ARISTADA than patients covered under a state Fee-for-Service (FFS) Medicaid program. It is important to verify which entity determines prescription drug coverage for long-acting injectable antipsychotics and benefit coverage for each individual patient, based on his or her insurance coverage at the time they are seeking treatment.

In some cases, even though a patient may be enrolled in a Managed Medicaid plan, the state retains the decision-making authority on coverage decisions for antipsychotic drugs. In other cases, the Managed Medicaid organization may be responsible for the coverage or formulary decision.

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IMPORTANT SAFETY INFORMATION (continued)
Seizures: ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain ARISTADA does not affect them adversely.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
MEDICAID FEE-FOR-SERVICE (FFS)

Until the migration toward Managed Medicaid, states purchased healthcare services for Medicaid beneficiaries largely on a Fee-For-Service (FFS) basis. Under state Medicaid FFS plans, providers are paid for services based on a set fee schedule, usually a fixed percentage of the Medicare rate. Some states continue to operate on a FFS basis or offer both Managed Medicaid and FFS options.

Although states are not required to include prescription drug coverage in their state Medicaid plan, currently all 50 states cover prescription drugs. Each state determines what medications will be included in the Medicaid formulary and whether the state will maintain authority over the formulary if it contracts with payers to administer and manage care for its Medicaid beneficiaries. Medicaid plans may have different names for their formulary, such as preferred drug list (PDL), contracted drug list (CDL), prescription injectable drug list (PIDL), or other state-determined name. Long-acting injectable antipsychotics are commonly included in these formularies. Some states provide a category-level protection and do not review antipsychotic agents. In these cases, new agents can be automatically added to the state’s drug list, or in other cases, covered without a formal addition. However, since there is considerable variation between states, it is important to understand the state’s coverage of ARISTADA® (aripiprazole lauroxil) as a long-acting injectable antipsychotic for the treatment of schizophrenia.

ARISTADA MAY BE COVERED AS EITHER A MEDICAL OR PHARMACY BENEFIT UNDER MEDICAID

When ARISTADA is covered by a Medicaid plan as a pharmacy benefit, the healthcare professional writes a prescription and submits it to the pharmacy (which can be specialty, retail, or mail order). The pharmacy then ships the medication to the healthcare professional’s site of service. In some cases, the Medicaid plan may specify that the prescription be filled by a specific pharmacy or pharmacy provider, such as a Specialty Pharmacy Provider (SPP). In these cases, the pharmacy provider is responsible for submitting the claim for ARISTADA and the healthcare professional bills for administering the injection and other professional services.

If ARISTADA is covered by a Medicaid plan under the medical benefit, healthcare professional offices and CMHCs may be able to purchase and administer ARISTADA in the healthcare professional-office setting. This process, also called “buy-and-bill,” may allow the healthcare professional or organization to use their National Provider Identifier (NPI) to bill for the different components of treatment, such as the cost of purchasing a medication, the injection/administration, and other services. The reimbursement methodology can vary based on each state’s reimbursement methodology for buy and bill, so it’s important to contact the state Medicaid program to verify the reimbursement amount for ARISTADA.

MEDICAID PATIENT FINANCIAL RESPONSIBILITY/COST-SHARING FOR TREATMENT WITH ARISTADA

Medicaid cost-sharing requirements for treatment with long-acting injectable antipsychotics such as ARISTADA vary by state, by site of care, and the patient’s coverage. In general, Medicaid plans offer patients living with schizophrenia access to antipsychotic medications at a nominal cost. Many states waive co-pay policies for drugs used to treat severe mental illness. To encourage the use of lower-cost drugs, states may establish different co-pays for generic drugs and brand-name drugs, or for drugs included on a preferred drug list. For people with incomes at or below the 100% of the federal poverty level (FPL), co-pays will generally be lower for nonpreferred drugs. Contact the state Medicaid plan, search its website for information, or contact ARISTADA Care Support at 1-866-ARISTADA (1-866-274-7823) for information about co-pay for Medicaid beneficiaries.

IMPORTANT SAFETY INFORMATION (continued)

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
MANAGED MEDICAID AND MEDICAID APPEALS

If a Managed Medicaid or Medicaid payer denies a prescription, PA, or claim for ARISTADA® (aripiprazole lauroxil), the plan is required to include information in the denial notice about how to appeal, with details about who to contact for more information. For questions about denial of a PA or claim, the first step is to contact the state Medicaid plan, or the Managed Medicaid plan.

The specific processes, levels, and deadlines or time limits in state Medicaid appeals processes vary from state to state. However, the federal rules governing Medicaid require that plans offer opportunities to request an appeal, or “fair hearing” as the process is called by many programs, in specific situations. These required opportunities for a fair hearing include:

- A patient’s claim for services is denied or not acted on with reasonable promptness
- The patient or healthcare professional believes that the plan has acted erroneously in delaying the delivery of, terminating, suspending, or reducing Medicaid covered services on the grounds of medical necessity
- A managed care plan enrollee wishes to challenge the denial of coverage or payment for services

For Medicaid FFS, the appeals process generally includes the following steps and deadlines:

- The state agency notifies the beneficiary of a claim denial or intended action
- The beneficiary (or representative) requests a hearing within a reasonable time established by the state agency (at least 20 days and not more than 90 days)
- The state has the option to provide a local-level evidentiary hearing
- If the hearing decision is adverse to the beneficiary, a state fair hearing can be requested within 15 days of the date the decision was mailed
- If the state fair-hearing decision is adverse, the beneficiary may seek judicial review in the state court, as available. All states make some review available as a matter of state law

Patients enrolled in Managed Medicaid plans may have access to supplementary appeals procedures. The federal Medicaid Act requires Managed Care Organizations (MCOs) to establish internal appeal procedures that allow enrollees to challenge the denial of coverage or payment for medical services. These internal appeal procedures may be faster than a state fair hearing, or they may delay the time in which a patient has access to a fair hearing.

In general, the MCO appeals process begins with a written Notice of Action and federal law requires that specific information be included in these notices of action. It is important to follow state regulations and designated processes and deadlines to ensure the patients’ rights are upheld during a Medicaid appeal.

**Important Safety Information (continued)**

**Dysphagia:** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ADDITIONAL PATHWAYS TO MEDICATION ACCESS FOR PATIENTS WHO ARE MEDICAID ELIGIBLE

Many people with low incomes and disabilities are eligible for Medicaid but may not be enrolled. It is not unusual for people living with schizophrenia to move in and out of insurance coverage during different periods of their lives. This may include eligibility for different types of government-sponsored health coverage programs, such as Medicaid, Medicare, or both.

If a patient was recently hospitalized or moved into a community-based living situation from another type of care site, ask whether he or she has Medicaid. If the patient is not enrolled (or does not know if he or she is enrolled), the patient can apply through the state Medicaid offices. Once the application process is completed, the patient can be enrolled in the appropriate level or type of Medicaid program that meets his or her individual needs, history, and current situation, if he or she qualifies.

For more information about different types of Medicaid eligibility and some of the programs that may be available to help patients obtain the coverage and benefits they need, please refer to the Dual eligibility: Medicare and Medicaid coverage section of this document. Contact ARISTADA Care Support 1-866-ARISTADA (1-866-274-7823) for more information about programs that can help patients access treatment with ARISTADA® (aripiprazole lauroxil).

ARISTADA Care Support can help determine coverage for patients with Medicaid. Call 1-866-ARISTADA (1-866-274-7823) for more information.

IMPORTANT SAFETY INFORMATION (continued)

Concomitant Medication: Decreasing the ARISTADA dosage is recommended in patients taking strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for longer than 2 weeks. Increasing the ARISTADA dosage from 441 mg to 662 mg is recommended in patients taking CYP3A4 inducers for longer than 2 weeks. No ARISTADA dosage changes are recommended for patients taking CYP450 modulators for less than 2 weeks.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicare

Medicare, the healthcare benefit plan administered by the federal government, covers individuals 65 years of age and older, certain disabled individuals, and individuals diagnosed with end stage renal disease. For people living with schizophrenia who are eligible for Medicare, it is an important payer for medications such as ARISTADA® (aripiprazole lauroxil).

As a patient with schizophrenia who is Medicare-eligible moves through different sites of care, coverage for the cost of their prescriptions and medical care will change, based on the Medicare four-part benefit design. Services covered in each of the four parts of Medicare are summarized in Figure 4.

**Figure 4: Medicare at a Glance**

**Medicare**
- Aged ≥65 years
- Aged <65 years with certain disabilities

**Medicare Part A** (Hospital Insurance)
- Includes inpatient hospital care, skilled nursing facility, home health care, and hospice care

**Medicare Part B** (Medical Insurance)
- Includes medically necessary outpatient hospital services, doctor visits, home health care, laboratory services, durable medical equipment, preventive services, and limited provider-administered drugs, including some oral drugs

**Medicare Advantage (MA)**
Combines Part A and Part B through a managed care plan OR **Medicare Advantage-Prescription Drug (MA-PD)**
Combines Part A and Part B, along with Part D, through a managed care plan

**Medicare Part D** (Outpatient Prescription Drug Coverage)

**Important Safety Information (continued)**

**Most Commonly Observed Adverse Reaction:** The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg monthly) was akathisia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicare Part A (Hospital Insurance): Inpatient care for Medicare beneficiaries is covered under Medicare Part A. This covers inpatient services in acute care and psychiatric hospitals. Hospitals are paid by Medicare under a bundled payment that may include prescription medications, such as ARISTADA® (aripiprazole lauroxil), used during the inpatient stay.

Medicare Part B (Medical Insurance): Outpatient hospital care and outpatient mental healthcare are covered under Medicare Part B. Part B also may cover partial hospitalization by a CMHC, which could include provider-administered medications such as ARISTADA. In these settings, healthcare professionals may be able to purchase covered medications and bill for the medication along with any related services.

Medicare Advantage: Most people sign up for original Medicare, which consists of Part A and Part B. However, a growing number of individuals are signing up for Medicare Advantage plans, which combine Part A and Part B with additional benefits, such as prescription drug coverage. Medicare Advantage plans are managed by private/commercial insurance companies under contract with the CMS. Patients in most areas can choose from a wide variety of different plans and benefit options. Prescription drug plans that are offered as part of a Medicare Advantage plan are called Medicare Advantage-Prescription Drug (MA-PD) plans, which may cover long-acting injectable antipsychotics under Part B; others may cover them under Part D. Some Medicare Advantage plans include special options for patients who may be institutionalized, are eligible for both Medicare and Medicaid, or who have chronic conditions; these are known as Medicare Advantage Special Needs Plans (SNPs).

Medicare Part D (Outpatient Prescription Drugs): Medicare Part D was created in 2006 to provide beneficiaries with coverage for outpatient prescription medications. It is an optional benefit, which means that most patients must choose to enroll and pay an additional premium for coverage. All Part D plans are managed by private/commercial insurance companies and individuals can choose a Prescription Drug Plan (PDP) that best meets their needs.

Some people with low incomes or disabilities may qualify for automatic enrollment in the Part D Low-Income Subsidy (LIS) program, also known as Medicare Extra Help. For more information, please see “Dual eligibility: Medicare and Medicaid coverage” on page 20.

MEDICARE PART D PROTECTED DRUG CLASSES

CMS requires that all Part D plan formularies include “all or substantially all” drugs in 6 categories:

- Antipsychotic
- Anticonvulsant
- Antidepressant
- Antineoplastic
- Antiretroviral
- Immunosuppressant (for prophylaxis of organ transplant rejection)

IMPORTANT SAFETY INFORMATION (continued)

Injection-Site Reactions: Injection-site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection-site pain and associated with the first injection and decreased with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) occurred at less than 1%.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
IMPORTANT SAFETY INFORMATION (continued)

**Dystonia:** Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

**Pregnancy/Nursing:** May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA during pregnancy. Aripiprazole is present in human breast milk. The benefits of breastfeeding should be considered along with the mother’s clinical need for ARISTADA and any potential adverse effects on the infant from ARISTADA or from the underlying maternal condition.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicare Part B

Medicare Part B covers services and supplies that are deemed medically necessary to treat a health condition. This includes outpatient and physician office visits. For patients who are not dual eligible, most beneficiaries will pay a monthly premium along with an annual deductible. Costs are subject to change each benefit year. Medicare pays 80% of allowable costs, while beneficiaries are responsible for a 20% coinsurance for most professional services and drugs. When services are provided in a hospital outpatient setting, the beneficiary coinsurance for separately covered drugs is 20% of the allowable, but coinsurance ranges from 20% to 40% of the amount allowed by Medicare for other items and services provided by the hospital. This is in addition to the 20% coinsurance that applies to professional services rendered in the hospital outpatient setting.

If a patient is covered for treatment with ARISTADA® (aripiprazole lauroxil) under Medicare Part B, it is important to determine whether the patient has supplemental coverage that will help pay for his or her coinsurance.

Medicare Advantage

Medicare Advantage (MA) plans provide both Medicare Part A and Medicare Part B benefits and in some cases, outpatient prescription drug (Part D) benefits as well. Medicare Advantage-Prescription Drug (MA-PD) plans include the Medicare Part D benefit described in the Part D section on the following page.

Premiums, deductibles, co-pays, and coinsurance vary from plan to plan. There is no supplemental coverage associated with these plans. MA and MA-PD plans should be contacted to determine each patient’s specific financial obligations.

IMPORTANT SAFETY INFORMATION (continued)

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Reactions, Including Stroke: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicare Part D

Medicare Part D PDPs and MA-PDs vary in their coverage of long-acting injectable antipsychotic medications, such as ARISTADA® (aripiprazole lauroxil). A plan may cover ARISTADA under Part D without restriction or require a Prior Authorization. The patient cost of prescription drugs, including ARISTADA, can vary significantly by plan, medication and even pharmacy. If not eligible for the Low-Income Subsidy, patients may be responsible for paying a monthly premium, deductible, co-pay, or coinsurance, depending on the plan.8

There are 3 different levels of beneficiaries within Part D10:

- **Standard beneficiaries** – Beneficiaries are not eligible for the Medicare Low-Income Subsidy (LIS), but may be eligible for a senior State Pharmaceutical Assistance Program (SPAP) based on income, resource levels, and other state criteria. The Part D cost structure can change annually. The standard Medicare Part D benefit has an annual deductible and an initial coverage limit.12 After reaching the initial coverage limit, beneficiaries are responsible for a percentage of the cost of prescription medications until they reach the out-of-pocket threshold. After reaching the out-of-pocket threshold, beneficiaries are responsible for a cost-share after the out-of-pocket threshold is reached.

- **Dual eligibility** – Individuals with dual eligibility for Medicare and Medicaid, also known as full subsidy-Full Benefit Dual Eligibles (FBDEs), are automatically enrolled in the Part D LIS and are responsible for a modest co-pay.

- **Other Low-Income Subsidy beneficiaries** – These beneficiaries have incomes less than 150% of the Federal Poverty Level. They may be eligible to receive partial assistance from Medicaid in paying for their Part D out-of-pocket expenses.

For more information please refer to the **Dual eligibility: Medicare and Medicaid coverage** section of this guide.

**IMPORTANT SAFETY INFORMATION (continued)**

**Tardive Dyskinesia (TD):** The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Medicare appeals
CMS has a defined process for appeals of both original Medicare, Medicare Advantage, and Part D coverage decisions. Both follow a similar five-level structure, with specific deadlines and time limits for both standard and expedited requests. If there is concern that a patient could be harmed by waiting the standard 14 days for a decision, a healthcare professional can request an expedited decision within 72 hours.

ORIGINAL MEDICARE AND MEDICARE ADVANTAGE APPEALS
When ARISTADA® (aripiprazole lauroxil) is covered under the Medicare Part B medical benefit, the process for appealing a denial of coverage is similar to the Part D appeals process described below. It involves 5 sequential levels of appeals, from a Request for Redetermination from the plan to a hearing or review by an appeals council or in a Federal District Court. For more information about the Medicare Part B appeals process, consult the Medicare Claims Processing Manual, Chapter 4 – Part B Hospital. This is available for download at:


Patients with coverage through Medicare Advantage plans follow a similar process, with established procedures for advancing to the next level of appeal defined in writing.

PART D DRUG COVERAGE APPEALS
CMS has defined a five-step process for prescription drug coverage appeals, with specific deadlines and procedures for each level. The levels of appeal range from a coverage redetermination, requesting that a plan reevaluate an initial denial, to the highest level of judicial review in a Federal District Court. The Medicare Part D Prescription Drug Coverage Determination and Appeals Process in Figure 5 summarizes the coverage determination and appeals process, and the key time limits and dollar amount criteria associated with each level of appeal.

Plans are required to accept any written request for a redetermination of coverage from patients, appointed representatives, the patient’s healthcare professional, or other prescriber. A written request to appeal should include:

- The patient’s name, address, Medicare number and/or plan member identification number
- The name of the drug submitted for the appeal
- Stated reason from initial denial of claim, date the denial was issued, and a copy of the denial
- The reasons for the appeal; consider including information similar to that outlined in the sample Letter of Medical Necessity or Appeals Letter
- If the healthcare professional is acting as the patient’s appointed representative in the appeal process, include proof of representation
- Include any other information that may help support the appeal, such as medical records, patient history, or recent chart notes

For more information about Part D drug coverage appeals, consult the Medicare Prescription Drug Benefit Manual, Chapter 18 – Part D Enrollee Grievances, Coverage Determinations and Appeals. This is available for download at:


IMPORTANT SAFETY INFORMATION (continued)
Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- **Hyperglycemia/Diabetes Mellitus**: Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
FIGURE 5: MEDICARE PART D PRESCRIPTION DRUG COVERAGE DETERMINATION* AND APPEALS PROCESS†

Medicare Prescription Drug (Part D)
Coverage determination* / appeals process

Standard process
72-hour time limit†

Expedited process
24-hour time limit†

PDP/MA-PD
Standard redetermination
7-day time limit

PDP/MA-PD
Expedited redetermination
72-hour time limit

Part D IRE
Standard redetermination
7-day time limit

Part D IRE
Expedited redetermination
72-hour time limit

Office of Medicare Hearings and Appeals
Standard decision
90-day time limit

Office of Medicare Hearings and Appeals
Expedited decision
AIC‡

Medicare Appeals Court
Standard decision
90-day time limit

Medicare Appeals Court
Expedited decision
AIC‡

Federal District Court
AIC‡

Coverage Determination

First Appeal Level
60 days to file

Second Appeal Level
60 days to file

Third Appeal Level
60 days to file

Fourth Appeal Level
60 days to file

* A request for a coverage determination includes a request for a tiering exception or a formulary exception. A request for coverage determination may be filed by the Medicare enrollee (patient), by an appointed representative, or by the enrollee’s healthcare provider or other prescriber.
† The adjudication time frames generally begin when the request is received by the plan sponsor. However, if the request involves a formulary exception request, the adjudication time frame begins when the plan sponsor receives the physician’s supporting statement.
‡ The AIC requirement for an ALJ hearing and Federal District Court appeal is adjusted annually in accordance with the medical care component of the consumer price index. For a current price index, visit: https://www.cms.gov/Medicare/Appeals-and-Grievances/MedPrescriptDrugApplGriev/index.html.

MAXIMUS Federal Services currently manages the Medicare Part D IRE process.
All requests from an authorized person must be submitted in writing via mail or fax to MAXIMUS at:
MAXIMUS Federal Services
3750 Monroe Avenue, Suite 703
Pittsford, NY 14534-1302
Toll-free fax: 1-866-825-9507
Additional information, including a Request for Reconsideration of Medicare Prescription Denial form, is available on the Medicare Part D appeals website (http://www.medicarepartdappeals.com/).

IMPORTANT SAFETY INFORMATION (continued)

• Dyslipidemia: Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
• Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
In 2011, there were approximately 10 million low-income elderly and disabled people who were covered under both Medicare and Medicaid. These beneficiaries include many people living with schizophrenia. Medicare is the primary source of health insurance coverage for these individuals. Medicaid supplements Medicare, paying for services not covered by Medicare, such as dental care and long-term care, and by helping to cover Medicare premiums and patient cost-sharing requirements.

The Medicare Part D benefit includes special assistance for Medicare-eligible beneficiaries with limited resources and income. This program, known as the Medicare Low-Income Subsidy (LIS), or Extra Help, can decrease or eliminate any out-of-pocket costs for patients with Medicare Part D.

Three groups of Medicare beneficiaries are automatically enrolled in LIS with full benefits and do not have to apply. These are:

1. Medicare beneficiaries who qualify for full Medicaid benefits (dual eligibility)

2. Beneficiaries enrolled in 1 of 4 Medicare Savings Programs (MSP):
   - **Qualified Medicare Beneficiary (QMB) Program** — Eligibility for the QMB program automatically qualifies an individual for LIS. The QMB program helps pay for Parts A and B out-of-pocket cost-sharing (premiums, deductibles, coinsurance, and co-pay). CMS automatically enrolls these qualified individuals into PDPs with premiums at or below the regional average (also known as low-income benchmark plans).
   - **Specified Low Income Medicare Beneficiary (SLMB) Program** — Eligibility for the SLMB program automatically qualifies an individual for LIS. The SLMB program helps pay for Part B premiums only.
   - **Qualified Individual (QI) Program** — Eligibility for the QI program automatically qualifies an individual for LIS. The QI program helps pay for Part B premiums only.
   - **Qualified Disabled and Working Individuals (QDWI) Program** — Helps pay Part A premiums for individuals that are disabled and working.

3. Beneficiaries receiving Supplemental Security Income (SSI) from the Social Security Administration. SSI patients receive support from both Medicare and Medicaid.

Again, some people, such as individuals who are dual eligible for Medicaid and Medicare, are automatically enrolled in the LIS program. However, many people who are eligible for LIS are not aware of the program and are not enrolled. People who are not automatically enrolled can apply for LIS.

### IMPORTANT SAFETY INFORMATION (continued)

**Pathological Gambling and Other Compulsive Behaviors:** Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping ARISTADA if a patient develops such urges.

**Orthostatic Hypotension:** Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

**Falls:** Antipsychotics including ARISTADA may cause somnolence, postural hypotension, or motor and sensory instability, which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Questions to help determine if a patient is enrolled in or eligible for LIS

Here are some questions to ask patients to help determine whether they are enrolled in LIS:

• How much do you pay for your prescriptions at the pharmacy?
  If the response is in the range of $1 to $8, they may be receiving LIS

• Could you show me all of your insurance cards, including the card you use at the pharmacy for prescriptions?
  If the patient has both Medicaid and Medicare cards, he or she may be eligible for or already receiving LIS

To help patients learn more about the LIS program, especially if they may be eligible, encourage them to:

• Visit www.socialsecurity.gov/extrahelp

• Contact the Social Security Administration (SSA) at 1-800-772-1213, where they can speak to a customer service representative for help with the application

• Contact the state Medicaid program

ARISTADA Care Support can help determine coverage for patients who may qualify as dual eligible. Call 1-866-ARISTADA (1-866-274-7823) for more information.

IMPORTANT SAFETY INFORMATION (continued)

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm³) and follow their WBC until recovery.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Most commercial insurance plans, including those offered through the healthcare exchange, or marketplace, cover professional services by healthcare providers as a standard benefit. Benefit design and coverage restrictions vary by plan, including patient co-pay, coinsurance, and deductible requirements.

Commercial payers may cover ARISTADA® (aripiprazole lauroxil) under either the medical or pharmacy benefit, or may require that ARISTADA be obtained through a specialty pharmacy. Thoroughness during the benefit verification process can help patients obtain medications they need in a timely manner.

**Commercially insured patient cost-sharing/financial responsibility for ARISTADA**

For patients covered by a commercial insurance plan, cost-sharing will depend on benefit coverage. If the payer covered ARISTADA under the medical benefit, the patient may only be responsible for the office visit co-pay. Patients also may be responsible for a co-pay or coinsurance for the medication. If ARISTADA is covered under the pharmacy benefit, the patient may be responsible for the plan’s designated co-pay or coinsurance for the medication.

Complete information about each patient’s cost-sharing obligations for treatment with ARISTADA should be obtained during the initial benefit verification process.

**Appealing coverage decisions from commercial payers**

For patients with commercial insurance, the process for appealing a coverage decision will be plan specific, although plans are required by law to have a defined appeals process. ARISTADA Care Support is available to assist with coverage, claims, and appeals for treatment with ARISTADA.

**IMPORTANT SAFETY INFORMATION (continued)**

**Seizures:** ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

**Potential for Cognitive and Motor Impairment:** ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain ARISTADA does not affect them adversely.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Coding for ARISTADA: An Overview

When submitting claims for a patient’s treatment with ARISTADA® (aripiprazole lauroxil), it is important to use codes that accurately reflect the patient’s condition, treatment, and other services rendered. Different coding systems are used to describe a patient’s medical condition, the drugs administered, and services provided. Submission of claims with inaccurate or incomplete codes may result in delayed or incorrect payment or denial of claims. This section of the ARISTADA reimbursement guide describes a general approach for providers to coding claims for treatment with ARISTADA using nationally recognized code sets. Additional details about site-specific variations in coding are discussed in the Sites of care and claim forms section of this guide.

This is not a guarantee of payment, coverage, or reimbursement. Alkermes does not provide any advice, recommendation, guarantee, or warranty relating to coverage, reimbursement, or coding for any product or service. Healthcare providers are responsible for determining coverage and reimbursement information and ensuring the accuracy and completeness of claim submissions for their patients. Coding, coverage, and reimbursement vary significantly by payer, patient, and setting of care and are subject to change. Additional information may exist. Actual coverage and reimbursement decisions are made by individual payers.

IMPORTANT SAFETY INFORMATION (continued)

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
National Drug Codes (NDCs)

The U.S. Food and Drug Administration (FDA) has established a list of unique, 3-segment numbers that identify all drugs available for commercial distribution in the U.S. called the NDC Directory. Many payers require the use of NDCs on claim submissions for provider-administered drugs. In some cases, the NDC code may be required instead of, or in addition to, the Healthcare Common Procedure Coding System (HCPCS) code.

The NDCs for ARISTADA® (aripiprazole lauroxil) are as follows:

<table>
<thead>
<tr>
<th>Dosage Strength</th>
<th>11-digit NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>441 mg</td>
<td>65757-0401-03</td>
</tr>
<tr>
<td>662 mg</td>
<td>65757-0402-03</td>
</tr>
<tr>
<td>882 mg</td>
<td>65757-0403-03</td>
</tr>
<tr>
<td>1064 mg</td>
<td>65757-0404-03</td>
</tr>
</tbody>
</table>

IMPORTANT SAFETY INFORMATION (continued)

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Billing for treatment with ARISTADA: HCPCS codes

HCPCS Level II codes are a standardized coding system for identifying medically related items and services. Prescription drugs are typically reported using product-specific HCPCS codes. These codes are assigned by CMS. Medicare, Medicaid, and most commercial payers require the use of HCPCS codes to report provider-administered drugs and facilitate coverage and payment determinations. Effective January 1, 2017, ARISTADA® (aripiprazole lauroxil) has been assigned the J-Code, J1942. This code should be used on a medical claim form when purchasing and administering ARISTADA.

<table>
<thead>
<tr>
<th>HCPCS code</th>
<th>Description</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1942</td>
<td>Injection, aripiprazole lauroxil, 1 mg</td>
<td>Most payers and care settings</td>
</tr>
</tbody>
</table>

When submitting a claim to a Medicare Administrative Contractor (MAC), if the MAC requires pricing or other additional information, it will issue an Additional Documentation Request (ADR). Your site should be prepared to provide the additional information requested in a timely manner if an ADR is issued.

The ADR may request information such as clinical notes, invoice, or a Letter of Medical Necessity.

NATIONAL PROVIDER IDENTIFIER (NPI)

The NPI is a unique 10-digit, intelligence-free numeric identifier used to identify each covered healthcare provider. NPIs must be used for all administrative and financial transactions adopted as a result of the Health Insurance Portability and Accountability Act (HIPAA) Administrative Simplification Standard by all covered healthcare providers, health plans, and healthcare clearinghouses. It is important to verify that each claim is billed with the performing provider’s assigned NPI.

NPI information is centralized within the National Plan and Provider Enumeration System (NPPES) registry, which enables you to search for a provider’s NPPES information. For more information, visit https://npiregistry.cms.hhs.gov/.

IMPORTANT SAFETY INFORMATION (continued)

Concomitant Medication: Decreasing the ARISTADA dosage is recommended in patients taking strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for longer than 2 weeks. Increasing the ARISTADA dosage from 441 mg to 662 mg is recommended in patients taking CYP3A4 inducers for longer than 2 weeks. No ARISTADA dosage changes are recommended for patients taking CYP450 modulators for less than 2 weeks.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
American Psychiatric Association, Diagnostic and Statistical Manual (DSM) code set

Mental health professionals use the DSM standard classification of mental disorders in clinical practice and research. These codes are not intended for billing use unless directed by the payer.

**DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS, 5TH EDITION (DSM-5): DSM CODE SET**

The DSM diagnosis codes for mental health disorders were updated, as of May 2013, in the DSM-5. DSM-5 codes and descriptors should be used as required by the payer.

<table>
<thead>
<tr>
<th>DSM-5 Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F20.9</td>
<td>Schizophrenia</td>
</tr>
</tbody>
</table>

**Diagnostic Codes**

The International Classification of Diseases (ICD) code sets are used by most provider offices and CMHCs to report a patient’s specific mental health disorder. Some may also use DSM-5 codes within the patient’s medical record or supporting clinical documentation. Selection of appropriate codes should be supported by the patient’s medical record and the healthcare professional’s clinical judgment. Check with individual payers about any questions about coding documentation for a particular patient.

**IMPORTANT SAFETY INFORMATION (continued)**

**Most Commonly Observed Adverse Reaction:** The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg monthly) was akathisia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
INTERNATIONAL CLASSIFICATION OF DISEASES, 10TH REVISION, CLINICAL MODIFICATION (ICD-10-CM)\(^2\)

Prior to October 1, 2015, payers were required to use the ICD-9-CM diagnosis code set. **For services delivered on or after October 1, 2015,** all claims for services submitted to payers that use the ICD-CM code set are required to use the ICD-10-CM diagnosis code set, which includes codes such as those listed in the table below.

<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F20.0</td>
<td>Paranoid schizophrenia</td>
</tr>
<tr>
<td>F20.1</td>
<td>Disorganized schizophrenia</td>
</tr>
<tr>
<td>F20.2</td>
<td>Catatonic schizophrenia</td>
</tr>
<tr>
<td>F20.3</td>
<td>Undifferentiated schizophrenia</td>
</tr>
<tr>
<td>F20.5</td>
<td>Residual schizophrenia</td>
</tr>
<tr>
<td>F20.89</td>
<td>Other schizophrenia</td>
</tr>
<tr>
<td>F20.9</td>
<td>Unspecified schizophrenia</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (continued)**

**Injection-Site Reactions:** Injection-site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection-site pain and associated with the first injection and decreased with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) occurred at less than 1%.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Current Procedural Terminology codes and ICD Procedure Codes: administration/intramuscular injection procedure codes in the outpatient and inpatient settings

The use of procedure codes for intramuscular injections can vary by sites of care and payer.

To report the administration of an intramuscular injection of ARISTADA® (aripiprazole lauroxil) in the office setting with direct physician or other qualified health professional supervision, it may be appropriate to use the following:

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Code Set</strong></td>
</tr>
<tr>
<td>CPT® code*</td>
</tr>
</tbody>
</table>

*CPT®=Current Procedural Terminology. CPT® is a registered trademark of the American Medical Association.
* This code is not intended to be reported by the physician in the facility setting.
† ARISTADA is administered as an IM injection only.

It may also be appropriate for hospitals to use CPT® code 96372 when reporting the facility fee associated with administration of the injection to an outpatient.23

To report the administration of an intramuscular injection of ARISTADA in the inpatient hospital setting, payers may require ICD procedure codes.24 The following ICD procedure codes may be appropriate to report the administration of ARISTADA in the inpatient hospital setting:

<table>
<thead>
<tr>
<th>Procedure Codes: Inpatient Hospital Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedure Code Set</strong></td>
</tr>
<tr>
<td>ICD-10-PCS25</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (continued)**

**Dystonia:** Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Other codes that may be appropriate for billing for ARISTADA

Depending on the site of care, providers may need to use a variety of codes to bill for other types of services provided to a patient. Rules regarding coverage and payment for services vary according to payer and should be verified before submitting claims.

Hospital Outpatient and Ambulatory Payment Classifications

Under the Medicare hospital OPPS, most services are reimbursed based on groups of procedures known as Ambulatory Payment Classifications (APCs). The table below shows the mapping of HCPCS codes to APC that may be appropriate for treatment with ARISTADA® (aripiprazole lauroxil).

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Maps to APC</th>
<th>HCPCS Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9637223</td>
<td>0436</td>
<td>Therapeutic, prophylactic, or diagnostic injection; subcutaneous or intramuscular*</td>
</tr>
<tr>
<td>J194219</td>
<td>9470</td>
<td>Injection, aripiprazole lauroxil, 1 mg</td>
</tr>
</tbody>
</table>

* ARISTADA is administered as an IM injection only.

REVENUE CODES

Hospitals report revenue codes on the UB-04 claim form (or its electronic equivalent) to categorize services by revenue center. Revenue codes can be used in both the inpatient and outpatient hospital setting. Payers use revenue codes to capture hospital cost data. Many payers require that claims include revenue codes for some or all services provided in the hospital setting. Examples of revenue codes that may be relevant for the administration of ARISTADA in the hospital setting are shown in the following table.

<table>
<thead>
<tr>
<th>Revenue Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0250</td>
<td>General classification, pharmacy</td>
</tr>
<tr>
<td>0510</td>
<td>Clinic</td>
</tr>
<tr>
<td>0636</td>
<td>Drugs requiring detailed coding</td>
</tr>
</tbody>
</table>

IMPORTANT SAFETY INFORMATION (continued)

Pregnancy/Nursing: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA during pregnancy. Aripiprazole is present in human breast milk. The benefits of breastfeeding should be considered along with the mother’s clinical need for ARISTADA and any potential adverse effects on the infant from ARISTADA or from the underlying maternal condition.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
**CPT® Codes: Evaluation and Management Services (E/M)**

A provider office, CMHC, or hospital outpatient clinic may sometimes also bill for an E/M or office visit, in addition to the drug and administration service if there is a separately identifiable reason for the E/M service. Determination of the E/M category (e.g., new vs established patient, hospital inpatient vs hospital outpatient vs hospital observation care) and the level of service to report is up to the discretion of the individual healthcare professional. The separate service should be clearly documented in the patient’s medical record and an appropriate E/M code used. The CPT® Manual, available from the American Medical Association (AMA), can provide guidance to provider offices regarding selection of the correct E/M code for each patient visit.

<table>
<thead>
<tr>
<th>Select E/M codes</th>
<th>Description</th>
</tr>
</thead>
</table>
| 99212 | Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components:  
- A problem-focused history  
- A problem-focused examination  
- Straightforward medical decision-making  
Counseling and/or coordination of care with other physicians, other qualified healthcare professionals, or agencies are provided consistent with the nature of the problem(s) and the patient’s family’s needs. Usually, the presenting problem(s) are self-limited or minor. Typically 10 minutes are spent face-to-face with the patient and/or family. |
| 99213 | Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components:  
- An expanded problem-focused history  
- An expanded problem-focused examination  
- Medical decision-making of low complexity  
Counseling and/or coordination of care with other physicians, other qualified healthcare professionals, or agencies are provided consistent with the nature of the problem(s) and the patient’s family’s needs. Usually, the presenting problem(s) are of low to moderate severity. Typically 15 minutes are spent face-to-face with the patient and/or family. |
| 99214 | Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components:  
- A detailed history  
- A detailed examination  
- Medical decision-making of moderate complexity  
Counseling and/or coordination of care with other physicians, other qualified healthcare professionals, or agencies are provided consistent with the nature of the problem(s) and the patient’s family’s needs. Usually, the presenting problem(s) are of moderate to high severity. Typically 25 minutes are spent face-to-face with the patient and/or family. |

**Contraindication:** Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

**Cerebrovascular Adverse Reactions, Including Stroke:** Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
E/M CODE MODIFIER

When an E/M service is provided separately from a procedural service, a modifier may be used to identify the separate service provided. The modifier -25 (significant, separately identifiable evaluation and management service by the same physician on the same day of the procedure or other service) may be appropriate for patients receiving other services in addition to treatment with ARISTADA® (aripiprazole lauroxil). The healthcare professional’s site should consult with a patient’s payer to identify whether it will cover an office visit on the same day as other healthcare professional services and the appropriate modifier codes to use. In some circumstances, it may be appropriate to report psychiatric services or procedures in lieu of, or in addition to, E/M services. These services are described by CPT® codes 90791 – 90899. See the current edition of CPT® for descriptions of these codes and guidelines for their use.

ADDITIONAL CPT® CODES: TRANSITIONAL CARE MANAGEMENT (TCM)

There are 2 current CPT® codes for TCM that support transitions of care associated with the management of patients who have recently been discharged from a hospital, skilled nursing facility, or CMHC stay. The codes include services provided to a patient with medical and/or psychosocial problems that necessitate moderate- or high-complexity medical decision-making during a care transition from a hospital setting to the patient’s community setting. Inpatient hospital settings include acute hospital, rehabilitation hospital, long-term acute care hospital, partial hospitalization, observation status while in a hospital, or skilled nursing facility/nursing facility. The community setting includes a patient’s home, domicile, or other assisted living facility.

The codes permit reporting of time spent discussing a patient’s care plan, connecting patients to community services, transitioning a patient from an inpatient setting, and discussions to prevent readmissions.

<table>
<thead>
<tr>
<th>Select E/M codes</th>
<th>Description</th>
</tr>
</thead>
</table>
| 99495            | Includes communication via direct contact, telephone, or electronic means with the patient and/or caregiver within 2 business days of discharge. Additionally, includes the following requirements:  
• Medical decision-making is at least of a moderate complexity during the service period  
• Face-to-face visit within 14 calendar days of discharge |
| 99496            | Includes communication via direct contact, telephone, or electronic means with the patient and/or caregiver within 2 business days of discharge. Additionally, includes the following requirements:  
• Medical decision-making of high complexity during the service period  
• Face-to-face visit within 7 calendar days of discharge |


IMPORTANT SAFETY INFORMATION (continued)

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Place of Service (POS) Codes

POS codes are used on claims to designate where a service is rendered. Different codes may be appropriate for physician offices, non–Medicare-certified CMHCs, and hospital outpatient clinics.

The POS codes that may commonly be used for treatment with ARISTADA® (aripiprazole lauroxil) are:

- POS 11 – Office
- POS 21 – Inpatient Hospital
- POS 22 – Outpatient Hospital
- POS 52 – Psychiatric Facility-Partial Hospitalization
- POS 53 – Community Mental Health Center

### IMPORTANT SAFETY INFORMATION (continued)

**Tardive Dyskinesia (TD):** The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

### Place of Service (POS) Codes

<table>
<thead>
<tr>
<th>POS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS 11</td>
<td>Office</td>
</tr>
<tr>
<td></td>
<td>This code applies to healthcare professional offices or other sites that provide services to patients who do not require hospitalization.</td>
</tr>
<tr>
<td>POS 14</td>
<td>Group Home</td>
</tr>
<tr>
<td></td>
<td>A residence, with shared living areas, where clients receive supervision and other services such as social and/or behavioral services, custodial service, and minimal services (e.g., medication administration).</td>
</tr>
<tr>
<td>POS 17</td>
<td>Walk-in Retail Health Clinic</td>
</tr>
<tr>
<td></td>
<td>A walk-in health clinic, other than an office, urgent care facility, pharmacy, or independent clinic, and not described by any other Place of Service code, that is located within a retail operation and provides, on an ambulatory basis, preventive and primary care services.</td>
</tr>
<tr>
<td>POS 21</td>
<td>Inpatient Hospital</td>
</tr>
<tr>
<td></td>
<td>A facility, other than psychiatric, which primarily provides diagnostic, therapeutic, and rehabilitation services. Physicians provide or supervise services to admitted patients for a variety of medical conditions.</td>
</tr>
<tr>
<td>POS 22</td>
<td>Outpatient Hospital</td>
</tr>
<tr>
<td></td>
<td>This code applies to outpatient sites of care where the patient is not required to be hospitalized or institutionalized.</td>
</tr>
<tr>
<td>POS 26</td>
<td>Military Treatment Facility</td>
</tr>
<tr>
<td></td>
<td>A medical facility operated by one or more of the Uniformed Services. Military Treatment Facility (MTF) also refers to certain former U.S. Public Health Service (USPHS) facilities not designated as Uniformed Service Treatment Facilities (USTF).</td>
</tr>
</tbody>
</table>
POS code | Description
--- | ---
POS 50 | Federally Qualified Health Center
A facility located in a medically underserved area that provides Medicare beneficiaries with preventive primary medical care under the general direction of a physician.

POS 51 | Inpatient Psychiatric Facility
A facility that provides inpatient psychiatric services for the diagnosis and treatment of mental illness on a 24-hour basis, by or under the supervision of a physician.

POS 52 | Psychiatric Facility-Partial Hospitalization
A facility for the diagnosis and treatment of mental illness that provides a planned therapeutic program for patients who do not require full time hospitalization, but who need broader programs than are possible from outpatient visits to a hospital-based or hospital-affiliated facility.

POS 53 | Community Mental Health Center
A facility that provides the following services: outpatient services including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the CMHC’s mental health services area who have been discharged from inpatient treatment at a mental health facility; 24-hour-a-day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to state mental health facilities to determine the appropriateness of such admission; and consultation and education services.

POS 56 | Psychiatric Residential Treatment Center
A facility or distinct part of a facility for psychiatric care that provides a 24-hour therapeutically planned and professionally staffed group living and learning environment.

POS 71 | Public Health Clinic
A facility maintained by either state or local health departments that provides ambulatory primary medical care under the general direction of a physician.

Please refer to the POS guidance document published by CMS for additional information and descriptions associated with specific POS codes. This document can be accessed at: [http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/Website-POS-database.pdf](http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/Website-POS-database.pdf).

**IMPORTANT SAFETY INFORMATION (continued)**

**Metabolic Changes:** Atypical antipsychotic drugs have been associated with metabolic changes that include:
- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.
Provider office or Community Mental Health Center (CMHC)*

Coverage for ARISTADA® (aripiprazole lauroxil) administered in a CMHC or provider’s office varies by payer type.

State Medicaid programs use a variety of different reimbursement methods, including fee schedules, discounted charges, or other predetermined rates. Reimbursement for drugs is separate from professional services and may be based on Wholesale Acquisition Cost (WAC), invoice cost, a percentage of Average Sales Price (ASP), Average Wholesale Price (AWP), or other variable formulas as determined by the individual payer. Contact the state Medicaid program for more information about state-specific coverage for ARISTADA in the CMHC or provider office.

Patients covered by Medicare plans, including those who qualify for benefits under Medicare and Medicaid, may have coverage for ARISTADA under either Part D or Part B. Reimbursement for drugs under Part B is separate from professional services and is generally based on ASP. Coverage of ARISTADA under Part D will vary by plan, depending on formulary and benefit design.

Commercial plans use a variety of different reimbursement methods, including fee schedules, discounted charges, or other predetermined rates. Reimbursement for drugs is separate from professional services and may be based on WAC, AWP, invoice cost, a percentage of ASP, or other payer-specific methodologies. Contact the commercial plan or review the payer contract for more information about specific coverage for ARISTADA in the CMHC or provider office.

*For Medicare billing purposes, this section refers to CMHCs that function as a clinic and are not certified by Medicare to provide partial hospitalization services.

This is not a guarantee of payment, coverage, or reimbursement. Alkermes does not provide any advice, recommendation, guarantee, or warranty relating to coverage, reimbursement, or coding for any product or service. Healthcare providers are responsible for determining coverage and reimbursement information and ensuring the accuracy and completeness of claim submissions for their patients. Coding, coverage, and reimbursement vary significantly by payer, patient, and setting of care and are subject to change. Additional information may exist. Actual coverage and reimbursement decisions are made by individual payers.

IMPORTANT SAFETY INFORMATION (continued)

- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping ARISTADA if a patient develops such urges.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Codi‌ng for treatment with ARISTADA: claim forms CMS-1500/837P (physician offices and CMHCs)

The 837P (Professional) is the standard format used by healthcare professionals and suppliers to transmit claims electronically. The form CMS-1500 is the standard paper claim form used to bill most insurance carriers, including Medicare, Medicaid, and commercial carriers when a paper claim is allowed. Data elements in the CMS uniform electronic billing specifications for 837P are consistent with the hard copy data set. Healthcare professionals and other qualified providers should submit all electronic claims using the 837P claims format, following ANSI ASC X12N 837P Version 5010A1 electronic data interchange transaction standards. Healthcare providers in a healthcare professional’s office who treat Medicare beneficiaries may use Form CMS-1500 (02/12) for most payers who accept paper claims if a paper claim is necessary.

<table>
<thead>
<tr>
<th>ARISTADA® (aripiprazole lauroxil) Dosage Strengths and NDCs1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage Strength</strong></td>
</tr>
<tr>
<td>![Image]</td>
</tr>
<tr>
<td>![Image]</td>
</tr>
<tr>
<td>![Image]</td>
</tr>
<tr>
<td>![Image]</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (continued)**

**Falls:** Antipsychotics including ARISTADA may cause somnolence, postural hypotension, or motor and sensory instability, which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

**Leukopenia, Neutropenia, and Agranulocytosis:** Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm³) and follow their WBC until recovery.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
The following information highlights some of the key product-specific fields in the 837P and the coordinating location on the CMS-1500 for Medicare claims reporting purposes. Please check with other payers for specific details and processes for use of appropriate forms and processes.

<table>
<thead>
<tr>
<th>Code Set</th>
<th>Code</th>
<th>Description</th>
<th>Settings of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS&lt;sup&gt;19&lt;/sup&gt;</td>
<td>J1942</td>
<td>Injection, aripiprazole lauroxil, 1 mg</td>
<td>Most payers and care settings</td>
</tr>
</tbody>
</table>

### Diagnostic Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F20.0</td>
<td>Paranoid schizophrenia</td>
</tr>
<tr>
<td>F20.1</td>
<td>Disorganized schizophrenia</td>
</tr>
<tr>
<td>F20.2</td>
<td>Catatonic schizophrenia</td>
</tr>
<tr>
<td>F20.3</td>
<td>Undifferentiated schizophrenia</td>
</tr>
<tr>
<td>F20.5</td>
<td>Residual schizophrenia</td>
</tr>
<tr>
<td>F20.89</td>
<td>Other schizophrenia</td>
</tr>
<tr>
<td>F20.9</td>
<td>Unspecified schizophrenia</td>
</tr>
</tbody>
</table>

### Procedural Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96372</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
</tr>
</tbody>
</table>

CMHC=Community Mental Health Center.
ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification.
CPT<sup>®</sup>=Current Procedural Terminology. CPT<sup>®</sup> is a registered trademark of the American Medical Association.
* This code is not intended to be reported by the physician in the facility setting.
† ARISTADA is administered as an IM injection only.

### IMPORTANT SAFETY INFORMATION (continued)

**Seizures:** ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

**Potential for Cognitive and Motor Impairment:** ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain ARISTADA does not affect them adversely.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
### Quick Reference Table for CMS-1500/837P

<table>
<thead>
<tr>
<th>Field/Category Name</th>
<th>Example</th>
<th>837P Loop ID, Segment/Data Element</th>
<th>CMS-1500 (02/12) Field Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures, Services, or Supplies (e.g., HCPCS code)</td>
<td>J1942</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedures, Services, or Supplies (e.g., NDCs)</td>
<td>ARISTADA 441 mg: NDC 65757-0401-03 662 mg: NDC 65757-0402-03 882 mg: NDC 65757-0403-03 1064 mg: NDC 65757-0404-03</td>
<td>Loop 2400/SV101</td>
<td>Field 24D</td>
</tr>
<tr>
<td>Procedures, Services, or Supplies (e.g., CPT® code)</td>
<td>96372 therapeutic, prophylactic, or diagnostic injection†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Units</td>
<td>441 units for 441 mg 662 units for 662 mg 882 units for 882 mg 1064 units for 1064 mg</td>
<td>Loop 2400/SV104</td>
<td>Field 24G</td>
</tr>
<tr>
<td>Diagnosis or Nature of Illness or Injury</td>
<td>F20.x</td>
<td>Loop 2300/HI01-2 to HI12-2</td>
<td>Field 21</td>
</tr>
</tbody>
</table>


* All examples indicated should also include any placeholder digits required by the 837P format.
† This code is not intended to be reported by the physician in the facility setting.
‡ ARISTADA is administered as an IM injection only.

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**IMPORTANT SAFETY INFORMATION (continued)**

**Body Temperature Regulation:** Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Compressing the CMS-1500 Claim Form (Physician Office Billing)

1. **DIAGNOSIS CODE (Field 21)**
   Enter appropriate ICD-10-CM code for schizophrenia (F20.x) and any additional codes appropriate for the patient.

2. **ICD INDICATOR (Field 21)**
   Enter “0” for ICD-10 codes.

3. **PRIOR AUTHORIZATION NUMBER (Field 23)**
   Document Prior Authorization number issued by the payer.

4. **PRODUCT CODE (Field 24D)**
   Document product use with HCPCS code, J1942.

5. **DIAGNOSIS POINTER (Field 24E)**
   Specify diagnosis, from Field 21, for each HCPCS/CPT® code listed.

6. **SERVICE UNITS (Field 24G)**
   Report number of units of ARISTADA® (aripiprazole lauroxil) (one unit of J1942 is equal to 1 mg):
   - 441 units for 441 mg
   - 662 units for 662 mg
   - 882 units for 882 mg
   - 1064 units for 1064 mg
   Note: Some payers may require a drug to be billed over two lines due to limitations in the amount of digits allowed in Field 24G – For example, bill one line of J1942 with 999 Service Units and bill a second line of J1942 with 65 Service Units.

7. **PROCEDURE CODE (Field 24D)**
   Document administration of ARISTADA with CPT® code 96372 (therapeutic, prophylactic, or diagnostic injection [specify substance or drug], subcutaneous or intramuscular†).

8. **ADDITIONAL CLAIM INFORMATION (Field 19)**
   This field should be filled out when a payer requires split billing for 4 digit service units.
   Input: ARISTADA (aripiprazole lauroxil) NDC 65757-0404-03, 1064 mg, IM.

CPT® = Current Procedural Terminology, CPT® is a registered trademark of the American Medical Association.
† ARISTADA is administered as an IM injection only.

**IMPORTANT SAFETY INFORMATION (continued)**

**Dysphagia:** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Hospital outpatient or partial hospitalization CMHCs

Coverage for ARISTADA® (aripiprazole lauroxil) when administered in the hospital outpatient (POS 22), Psychiatric Facility-Partial Hospitalization (POS 52), or partial hospitalization in the CMHC setting (POS 53) may vary by payer type. Organizations should use the appropriate POS code based on their structure or services or otherwise consistent with their organizational guidance when filing claims.

State Medicaid programs use a variety of payment methodologies: Maximum Allowable Cost (MAC) cost-sharing limits, discounted charges, or other predetermined rates. Drugs administered in the hospital outpatient setting may be reimbursed separately from professional services based on a set rate, such as Wholesale Acquisition Cost (WAC), Average Wholesale Price (AWP), invoice cost, or a percentage of Average Sales Price (ASP). Actual reimbursement methodologies vary by state and healthcare professionals should contact the state Medicaid program for more information about coverage for ARISTADA.

Medicare beneficiaries, those who are dual eligible, generally have coverage for hospital outpatient services under Part B. Reimbursement is based on the hospital OPPS and payment is based on APCs. Coverage and reimbursement may also vary according to facility designation: hospital or partial hospitalization setting. Medicare has specific criteria for what it will cover under Part B as “partial hospitalization” services and recently updated its definition of the criteria CMHCs must meet to qualify as providers of partial hospitalization services (see box on next page). CMHCs that meet the Medicare criteria may be able to bill Medicare for partial hospitalization through hospital OPPS.¹⁰

Commercial payers may reimburse services and drugs provided in the hospital outpatient and partial hospitalization settings in a variety of ways, including fee schedules based on payer contract, usual and customary charges, a percentage of WAC, AWP, ASP, or other prenegotiated rates.

IMPORTANT SAFETY INFORMATION (continued)

Most Commonly Observed Adverse Reaction: The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg monthly) was akathisia.
Hospital outpatient or partial hospitalization coding for treatment with ARISTADA: claim form UB-04/CMS-1450/837I

The 837I (Institutional) is the standard format used by institutional providers to transmit claims electronically. The form UB-04, also known as the CMS-1450, is the standard claim form to bill Medicare Administrative Contractors (MACs) when a paper claim is allowed. Data elements in the CMS uniform electronic billing specifications for 837I are consistent with the hard copy data set.

The 837I and UB-04 also may be suitable for billing various government and some commercial insurers. Please check with Medicaid programs and private payers for specific details and processes.

Medicare criteria for CMHC to provide partial hospitalization services (POS 53)

A CMHC may receive Medicare payment for partial hospitalization services if:

- It provides outpatient services, including specialized outpatient services for children, elderly individuals, individuals with chronic mental illness, and residents of the community that have been discharged from inpatient treatment at a mental health facility
- It provides 24-hour-a-day emergency care
- It provides day treatment, partial hospitalization, or psychosocial rehabilitation services
- It provides screening and evaluation for clients being considered for admission to state mental health facilities
- It provides at least 40% of its services to individuals who are not eligible for benefits under Medicare
- Services are furnished under the general supervision of a physician
- Services are subject to certification that the individual patient would require inpatient psychiatric care if partial hospitalization services were not provided
- Services are provided under an individualized treatment plan

Hospital outpatient or partial hospitalization coding for treatment with ARISTADA: claim form UB-04/CMS-1450/837I

The 837I (Institutional) is the standard format used by institutional providers to transmit claims electronically. The form UB-04, also known as the CMS-1450, is the standard claim form to bill Medicare Administrative Contractors (MACs) when a paper claim is allowed. Data elements in the CMS uniform electronic billing specifications for 837I are consistent with the hard copy data set.

The 837I and UB-04 also may be suitable for billing various government and some commercial insurers. Please check with Medicaid programs and private payers for specific details and processes.

Medicare criteria for CMHC to provide partial hospitalization services (POS 53)

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- Services are furnished under the general supervision of a physician
- Services are subject to certification that the individual patient would require inpatient psychiatric care if partial hospitalization services were not provided
- Services are provided under an individualized treatment plan

IMPORTANT SAFETY INFORMATION (continued)

Injection-Site Reactions: Injection-site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection-site pain and associated with the first injection and decreased with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) occurred at less than 1%.

Dystonia: Symptons of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
**Quick Reference Table for UB-04/CMS-1450/837I**

<table>
<thead>
<tr>
<th>Field/Category Name</th>
<th>Example</th>
<th>837I Loop ID, Segment/Data Element</th>
<th>UB-04/CMS-1450</th>
</tr>
</thead>
</table>
| Revenue Code        | • Medicare, revenue code 0636 (drugs that require detailed coding)  
                     • For non-Medicare payers, revenue code 0250 (general pharmacy)  
                     • Injection services may be reported with revenue code 0510 (clinic, general service) | Loop 2400, SV201 | Field 42 |
| Description         | Medicare requirements for claims crossing over to Medicaid include the NDC qualifier N4 followed by the 11-digit NDC (e.g., N465757-XXXX-03) | Check with payer (instructions may vary) | Field 43 |
| HCPCS Code          | J1942   | Loop 2400, SV202-2                | Field 44 |
| CPT® Code*          | 96372 (therapeutic, prophylactic, or diagnostic injection)† | Loop 2400, SV205 | Field 46 |
| Service Units       | 441 units for 441 mg  
                     662 units for 662 mg  
                     882 units for 882 mg  
                     1064 units for 1064 mg | Loop 2300, HI01-2  
                     (HI01-1=8K) | Fields 67A-Q |
| Diagnosis           | F20.x |                                  |                |


* This code is not intended to be reported by the physician in the facility setting.

† ARISTADA is administered as an IM injection only.

**IMPORTANT SAFETY INFORMATION (continued)**

**Pregnancy/Nursing:** May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA during pregnancy. Aripiprazole is present in human breast milk. The benefits of breastfeeding should be considered along with the mother’s clinical need for ARISTADA and any potential adverse effects on the infant from ARISTADA or from the underlying maternal condition.

**Contraindication:** Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Sample the CMS-1450* Claim Form (Institutional Billing)

Please verify with the payer any character/digit limitations, e.g., 3-digit limitation in Field 46 (Service Units) when billing for the 1064 mg dose of ARISTADA.

Field 46

Some payers may not allow 4 digits in Field 46. Please confirm billing guidelines with the payer. Note: See sample below for split-line billing if payer cannot accept 4 digits in Field 46.

For payers that do not allow 4-digit billing in Field 46, please see the method below for billing the 1064 mg dose.

When billing 1064 units and payer requires 3 digits, split the units over 2 lines: 999 + 65 = 1064 units

Field 80

Should be utilized when the payer has confirmed split billing is necessary.


* This illustration represents excerpts of the CMS-1450 form applicable to ARISTADA.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
REVENUE CODE (Field 42)
Enter the appropriate revenue code(s).
Revenue code examples:
- For Medicare, revenue code 0636 (drugs that require detailed coding) may be appropriate
- For Non-Medicare payers, revenue code 0250 (general pharmacy) may be appropriate
- Injection services may be reported with revenue code 0510 (clinic, general service)

DESCRIPTION (Field 43)
This field is not required. However, for Medicare claims where Medicaid is the secondary payer, Field 43 should be used to report drug rebate information for Medicaid crossover purposes. The format required by Medicare includes the NDC qualifier N4 followed by the 11-digit NDC in positions 01-13 (e.g., N465757-XXXX-03). Report the NDC quantity qualifier followed by the quantity beginning in position 14. The Description Field on Form CMS-1450 is 24 characters long.

HCPCS CODE (Field 44)
In Field 44, enter the applicable HCPCS or CPT® code (including any modifiers needed) to describe the drug and other separately billable services provided.
HCPCS: J1942 should be used for ARISTADA® (aripiprazole lauroxil)
HCPCS (CPT®) procedure example: 96372 (therapeutic, prophylactic, or diagnostic injection [specify substance or drug], subcutaneous or intramuscular†)

SERVICE UNITS (Field 46)
Report number of units of ARISTADA (one unit of J1942 is equal to 1 mg):
• 441 units for 441 mg
• 662 units for 662 mg
• 882 units for 882 mg
• 1064 units for 1064 mg

DIAGNOSIS AND PROCEDURE CODE QUALIFIER (Field 66)
Enter “0” to identify as an ICD-10 code.

DIAGNOSIS CODE (Field 67)
Enter the appropriate ICD-10 codes for schizophrenia, such as F20.x. This field should contain the ICD-10 diagnosis code that describes the primary reason that the patient is receiving the outpatient services described on the claim. Additional diagnosis codes should be included within Fields 67A-Q.

REMARKS (Field 80)
This field should be filled out when a payer requires split billing for 4-digit service units.
Input: ARISTADA (aripiprazole lauroxil) NDC 65757-0404-03, 1064 mg, IM.

IMPORTANT SAFETY INFORMATION (continued)
Cerebrovascular Adverse Reactions, Including Stroke: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
**Hospital outpatient and Ambulatory Payment Classifications (APCs)**

Under the Medicare hospital OPPS, most services are reimbursed based on groups of procedures known as Ambulatory Payment Classifications (APCs). The information in the table below shows the mapping of HCPCS codes entered onto the claim form to APCs that may be appropriate for treatment with ARISTADA® (aripiprazole lauroxil).

<table>
<thead>
<tr>
<th>HCPCS code</th>
<th>Maps to APC</th>
<th>HCPCS Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9637223</td>
<td>0436</td>
<td>Therapeutic, prophylactic, or diagnostic injection; subcutaneous or intramuscular*</td>
</tr>
<tr>
<td>J194219</td>
<td>9470</td>
<td>Injection, aripiprazole lauroxil, 1 mg</td>
</tr>
</tbody>
</table>

* ARISTADA is administered as an IM injection only.

**Checklist for submitting electronic or paper hospital claims for ARISTADA**

Prior to treatment or submitting a claim, ensure that all payer requirements for coverage are met, such as:

- Letter of Medical Necessity, if needed
  - Documentation, as needed, if a step edit exists
  - Attaching prescribing information
- Claim form completion and submission
  - Use the claim form and preferred format (e.g., electronic or paper) designated by the payer
  - Identify correct date of service
  - Provide correct and accurate coding
  - Correctly specify number of units
  - Provide the full documentation required by the payer including healthcare professional order if requested
  - Ensure documentation includes a valid and legible healthcare professional signature or acceptable e-signature
  - Submit claim within the payer’s designated claim filing time frame

**Channels for obtaining ARISTADA: hospital outpatient settings**

In most cases, drugs administered in the hospital outpatient setting will be obtained through normal hospital procurement channels. Contact ARISTADA Care Support (1-866-ARISTADA [1-866-274-7823]) or your Territory Business Manager for questions on how to obtain ARISTADA.

**IMPORTANT SAFETY INFORMATION (continued)**

**Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Hospital inpatient

Coverage for ARISTADA® (aripiprazole lauroxil) administered in the hospital inpatient setting varies by type of payer but is similar for both acute-care hospitals and psychiatric facilities. There are several primary payment methodologies used in the hospital inpatient setting:

- Diagnosis-Related Groups (DRGs)
  - Medicare Severity DRGs (MS-DRGs)
  - All Patient Refined DRGs (APR-DRGs)
- Global case rates
- Per diem rates

Medicaid

Medicaid regulations require that each state pay for inpatient hospital and long-term care services. Medicaid payment for inpatient services provided in general or psychiatric hospitals varies by state agency.

Medicare

Medicare reimburses for most hospital inpatient stays (except for psychiatric hospitals and most inpatient psychiatric units) according to a prospective payment system based on DRGs. These are determined by the ICD-10 diagnostic and procedure codes entered onto the claims form, which are then grouped to determine the appropriate MS-DRG. Most services and supplies provided during the stay, including medications, are bundled in the MS-DRG reimbursement rate. Hospitals receive one global MS-DRG payment per patient inpatient stay and under certain circumstances are also eligible for additional outlier payments. Drugs such as ARISTADA are typically not reimbursed separately.

Medicare reimburses qualified psychiatric hospitals and inpatient psychiatric units in acute care and Critical Access Hospitals on a per diem basis. As with the DRG system, the per diem method does not typically make separate reimbursement for drugs.33

Commercial

Commercial payers may cover inpatient treatment with ARISTADA in several different ways. Many payers use a global payment rate that includes most or all services and medications that are usually based on modified MS-DRGs and does not include a separate payment for drugs. Other commercial and managed care plans reimburse based on case rates, Usual, Customary and Reasonable (UCR) charges, discounted charges, or per diem rates. If you are researching coverage for ARISTADA for a hospital inpatient, contact the patient’s plan to determine if it will reimburse separately for medications provided in the hospital inpatient setting.

IMPORTANT SAFETY INFORMATION (continued)

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Payment Methodologies for Hospital Inpatient

<table>
<thead>
<tr>
<th>Medicaid</th>
<th>Medicare</th>
<th>Commercial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inpatient Hospital Payment</strong></td>
<td><strong>Inpatient Hospital Payment</strong></td>
<td><strong>Inpatient Hospital Payment</strong></td>
</tr>
<tr>
<td>• Payment methodology varies by state</td>
<td>• Bundled payment based on MS-DRGs except for inpatient psychiatric facilities and units, which are paid on a per diem basis</td>
<td>• Payment methodology varies by plan although most use a global rate or per diem rate</td>
</tr>
<tr>
<td>• Variations of DRG bundled-payment systems or per diems, such as MS-DRGs or APR-DRGs</td>
<td>• Payments will vary based on complications and comorbidities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• For more information, review the Medicare Prospective Payment System (PPS) fee schedule for hospital inpatient services at: <a href="http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PCPricer/inpatient.html">http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PCPricer/inpatient.html</a> Also see information related to the Inpatient Psychiatric Prospective Payment System at: <a href="https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/InpatientPsychFac.pdf">https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/InpatientPsychFac.pdf</a></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Inpatient Drug Payment</strong></th>
<th><strong>Inpatient Drug Payment</strong></th>
<th><strong>Inpatient Drug Payment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Drug payment is usually included in DRG or per diem bundled payments</td>
<td>• Drug payment is included in MS-DRG or per diem bundled payment</td>
<td>• Drug payment is usually included in DRG or per diem bundled payments</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (continued)**

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

• **Hyperglycemia/Diabetes Mellitus**: Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.
ARISTADA® (aripiprazole lauroxil) is a long-acting injectable antipsychotic for the treatment of schizophrenia, a severe mental illness. ARISTADA is a medication that was approved by the U.S. FDA in October 2015.

Payers often require PAs for mental health services. For antipsychotic medications, PAs generally are based on clinical criteria (e.g., the patient’s diagnosis and on-label use of the medication). Some payers allow the healthcare professional to request a PA by telephone, or to submit PA requests electronically. However, for treatments that are considered expensive, payers may require a written request for treatment and require specific documentation from the healthcare professional. Payers also may have specific forms that must be completed for a PA. The letter within this section is an example of a Letter of Medical Necessity (LOMN) for use when requesting PA or a formulary exception for ARISTADA.

In some cases and geographies, ARISTADA may be in a drug category that is protected to ensure patient access. Please refer to the Benefit Verification Tips section of this guide for more information about the importance of a thorough benefit investigation prior to treatment.

If, during the benefit investigation, it is determined that ARISTADA is listed as “not covered” on the payer’s formulary and a patient needs treatment with ARISTADA, the healthcare professional can submit an appeal for coverage, or a formulary exception.

General guidance for seeking prior authorization or a formulary exception is as follows:

• Ask the payer about the preferred format for PA requests and whether there is a product-specific or category-specific PA request form for long-acting injectable antipsychotics such as ARISTADA
• Determine the documentation the payer may accept to support the request, such as a Letter of Medical Necessity, patient history, and chart notes
• If unfamiliar with the coverage of ARISTADA, contact the payer to discuss coverage for the patient

ARISTADA Care Support is available to help identify a payer’s coverage and to assist in obtaining access for a patient. Contact the ARISTADA care support at (1-866-ARISTADA [1-866-274-7823]).

IMPORTANT SAFETY INFORMATION (continued)

• Dyslipidemia: Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
• Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping ARISTADA if a patient develops such urges.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
IMPORTANT SAFETY INFORMATION (continued)

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

Falls: Antipsychotics including ARISTADA may cause somnolence, postural hypotension, or motor and sensory instability, which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Sample LOMN to support prior authorization/formulary exception request for ARISTADA

Letter of Medical Necessity/Prior Authorization

Dear [Name of contact],

I am writing on behalf of my patient, [Patient name], to request prior authorization for ARISTADA® (aripiprazole lauroxil) long-acting injectable atypical antipsychotic. The patient will be treated with ARISTADA for [diagnosis]. ARISTADA is indicated for the treatment of schizophrenia.

This letter outlines medical history, prognosis, and treatment rationale.

Summary of Patient History:

- Patient's diagnosis, condition, and history:
- Previous treatments the patient has taken for the symptoms associated with [diagnosis]:
- Patient's response to previous treatments:
- Description of the patient's recent symptoms:
- Need for ARISTADA:

Based on these facts, ARISTADA is indicated and medically necessary for this patient. If you have further questions, please feel free to call me at [XX-XX-XXXX] to discuss.

Thank you in advance for your immediate attention to this request.

Sincerely,

[Name]

[Name of Practice]

[Address]

Please see additional Important Safety Information on the following pages and accompanying full Prescribing Information, including Boxed Warning.

IMPORTANT SAFETY INFORMATION (continued)

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm³) and follow their WBC until recovery.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Managing PA denials

If the healthcare professional receives a PA denial because a payer does not cover ARISTADA® (aripiprazole lauroxil), resubmit the request with additional documentation supporting medical necessity. The healthcare professional may also call ARISTADA Care Support at 1-866-ARISTADA (1-866-274-7823) for assistance.

If the healthcare professional has not done so previously, it is strongly recommended to include a detailed LOMN in the appeal packet. Please see the sample LOMN for examples of the types of information that should be included.

In addition, the healthcare professional should include a copy of the original PA request and denial notification; the patient’s complete medical history; the provider’s plan for continuing treatment; and relevant journal articles supporting the use of ARISTADA extended release injectable suspension.

If the second submission is denied, it may be necessary to contact the payer’s medical director. PA denials may be reversed following medical review of an accurate and complete appeal request.

Appealing a claim denial

If a claim for treatment with ARISTADA submitted by an office is improperly reimbursed or denied, providers may consider submitting an appeal. The following checklist provides some tips for appealing denied claims:

**Checklist for appealing denied claims**

- Review the Explanation of Benefits (EOB) to determine the reason for the claim denial
  - If additional information is requested, submit it immediately or within the required time frame for processing
- If the denial was due to a technical error, amend it and submit a corrected claim
- Verify the appeals process with the payer:
  - Does the payer require use of a specific form?
  - Can the appeal be conducted over the telephone?
  - If the appeal must be submitted in writing, to whom should it be directed?
  - What information must be included with the appeal (e.g., a copy of the original claim, EOB, LOMN, or other documentation)?
  - How long does the appeals process usually take?
  - How will the payer communicate the appeals decision?
- Review the appeal request for accuracy and completeness, including patient identification numbers, coding and additional information requested
- Request that a psychiatrist or other designated provider who is familiar with treating patients with ARISTADA review the appeal
- File the appeal as soon as possible and within filing time limits
- Reconcile responses to the appeal promptly and thoroughly to ensure an appeal has been processed appropriately
- Record appeals result (e.g., payment amount or if further action is required)

**IMPORTANT SAFETY INFORMATION (continued)**

**Seizures:** ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Sample appeals letter

Appeal Letter

Payer Contact Name: 
Title: 
Name of Health Insurance Company:  
Address: 
City, State, ZIP Code: 

Patient Information

Patient Name: 
Policy Number: 
Insured Name: 
Group Number: 

Schizophrenia Diagnosis Code(s):  

Claim Number:  

Dear:  

This letter serves as a request for reconsideration of payment for a claim representing charges for ARISTADA® (aripiprazole lauroxil) administered to 

Patient’s name has been under my treatment for schizophrenia. Because of I have administered ARISTADA as a medically necessary part of this patient’s treatment and request your reconsideration of the denied ARISTADA claim for . Please contact me at (XXX) XXX-XXXX if you require additional information.

Thank you in advance for your immediate attention to this request.

Sincerely,

Name 
Name of Practice 
Address of Practice 

Attachments:

Original Claim Form 
Letter of Medical Necessity 
Explanation of Benefits 
Additional Supporting Documents 

Please see additional Important Safety Information on the following pages and accompanying full Prescribing Information, including Boxed Warning.

IMPORTANT SAFETY INFORMATION (continued)

Potential for Cognitive and Motor Impairment: ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain ARISTADA does not affect them adversely.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Indication

ARISTADA is indicated for the treatment of schizophrenia.

Recommended dosing

Depending on individual patient’s needs, treatment with ARISTADA® (aripiprazole lauroxil) can be initiated at a dose of 441 mg, 662 mg or 882 mg administered monthly, 882 mg administered every 6 weeks, or 1064 mg administered every 2 months.

For patients who have never taken aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment with ARISTADA.

ARISTADA IM injection should be administered by a healthcare professional in either the deltoid muscle (441 mg only) or gluteal muscle (441 mg, 662 mg, 882 mg or 1064 mg).

For all dosage strengths, administer treatment with oral aripiprazole for 21 consecutive days in conjunction with the first ARISTADA injection.

Dose may be adjusted as needed. When making dose and dosing interval adjustments, the pharmacokinetics and prolonged-release characteristics of ARISTADA should be considered.

Early dosing

The recommended ARISTADA dosing interval is monthly for the 441 mg, 662 mg and 882 mg doses, every 6 weeks for the 882 mg dose, or every 2 months for the 1064 mg dose and should be maintained. In the event of early dosing, an ARISTADA injection should not be given earlier than 14 days after the previous injection.

Recommendations for missed doses

When any dose is missed, administer the next injection of ARISTADA as soon as possible. If the time elapsed since the last ARISTADA injection exceeds the length of time noted below, use the oral aripiprazole supplementation with the next ARISTADA injection as recommended below.

### Recommendation for Reinitiating Concomitant Oral Aripiprazole Supplementation Following Missed Doses*

<table>
<thead>
<tr>
<th>Dose of Last Injection</th>
<th>Length of Time Since Last Injection</th>
<th>Oral Aripiprazole Supplementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1064 mg every 2 months</td>
<td>≤10 weeks</td>
<td>Supplement with 7 Days Oral Aripiprazole</td>
</tr>
<tr>
<td></td>
<td>&gt;10 and ≤12 weeks</td>
<td>Supplement with 21 Days Oral Aripiprazole</td>
</tr>
<tr>
<td>882 mg monthly or every 6 weeks</td>
<td>&gt;12 weeks</td>
<td>Supplement with 21 Days Oral Aripiprazole</td>
</tr>
<tr>
<td>662 mg monthly</td>
<td>≤8 weeks</td>
<td>Supplement with 7 Days Oral Aripiprazole</td>
</tr>
<tr>
<td>441 mg monthly</td>
<td>&gt;8 and ≤12 weeks</td>
<td>Supplement with 21 Days Oral Aripiprazole</td>
</tr>
<tr>
<td></td>
<td>&gt;12 weeks</td>
<td>Supplement with 21 Days Oral Aripiprazole</td>
</tr>
<tr>
<td></td>
<td>&gt;7 weeks</td>
<td>Supplement with 21 Days Oral Aripiprazole</td>
</tr>
</tbody>
</table>

* The patient should supplement with the same dose of oral aripiprazole as when the patient began ARISTADA.

IMPORTANT SAFETY INFORMATION (continued)

**Body Temperature Regulation:** Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
How supplied

ARISTADA® (aripiprazole lauroxil) extended-release injectable suspension is available in dose strengths of 441 mg in 1.6 mL, 662 mg in 2.4 mL, 882 mg in 3.2 mL, and 1064 mg in 3.9 mL. The kit contains a 5-mL pre-filled, single use syringe containing ARISTADA sterile aqueous suspension and safety needles.

- The 441 mg strength kit (NDC 65757-0401-03; light blue label) contains 3 safety needles:
  - a 1-inch (25 mm) 21 gauge needle
  - a 1½-inch (38 mm) 20 gauge needle
  - a 2-inch (50 mm) 20 gauge needle
- The 662 mg strength kit (NDC 65757-0402-03; green label) contains 2 safety needles:
  - a 1½-inch (38 mm) 20 gauge needle
  - a 2-inch (50 mm) 20 gauge needle
- The 882 mg strength kit (NDC 65757-0403-03; burgundy label) contains 2 safety needles:
  - a 1½-inch (38 mm) 20 gauge needle
  - a 2-inch (50 mm) 20 gauge needle
- The 1064 mg strength kit (NDC 65757-0404-03; dark blue label) contains 2 safety needles:
  - a 1½-inch (38 mm) 20 gauge needle
  - a 2-inch (50 mm) 20 gauge needle

IMPORTANT SAFETY INFORMATION (continued)

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Ordering and procurement

Providers have several options for ordering and procuring ARISTADA® (aripiprazole lauroxil), depending on their site of care. In general, Alkermes has established an open network for ARISTADA. The following chart shows some of the wholesalers that can provide distribution support for obtaining ARISTADA.

<table>
<thead>
<tr>
<th>Wholesaler/Distributor</th>
<th>Phone</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>AmerisourceBergen®</td>
<td>1-844-222-2273</td>
<td><a href="http://www.amerisourcebergen.com">http://www.amerisourcebergen.com</a></td>
</tr>
<tr>
<td>Cardinal Health™</td>
<td>1-800-926-3161</td>
<td><a href="http://www.cardinalhealth.com">http://www.cardinalhealth.com</a></td>
</tr>
<tr>
<td>McKesson</td>
<td>1-885-625-7385</td>
<td><a href="http://www.mckesson.com">http://www.mckesson.com</a></td>
</tr>
</tbody>
</table>

Alkermes, Inc. does not endorse the use of any specific company shown here. This information is provided as a service to our customers.

Storage

Store at room temperature 20°C to 25°C (68°F to 77°F) with excursions between 15°C and 30°C (between 59°F to 86°F).

Product returns and replacements

For product returns, call 1-855-318-4160 or send an email to AlkermesReturns@icsconnect.com. For product replacements, call 1-888-235-8008.

IMPORTANT SAFETY INFORMATION (continued)

Concomitant Medication: Decreasing the ARISTADA dosage is recommended in patients taking strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for longer than 2 weeks. Increasing the ARISTADA dosage from 441 mg to 662 mg is recommended in patients taking CYP3A4 inducers for longer than 2 weeks. No ARISTADA dosage changes are recommended for patients taking CYP450 modulators for less than 2 weeks.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
ARISTADA Care Support

ARISTADA Care Support provides a comprehensive suite of services to help make ARISTADA® (aripiprazole lauroxil) therapy more accessible for patients.

ARISTADA Care Support services include:

• **Access Services**: Reimbursement support and financial assistance programs to help patients access treatment

• **Hospital Services**:
  - A program to help hospitalized patients trial ARISTADA in the hospital
  - A program to help patients secure potential sites and providers for follow-up care

• **Product Support**: Samples, ordering information, and answers to questions about ARISTADA

• **Patient Support**: Educational materials, transition assistance, injection services, and appointment reminders are available for patients and caregivers who need them

Reimbursement support

Insurance coverage may pose challenges for patients. We’ll provide the most up-to-date coverage information and, if requested, help navigate access barriers. There are both phone and Web options for reimbursement support.

• Live representative – Call 1-866-ARISTADA (1-866-274-7823) to receive general coverage information, including prior authorization requirements or visit ARISTADACareSupport.com. We can also execute a full benefit investigation upon receiving a patient’s enrollment with ARISTADA Care Support. We’ll follow up with patient-specific research, including plan-specific prior authorization requirements, usually within 24 hours

Learn more at ARISTADACareSupport.com, or call us at 1-866-ARISTADA (1-866-274-7823) Monday through Friday, 8 AM to 8 PM EST

**IMPORTANT SAFETY INFORMATION (continued)**

**Most Commonly Observed Adverse Reaction**: The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg monthly) was akathisia.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Hospital Inpatient Free Trial Program

ACCESS TO THERAPY WHEN PATIENTS NEED IT
Free trial units of all ARISTADA® (aripiprazole lauroxil) doses, including the first and only 2-month option (1064 mg) for schizophrenia, are available to hospitalized patients.

PROGRAM HIGHLIGHTS
• ARISTADA is being provided free of charge for appropriate hospitalized patients
• Program is available throughout the United States (not including its territories)
• Free trial units are commercially labeled as trade product and not labeled as samples
• You may NOT bill the patient, the patient’s insurance carrier, or any government healthcare program for any ARISTADA dispensed as part of this program
• You may NOT sell, trade, barter, or return for credit any ARISTADA provided as part of the program
• Where drug costs are included in a capitated rate or there is submission of a cost report or other insurer or government program reporting requirements, you must properly report the free trial units because the ARISTADA you receive is not a sample, it is a free commercial trade product
• Available only to hospital inpatient pharmacies for use in a licensed hospital that cannot accept PDMA-compliant samples
• There is no requirement for subsequent use of ARISTADA for any patient receiving a free trial unit through this program

Additional limits may apply per institution. This program, as amended from time to time, will be available through December 31, 2019.

* Alkermes, Inc. may terminate the program prior to December 31, 2019, upon 60 days’ notice to all participating inpatient pharmacies, or upon less or no notice if there is a change in interpretation of federal or state laws supporting the continuation of this program.

IMPORTANT SAFETY INFORMATION (continued)
Injection-Site Reactions: Injection-site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection-site pain and associated with the first injection and decreased with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) occurred at less than 1%.

Dystonia: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Transition Support Program

HELPING PATIENTS TRANSITION TO OUTPATIENT CARE

• Meet the challenges associated with hospital transitions by enrolling your patients in ARISTADA Care Support
• ARISTADA Care Support staff can assist with contacting your patient’s health plan to obtain specific coverage details
• A representative will provide a written Summary of Benefits within 24 hours
• They can also help your patients navigate other obstacles in receiving their prescribed ARISTADA® (aripiprazole lauroxil) treatment when needed, such as financial assistance

THE TRANSITION SUPPORT PROGRAM HELPS TO ENSURE CONTINUITY OF CARE

Following hospitalization, it is critical that there are no gaps in treatment because patients are vulnerable and need support adjusting to community life. Enrolling patients in the Transition Support Program can help them during this crucial time:

• Nurse coordinators can work with both inpatient and outpatient staff to assist with coordinating a patient’s transition to the outpatient setting
• They can schedule appointments and provide appointment confirmations and reminders, if needed
• If requested, nurse coordinators can also identify potential sites for follow-up care

For more information, ask your Alkermes representative, or call 1-866-ARISTADA (1-866-274-7823)
Monday through Friday, 8 AM to 8 PM EST

iAssist

iAssist is an e-prescribing and electronic prior authorization technology platform that is designed to support patient access to specialty therapies. ARISTADA is available to order on iAssist, which allows for the following:

• Electronic enrollment into ARISTADA Care Support services
• Verification of patient health plan eligibility information in real time
• Electronic access and completion of various health plan prior authorization forms (if applicable)
• Attachment and submission of electronic medical records (EMRs) and electronic prescriptions (eRX) via Surescripts directly to almost 93% of pharmacies

IMPORTANT SAFETY INFORMATION (continued)

Pregnancy/Nursing: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA during pregnancy. Aripiprazole is present in human breast milk. The benefits of breastfeeding should be considered along with the mother’s clinical need for ARISTADA and any potential adverse effects on the infant from ARISTADA or from the underlying maternal condition.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
INDICATION and IMPORTANT SAFETY INFORMATION for ARISTADA® (aripiprazole lauroxil) extended-release injectable suspension, for intramuscular use

INDICATION
ARISTADA is indicated for the treatment of schizophrenia.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Reactions, Including Stroke: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- Hyperglycemia/Diabetes Mellitus: Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

- Dyslipidemia: Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.

- Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping ARISTADA if a patient develops such urges.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

Please see additional Important Safety Information on pages 60 to 61 and accompanying full Prescribing Information, including Boxed Warning.
Falls: Antipsychotics including ARISTADA may cause somnolence, postural hypotension, or motor and sensory instability, which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm^3) and follow their WBC until recovery.

Seizures: ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain ARISTADA does not affect them adversely.

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Concomitant Medication: Decreasing the ARISTADA dosage is recommended in patients taking strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for longer than 2 weeks. Increasing the ARISTADA dosage from 441 mg to 662 mg is recommended in patients taking CYP3A4 inducers for longer than 2 weeks. No ARISTADA dosage changes are recommended for patients taking CYP450 modulators for less than 2 weeks.

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