ARIPiprazole (a-ri-pip-raz-ole)
Abilify, Abilify Maintena

Classification
Therapeutic: antipsychotics, mood stabilizers
Pharmacologic: dihydrocarbostyril

Pregnancy Category C

Indications
Schizophrenia (Abilify and Abilify Maintena). Acute and maintenance treatment of mania and mixed episodes associated with bipolar disorder (as monotherapy or with lithium or valproate) (Abilify-only). Adjunctive treatment of depression in adults (Abilify-only). Agitation associated with schizophrenia or bipolar disorder (Abilify only). Irreversible associated with autism spectrum disorder in children (Abilify only).

Action
Psychoactive activity may be due to agonist activity at dopamine D₂ and serotonin 5-HT₆ receptors and antagonist activity at the 5-HT₃ receptor. Also has alpha, adrenergic blocking activity. Therapeutic Effects: Decreased manifestations of schizophrenia. Decreased manic in bipolar patients. Decreased symptoms of depression. Decreased agitation associated with schizophrenia or bipolar disorder. Decreased emotional and behavioral symptoms of irritability.

Pharmacokinetics
Absorption: Well absorbed (87%) following oral administration; 100% following IM injection.
Distribution: Extensive extravascular distribution.
Protein Binding: Aripiprazole and dehydro-aripiprazole—99%.
Metabolism and Excretion: Mostly metabolized by the liver (CYP3A4 and CYP2D6 isoenzymes). The CYP2D6 enzyme system exhibits genetic polymorphism; 7% of population may be poor metabolizers (PMs) and may have significantly decreased aripiprazole concentrations and an increased risk of adverse effects (dose by 50% in PMs); one metabolite (dehydro-aripiprazole) has antipsychotic activity. 85% excreted unchanged in urine; 5% excreted unchanged in stool.
Half-life: Aripiprazole—75 hr; dehydro-aripiprazole—94 hr; extended release injectable suspension: 30–46 days.

Contraindications/Precautions
Contraindicated in: Hypersensitivity. Lactation: Excreted in breast milk, discontinue drug or breast feed.

Use Cautiously in:
- Known cardiovascular or cerebrovascular disease. Conditions which cause hypotension (decreased treatment with antihypertensives or diuretics), Diabetes (may ↑ risk of hyperglycemia), Severe disorders. Patients at risk for aspiration pneumonia. Concomitant ketoconazole or other potential CYP3A4 inhibitors (↑ aripiprazole dose by 50%). Concurrent pimozide, flavoxate, propoxyphene, or other potent (CYP2D6 inhibitors). Concurrent carbamazepine or other potent CYP3A4 inducers. GI: Nausea at ↑ risk for extrapyramidal symptoms and withdrawal delirium when repositioned during the 3rd trimester; use of minimal benefit hormonal therapies for menopause. ↑ risk of suicide attempts in patients with depression. Decreased agitation associated with schizophrenia or bipolar disorder. Decreased emotional and behavioral symptoms of irritability.

Adverse Reactions/Side Effects
CNS: Sedation, insufficiency, drowsiness, extrapyramidal reactions, akathisia, confusion, depression, fatigue, hyperreflexia, hypotonia, rebound insomnia, tardive dyskinesia.
Resp: dyspnea, chest pain, edema, hyperventilation, orthostatic hypotension, respiratory arrest.
EENT: blurred vision, conjunctivitis, ear pain.
CV: hypotension, tachycardia.
EENT: hearing loss.
Resp: tachypnea.
Derm: rash, urticaria, pruritus, alopecia, sweating, pruritus, tachycardia.
GI: constipation, dry mouth, dyspepsia, flatulence, nausea, vomiting, weight gain, weight loss.
GU: dysuria.
Metab: hyperglycemia, hyperlipidemia.
Mus: myalgia, weakness.
Misc: mood swings, anorexia, salivation, nausea, vomiting, weight gain, weight loss.

Drugs: Strong CYP3A4 inhibitors: ↑ risk for extrapyramidal symptoms and withdrawal delirium when repositioned during the 3rd trimester; use of minimal benefit hormonal therapies for menopause. ↑ risk of suicide attempts in patients with depression. Decreased agitation associated with schizophrenia or bipolar disorder. Decreased emotional and behavioral symptoms of irritability.

Drug Interactions
Ketoconazole, clarithromycin, or other strong CYP3A4 inhibitors: ↑ aripiprazole concentrations and an ↑ risk of adverse effects (dose by 50%).

Time/Action Profile (antipsychotic effect)
ROUTE ONSET PEAK DURATION
IM 1–3 hr 1–3 hr 1–3 hr
PO unknown 2 wk unknown

Interactions
Drug-Drug: Ketoconazole, clarithromycin, or other strong CYP3A4 inhibitors; Concurrent pimozide, flavoxate, propoxyphene, or other potent (CYP2D6 inhibitors). Concurrent carbamazepine or other potent CYP3A4 inducers. GI: Nausea at ↑ risk for extrapyramidal symptoms and withdrawal delirium when repositioned during the 3rd trimester; use of minimal benefit hormonal therapies for menopause. ↑ risk of suicide attempts in patients with depression. Decreased agitation associated with schizophrenia or bipolar disorder. Decreased emotional and behavioral symptoms of irritability.

Therapeutic Effects:
Decreased manifestation of schizophrenia. Decreased mania in bipolar patients. Decreased symptoms of depression. Decreased agitation associated with schizophrenia or bipolar disorder. Decreased emotional and behavioral symptoms of irritability.

Pharmacologic:
Antipsychotics, mood stabilizers

Therapeutic:
Classification:
Abilify, Abilify Maintena
Route/Dosage

If used concurrently with combination of strong, moderate, or weak CYP3A4 and CYP2D6 inhibitors, oral aripiprazole dose by 75%. Aripiprazole dose should be by 75% in CYP2D6 PMs who are concomitantly receiving a strong CYP3A4 inhibitor.

Schizophrenia

PO (Adults): 10 or 15 mg daily; doses up to 30 mg daily have been used; increments in dosing should be made before week 2 and after 2 days, and then to target dose of 10 mg daily after another 2 days; may further reduce dose in 5-mg increments if needed (max: 30 mg/day).

IM (Adults): 400 mg every month; after 1st injection, continue treatment with oral aripiprazole daily (30 mg daily) for 14 days; if no adverse reactions to 400 mg/month dose, may titrate upward to 500 mg every month. CYP2D6 PMs — dose to 500 mg monthly; CYP2D6 PM concomitantly receiving strong CYP2D6 inhibitor — dose to 200 mg monthly. Concomitant therapy with strong CYP2D6 and CYP3A4 inhibitor — dose to 200 mg monthly (if originally receiving 400 mg/month) or 160 mg monthly (if originally receiving 300 mg/month). Concomitant therapy with CYP2D6 and CYP3A4 inhibitors — avoid use.

Acute Manic or Mixed Episodes Associated with Bipolar I Disorder

PO (Adults): 15 mg daily as monotherapy or 10–15 mg daily with lithium or valproate; target dose is 15 mg daily; may increase dose at 3-wk intervals to 30 mg daily, if needed.

PO (Children 10–17 yr): 2 mg daily; q 2 days, and then to target dose of 5 mg daily after another 2 days; may further reduce dose in 5-mg increments if needed (max: 30 mg/day).

Maintenance Treatment of Bipolar I Disorder

PO (Adults): Continue same dose needed to stabilize patient during acute treatment.

PO (Children 10–17 yr): Continue same dose needed to stabilize patient during acute treatment.

Depression

PO (Adults): 2–5 mg daily, may titrate upward at 1-wk intervals to 5–10 mg daily; not to exceed 15 mg/day.

Agitation Associated with Schizophrenia or Bipolar Disorder

IM (Adults): 5–7.5 mg/day; may use a dose of 5–25 mg based on clinical situation. May give additional doses up to a cumulative dose of 10 mg/day, if needed.

Irritability Associated with Autistic Disorder

PO (Children 4–7 yr): 2 mg daily; q 2 days, and then to target dose of 5 mg daily after at least 5 wk; may further reduce dose in 5-mg increments if needed (max: 15 mg/day).

NURSING IMPLICATIONS

Assessment

● Assess mental status (orientation, mood, behavior) before and periodically during therapy. Assess for suicidal tendencies, especially during early therapy for depression. Restrict amount of drug available to patient. Risk may be increased in children, adolescents, and adults ≥50 yrs.

● Assess weight and BMI initially and throughout therapy. Compare weight of children and adolescents with that expected during normal growth.

● Obtain fasting blood glucose and cholesterol levels initially and periodically during therapy.

● Monitor BP (sitting, standing, lying), pulse, and respiratory rate before and periodically during therapy.

● Observe patient carefully when administering medication to ensure that medication is actually taken and not hoarded or chewed.

● Monitor patient for onset of akathisia (restlessness or desire to keep moving) and extrapyramidal side effects (parkinsonian — difficulty speaking or swallowing, loss of balance control, pill rolling of hands, masked face, shuffling gait, rigidity, tremors; and dystonic — muscle spasms, twisting motions, twitching, inability to move eyes, weakness of arms or legs) periodically throughout therapy. Report these symptoms.

● Monitor for tardive dyskinesia (uncontrolled rhythmic movement of mouth, face, and extremities; lip smacking or puckering; puffing of cheeks; uncontrolled chewing; rapid or worm-like movements of tongue). Notify health-care professional immediately if these symptoms occur, as these side effects may be irreversible.

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CONTINUED
ARIPiprazole

- Monitor for development of neuroleptic malignant syndrome (fever, muscle rigidity, altered mental status, respiratory distress, tachycardia, seizures, diaphoresis, hyperpyrexia or hypothermia, pallor, tachycardia, loss of bladder control). Notify health care professional immediately if these symptoms occur.

- Lab Test Considerations: May cause 7 creatinine phosphokinase.

- Monitor CBC during initial months of therapy in patients with pre-existing or history of low WBC. May cause leukopenia, neutropenia, or agranulocytosis. Discontinue therapy if this occurs.

- Monitor blood glucose and cholesterol levels initially and periodically during therapy.

Potential Nursing Diagnoses

- Disturbed thought process (Indications)

- Imbalanced nutrition: risk for more than body requirements (Side Effects)

Lab Test Considerations:

- Monitor for development of neuroleptic malignant syndrome (fever, muscle rigidity, altered mental status, respiratory distress, tachycardia, seizures, diaphoresis, hyperpyrexia or hypothermia, pallor, tachycardia, loss of bladder control). Notify health care professional immediately if these symptoms occur.

- Do not confuse aripiprazole with rabeprazole.

- Do not confuse short-acting aripiprazole injection (Abilify Maintena) with long-acting aripiprazole (Abilify Maintenance). Genetic Implication. CAPI TALS indicate life-threatening, underlines indicate most frequent. Strikethrough indicate discontinued.

- Do not attempt to split the tablet. Rapidly in saliva. Take tablet without liquid; but if needed, it can be taken with liquid.

- Advise patient and family to notify health care professional if thoughts about suicide or dying, attempts to commit suicide, new or worse depression; new or worse anxiety; feeling very agitated or restless; panic attacks; trouble sleeping; new or worse irritability; acting aggressive; being angry or violent; acting on dangerous impulses; an extreme increase in activity and talking; other unusual changes in behavior or mood occur.

- Advise patient to take medication as directed and not to skip doses or double up on missed doses. Take missed doses as soon as remembered unless almost time for the next dose. Emphasize importance of maintaining regular scheduled injections when taking Abilify Maintena.

- Advise patient to report these symptoms immediately.

- Advise patient to avoid driving or other activities requiring alertness until response to medication is known.

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- Monitor blood glucose and cholesterol levels initially and periodically during therapy.

- Monitor CBC frequently during initial months of therapy in patients with pre-existing or history of low WBC. May cause leukopenia, neutropenia, or agranulocytosis. Discontinue therapy if this occurs.

- Extended-Release IM: Reconstitute the 300 mg dose with 1.5 mL and 400 mg dose with 2 mL of Sterile Water for Injection, discard extra sterile water. Wipe-dry air to equalize pressure in vial. Shake vial temporarily until suspension is uniform. Injections are opaque and milky white. If injection is not given immediately, shake vial temporarily to re-suspend prior to injection. Do not store suspension in syringe. Determine volume needed for dose: from 400 mg vial: 400 mg = 2 mL, 300 mg = 1.5 mL, 200 mg = 1.0, and 160 mg = 0.5 mL. Use 21 gauge needle, 1.5 inches in length for non-obese patients and 2 inches for obese patients. Inject into gluteal site; do not massage. Continue oral dosing of aripiprazole for 2 to 6 weeks after first dose of Abilify Maintena. If second or third doses of Abilify Maintena are missed and 3 to 4 weeks since last injection, administer the injection as soon as possible. 4 to 5 weeks since last injection, restart concomitant oral aripiprazole for 14 days with the next administered injection. If fourth or subsequent doses are missed and 3 to 4 weeks since last injection, administer injection as soon as possible. If 5 to 6 weeks since last injection, restart concomitant oral aripiprazole for 14 days with next administered injection.

- Do not open the blister until ready to administer. Do not push the tablets through the foil, may damage tablet. Im mediately open opening the blister, using dry hands, remove the tablet and place the entire orally disintegrating tablet on the tongue. Tablet disintegration occurs rapidly in saliva. Take tablet without liquid, but if needed, it can be taken with liquid.

- Medication may cause dizziness and lightheadedness. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.

- Advise patient to report these symptoms immediately.

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Inform patient that aripiprazole may cause weight gain. Advise patient to monitor weight periodically. Notify health care professional of significant weight gain.

Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken, to avoid alcohol, and to consult health care professional before taking any new medications. Caution patient to avoid taking alcohol or other CNS depressants concurrently with this medication.

Advise patient that extremes in temperature should be avoided, because this drug impairs body temperature regulation.

Advise patient to notify health care professional of medication regimen prior to treatment or surgery.

Advise female patients to notify health care professional if pregnancy is planned or suspected and to avoid breast feeding during therapy.

Emphasize the importance of routine follow-up exams and continued participation in psychotherapy as indicated.

Evaluation/Desired Outcomes

- Decrease in excitable, paranoid, or withdrawn behavior.
- Decrease in incidence of mood swings in patients with bipolar disorder.
- Increased sense of well-being in patients with depression.
- Decrease of agitation associated with schizophrenia or bipolar disorder.
- Decrease of emotional and behavioral symptoms of irritability.

Why was this drug prescribed for your patient?