Aplefi

(Aripiprazole USP)

Tablet

اپلیفی

(ایری پیپرازول یو ایس پی)

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Composition:
Each film-coated tablet of Aripip 10 contains:
Aripiprazole 10mg
Each film-coated tablet of Aripip 15 contains:
Aripiprazole 15mg

Mechanism of action:
Aripiprazole is the first "dopamine system stabilizer". The mechanism of action of aripiprazole has been proposed through a combination of partial agonist activity at D_2 and 5-HT_{1A} receptors and antagonist activity at 5-HT_{2A} receptor. Actions at receptors other than D_2, 5-HT_{1A}, and 5-HT_{2A} may explain some of the other clinical effects of aripiprazole, e.g. the orthostatlc hypotension observed with aripiprazole may be explained by its antagonist activity at adrenergic α_1, receptors. Aripiprazole exhibits high affinity for dopamine D_2 and D_3, serotonin 5-$HT_A$and 5-HT_{2A} receptors, moderate affinity for dopamine D_4, serotonin 5-HT_{2c} and 5-HT_7,α_1-adrenergic and histamine H_1 receptors, and moderate affinity for the serotonin reuptake site. Aripiprazole has no appreciable affinity for cholinergic and muscarinic receptors. Aripiprazole functions as a partial agonist at the dopamine $D_2$and the serotonin 5-HT_A receptors, and as an antagonist at serotonin 5-HT_{2A}receptor.

Pharmacokinetics:
Absorption:
Aripiprazole is well absorbed, with peak plasma concentrations occurring within 3 to 5 hours; the absolute oral bioavailability of the tablet formulation is 87%.

Distribution:
At therapeutic concentrations, aripiprazole and its major metabolite are greater than 99% bound to serum proteins, primarily to albumin.

Metabolism and Elimination:
Primarily three biotransformation pathways metabolize Aripiprazole: dehydrogenation, hydroxylation, and N-dealkylation. Aripiprazole activity is presumably primarily due to the parent drug, aripiprazole, and to a lesser extent, to its major metabolite dehydro-aripiprazole The mean elimination half-lives are about 75 hours and 94 hours for aripiprazole and dehydro-aripiprazole, respectively. Following a single oral dose of [^{14}C]-labeled aripiprazole, approximately 25% and 55% of the administered radioactivity was recovered in the urine and feces, respectively. Less than 1% of unchanged aripiprazole was excreted in the urine and approximately 18% of the oral dose was recovered unchanged in the feces.

Indications:
Aripiprazole is indicated for the treatment of schizophrenia, schizoaffective disorders, maintenance treatment of schizophrenia and acute bipolar mania.

Contraindication:
Aripiprazole is contraindicated in patients with a known hypersensitivity to the product.

Dosage:
The recommended starting and target dose for aripiprazole is 10 or 15 mg/day administered on a once-a-day schedule with or without meals. Aripiprazole has been systematically evaluated and shown to be effective in a dose range of 10 to 30 mg/day. The dose may be increased to a maximum of 30mg daily. The dose may be taken without regard to meals. Dosage adjustment is not needed for patients with renal insufficiency, hepatic insufficiency, or the elderly. Safety and effectiveness in pediatric and adolescent patients have not been established.

Maintenance Therapy:
The answer to the question of how long a patient treated with aripiprazole should remain on aripiprazole, is still under clinical evaluation. Patients should be periodically reassessed to determine the need for maintenance treatment.

Switching from other Antipsychotics:
Switch study:
Three different switching strategies were evaluated over an 8-week period in a clinical report. Patients receiving prior treatment with olanzapine, risperidone, or haloperidol were switched to aripiprazole using 1 of 3 strategies. For strategy 1, the current antipsychotic was immediately stopped and aripiprazole 30mg was immediately started. Strategy 2 involved a 2-week taper of the current antipsychotic with the immediate start of aripiprazole 30mg. The strategy 3 involved a 2-week taper of the current antipsychotic with start of aripiprazole titrated to 30mg over a 2 week period. The mean baseline PANSS-total score was approximately 69 for the 3 groups. There was no significant difference in improvement in the PANSS-total score between the groups at any of the time points measured.

Adverse effects:
Headache, insomnia, somnolence, dyspepsia, constipation, abdominal pain, nausea, vomiting, asthenia, dizziness, dry mouth, anxiety, akathisia, orthostatic hypotension, hypertonia, tremor, blurred vision are frequent complaints. Aripiprazole may result in extra pyramidal symptoms, slight weight gain, tended to slightly shorten the QTc interval, slight prolactin level increase and others related to use of atypical antipsychotic drugs.

Precautions:
Orthostatic Hypotension: Aripiprazole may be associated with orthostatic hypotension, perhaps due to its a_1- adrenergic receptor antagonism. ***Seizure:*** Seizures occurred in 0.1%. ***Body Temperature Regulation:*** Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. **Suicide:** The possibility of a suicide attempt is inherent in psychotic illnesses, and close supervision of high-risk, patients should accompany drug therapy. ***Hepatic Impairment / Renal Impairment:*** No dosage adjustment is required.

Pregnancy and Lactation:
In animal studies aripiprazole demonstrated developmental toxicity, including possible teratogenic effects in rats and rabbits. Aripiprazole is Pregnancy Category C. Aripiprazole should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus. The effect of aripiprazole on labor and delivery in humans is unknown. Aripiprazole was excreted in milk of rats during lactation. It is not known whether aripiprazole or its metabolites are excreted in human milk. It is recommended that women receiving aripiprazole should not breast-feed.

Drug-Drug Interactions:
Potential for other drugs to affect aripiprazole: Agents that induce CYP3A4 (e.g. carbamazepine) could cause an increase in aripiprazole clearance and lower blood levels. Inhibitors of CYP3A4 (e.g. ketoconazole) or CYP2D6 (e.g. quinidine, fluoxetine, or paroxetine) can inhibit aripiprazole elimination and cause increased blood levels.
Potential for aripiprazole to affect Other Drugs: Aripiprazole is unlikely to cause clinically important pharmacokinetic interactions with drugs metabolized by cytochrome P450 enzymes. In in vivo studies, 10- to 30-mg/day doses of aripiprazole had no significant effect on metabolism by CYP2D6 (dextromethorphan), CYP2C9 (warfarin), CYP2C19 (omeprazole, warfarin), and CYP3A4 (dextromethorphan) substrates. Additionally, aripiprazole and dehydro Aripiprazole did not show potential for altering CYP1A2-mediated metabolism in vitro.

Warnings: Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including aripiprazole. T**ardive Dyskinesia** has also been reported.

Overdosage: Overdose of 180mg have been reported in two patients. The only symptoms reported were somnolence and vomiting in one of the two patients. There were no observations indicating an adverse change in vital signs, laboratory assessments or ECG.
Management of over dosage: No specific information is available on the treatment of overdose with aripiprazole. An electrocardiogram should be obtained in case of overdosage and, if QT_c interval prolongation is present, cardiac monitoring should be instituted. Otherwise, management of overdose should concentrate on supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. Close medical supervision and monitoring should continue until the patient recovers.

Storage: Store below 30 °C, protect from light and moisture.

How supplied:
Aplefi 10mg pack of 30 tablets (3 X 10's blister)
Aplefi 15mg pack of 30 tablets (3 X 10's blister)
Aplefi 20mg pack of 30 tablets (3 X 10's blister)

خوراک:
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

- دوا کو روشنی اور نمی سے محفوظ، 30 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
- دواؤں کو بچوں کی پہنچ سے دور رکھیں۔
- صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کریں۔

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ORGANIC Pharmaceuticals

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