

Abiprex®

Aripiprazole

FORMS AND PRESENTATION

Abiprex® 10: Tablets: Box of 30.
Abiprex® 15: Tablets: Box of 30.
Abiprex® 20: Tablets: Box of 30.
Abiprex® 30: Tablets: Box of 30.

COMPOSITION

Abiprex® 10: Each tablet contains Aripiprazole 10mg.
Abiprex® 15: Each tablet contains Aripiprazole 15mg.
Abiprex® 20: Each tablet contains Aripiprazole 20mg.
Abiprex® 30: Each tablet contains Aripiprazole 30mg.

Excipients: Lactose monohydrate, maize starch, microcrystalline cellulose, hydroxypropyl cellulose, magnesium stearate, red iron oxide (Abiprex® 10 and Abiprex® 30), yellow iron oxide (Abiprex® 15).

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics, other antipsychotics.

ATC code: N05AX12

Mechanism of action

It has been proposed that aripiprazole's efficacy in schizophrenia and Bipolar I Disorder is mediated through a combination of partial agonism at dopamine D₂ and serotonin 5-HT_{1A} receptors and antagonism of serotonin 5-HT_{2A} receptors. Aripiprazole exhibited antagonist properties in animal models of dopaminergic hyperactivity and agonist properties in animal models of dopaminergic hypoactivity. Aripiprazole exhibited high binding affinity in vitro for dopamine D₂ and D₃, serotonin 5-HT_{1A} and 5-HT_{2A} receptors and moderate affinity for dopamine D₄, serotonin 5-HT_{2C} and 5-HT_{2B}, alpha-1 adrenergic and histamine H₁ receptors. Aripiprazole also exhibited moderate binding affinity for the serotonin reuptake site and no appreciable affinity for muscarinic receptors. Interaction with receptors other than dopamine and serotonin subtypes may explain some of the other clinical effects of aripiprazole.

Pharmacokinetic properties

Absorption

Aripiprazole is well absorbed, with peak plasma concentrations occurring within 3-5 hours after dosing. Aripiprazole undergoes minimal pre-systemic metabolism. The absolute oral bioavailability of the tablet formulation is 87 %. There is no effect of a high fat meal on the pharmacokinetics of aripiprazole.

Distribution

Aripiprazole is widely distributed throughout the body with an apparent volume of distribution of 4.9 l/kg, indicating extensive extravascular distribution. At therapeutic concentrations, aripiprazole and dehydro-aripiprazole are greater than 99 % bound to serum proteins, binding primarily to albumin.

Biotransformation

Aripiprazole is extensively metabolised by the liver primarily by three biotransformation pathways: dehydrogenation, hydroxylation, and N-dealkylation. Based on in vitro studies, CYP3A4 and CYP2D6 enzymes are responsible for dehydrogenation and hydroxylation of aripiprazole, and N-dealkylation is catalysed by CYP3A4. Aripiprazole is the predominant medicinal product moiety in systemic circulation. At steady state, dehydro-aripiprazole, the active metabolite, represents about 40 % of aripiprazole AUC in plasma.

Elimination

The mean elimination half-lives for aripiprazole are approximately 75 hours in extensive metabolisers of CYP2D6 and approximately 146 hours in poor metabolisers of CYP2D6. The total body clearance of aripiprazole is 0.7 ml/min/kg, which is primarily hepatic. Following a single oral dose of [¹⁴C]-labelled aripiprazole, approximately 27% of the administered radioactivity was recovered in the urine and approximately 60% in the faeces. Less than 1% of unchanged aripiprazole was excreted in the urine and approximately 18% was recovered unchanged in the faeces.

Paediatric population

The pharmacokinetics of aripiprazole and dehydro-aripiprazole in paediatric patients 10 to 17 years of age were similar to those in adults after correcting for the differences in body weights.

Pharmacokinetics in special patient groups

Renal impairment

The pharmacokinetic characteristics of aripiprazole and dehydro-aripiprazole were found to be similar in patients with severe renal disease compared to young healthy subjects.

INDICATIONS

Abiprex® is indicated for the treatment of schizophrenia in adults and in adolescents aged 15 years and older.

Abiprex® is indicated for the treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in adults who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment.

Abiprex® is indicated for the treatment up to 12 weeks of moderate to severe manic episodes in Bipolar I Disorder in adolescents aged 13 years and older.

CONTRAINDICATIONS

Hypersensitivity to the active substance, or any of the excipients of this medicine.

PRECAUTIONS

During antipsychotic treatment, improvement in the patient's clinical condition may take several days to some weeks. Patients should be closely monitored throughout this period.

Suicidality

The occurrence of suicidal behaviour is inherent in psychotic illnesses and mood disorders and in some cases has been reported early after initiation or switch of antipsychotic therapy, including treatment with aripiprazole. Close supervision of high-risk patients should accompany antipsychotic therapy.

Cardiovascular disorders

Aripiprazole should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, conditions which would predispose patients to hypotension or hypertension, including accelerated or malignant.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with aripiprazole and preventive measures undertaken.

QT prolongation

In clinical trials of aripiprazole, the incidence of QT prolongation was comparable to placebo. Abiprex® should be used with caution in patients with a family history of QT prolongation.

Tardive dyskinesia

If signs and symptoms of tardive dyskinesia appear in a patient on aripiprazole, dose reduction or discontinuation should be considered. These symptoms can temporally deteriorate or can even arise after discontinuation of treatment.

Other extrapyramidal symptoms

If signs and symptoms of other EPS appear in a patient taking aripiprazole, dose reduction and close clinical monitoring should be considered.

Neuroleptic Malignant Syndrome (NMS)

NMS is a potentially fatal symptom complex associated with antipsychotic medicinal products. In clinical trials, rare cases of NMS were reported during treatment with aripiprazole. Clinical manifestations of NMS are 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. However, elevated creatine phosphokinase and rhabdomyolysis, not necessarily in association with NMS, have also been reported. If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fever without additional

clinical manifestations of NMS, all antipsychotic active substances, including aripiprazole, must be discontinued.

Seizure

In clinical trials, uncommon cases of seizure were reported during treatment with aripiprazole. Therefore, Abiprex® should be used with caution in patients who have a history of seizure disorder or have conditions associated with seizures.

Elderly patients with dementia-related psychosis

Increased mortality

In three placebo-controlled trials (n= 938; mean age: 82.4 years; range: 56-99 years) of aripiprazole in elderly patients with psychosis associated with Alzheimer's disease, patients treated with aripiprazole were at increased risk of death compared to placebo. The rate of death in aripiprazole-treated patients was 3.5% compared to 1.7% in the placebo group. Although the causes of deaths were varied, most of the deaths appeared to be either cardiovascular (e.g. heart failure, sudden death) or infectious (e.g. pneumonia) in nature.

Cerebrovascular adverse reactions

In the same trials, cerebrovascular adverse reactions (e.g. stroke, transient ischaemic attack), including fatalities, were reported in patients (mean age: 84 years; range: 78-88 years). Overall, 1.3% of aripiprazole-treated patients reported cerebrovascular adverse reactions compared with 0.6% of placebo-treated patients in these trials. This difference was not statistically significant. However, in one of these trials, a fixed-dose trial, there was a significant dose response relationship for cerebrovascular adverse reactions in patients treated with aripiprazole.

Abiprex® is not indicated for the treatment of dementia-related psychosis.

Hyperglycaemia and diabetes mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotic medicinal products, including aripiprazole. Risk factors that may predispose patients to severe complications include obesity and family history of diabetes. In clinical trials with aripiprazole, there were no significant differences in the incidence rates of hyperglycaemia-related adverse reactions (including diabetes) or in abnormal glycaemia laboratory values compared to placebo. Precise risk estimates for hyperglycaemia-related adverse reactions in patients treated with aripiprazole and with other atypical antipsychotic medicinal products are not available to allow direct comparisons. Patients treated with any antipsychotic agents, including aripiprazole, should be observed for signs and symptoms of hyperglycaemia (such as polydipsia, polyuria, polyphagia and weakness) and patients with diabetes mellitus or with risk factors for diabetes mellitus should be monitored regularly for worsening of glucose control.

Hypersensitivity

As with other medicinal products, hypersensitivity reactions, characterised by allergic symptoms, may occur with aripiprazole.

Weight gain

Weight gain is commonly seen in schizophrenic and bipolar mania patients due to comorbidities, use of antipsychotics known to cause weight gain, poorly managed life-style, and might lead to severe complications. Weight gain has been reported post-marketing among patients prescribed aripiprazole. When seen, it is usually in those with significant risk factors such as history of diabetes, thyroid disorder or pituitary adenoma. In clinical trials aripiprazole has not been shown to induce clinically relevant weight gain in adults. In clinical trials of adolescent patients with bipolar mania, aripiprazole has been shown to be associated with weight gain after 4 weeks of treatment. Weight gain should be monitored in adolescent patients with bipolar mania. If weight gain is clinically significant, dose reduction should be considered.

Dysphagia:

Oesophageal dysmotility and aspiration have been associated with antipsychotic medicinal product use, including aripiprazole. Aripiprazole and other antipsychotic active substances should be used cautiously in patients at risk for aspiration pneumonia.

Pathological gambling

Patients can experience increased urges, particularly for gambling, and the inability to control these urges while taking aripiprazole. Other urges, reported, include: increased sexual urges, compulsive shopping, binge or compulsive eating, and other impulsive and compulsive behaviours. It is important for prescribers to ask patients or their caregivers specifically about the development of new or increased gambling urges, sexual urges, compulsive shopping, binge or compulsive eating, or other urges while being treated with aripiprazole. It should be noted that impulse-control symptoms can be associated with the underlying disorder; however, in some cases, urges were reported to have stopped when the dose was reduced or the medication was discontinued. Impulse control disorders may result in harm to the patient and others if not recognised. Consider dose reduction or stopping the medication if a patient develops such urges while taking aripiprazole.

Falls

Aripiprazole may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls. Caution should be taken when treating patients at higher risk, and a lower starting dose should be considered (e.g. elderly or debilitated patients).

Lactose

Abiprex® tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Patients with ADHD comorbidity

Despite the high comorbidity frequency of Bipolar I Disorder and A DHD, very limited safety data are available on concomitant use of aripiprazole and stimulants; therefore, extreme caution should be taken when these drugs are co-administered.

Ability to drive and use machines

Abiprex® has minor to moderate influence on the ability to drive and use machines due to potential nervous system and visual effects, such as sedation, somnolence, syncope, vision blurred, diplopia.

PREGNANCY AND LACTATION

Pregnancy

There are no adequate and well-controlled trials of aripiprazole in pregnant women. Congenital anomalies have been reported; however, causal relationship with aripiprazole could not be established. Animal studies could not exclude potential developmental toxicity. Patients must be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with Abiprex®. Due to insufficient safety information in humans and concerns raised by animal reproductive studies, this medicinal product should not be used in pregnancy unless the expected benefit clearly justifies the potential risk to the foetus.

Newborn infants exposed to antipsychotics (including aripiprazole) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborn infants should be monitored carefully.

Breast-feeding

Aripiprazole/metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from aripiprazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Aripiprazole did not impair fertility based on data from reproductive toxicity studies.

DRUG INTERACTIONS

Due to its α1-adrenergic receptor antagonism, aripiprazole has the potential to enhance the effect of certain antihypertensive medicinal products.

Given the primary CNS effects of aripiprazole, caution should be used when aripiprazole is administered in combination with alcohol or other CNS medicinal products with

overlapping adverse reactions such as sedation.

If aripiprazole is administered concomitantly with medicinal products known to cause QT prolongation or electrolyte imbalance, caution should be used.

Potential for other medicinal products to affect aripiprazole

A gastric acid blocker, the H₂ antagonist famotidine, reduces aripiprazole rate of absorption but this effect is deemed not clinically relevant.

Aripiprazole is metabolised by multiple pathways involving the CYP2D6 and CYP3A4 enzymes but not CYP1A enzymes. Thus, no dosage adjustment is required for smokers.

Quinidine and other CYP2D6 inhibitors

In a clinical trial in healthy subjects, a strong inhibitor of CYP2D6 (quinidine) increased aripiprazole AUC by 107 %, while C_{max} was unchanged. The AUC and C_{max} of dehydro-aripiprazole, the active metabolite, decreased by 32 % and 47 %, respectively. Aripiprazole dose should be reduced to approximately one-half of its prescribed dose when concomitant administration of aripiprazole with quinidine occurs. Other strong inhibitors of CYP2D6, such as fluoxetine and paroxetine, may be expected to have similar effects and similar dose reductions should therefore be applied.

Ketoconazole and other CYP3A4 inhibitors

In a clinical trial in healthy subjects, a strong inhibitor of CYP3A4 (ketoconazole) increased aripiprazole AUC and C_{max} by 63 % and 37 %, respectively. The AUC and C_{max} of dehydro-aripiprazole increased by 77 % and 43 %, respectively. In CYP2D6 poor metabolisers, concomitant use of strong inhibitors of CYP3A4 may result in higher plasma concentrations of aripiprazole compared to that in CYP2D6 extensive metabolizers. When considering concomitant administration of ketoconazole or other strong CYP3A4 inhibitors with aripiprazole, potential benefits should outweigh the potential risks to the patient. When concomitant administration of ketoconazole with aripiprazole occurs, aripiprazole dose should be reduced to approximately one-half of its prescribed dose. Other strong inhibitors of CYP3A4, such as itraconazole and HIV protease inhibitors may be expected to have similar effects and similar dose reductions should therefore be applied. Upon discontinuation of the CYP2D6 or CYP3A4 inhibitor, the dosage of aripiprazole should be increased to the level prior to the initiation of the concomitant therapy. When weak inhibitors of CYP3A4 (e.g. diltiazem) or CYP2D6 (e.g. escitalopram) are used concomitantly with aripiprazole, modest increases in plasma aripiprazole concentrations may be expected.

Carbamazepine and other CYP3A4 inducers

Following concomitant administration of carbamazepine, a strong inducer of CYP3A4, and oral aripiprazole to patients with schizophrenia or schizoaffective disorder, the geometric means of C_{max} and AUC for aripiprazole were 68 % and 73 % lower, respectively, compared to when aripiprazole (30 mg) was administered alone. Similarly, for dehydro-aripiprazole the geometric means of C_{max} and AUC after carbamazepine co-administration were 69 % and 71 % lower, respectively, than those following treatment with aripiprazole alone. Aripiprazole dose should be doubled when concomitant administration of aripiprazole occurs with carbamazepine. Concomitant administration of aripiprazole and other inducers of CYP3A4 (such as rifampicin, rifabutin, phenytoin, phenobarbital, primidone, efavirenz, nevirapine and St. John's Wort) may be expected to have similar effects and similar dose increases should therefore be applied. Upon discontinuation of strong CYP3A4 inducers, the dosage of aripiprazole should be reduced to the recommended dose.

Valproate and lithium

When either valproate or lithium was administered concomitantly with aripiprazole, there was no clinically significant change in aripiprazole concentrations and therefore no dose adjustment is necessary when either valproate or lithium is administered with aripiprazole.

Potential for aripiprazole to affect other medicinal products

In clinical studies, 10-30 mg/day doses of aripiprazole had no significant effect on the metabolism of substrates of CYP2D6 (dextromethorphan/3-methoxymorphinan ratio), CYP2C9 (warfarin), CYP2C19 (omeprazole), and CYP3A4 (dextromethorphan). Additionally, aripiprazole and dehydro-aripiprazole did not show potential for altering CYP1A2-mediated metabolism in vitro. Thus, aripiprazole is unlikely to cause clinically important medicinal product interactions mediated by these enzymes.

When aripiprazole was administered concomitantly with either valproate, lithium or lamotrigine, there was no clinically important change in valproate, lithium or lamotrigine concentrations.

Serotonin syndrome

Cases of serotonin syndrome have been reported in patients taking aripiprazole, and possible signs and symptoms for this condition can occur especially in cases of concomitant use with other serotonergic medicinal products, such as SSRIs/SNRIs, or with medicinal products that are known to increase aripiprazole concentrations.

ADVERSE EFFECTS

Adverse effects are listed by system organ class and frequency; very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) and not known (cannot be estimated from the available data).

Blood and lymphatic system disorders: leukopenia, neutropenia, thrombocytopenia (not known).

Immune system disorders: allergic reaction (e.g. anaphylactic reaction, angioedema including swollen tongue, tongue oedema, face oedema, pruritus, or urticaria) (not known).

Endocrine disorders: hyperprolactinaemia, blood prolactin decreased (uncommon); diabetic hyperosmolar coma, diabetic ketoacidosis (not known).

Metabolism and nutrition disorders: diabetes mellitus (common); hyperglycaemia (uncommon); hyponatraemia, anorexia (not known).

Psychiatric disorders: insomnia, anxiety, restlessness (common); depression, hypersexuality (uncommon); Suicide attempt, suicidal ideation and completed suicide, pathological gambling, impulse-control disorders, binge eating, compulsive shopping, poriomania, aggression, agitation, nervousness (not known).

Nervous system disorders: akathisia, extrapyramidal disorder, tremor, headache, sedation, somnolence, dizziness (common); tardive dyskinesia, dystonia, restless legs syndrome (uncommon); neuroleptic malignant syndrome, grand mal convulsion, serotonin syndrome, speech disorder (not known).

Eye disorders: vision blurred (common); diplopia, photophobia (uncommon); oculogyric crisis (not known).

Cardiac disorders: tachycardia (uncommon); sudden death unexplained, torsades de pointes, ventricular arrhythmias, cardiac arrest, bradycardia (not known).

Vascular disorders: orthostatic hypotension (uncommon); venous thromboembolism (including pulmonary embolism and deep vein thrombosis), hypertension, syncope (not known).

Respiratory, thoracic and mediastinal disorders: hiccups (uncommon); aspiration pneumonia, laryngospasm, oropharyngeal spasm (not known).

Gastrointestinal disorders: constipation, dyspepsia, nausea, salivary hypersecretion, vomiting (common); pancreatitis, dysphagia, diarrhoea, abdominal discomfort, stomach discomfort (not known).

Hepatobiliary disorders: hepatic failure, hepatitis, jaundice (not known).

Skin and subcutaneous tissue disorders: rash, photosensitivity reaction, alopecia, hyperhidrosis, drug reaction with Eosinophilia and Systemic Symptoms (DRESS) (not known).

Musculoskeletal and connective tissue disorders: rhabdomyolysis, myalgia, stiffness (not known).

Renal and urinary disorders: urinary incontinence, urinary retention (not known).

Pregnancy, puerperium and perinatal conditions: drug withdrawal syndrome neonatal (not known).

Reproductive system and breast disorders: priapism (not known).

General disorders and administration site conditions: fatigue (common); temperature regulation disorder (e.g. hypothermia, pyrexia), chest pain, peripheral oedema (not known).

DOSAGE AND ADMINISTRATION

Adults

Schizophrenia: the recommended starting dose for Abiprex® is 10 or 15mg/day with a maintenance dose of 15mg/day administered on a once-a-day schedule without regard to meals.

Abiprex® is effective in a dose range of 10 to 30 mg/day. Enhanced efficacy at doses higher than a daily dose of 15mg has not been demonstrated although individual patients may benefit from a higher dose. The maximum daily dose should not exceed 30mg.

Manic episodes in Bipolar I Disorder: the recommended starting dose for Abiprex® is 15mg administered on a once-a-day schedule without regard to meals as monotherapy or combination therapy. Some patients may benefit from a higher dose. The maximum daily dose should not exceed 30mg.

Recurrence prevention of manic episodes in Bipolar I Disorder: for preventing recurrence of manic episodes in patients who have been receiving Abiprex® as monotherapy or combination therapy, continue therapy at the same dose. Adjustments of daily dosage, including dose reduction should be considered on the basis of clinical status.

Paediatric population

Schizophrenia in adolescents aged 15 years and older: the recommended dose for Abiprex® is 10 mg/day administered on a once-a-day schedule without regard to meals. Treatment should be initiated at 2mg for 2 days, titrated to 5mg for 2 additional days to reach the recommended daily dose of 10mg. When appropriate, subsequent dose increases should be administered in 5 mg increments without exceeding the maximum daily dose of 30mg.

Abiprex® is effective in a dose range of 10 to 30mg/day. Enhanced efficacy at doses higher than a daily dose of 10mg has not been demonstrated although individual patients may benefit from a higher dose.

Abiprex® is not recommended for use in patients with schizophrenia below 15 years of age due to insufficient data on safety and efficacy.

Manic episodes in Bipolar I Disorder in adolescents aged 13 years and older: the recommended dose for Abiprex® is 10mg/day administered on a once-a-day schedule without regard to meals. Treatment should be initiated at 2mg for 2 days, titrated to 5mg for 2 additional days to reach the recommended daily dose of 10mg.

The treatment duration should be the minimum necessary for symptom control and must not exceed 12 weeks. Enhanced efficacy at doses higher than a daily dose of 10 mg has not been demonstrated, and a daily dose of 30 mg is associated with a substantially higher incidence of significant undesirable effects including EPS related events, somnolence, fatigue and weight gain. Doses higher than 10 mg/day should therefore only be used in exceptional cases and with close clinical monitoring.

Younger patients are at increased risk of experiencing adverse events associated with aripiprazole. Therefore, Abiprex® is not recommended for use in patients below 13 years of age.

Irritability associated with autistic disorder: the safety and efficacy of Abiprex® in children and adolescents aged below 18 years have not yet been established. Currently available but no recommendation on a posology can be made.

Special population

Hepatic impairment

No dosage adjustment is required for patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the data available are insufficient to establish recommendations. In these patients dosing should be managed cautiously. However, the maximum daily dose of 30 mg should be used with caution in patients with severe hepatic impairment.

Renal impairment

No dosage adjustment is required in patients with renal impairment.

Elderly

The safety and efficacy of Aripiprazole in the treatment of schizophrenia or manic episodes in Bipolar I Disorder in patients aged 65 years and older has not been established. Owing to the greater sensitivity of this population, a lower starting dose should be considered when clinical factors warrant.

Gender

No dosage adjustment is required for female patients as compared to male patients.

Smoking status

According to the metabolic pathway of aripiprazole no dosage adjustment is required for smokers.

Dose adjustments due to interactions

When concomitant administration of strong CYP3A4 or CYP2D6 inhibitors with aripiprazole occurs, the aripiprazole dose should be reduced. When the CYP3A4 or CYP2D6 inhibitor is withdrawn from the combination therapy, aripiprazole dose should then be increased.

When concomitant administration of strong CYP3A4 inducers with aripiprazole occurs, the aripiprazole dose should be increased. When the CYP3A4 inducer is withdrawn from the combination therapy, the aripiprazole dose should then be reduced to the recommended dose.

Method of administration

Abiprex® tablet is for oral use.

OVERDOSAGE

Signs and symptoms

The potentially medically important signs and symptoms observed included lethargy, increased blood pressure, somnolence, tachycardia, nausea, vomiting and diarrhoea. In addition, reports of accidental overdose with aripiprazole alone (up to 195 mg) in children have been received with no fatalities. The potentially medically serious signs and symptoms reported included somnolence, transient loss of consciousness and extrapyramidal symptoms.

Management of overdose

Management of overdose should concentrate on supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. The possibility of multiple medicinal product involvement should be considered. Therefore cardiovascular monitoring should be started immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. Following any confirmed or suspected overdose with Abiprex®, close medical supervision and monitoring should continue until the patient recovers.

Activated charcoal (50 g), administered one hour after Abiprex®, decreased aripiprazole C_{max} by about 41 % and AUC by about 51%, suggesting that charcoal may be effective in the treatment of overdose.

STORAGE CONDITIONS

Store below 30°C .

Keep it in the original package to protect from moisture

Date of revision: July 2023.

Marketing Authorization Holder and Manufacturer:

Benta S.A.L. – Lebanon

