APPROVED
leshania , 2021/12/20 ,08:19:45

Alebon tablets
P1528027

Alebon tablets
P1528027

Professional Information for Medicines for Human Use

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE
ALEBON 5 mg (tablet)
ALEBON 10 mg (tablet)
ALEBON 15 mg (tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
ALEBON 5 mg:
Each tablet contains 5 mg of aripiprazole.
Excipients with known effect:
Contains sugar: Lactose monohydrate 76,00 mg.

ALEBON 10 mg:
Each tablet contains 10 mg of aripiprazole.
Excipients with known effect:
Contains sugar: Lactose monohydrate 66,50 mg.

ALEBON 15 mg:
Each tablet contains 15 mg of aripiprazole.
Excipients with known effect:
Contains sugar: Lactose monohydrate 99,75 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
ALEBON 5 mg:
Blue coloured, modified rectangular shaped, uncoated tablets debossed with '62' on one side and 'H' on other side.

ALEBON 10 mg:
White coloured, modified rectangular shaped, uncoated tablets debossed with '63' on one side and 'H' on other side.

ALEBON 15 mg:
White coloured, round shaped, uncoated tablets debossed with '64' on one side and 'H' on other side.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
ALEBON is indicated for the treatment of schizophrenia and for the maintenance of clinical improvement in adults.

ALEBON is indicated for the treatment of acute manic episodes associated with Bipolar I Disorder and for prevention of recurrence of new manic episodes in patients who experienced predominantly manic episodes and who responded to **ALEBON** treatment.

4.2. Posology and method of administration
Schizophrenia
The recommended starting dose for **ALEBON** is 10 or 15 mg/day with a maintenance dose of 15 mg/day administered on a once-a-day schedule without regard to meals. **ALEBON** is effective in a dose range of 10 to 30 mg/day. Enhanced efficacy at doses higher than the recommended daily dose of 15 mg has not been demonstrated although individual patients may benefit from a higher dose. The maximum daily dose should not exceed 30 mg.

Bipolar Mania
The recommended starting dose for **ALEBON** is 15 mg administered on a once-a-day schedule without regard to meals as monotherapy or combination therapy (see section 4.5). Some patients may benefit from a higher dose. The maximum daily dose should not exceed 30 mg.

Recurrence prevention of manic episodes in Bipolar I disorder: For preventing recurrence of manic episodes in patients who have been receiving **ALEBON,** continue therapy at the same dose. Adjustments of daily dose, including dose reduction should be considered on the basis of clinical status. Prevention of depressive episodes using aripiprazole (as contained **ALEBON**) monotherapy has not been established. Supplementary therapy should be considered for the prevention or treatment of depressive episodes, as clinically appropriate.

Concomitant Medications
Dosage adjustment for patients taking **ALEBON** concomitantly with potent CYP3A4 or CYP2D6 inhibitors: When concomitant administration of a potent CYP3A4 or CYP2D6 inhibitor with **ALEBON** occurs, **ALEBON** dose should be reduced to one-half of the usual dose. When the CYP3A4 or CYP2D6 inhibitor is withdrawn from the combination therapy, the **ALEBON** dose should then be increased (see Section 5.2).

Dosage adjustment for patients taking potent CYP3A4 inducers: When a potent CYP3A4 inducer is added to **ALEBON** therapy, **ALEBON** dose should be doubled. Additional dose increases of **ALEBON** should be based on clinical evaluation. When the CYP3A4 inducer is withdrawn from the combination therapy, **ALEBON** dose should be reduced (see Section 5.2).

Method of administration:
ALEBON is for oral administration.

4.3. Contraindications
ALEBON is contraindicated in:

- Patients with hypersensitivity to aripiprazole or to any excipients in **ALEBON** (see Section 6.1).
- The safety and efficacy of **ALEBON** in patients under 18 years of age have not been established.

4.4. Special warnings and precautions for use
During antipsychotic treatment, improvement in the patient's clinical condition may take several days to some weeks. Patients should be closely monitored during this period.

Suicide
The possibility of a suicide attempt is inherent in psychotic illnesses, and mood disorders and in some cases has been reported early after initiation or switch of antipsychotic treatment, including treatment with aripiprazole (see section 4.8). Close supervision of high-risk patients should accompany **ALEBON** therapy. Prescriptions for **ALEBON** should be written for the smallest dose of tablets consistent with good patient management, in order to reduce the risk of overdose.

Cardiovascular disorders
ALEBON should be used with caution in patients with known cardiovascular disease (history of myocardial infarction or ischaemic heart disease, heart failure, or conduction abnormalities), cerebrovascular disease, conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medicinal products) or hypertension, including accelerated or malignant.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic medicinal products. 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 **ALEBON** and preventive measures undertaken.

Orthostatic hypotension
ALEBON may be associated with orthostatic hypotension, perhaps due to its α1-adrenergic receptor antagonism.

QT prolongation:
In clinical trials of aripiprazole, the incidence of QT prolongation was comparable to placebo. As with other antipsychotics, aripiprazole should be used with caution in patients with a family history of QT prolongation (see Section 4.8).

Tardive dyskinesia
As the risk of tardive dyskinesia increases with long-term exposure to antipsychotic treatment, if signs and symptoms of tardive dyskinesia appear in a patient on **ALEBON**, a dose reduction or medicine discontinuation should be considered. These symptoms can temporally deteriorate or even arise after discontinuation of treatment.

Other extrapyramidal symptoms
In paediatric clinical trials of aripiprazole, akathisia and parkinsonism were observed. If signs and symptoms of other EPS appear in a patient taking **ALEBON,** dose reduction and close clinical monitoring should be considered. Use of aripiprazole in patients under 18 years of age is contraindicated (see Section 4.3).

Neuroleptic malignant syndrome
A potentially fatal symptom complex sometimes referred to as neuroleptic malignant syndrome (NMS) has been reported. 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.

If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fiver without additional clinical manifestations of NMS, all antipsychotic medicines, including **ALEBON** must be discontinued.

Seizure
ALEBON should be used cautiously in patients who have a history of seizure disorder or have conditions associated with seizures.

Body temperature Regulation
Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing **ALEBON** for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g. exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Elderly patients with dementia-related psychosis
Elderly patients with dementia-related psychosis treated with **ALEBON,** are at increased risk of death compared to placebo. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g. heart failure, sudden death) or infectious (e.g. pneumonia) in nature.
ALEBON are not approved for the treatment of patients with 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 antipsychotics including aripiprazole, as contained in **ALEBON.** Patients treated with **ALEBON** should be monitored 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 (see section 4.8). Patients who develop symptoms of hyperglycaemia during treatment with **ALEBON** should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when **ALEBON** was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect medicine.

Hypersensitivity:
As with other medicinal products, hypersensitivity reactions, characterised by allergic symptoms, may occur with aripiprazole (see Section 4.8).

Weight gain
Weight gain is commonly seen in schizophrenic and bipolar mania patients due to co-morbidities, use of antipsychotics known to cause weight gain and poorly managed life-style might lead to severe complications. When seen, it is usually in those with significant risk factors such as history of diabetes, thyroid disorder or pituitary adenoma. Weight gain should be monitored in adolescent patients 18 years and older with bipolar mania. If weight gain is clinically significant, dose reduction should be considered (see Section 4.8).

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

Pathological gambling:
Increased urges, particularly for gambling, and the inability to control these urges while taking aripiprazole. Increased sexual urges, compulsive shopping, binge or compulsive eating, and other impulsive and compulsive behaviours have also been reported. Prescribers should 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. Post-marketing reports of pathological gambling have been reported among patients prescribed aripiprazole, regardless of whether these patients had a prior history of gambling. Patients with a prior history of pathological gambling may be at increased risk and should be monitored carefully. 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 medicine was discontinued. Impulse control disorders may result in harm to the patient and others if not recognized. Dose reduction or stopping the medication, should be considered if a patient develops such urges while taking aripiprazole (see Section 4.8).

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

Falls
ALEBON 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
ALEBON contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5. Interaction with other medicines and other forms of interaction
General
Given the primary CNS effects of **ALEBON**, caution should be used when **ALEBON** is taken in combination with other centrally acting medicines due to overlapping adverse reactions such as sedation (see Section 4.8). Similarly, combination use of **ALEBON** with alcohol should be avoided. Due to its α_1-adrenergic receptor antagonist activity, **ALEBON** has the potential to enhance the effect of certain antihypertensive agents.

There was no effect of a high fat meal on the pharmacokinetics of **ALEBON**.

If **ALEBON** is administered concomitantly with medicines 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.

Valproate and lithium
When either valproate or lithium were administered concomitantly with aripiprazole, there was no clinically significant change in aripiprazole concentrations.
ALEBON is metabolised by multiple pathways involving the CYP2D6 and CYP3A4 enzymes but not CYP1A enzymes.

Quinidine and other CYP2D6 inhibitors
Quinidine, a strong inhibitor of CYP2D6, increased plasma exposure (AUC) of aripiprazole in clinical trials. **ALEBON** dose should be reduced to approximately one-half of its prescribed dose when concomitant administration of **ALEBON** with quinidine occurs. Other potent 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
Ketoconazole, a strong inhibitor of CYP3A4, increases aripiprazole and metabolite dehydro-aripiprazole plasma exposure substantially.

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 metabolisers.

When concomitant administration of ketoconazole with aripiprazole occurs, **ALEBON** dose should be reduced to approximately one-half of its prescribed dose. Other potent 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 (see Section 4.2). 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.

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.

Carbamazepine and other CYP3A4 inducers
Concomitant administration of carbamazepine, a strong inducer of CYP3A4, and oral aripiprazole to patients with schizophrenia or schizoaffective disorder, resulted in decreased plasma exposure of aripiprazole and metabolite dehydro-aripiprazole compared to when aripiprazole was administered alone.

ALEBON dose should be doubled when concomitant administration of aripiprazole occurs with carbamazepine. Other potent 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 potent CYP3A4 inducers, the dosage of **ALEBON** should be reduced to the recommended dose.

Potential for ALEBON to affect other medicines
In clinical studies, 10 to 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.

Serotonin syndrome
Cases of serotonin syndrome have been reported in patients taking aripiprazole as contained in **ALEBON,** and possible signs and symptoms for this condition can occur especially in cases of concomitant use with other serotonergic medicinal products, such as SSRI/SNRI, or with medicinal products that are known to increase **ALEBON** concentrations (see Section 4.8).

When **ALEBON** was administered concomitantly with lamotrigine, there was no clinically important change in lamotrigine concentrations.

4.6. Fertility, pregnancy and lactation
Safety of use of **ALEBON** during pregnancy and lactation has not been established.

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 (see Section 5.3). Patients must be advised to notify their medical practitioner if they become pregnant or intend to become pregnant during treatment with aripiprazole. Due to insufficient safety information in humans and concerns raised by animal reproductive studies, this medicine.

New-born 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, new-born infants should be monitored carefully (see Section 4.8).

Lactation
Aripiprazole is excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from aripiprazole therapy.

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

4.7. Effects on ability to drive and use machines
ALEBON 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. (see Section 4.8).

Patients should be cautioned about operating hazardous machines, including motor vehicles, until they are reasonably certain that aripiprazole does not affect them adversely. Some paediatric patients with Bipolar I Disorder have an increased incidence of somnolence and fatigue (see Section 4.8).

4.8. Undesirable effects
a. Summary of the safety profile
The most commonly reported adverse reaction in placebo-controlled trials are akathisia and nausea each occurring in more than 3 % of patients treated with oral aripiprazole.

b. Tabulated list of adverse reactions
Adverse drug reactions are classified by system organ class and frequency; within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The table is based on adverse events reported during clinical trials and/or post-marketing use.

The frequency of adverse reactions reported during post-marketing use cannot be determined as they are derived from spontaneous reports. Consequently, the frequency of these adverse events is qualified as "Frequency unknown".

System organ class	Frequent	Less Frequent	Frequency not known
Blood and lymphatic system disorders			Leukopenia, Neutropenia, Thrombocytopenia
Immune system disorders			Allergic reaction (e.g. anaphylactic reaction, angioedema including swollen tongue, tongue oedema, face oedema, pruritus, or urticaria)
Endocrine disorders		Hyperprolactinaemia	Diabetic hyperosmolar coma, Diabetic ketoacidosis
Metabolism and nutrition disorders	Diabetes mellitus	Hyperglycaemia	Hyponatremia, Anorexia, Weight decreased, Weight gain,
Psychiatric disorders	Insomnia, Anxiety, Restlessness	Depression, Hypersexuality	Suicide attempt, suicidal ideation and completed suicide (see Section 4.4), Pathological gambling, Impulsive-control disorders, Binge eating, Compulsive shopping, Poriomania, Aggression, Agitation, Nervousness
Nervous system disorders	Akathisia, Extrapyramidal disorder, Tremor, Headache, Sedation, Somnolence, Dizziness	Tardive dyskinesia, Dystonia	Neuroleptic Malignant Syndrome (NMS), Grand mal convulsion, Serotonin syndrome, Speech disorder
Eye disorders	Vision blurred	Diplopia	Oculogyric crisis
Cardiac disorders		Tachycardia	Sudden unexplained death, Torsades de pointes, QT prolongation, Ventricular Dysrhythmias, Cardiac arrest, Bradycardia
Vascular disorders		Orthostatic hypotension	Venous thromboembolism (including pulmonary embolism and deep vein thrombosis), Hypertension, Syncope
Respiratory, thoracic and mediastinal disorders		Hiccups	Aspiration pneumonia, Laryngospasm, Oropharyngeal spasm
Gastrointestinal disorders	Constipation, Dyspepsia, Nausea, Salivary hypersecretion, Vomiting		Pancreatitis, Dysphagia, Diarrhoea, Abdominal discomfort, Stomach discomfort
Hepatobiliary disorders			Hepatic failure, Hepatitis, Jaundice, Increased Alanine Aminotransferase (ALT), Increased Aspartate Aminotransferase (AST), Increased Gamma Glutamyl Transferase (GGT) , Increased alkaline phosphatase
Skin and subcutaneous tissue disorders			Rash, Photosensitivity reaction, Alopecia, Hyperhidrosis
Musculoskeletal and connective tissue disorders			Rhabdomyolysis, Myalgia, Musculoskeletal stiffness
Renal and urinary disorders			Urinary incontinence, Urinary retention
Pregnancy, puerperium and perinatal conditions			Drug withdrawal syndrome neonatal (see Section 4.6)
Reproductive system and breast disorders			Priapism
General disorders and administration site conditions	Fatigue		Temperature regulation disorder (e.g. hypothermia, pyrexia), Chest pain, Peripheral oedema
Investigations			Blood glucose increased, Glycosylated haemoglobin increased, Blood glucose fluctuation, Increased creatine phosphokinase

c. Description of selected adverse reactions
Dystonia
Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic medicines. An elevated risk of acute dystonia is observed in males and younger age groups.

Prolactin
In clinical trials for the approved indications and post-marketing, both increase and decrease in serum prolactin as compared to baseline was observed with aripiprazole.

Paediatric population
Schizophrenia in adolescents aged 15 years and older
In a short-term clinical trial involving adolescents (13-17 years) with schizophrenia, the frequency and type of undesirable effects were similar to those in adults except for the following reactions that were reported more frequently in adolescents receiving aripiprazole than in adults receiving aripiprazole (and more frequently than placebo):

Somnolence /sedation, extrapyramidal disorders, dry mouth, increased appetite, and orthostatic hypotension.

The safety profile of a long-term trial was also similar except for the following reactions that were reported more frequently than paediatric patients taking placebo: weight decreased, blood insulin increased, dysrhythmia, and leukopenia.

Manic episodes in Bipolar I Disorder in adolescents aged 13 years and older
The frequency and type of undesirable effects in adolescents with Bipolar I Disorder were similar to those in adults except for the following reactions: somnolence, extrapyramidal disorder, akathisia, fatigue; and abdominal pain upper, heart rate increased, weight increased, increased appetite, muscle twitching, and dyskinesia.

d. Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the '6.04 Adverse Drug Reactions Reporting Form'. Found under SAHPRA's publications: **https://www.sahpra.org.za/Publications/Index/8**

4.9. Overdose
Symptoms
The potentially medically important signs and symptoms reported included lethargy, blood pressure increased, somnolence, tachycardia, nausea, vomiting and diarrhoea. The potentially medically serious signs and symptoms in children include: somnolence, transient loss of consciousness and extrapyramidal symptoms.

Treatment
Management of overdose should concentrate on supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. The possibility of multiple medicine involvement should be considered. Therefore, cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible dysrhythmias.

Following any confirmed or suspected overdose of **ALEBON,** close medical supervision and monitoring should continue until the patient recovers.

Activated charcoal (50 g), administered one hour after **ALEBON**, and decreased aripiprazole.

Although there is no information on the effect of haemodialysis in treating an overdose with **ALEBON,** haemodialysis is unlikely to be useful in overdose management since aripiprazole is not eliminated unchanged by the kidneys and is highly bound to plasma proteins.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Psycholeptics other antipsychotics, ATC code: N05AX12

Category and class: A 2.6.5 Tranquillisers – miscellaneous structures

Mechanism of action
It has been proposed that aripiprazole's efficacy in schizophrenia is mediated through a combination of partial agonist activity at dopamine D2 and serotonin 5HT1a receptors and antagonist activity at serotonin 5HT2a receptors.

Aripiprazole exhibited high binding affinity *in vitro* for dopamine D2 and D3, serotonin 5HT1a and 5HT2a receptors and moderate affinity for dopamine D4, serotonin 5HT2C and 5HT7, alpha1-adrenergic and histamine H1 receptors. Aripiprazole also exhibited moderate binding affinity for serotonin reuptake site and no appreciable affinity for muscarinic receptors. Aripiprazole exhibited antagonist properties in animal models of dopaminergic hyperactivity and agonist properties in animal models of dopaminergic hypoactivity. Interaction with receptors other than dopamine and serotonin subtypes may explain some of the other clinical effects of aripiprazole.

5.2. Pharmacokinetic properties
Absorption
Aripiprazole is well absorbed after oral administration of aripiprazole, 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 of aripiprazole is 87 %. The bioavailability of aripiprazole is not significantly affected by administration with food.

Distribution
Aripiprazole is widely distributed throughout the body with an apparent volume of distribution of 4,9 L/kg. At therapeutic concentrations, aripiprazole is greater than 99 % bound to serum proteins, primarily albumin. Aripiprazole did not alter the pharmacokinetics and pharmacodynamics of highly protein-bound warfarin, suggesting that protein displacement of warfarin did not occur.

Biotransformation
Aripiprazole undergoes minimal pre-systemic metabolism. 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 medicine moiety in systemic circulation. At steady-state, dehydro-aripiprazole, the active metabolite, represented about 39 % of aripiprazole AUC in plasma.

Elimination
The mean elimination half-life of aripiprazole is about 75 hours in extensive metabolisers of CYP2D6 and approximately 146 hours in poor metabolisers of CYP2D6.

Following single oral dose of [14^{C}]-labelled aripiprazole, approximately 27 % and 60 % of administered radioactivity was recovered in the urine and faeces, respectively. Less than 1 % of unchanged aripiprazole was excreted in the urine and approximately 18 % of the oral dose was recovered unchanged in the faeces. The total body clearance of aripiprazole is 0,7 mL/min/kg, which is primarily hepatic.

Linearity
Steady-state concentrations are attained within 14 days of dosing. Aripiprazole accumulation by a factor of 5 is predictable with multiple dosing. At steady-state, the pharmacokinetics of aripiprazole is dose-proportional. There is minimal diurnal variation in the disposition of aripiprazole and its active metabolite, dehydro-aripiprazole. This predominant metabolite in human plasma, dehydro-aripiprazole, has been shown to have similar affinities for D2 receptors as the parent compound.

Special Populations
Gender
C_{max} and AUC of aripiprazole and its active metabolite, dehydro-aripiprazole, are higher in women than in men, and correspondingly, the apparent oral clearance of aripiprazole is lower in women. These differences, however, are largely explained by differences in body weight between men and women. No dosage adjustment is recommended based on gender.

Smoking
Population pharmacokinetic evaluation has revealed no evidence of clinically significant effects from smoking on the pharmacokinetics of aripiprazole. Based on studies utilising human liver enzymes *in vitro*, aripiprazole is not a substrate for CYP1A2, and also does not undergo direct glucuronidation. Smoking should, therefore, not have an effect on the pharmacokinetics of aripiprazole. Consistent with these *in vitro* results, population pharmacokinetic evaluation did not reveal any significant pharmacokinetic differences between smokers and non-smokers. No dosage adjustment is recommended based on smoking status.

Race
Although no specific pharmacokinetic study was conducted to investigate the effects of race on the disposition of aripiprazole, population pharmacokinetic evaluation revealed no evidence of clinically significant race-related differences in the pharmacokinetics of aripiprazole. No dosage adjustment is recommended based on race.

Renal impairment
In patients with severe renal impairment (creatinine clearance < 30 mL/min). C_{max} of aripiprazole (given in a single dose of 15 mg) and dehydro-aripiprazole increased, but AUC was lower for aripiprazole and higher for dehydro-aripiprazole.

Renal excretion of both unchanged aripiprazole and dehydro-aripiprazole is less than 1 % of the dose. No dosage adjustment is required in subjects with renal impairment.

Hepatic impairment
In a single-dose study (15 mg of aripiprazole) in subjects with varying degrees of liver cirrhosis (Child-Pugh classes A, B and C), the AUC of aripiprazole, compared to healthy subjects, increased in mild hepatic impairment and, in moderate hepatic impairment and decreased in severe hepatic impairment. None of these differences would require dose adjustment.

Elderly patients
In pharmacokinetic studies (with aripiprazole given in a single dose of 15 mg), aripiprazole clearance was lower in elderly (≥ 65 years) subjects compared to younger adult subjects (18 to 64 years).

There was no detectable age effect, however, in the population pharmacokinetic analysis in schizophrenia patients. Also, the pharmacokinetics of aripiprazole after multiple doses in elderly patients appeared similar to that reported in young, healthy subjects. No dosage adjustment is recommended for elderly patients (see Section 4.4).

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.

5.3 Preclinical safety data
Animal studies in rats and rabbits could not exclude potential foetal developmental toxicity.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Cellulose microcrystalline, hydroxyl propyl cellulose, lactose monohydrate, magnesium stearate, maize starch and silica colloidal anhydrous.
In addition 5 mg contains FD & C blue No. 2 (C.I. No: 73015).

6.2. Incompatibilities
Not applicable

6.3. Shelf life
36 months

6.4. Special precautions for storage
Store at or below 25 °C.
Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container
Blister packs:
30 tablets are packed in aluminium foil/PVC film blister packs. Each carton contains 3 blisters of 10 tablets each.

HDPE containers:
30 tablets are packed in white opaque HDPE container with a white opaque polypropylene closure with wad, silica gel sachet and rayon.
Not all packs and pack sizes are necessarily marketed.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
AUROGEN SA (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8. REGISTRATION NUMBER
ALEBON 5 mg: 47/2.6.5/1080
ALEBON 10 mg: 47/2.6.5/1081
ALEBON 15 mg: 47/2.6.5/1082

9. DATE OF FIRST AUTHORISATION

18 May 2021

P1528027

DETACH BEFORE DISPENSING

SCHEDULING STATUS

S5

PATIENT INFORMATION LEAFLET
ALEBON (5 mg/ 10 mg/ 15 mg)
Aripiprazole
(Contains Sugar: Lactose monohydrate 76,00 mg/ 66,50 mg/ 99,75 mg)

Read all of this leaflet carefully before you start taking ALEBON
- **Keep this leaflet. You may need to read it again.**
- **If you have any further questions, ask your doctor, pharmacist, nurse or other health care provider.**
- **ALEBON has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.**

What is in this leaflet:
1. What ALEBON is and what it is used for.
2. What you need to know before you use ALEBON.
3. How to use ALEBON.
4. Possible side effects.
5. How to store ALEBON.
6. Contents of the pack and other information.

1. What ALEBON is and what it is used for
ALEBON is used to treat adults and adolescents aged 18 years and older who suffer from a disease called schizophrenia. This is a disorder whereby your thoughts or experiences seem out of touch with reality; Such as hearing, seeing or sensing things which are not there, suspiciousness, mistaken beliefs, you may experience disorganised speech or behaviour and decreased participation in daily activities. People with this condition may also feel depressed, guilty, anxious or tense.

ALEBON is used to treat adults who suffer from a condition with symptoms such as feeling "high", having excessive amounts of energy, needing much less sleep than usual, talking very quickly with racing ideas and sometimes severe irritability. In adults, ALEBON is also used to prevent this condition from returning in patients who responded to ALEBON treatment.

2. What you need to know before you take ALEBON
Do not take ALEBON:
- If you are hypersensitive (allergic) to aripiprazole or any of the ingredients of ALEBON.
- If you are younger than 18 years of age.

Take special care with ALEBON
- If you experience worsening of your depression, or if you have suicidal thoughts or behaviour, you should contact your doctor immediately.
- If you have known cardiovascular disease (a disease of the heart and circulation) or a family history of heart disease, heart attack, stroke or abnormal blood pressure.
- If you suffer from conditions that affect the blood vessels and blood supply to the brain. If you experience situations which would predispose you to low blood pressure (dehydration) and are receiving treatment with medications that lower your blood pressure.
- If signs and symptoms of tardive dyskinesia appear (a condition characterised by repetitive, involuntary movements especially in the face). Types of involuntary movements include: Grimacing, tongue movements, lip smacking, lip puckering, pursing of the lips and excessive eye blinking.
- If you experience conditions which may contribute to a raise in core body temperature, e.g. exercising strenuously, exposure to extreme heat, being subject to dehydration.
- If you experience spasms, muscle contractions, rigidity, slowness of movement.
- If you experience symptoms of a condition called Neuroleptic malignant syndrome which include high fever, muscle stiffness, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, fast heartbeat, sweating and abnormal heart beat).
- If you suffer from fits (seizure disorders).
- If you suffer with dementia-related psychosis (when you find that you have a decline in memory, language, problem-solving and other thinking skills) and are an elderly patient as your doctor may need to monitor you more closely.
- If you have too much sugar in the blood (a disease called diabetes). A disease characterised by symptoms such as excessive thirst, passing of large amounts of urine, increase in appetite, and feeling weak) or a family history of diabetes, thyroid disorder or pituitary adenoma.
- If you are notice that you are gaining weight, develop unusual movements, experience sleepiness that interferes with normal daily activities, have any difficulty in swallowing or allergic symptoms.

Taking other medicines with ALEBON

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines). See Do not take ALEBON.

Tell your doctor if you are taking medicine to lower your blood pressure.
ALEBON may increase the effect of medicines used to lower the blood pressure.
When taking ALEBON with some medicines your doctor may need to change your dose of ALEBON.
Tell your doctor if you are taking or using any of the following medicines:
- Quinidine (used to treat irregular heart rate or malaria).
- Fluoxetine (used to treat depression) or paroxetine (used to treat depression or anxiety).
- Ketoconazole or itraconazole (used to treat fungal infections),
- Certain medicines used to treat HIV, for example efavirenz or nevirapine and a class of HIV medication called HIV protease inhibitors, ask your doctor or pharmacist if you are not sure.
- Carbamazepine, phenytoin, phenobarbital (used to treat seizures.
- Certain antibiotics like rifampicin or rifabutin (used to treat bacterial infections.
- St. John's Wort (a complementary medicine used to treat depression).

These medicines may increase the risk of side effects or reduce the effect of ALEBON; if you get any unusual symptom taking any of these medicines together with ALEBON you should see your doctor.

Pregnancy, breastfeeding and fertility
ALEBON is excreted in human milk. You should not breastfeed if they are taking ALEBON.

If you are pregnant, think you might be pregnant or planning to become pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before ALEBON is administered to you.

The following symptoms may occur in newborn babies, of mothers that have used **ALEBON** in the last trimester (last three months of their pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor.

Driving and using machines
As with other antipsychotics, caution should be observed when operating hazardous machines, including motor vehicles, until you are reasonably certain that aripiprazole does not affect you adversely.

You may feel dizzy, confused or lightheaded and vision problems may occur after taking ALEBON. If this happens, do not drive or use any tool or machines. Ask your doctor if you are not sure.

Important information about some of the ingredients of ALEBON
ALEBON contains lactose, which is a type of sugar. So before taking ALEBON, please consult your doctor for advice if you have an intolerance to some sugars.

3. How to take ALEBON

Do not share medicines prescribed for you with any other person. Always take ALEBON exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.
Your doctor will tell you how long your treatment with ALEBON will last.

ALEBON should be swallowed whole with a half a glass of water. Do not chew.

Schizophrenia
The recommended starting dose for ALEBON is 10 or 15 mg/day with a maintenance dose of 15 mg/day administered on a once-a-day schedule.

Bipolar Mania
The recommended starting dose for ALEBON is 15 mg/day administered on a once a day schedule.

However, your doctor may prescribe a lower or higher dose to a maximum of 30 mg once a day.

If you have the impression that the effect of ALEBON is too strong or too weak, talk to your doctor or pharmacist. Try to take the ALEBON tablet at the same time each day.

Even if you feel better, do not alter or stop taking the daily dose of ALEBON without first [consulting] talking to your doctor. Your doctor will tell you how long your treatment with ALEBON will last.

Taking ALEBON with food and drink
ALEBON can be taken with or without food.
Alcohol should be avoided when taking ALEBON.

If you take more ALEBON than you should

If you realise you have taken more ALEBON then you should (or if someone else has taken your ALEBON), consult your doctor or pharmacist without delay. If neither is available, contact the nearest hospital or poison control centre and take your pack of ALEBON with you.

If you missed a dose of ALEBON
If you forgot to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects
ALEBON can have side effects but not everybody gets them.

Not all side effects reported for ALEBON are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ALEBON, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop taking ALEBON and tell your doctor immediately or go to the casualty department at your nearest hospital:
- Allergic reaction (e.g. anaphylactic reaction, difficulty breathing or swallowing, swelling including swollen tongue, swollen face, severe itching, or hives).

These are all very serious side effects. If you have them, you may have had a serious reaction to ALEBON. You may need urgent medical attention or hospitalisation.
Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- Neuroleptic malignant syndrome (NMS): If you notice that your heart beats faster than normal or beats irregularly, if you are sweating a lot, if your muscles are stiff, you might have a serious condition called Neuroleptic malignant syndrome (NMS)
- Hyperglycemia (High blood sugar): Increases in blood sugar can happen in some people who take ALEBON.Extremely high blood sugar can lead to coma or death. Symptoms of high blood sugar while taking ALEBON are: polydipsia (feel very thirsty), polyuria (need to urinate more than usual), polyphagia (excessive eating) and weakness
- Tardive dyskinesia: characterised by protrusion of the tongue ('fly catching'), lip smacking, sucking, lateral chewing, and pouting of the lips and cheeks
- Dystonia: Prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue
- Orthostatic hypotension (decreased blood pressure): light headedness or fainting when rising too quickly from a sitting or lying position.
- Seizures (convulsions).

These are all serious side effects. You may need urgent medical attention.
Tell your doctor if you notice any of the following:
Frequent side effects:
- Inability to sleep (insomnia), sleepiness (somnolence), anxiety, restlessness
- Headaches, sedation, dizziness
- Blurred vision
- Nausea, constipation, dyspepsia (heartburn), salivary hypersecretion, vomiting
- Fatigue

Less frequent side effects:
- Hyperprolactinaemia (elevated levels of hormone prolactin)
- Hyperglycaemia (elevated levels of glucose in the blood stream)
- Depression
- Hyper sexuality (extremely frequent or sudden increase in libido)
- Dystonia (involuntary muscle contractions that cause repetitive or twisting movements)
- Diplopia (double vision)
- Tachycardia (increased heart rate)
- Hiccups
- Dysphagia (difficulty swallowing)
- Diarrhoea

Unknown frequency:
- Leukopenia (A low level of white blood cells in the blood, which can interfere with the ability to fight infection)
- Neutropenia (Low level of neutrophils. Neutrophils are a type of white blood cell)
- Thrombocytopenia (Low blood platelet count. Platelets are colourless blood cells that help blood clot)
- Allergic reaction
- Diabetic hyperosmolar coma (Symptoms include signs of dehydration, weakness, leg cramps, vision problems, and an altered level of consciousness)
- Diabetic ketoacidosis (excessive thirst, frequent urination, nausea and vomiting, abdominal pain, weakness or fatigue, shortness of breath, fruity-scented breath and confusion)
- Hyponatremia (ow level of sodium in the blood)
- Anorexia
- Weight decreased
- Weight gain
- Suicide attempt, suicidal ideation and completed suicide
- Compulsive gambling
- Aggression
- Agitation
- Nervousness
- Grand mal convulsion (causes a loss of consciousness and violent muscle contractions)
- Serotonin syndrome (symptoms include high body temperature, agitation, increased reflexes, tremor, sweating, dilated pupils, and diarrhoea)
- Speech disorder
- Oculogyric crisis (involuntary movements of the eyeballs)
- Sudden unexplained death
- Torsades de pointes (abnormal heart rhythm that can lead to sudden cardiac death)
- QT prolongation
- Ventricular arrhythmias
- Cardiac arrest (sudden, unexpected loss of heart function, breathing and consciousness)
- Bradycardia (slow heart rate)
- Venous thromboembolism (blood clot)- [including pulmonary embolism (blood clot in the artery in the lung) and deep vein thrombosis]
- Hypertension (high blood pressure)
- Syncope (temporary loss of consciousness)
- Aspiration pneumonia (when you inhale food, stomach acid, or saliva into your lungs)
- Laryngospasm (spasm of the vocal cords that temporarily makes it difficult to speak or breathe)
- Oropharyngeal spasm
- Pancreatitis (inflamed pancreas. Symptoms include Upper abdominal pain that radiates into the back; it may be aggravated by eating, especially foods high in fat. Swollen and tender abdomen, nausea and vomiting, fever and increased heart rate)
- Abdominal discomfort
- Stomach discomfort
- Hepatic failure/ Liver failure (symptoms include nausea, loss of appetite, fatigue, diarrhoea, jaundice, a yellowish colour of the skin and eyes, weight loss, bruising or bleeding easily, itching and fluid build-up in the legs)
- Hepatitis (inflammation of the liver)
- Jaundice (A yellow colour to the skin or eyes)
- Increased Alanine Aminotransferase (ALT)
- Increased Aspartate Aminotransferase (AST)
- Increased Gamma Glutamyl Transferase (GGT)
- Increased alkaline phosphatase
- Rash
- Photosensitivity reaction
- Alopecia (Hair loss from the scalp or elsewhere on the body)
- Hyperhidrosis (excessive sweating)
- Rhabdomyolysis (A breakdown of muscle tissue that releases a damaging protein into the blood)
- Myalgia (pain in a muscle or group of muscles)
- Muscle Stiffness
- Urinary incontinence (Loss of bladder control)
- Urinary retention
- Priapism (A prolonged erection of the penis, usually without sexual arousal)
- Temperature regulation disorder (dangerously low body temperature or fever)
- Chest pain
- Peripheral oedema (accumulation of fluid causing swelling)
- Glycosylated haemoglobin increased
- Blood glucose fluctuation
- Increased creatine phosphokinase

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects via https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store ALEBON
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
Store at or below 25 °C.
- Keep in original packaging until required for use.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What ALEBON contains
The active substance is aripiprazole.
Each tablet of ALEBON 5 mg contains 5 mg of aripiprazole.
Contains Sugar: Lactose monohydrate 76,00 mg.

Each tablet of ALEBON 10 mg contains 10 mg of aripiprazole.
Contains Sugar: Lactose monohydrate 66,50 mg

Each tablet of ALEBON 15 mg contains 15 mg of aripiprazole.
Contains Sugar: Lactose monohydrate 99,75 mg

The other ingredients are cellulose microcrystalline, hydroxyl propyl cellulose, lactose monohydrate, magnesium stearate, maize starch and silica colloidal anhydrous.
In addition, ALEBON 5 mg contains FD & C blue No: 2 (C.I. No: 73015).

What ALEBON looks like and contents of the pack
ALEBON 5 mg:
Blue coloured, modified rectangular shaped, uncoated tablets debossed with '62' on one side and 'H' on other side.

ALEBON 10 mg:
White coloured, modified rectangular shaped, uncoated tablets debossed with '63' on one side and 'H' on other side.

ALEBON 15 mg:
White coloured, round shaped, uncoated tablets debossed with '64' on one side and 'H' on other side.

Blister packs:
30 tablets are packed in aluminium foil/PVC film blister packs. Each carton contains 3 blisters of 10 tablets each.

HDPE containers:
30 tablets are packed in white opaque HDPE container with a white opaque polypropylene closure with wad, silica gel sachet and rayon.
Not all packs and pack sizes are necessarily marketed.

NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
AUROGEN SA (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

Registration number:
ALEBON 5 mg: 47/2.6.5/1080
ALEBON 10 mg: 47/2.6.5/1081
ALEBON 15 mg: 47/2.6.5/1082

This leaflet was last revised in:
18 May 2021

A/s: 420 x 680 mm ■ Black

AUROBINDO Packaging Development		Product Name	Component	Item Code	Date & Time
		Novalute Tablets	Leaflet	P1528027	16.12.2021 & 10.50 am
		Country	**Version No.**	**Reason Of Issue**	**Reviewed / Approved by**
		South Africa - Aurogen	05	Submission	
Team Leader	Kiran K	**Dimensions (mm)**	**Colours: 01**	**UNIT_7**	
Initiator	Bhogi	A/s: 420 x 680 mm	28027		
Artist	Sree Designers	Pharma Code: 28027			
Additional Information: Sai Charan					

Professionele inligting oor medisyne vir menslike gebruik

SKEDULERINGSTATUS

S5

1. NAAM VAN DIE MEDISYNE
ALEBON 5 mg (tablette)
ALEBON 10 mg (tablette)
ALEBON 15 mg (tablette)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
ALEBON 5 mg:
Elke tablet bevat 5 mg aripiprasool.
Hulpstowwe met 'n bekende effek:
Bevat suiker: laktosemonohidraat 76,00 mg.

ALEBON 10 mg:
Elke tablet bevat 10 mg aripiprasool.
Hulpstowwe met 'n bekende effek:
Bevat suiker: laktosemonohidraat 66,50 mg.

ALEBON 15 mg:
Elke tablet bevat 15 mg aripiprasool.
Hulpstowwe met 'n bekende effek:
Bevat suiker: laktosemonohidraat 99,75 mg.
Raadpleeg afdeling 6.1 vir die volledige lys hulpstowwe.

3. FARMASEUTIESE VORM
ALEBON 5 mg:
Blou, gemodifiseerde reghoekige onbedekte tablette met "62" op die een kant gedruk en "H" op die ander kant.

ALEBON 10 mg:
Wit, gemodifiseerde reghoekige onbedekte tablette met "63" op die een kant gedruk en "H" op die ander kant.

ALEBON 15 mg:
Wit, gemodifiseerde ronde onbedekte tablette met "64" op die een kant gedruk en "H" op die ander kant.

4. KLINIESE BESONDERHEDE
4.1. Terapeutiese indikasies
ALEBON is aangedui vir die behandeling van skisofrenie en vir die onderhoud van kliniese verbetering in volwassenes.
ALEBON is aangedui vir die behandeling van akute maniese episodes van bipolêre I-versteuring en vir die voorkoming van die herhaling van nuwe maniese episodes in pasiënte wat oorwegend maniese episodes ervaar en wat op behandeling met **ALEBON** gereageer het.

4.2. Dosis en metode van toediening
Skisofrenie
Die aanbevole aanvangsdosis van **ALEBON** is 10 of 15 mg/dag met 'n instandhoudingsdosis van 15 mg/dag een keer per sonder inagneming van maaltye. **ALEBON** is effektief in die dosisgebied van 10 tot 30 mg/dag. Groter effektiwiteit teen dosisse hoër as die aanbevole daaglikse dosis van 15 mg is nie aangetoon nie hoewel individuele pasiënte by 'n hoër dosis kan baat. Die maksimum daaglikse dosis moet 30 mg nie oorskry nie.

Bipolêre manie
Die aanbevole aanvangsdosis van **ALEBON** is 15 mg een keer per dag, sonder inagneming van maaltye as monoterapie of kombinasieterapie (kyk afdeling 4.5). Vir sommige pasiënte kan 'n hoër dosis voordelig wees. Die maksimum daaglikse dosis moet 30 mg nie oorskry nie.

Voorkoming van herhaling van maniese episodes in bipolêre I-versteuring: Om die herhaling van maniese episodes te voorkom in pasiënte wat **ALEBON** ontvang het, moet die behandeling teen dieselfde dosis voortgesit word. Aanpassings in die daaglikse dosis, waaronder verlaging van die dosis, moet op grond van die kliniese status oorweeg word. Die voorkoming van depressiewe episodes met aripiprasool (soos in **ALEBON**) is nie bepaal nie. Aanvullende behandeling moet soos dit klinies toepaslik oorweeg word vir die voorkoming of behandeling van depressiewe episodes.

Meegaande medikasie
Aanpassing in die dosis vir pasiënte wat **ALEBON** saam met kragtige CYP3A4- of CYP2D6-remmers gebruik: As kragtige remmers van CYP3A4- of CYP2D6 saam met **ALEBON** gegee word, moet die dosis van **ALEBON** tot die helfte van die gewone dosis verminder word. Wanneer die CYP3A4- of CYP2D6-remmer uit kombinasieterapie onttrek word, moet die dosis **ALEBON** verhoog word (kyk afdeling 5.2).
Dosisaanpassing vir pasiënte wat kragtige CYP3A4-induseerders gebruik: Wanneer 'n kragtige CYP3A4-induseerder by **ALEBON** gevoeg word, moet die dosis **ALEBON** verdubbel word. Bykomende verhogings in de dosis van **ALEBON** moet op kliniese evaluering gebaseer wees. Wanneer die CYP3A4-induseerder aan die kombinasieterapie onttrek word, moet die dosis **ALEBON** verlaag word (kyk afdeling 5.2).

Metode van toediening:
ALEBON is vir orale toediening.

4.3. Kontra-indikasies
ALEBON is teenaangedui vir:
- Pasiënte met hipersensitiwiteit vir aripiprasool of vir enige van die hulpstowwe in **ALEBON** (kyk afdeling 6.1).
- Die veiligheid en effektiwiteit van **ALEBON** vir pasiënte jonger as 18 jaar is nie bepaal nie

4.4. Spesiale waarskuwings en voorsorgmaatreëls tydens gebruik
'n Verbetering in die pasiënt se kliniese toestand kan eers etlike dae tot weke na behandeling met die antipsigotikum voorkom. Pasiënte moet in hierdie periode noukeurig gemonitor word.

Selfdood
Die moontlikheid van 'n selfdoodpoging is inherent aan psigotiese siektes en gemoedsversteurings, en in sommige gevalle is dit vroeg na aanvang of omskakeling van antipsigotiese behandeling, waaronder behandeling met aripiprasool, aangemeld (kyk afdeling 4.8). Pasiënte met 'n hoë risiko moet tydens behandeling met **ALEBON** noukeurig dopgehou word. Voorskrifte vir **ALEBON** moet vir die kleinste aantal tablette wees wat die pasiënt goed sal beheer ten einde die risiko vir oordosering te verlaag.

Kardiovaskulêre versteurings
ALEBON moet versigtig gebruik word deur pasiënte met bekende kardiovaskulêre siekte (geskiedenis van miokardiale infarksie of iskemiese hartsiekte, hartversaking of geleidingsabnormaliteite), serobrovaskulêre siekte of toestande wat die pasiënt aan hipotensie blootstel (dehidrasie, hipovolemie en behandeling met anti-hipertensiewe produkte) of hipertensie, waaronder versnelde of kwaadaardige.

Gevalle van veneuse trombo-embolisme (VTE) is met antipsigotiese medisyne aangemeld. Aangesien pasiënte wat met antipsigotika behandel word, dikwels verworwe risikofaktore vir VTE het, moet alle moontlike risikofaktore vir VTE voor en tydens behandeling met **ALEBON** geïdentifiseer en voorkomende maatreëls getref word.

Ortostatiese hipotensie
ALEBON kan met ortostatiese hipotensie gepaardgaan wat miskien vanweë sy antagonisme van die α1-adrenergiese reseptor is.

Verlenging van QT-interval
In kliniese toetse met aripiprasool was die voorkoms van QT-verlenging vergelykbaar met placebo. Soos met ander antipsigotika, moet aripiprasool versigtig gebruik word deur pasiënte met 'n familiegeskiedenis van QT-verlenging (kyk afdeling 4.8).

Laat diskinesie
Omdat die risiko vir dralende diskinesie met langtermynblootstelling aan anti-psigotiese middels verhoog, moet die dosis verlaag of die middel gestaak word as tekens en simptome van dralende diskinesie in 'n pasiënt voorkom. Hierdie simptome kan tydelik na staking van behandeling vererger of selfs verskyn.

Ander ekstrapiramidale simptome
In kliniese proewe met aripiprasool is akatisie en parkinsonisme in kinders waargeneem. As tekens en simptome van ander EPS voorkom in 'n pasiënt wat **ALEBON** gebruik, moet verlaging in die dosis en noukeurige kliniese monitering oorweeg word. Gebruik van aripiprasool deur pasiënte jonger as 18 jaar is teenaangedui (kyk afdeling 4.3).

Neuroleptiese kwaadaardige sindroom
'n Moontlik dodelike simptoomkompleks, waarna soms as die neuroleptiese kwaadaardige sindroom (NKS) verwys word, is aangemeld. Kliniese manifestasies van NKS is hiperpireksie, spierstyfheid, veranderde verstandelike status en getuienis van outonome onstabiliteit (onreëlmatige polsslag of bloeddruk, tagikardie, diaforese en hartdisritmie). Bykomende tekens kan hoër vlakke kreatinienfosfokinase, mioglobinurie (rabdomiolise) en akute nierversaking wees.
As 'n pasiënt tekens en simptome ontwikkel wat op NKS dui, of 'n onverklaarbare hoë koors sonder verdere kliniese manifestasies van NKS, moet alle antipsigotiese medisyne, waaronder **ALEBON**, gestaak word.

Toevalle
ALEBON moet versigtig gebruik word deur pasiënte met 'n geskiedenis van toevalle of wat toestande het wat met toevalle gepaardgaan.

Regulering van liggaamstemperatuur
Versteuring van die liggaam se vermoë om liggaamstemperatuur te beheer is aan antipsigotiese middels toegeskryf. Toepaslike sorg word aanbeveel as aripiprasool voorgeskryf word aan pasiënte wat toestande sal ervaar wat bydra tot 'n verhoging in liggaamstemperatuur, bv. strawwe oefening, blootstelling aan buitengewone hitte, gelyktydige behandeling met anticholinergiese middels of blootstelling aan dehidrasie.

Bejaarde pasiënte met psigoses vanweë dimensie
Bejaarde pasiënt met psigoses vanweë dimensie wat met **ALEBON** behandel word, het 'n hoër risiko vir sterftes vergeleke met placebo. Hoewel die oorsake van dood gewissel het, het dit gelyk asof die meeste sterftes vanweë kardiovaskulêre effekte (bv. hartversaking, sieklike dood) of infeksies (bv. longontsteking) was. **ALEBON** is nie vir die behandeling van pasiënte met psigoses vanweë dimensie goedgekeur nie.

Hiperglisemie en diabetes mellitus
Hiperglisemie is aangemeld in pasiënte wat met atipiese antipsigotika, waaronder aripiprasool soos in **ALEBON**, behandel is en dit was in party gevalle ernstig en het met ketoasidose of hiperosmolêre koma of sterftes gepaardgegaan. Pasiënte wat met **ALEBON** behandel word, moet dopgehou word vir tekens en simptome van hiperglisemie (soos polidipsie, poliurie, polifagie en swakheid) en pasiënte met diabetes mellitus of risikofaktore vir diabetes mellitus moet gereeld gemonitor word vir agteruitgang in die beheer van bloedsuiker (kyk afdeling 4.8). Pasiënte wat tydens behandeling met **ALEBON** simptome van hiperglisemie ontwikkel, moet vastende bloedglukosetoetse ondergaan. In party gevalle het hiperglisemie opgeklaar nadat **ALEBON** gestaak is, hoewel party pasiënte steeds antidiabetiese behandeling nodig gehad het ten spyte van staking van die verdagte medisyne.

Hipersensitiwiteit
Soos met ander medisyne, kan hipersensitiwiteitsreaksies met aripiprasool voorkom (kyk afdeling 4.8).

Toename in gewig
Gewigstoename word algemeen gesien in pasiënte met skisofreniese en bipolêre manie as gevolg van komorbiditeite, die gebruik van antipsigotika wat gewigstoename veroorsaak en 'n swak bestuurde lewenswyse kan ernstige komplikasies veroorsaak. As dit gesien word, is dit gewoonlik diegene met beduidende risikofaktore soos 'n geskiedenis van diabetes, skildklierafwyking of hipofise-adenoom. Gewigstoename in adolessente pasiënte van 18 jaar en ouer met bipolêre manie moet gemonitor word. As gewigstoename klinies beduidend is, moet 'n verlaging in die dosis oorweeg word (kyk afdeling 4.8).

Disfagie
Esofageale dismotiliteit en aspirasie het met gebruik van antipsigotiese middels voorgekom. **ALEBON** en ander anti-psigotiese middels moet versigtig gebruik word deur pasiënte met 'n risiko vir longontsteking vanweë aspirasie.

Patologiese dobbelary
Sterker drange, veral vir dobbel, en die onvermoë om hierdie drange te beheer, kom voor as aripiprasool gebruik word. Daar was ook berigte van erger seksuele drange, kompulsiewe inkope, ooreet of kompulsiewe eet, en ander impulsiewe en kompulsiewe gedrag. Voorskrywers moet pasiënte of hul versorgers spesifiek uitvra oor die ontwikkeling van nuwe of erger drang vir dobbel, seksuele drange, kompulsiewe inkope, ooreet of kompulsiewe eet of ander drange terwyl hulle met aripiprasool behandel word. Patologiese dobbel van pasiënte vir wie aripiprasool voorgeskryf is, is na bemarking aangemeld, ongeag daarvan of hierdie pasiënte 'n geskiedenis van dobbel gehad het. Pasiënte met 'n vroeëre geskiedenis van patologiese dobbelary kan 'n groter risiko hê en moet noukeurig dopgehou word. Daar moet kennis geneem word dat simptome van swak impulsbeheer met die onderliggende siekte kan voorkom; in sommige gevalle is daar egter berig dat die drange opgehou het toe die dosis verlaag of die medisyne gestaak is. Swak impulsbeheer lei tot skade aan die pasiënt en ander kan as dit nie raakgesien word nie. Verlaging van die dosis of die staking van die medikasie moet oorweeg word as 'n pasiënt sulke drange ontwikkel terwyl aripiprasool gedrink word (kyk afdeling 4.8).

Pasiënte met ADHD as komorbiditeit
Ten spyte van die hoë frekwensie van komorbiditeit van bipolêre I-versteuring en ADHD, is daar baie beperkte veiligheidsdata beskikbaar oor gelyktydige gebruik van aripiprasool en stimulante; wees daarom baie versigtig wanneer hierdie middels saam gegee word.

Struikeling
ALEBON kan slaperigheid, posturale hipotensie, motoriese en sensoriese onstabiliteit veroorsaak, wat tot struikelings kan lei. Wees versigtig wanneer pasiënte met 'n hoër risiko behandel word, en 'n laer aanvangsdosis moet oorweeg word (bv. bejaarde of verswakte pasiënte).

Laktose
ALEBON bevat laktosemonohidraat. Pasiënte met die skaars oorerflike probleem van onverdraagbaarheid van galaktose, die Laplandse laktasetekort of wanabsorpsie van glukose/galaktose, moet nie hierdie medisyne gebruik nie.

4.5. Interaksies met ander medisyne en ander vorms van interaksie:
Algemeen
Gegewe die primêre effekte van **ALEBON** op die SSS, moet **ALEBON** as gevolg van oorvleuelende newe-effekte soos sedasie versigtig in kombinasie met ander sentraalwerkende medisyne gebruik word (kyk afdeling 4.8). Net so moet gebruik van **ALEBON** saam met alkohol vermy word. As gevolg van die aktiwiteit as antagonis van die α_1-adrenergiese reseptor, kan **ALEBON** die effek van sekere antihipertensiewe middels verhoog.

Daar was geen effek van 'n hoëvetmaaltyd op die farmakokinetika van **ALEBON** nie.

Wees versigtig as **ALEBON** toegedien word saam met medisyne wat bekend is dat dit QT-verlenging of elektrolietwanbalans veroorsaak.

Die moontlikheid dat ander medisyne aripiprasool kan beïnvloed
'n Maagsuurblokker, die H2-antagonis famotidien, verminder die absorpsiesnelheid van aripiprasool, maar hierdie effek word nie as klinies relevant beskou nie.

Valproaat en litium
Daar was geen klinies beduidende verandering in aripiprasool-konsentrasies toe valproaat of litium saam met aripiprasool toegedien is nie.
ALEBON word volgens verskeie roetes deur die CYP2D6- en CYP3A4-ensieme gemetaboliseer maar nie deur CYP1A-ensieme nie.

Kinidien en ander CYP2D6-remmers
Kinidien, 'n sterk remmer van CYP2D6, het plasmablootstelling (AOK) van aripiprasool in kliniese toetse verhoog. Die dosis van **ALEBON** moet tot ongeveer die helfte verminder word as dit saam met kinidien gegee word. Dit kan verwag word dat ander kragtige remmers van CYP2D6, soos fluoksetien en paroksetien, dieselfde effekte kan uitoefen en die dosisse moet dus dienooreenkomstig verlaag word.

Ketokonasool en ander CYP3A4-remmers
Ketokonasool, 'n sterk remmer van CYP3A4, verhoog die blootstelling aan aripiprasool en metaboliet dehidro-aripiprasool in die plasma.

Met swak CYP2D6-metaboliseerders kan gelyktydige gebruik van kragtige remmers van CYP3A4 'n hoër plasmakonsentrasie van aripiprasool veroorsaak vergeleke met dié met sterk metaboliseerders van CYP2D6.

As ketokonasool saam met aripiprasool toegedien word, moet die dosis van **ALEBON** tot die helfte van die voorgeskrewe dosis verlaag word. Dit kan verwag word dat ander kragtige remmers van CYP3A4, soos itrakonasool en MIV-proteaseremmers, dieselfde effekte kan uitoefen en die dosisse moet dus dienooreenkomstig verlaag word (kyk afdeling 4.2). Wanneer swak remmers van CYP3A4 (bv. diltiasem) of CYP2D6 (bv. essitalopraam) saam met aripiprasool gebruik word, kan 'n matige toename in plasmakonsentrasies van aripiprasool verwag word.

Na staking van die CYP2D6- of CYP3A4-remmer, moet die dosis van aripiprasool verhoog word tot die vlak voor die aanvang van gelyktydige behandeling.

Karbaamasepien en ander CYP3A4-induseerders
Gelyktydige toediening van karbaamasepien, 'n sterk induseerder van CYP3A4, en orale aripiprasool aan pasiënte met skisofrenie of skiso-affektiewe versteuring, het gelei tot 'n laer plasmablootstelling aan aripiprasool en die metaboliet dehidro-aripiprasool in vergelyking met toe aripiprasool alleen toegedien was.

Die dosis van **ALEBON** moet verdubbel word as dit saam met karbaamasepien gegee word. Dit kan verwag word dat ander kragtige induseerders van CYP3A4 (soos rifampisien, rifabutien, fenitoïen, fenobarbitoon, primidoon, efavirens, nevirapien en die Sint Janskruid) soortgelyke effekte sal uitoefen en die dosis moet dienooreenkomstig verhoog word. Na staking van kragtige CYP3A4-induseerders moet die dosis van **ALEBON** tot die aanbevole dosis verlaag word.

Moontlike effek van ALEBON op ander medisyne
In kliniese studies het dosisse van 10 tot 30 mg/dag aripiprasool geen beduidende effek op die metabolisme van substrate van CYP2D6 (dekstrometorfaan/3-metoksimorfinaan-verhouding), CYP2C9 (warfarien), CYP2C19 (omeprasool) en CYP3A4 (dekstrometorfaan) gehad nie. Daarby het aripiprasool en dehidro-aripiprasool in vitro geen potensiaal getoon om die metabolisme deur CYP1A2 te verander nie. Dit is dus onwaarskynlik dat aripiprasool enige klinies beduidende medisinale interaksies vanweë hierdie ensieme sal veroorsaak.

Serotoniensindroom
Gevalle van die serotonien-sindroom is aangemeld in pasiënte wat aripiprasool soos in **ALEBON** gebruik het, en moontlike tekens en simptome vir hierdie toestand kan veral voorkom in gevalle van gebruik saam met ander serotonergiese middels, soos SSHR's/SNHR's, of saam met medisyne wat bekend is daarvoor dat dit **ALEBON**-konsentrasies verhoog (kyk afdeling 4.8).

Toe **ALEBON** saam met lamotrigien gegee was, was daar geen klinies belangrike verandering in die konsentrasies van lamotrigien nie.

4.6. Fertiliteit, swangerskap en borsvoeding
Die veiligheid van **ALEBON** tydens swangerskap en borsvoeding is nie bepaal nie.

Swangerskap
Geen voldoende en behoorlik gekontroleerde studies is met aripiprasool en swanger vroue gedoen nie. Aangebore afwykings is aangemeld; 'n oorsaaklike verband met aripiprasool kon egter nie bepaal word nie. Studies met diere kon moontlike toksisiteit op ontwikkeling nie uitsluit nie (kyk afdeling 5.3). Pasiënte moet inlig word om hulle mediese praktisyns in kennis te stel as hulle tydens behandeling met aripiprasool swanger raak of beplan om swanger te raak. As gevolg van onvoldoende veiligheidsinligting vir mense en kommer wat uit studies van voortplanting in diere voorkom, is hierdie medisyne teenaangedui.

Pasgebore babas wat gedurende die derde trimester van die swangerskap aan antipsigotika (insluitend aripiprasool) blootgestel is, loop die risiko vir newe-reaksies, waaronder ekstrapiramidale en/of onttrekkingsimptome, wat in erns en duur na die bevalling kan wissel. Daar was verslae van agitasie, hipertonie, hipotonie, bewing, slaperigheid, asemhalingsnood of voedingstoornis. Pasgebore babas moet gevolglik noukeurig gemonitor word (kyk afdeling 4.8).

Borsvoeding
Aripiprasool word in borsmelk uitgeskei. Daar moet besluit word om borsvoeding of behandeling met aripiprasool te staak.

Fertiliteit
Op grond van data uit studies van toksisiteit op voortplanting benadeel aripiprasool nie vrugbaarheid nie.

4.7. Effek op vermoë om 'n voertuig te bestuur en masjiene te gebruik
ALEBON het as gevolg van moontlike effekte op die senustelsel en visie, soos sedasie, slaperigheid, sinkopee, dowwe visie, diplopie 'n geringe tot matige invloed op die vermoë om te bestuur en masjiene te gebruik (kyk afdeling 4.8).

Pasiënte moet gewaarsku word teen die gebruik van gevaarlike masjiene, waaronder motorvoertuie, totdat hulle redelik seker is dat aripiprasool hulle nie nadelig beïnvloed nie. Sommige pediatriese pasiënte met 'n bipolêre I-versteuring ervaar 'n groter voorkoms van slaperigheid en moegheid (kyk afdeling 4.8).

4.8. Ongewensde effekte
a. Opsomming van die veiligheidsprofiel
Die mees algemene aangemelde newe-effek in plasebogekontroleerde proewe was akatisie en naarheid wat elk voorgekom het in meer as 3 % van die pasiënte wat met orale aripiprasool behandel is.

b. Getabuleerde opsomming van nadelige reaksies
Ongunstige geneesmiddelreaksies word volgens die orgaanklas en frekwensie geklassifiseer; binne elke frekwensiegroepering word nadelige reaksies in volgorde van dalende erns gegee. Die tabel is gebaseer op newe-effekte wat tydens kliniese toetse en/of na bemarking aangemeld is.

Die frekwensie van ongewenste reaksies wat tydens gebruik na bemarking aangemeld is, kan nie bepaal word nie, aangesien dit van spontane verslae verkry is. Gevolglik word die frekwensie van hierdie newe-effekte as "Frekwensie onbekend" gekwalifiseer.

Orgaanstelsel	Dikwels	Minder dikwels	Frekwensie nie bekend nie
Versteurings van die bloed en limfstelsel			Leukopenie, Neutropenie, Trombositopenie
Versteurings van die immuunstelsel			Allergiese reaksie (bv. anafilaktiese reaksie, angio-edeem, waaronder geswelde tong, tongedeem, gesigsedeem, pruritus of urtikarie)
Versteurings van endokrien-stelsel		Hiperprolaktinemie	Diabetiese hiperosmolêre koma, Diabetiese ketoasidose
Versteurings in metabolisme en voeding	Diabetes mellitus	Hiperglisemie	Hiponatremie, Anoreksie, Gewigsverlies, Toename in gewig
Psigiatriese versteurings	Slaaploosheid, Angs, Rusteloosheid	Depressie, Hiperseksualiteit	Selfdoodpoging, selfdoodgedagtes en suksesvolle selfdood (kyk afdeling 4.4) , Patologiese dobbel, Versteuring in impulsbeheer, Ooreet, Kompulsiewe inkopies, Poriomanie, Aggressie, Agitasie, Senuagtigheid
Versteurings van die senustelsel	Akatisie, Ekstrapiramidale versteurings, Bewerasie, Hoofpyn, Sedasie, Lomerigheid, Duiseligheid	Laat diskinesie , Distonie	Neuroleptiese kwaadaardige sindroom (NKS), Grand mal-stuipe, Serotoniensindroom, Spraakversteuring
Oogversteurings	Dowwe visie	Dubbelvisie	Okulogiriese krisis
Hartversteurings		Tagikardie	Skielike onverklaarbare dood, Torsades de pointes, Verlenging van QT-interval, Ventrikulêre disritmie, Hartarres, Bradikardie
Vaskulêre versteurings		Ortostatiese hipotensie	Veneuse trombo-embolisme (waaronder pulmonale embolisme en diep veneuse trombose), Hipertensie, Sinkopee
Respiratoriese, toragiese en mediastinale versteurings		Hik	Longontsteking vanweë aspirasie, Laringospasma, Orofaringeale spasma
Gastro-intestinale versteuring	Hardlywigheid, Dispepsie, Naarheid, Oorafskeiding van speeksel, Braking		Pankreatitis, Disfagie, Diarree, Buikongemak, Maagongemak
Hepatobiliêre versteurings			Lewerversaking, Hepatitis, Geelsug, Hoër vlakke alanienaminotransferase (ALT), Hoër vlakke aspartaataminotransferase (AST), Hoër vlakke gammaglutamieltransferase (GGT), Hoër vlakke alkaliese fosfatase
Versteurings van die vel en subkutane weefsel			Veluitslag, Fotosensitiwiteitsreaksies, Alopesie, Hiperhidrose
Versteurings van die muskuloskeletale stelsel en van bindweefsel			Rabdomiolise, Mialgie, Muskuloskeletale styfheid
Versteurings van die niere en urienweg			Urieninkontinensie, Urienretensie
Swangerskap, puerperium en perinatale toestande			Neonatale geneesmiddelonttrekkingsindroom (kyk afdeling 4.6)
Versteurings in die voortplantingstelsel en borste			Priapisme
Algemene versteurings en effekte by die plek van toediening	Moegheid		Versteuring van temperatuurregulering (bv. hipotermie, pireksie), Pyn in die borskas, Perifere edeem
Laboratoriumtoetse			Hoër vlakke bloedglukose, Hoër vlakke geglikosileerde hemoglobien, Fluktuasie in bloedglukosevlakke, Hoër vlakke kreatinienfosfokinase

c. Beskrywing van spesifieke nadelige reaksies
Distonie
Simptome van distonie, langdurige abnormale sametrekkings van spiergroepe, kan gedurende die eerste paar dae van behandeling in vatbare individue voorkom. Simptome van distonie is onder meer krampe in die nekspiere, wat soms tot styfheid in die keel lei, slukprobleme, asemhalingsprobleme en/of uitsteek van die tong. Alhoewel hierdie simptome by lae dosisse kan voorkom, kom dit meer gereeld voor en met 'n erger graad met kragtige eerste generasie antipsigotiese medisyne en teen hoër dosisse. 'n Hoër risiko van akute distonie word in mans en in jonger ouderdomsgroepe waargeneem.

Prolaktien
In kliniese proewe vir die goedgekeurde indikasies en na bemarking is sowel 'n styging as daling in die vlakke van prolaktien in die serum met aripiprasool waargeneem.

Pediatriese populasie
Skisofrenie in adolessente van 15 jaar en ouer
In 'n korttermyn kliniese proef met adolessente (13-17 jaar) met skisofrenie, was die frekwensie en tipe ongewenste effekte soortgelyk aan dié in volwassenes, behalwe vir die volgende reaksies wat meer dikwels aangemeld is deur adolessente wat aripiprasool ontvang het as deur volwassenes (en meer dikwels as plasebo): slaperigheid/sedasie, ekstrapiramidale afwykings, droë mond, groter eetlus en ortostatiese hipotensie.

Die veiligheidsprofiel van 'n langtermynproef was ook soortgelyk behalwe vir die volgende reaksies wat meer dikwels aangemeld is as pediatriese pasiënte wat plasebo gekry het: gewigsverlies, hoër vlakke insulien in die bloed, disritmie en leukopenie.

Maniese episodes in bipolêre I-versteuring in tieners van 13 jaar en ouer
Die frekwensie en tipe ongewenste effekte in adolessente met bipolêre I-versteuring was soortgelyk aan dié in volwassenes, behalwe vir die volgende reaksies: slaperigheid, ekstrapiramidale afwyking, akatisie, moegheid, boonstebuikpyn, vinniger hartklop, gewigstoename, groter eetlus, spiertrekkings en diskinesie.

d. Aanmeld van vermeende nadelige reaksies
Dit is belangrik om vermeende nadelige reaksies wat na magtiging van die medisinale produk voorkom, aan te meld. Dit maak voortgesette monitering van die balans tussen voordeel en risiko van die medisinale produk moontlik. Gesondheidspraktisyns word versoek om alle vermeende nadelige reaksies by SAHPRA aan te meld met die vorm "6.04 Adverse Drug Reaction Reporting Form" wat aanlyn by SAHPRA se publikasies gekry kan word:
https://www.sahpra.org.za/Publications/Index/8.

4.9. Oordosis
Simptome
Die potensieel medies belangrike tekens en simptome wat aangemeld is, was lusteloosheid, hoë bloeddruk, slaperigheid, tagikardie, naarheid, braking en diarree. Die potensieel medies ernstige tekens en simptome in kinders is onder meer slaperigheid, kortstondige verlies van bewussyn en ekstrapiramidale simptome.

Behandeling
Behandeling van oordosering is ondersteunende terapie, handhawing van 'n oop lugweg, oksigenering en ventilasie en beheer van simptome. Die moontlikheid dat talle medisyne gebruik kan word, moet in gedagte gehou word. Kardiovaskulêre monitering moet daarom onmiddellik begin en moet kontinue elektrokardiografiese monitering insluit om moontlike aritmie op te spoor.

Na enige bevestigde of vermoedelike oordosering met **ALEBON** moet noukeurige mediese toesig en monitering volgehou word totdat die pasiënt herstel.

Geaktiveerde houtskool (50 g), toegedien een uur na **ALEBON** verlaag aripiprasoolvlakke.

Hoewel daar geen inligting is oor die effek van hemodialise vir behandeling van oordosering met **ALEBON** nie, is dit onwaarskynlik dat hemodialise nuttig sal wees omdat aripiprasool nie onveranderd deur die niere uitgeskei word nie en sterk aan plasmaproteïene bind.

5. FARMAKOLOGIESE EIENSKAPPE
5.1. Farmakodinamiese eienskappe
Farmakoterapeutiese groep: Psigoleptika, ander antipsigotika, ATC-kode: N05AX12
Kategorie en klas: A 2.6.5 Bedaarmiddels – diverse strukture

Werkingsmeganisme
Dit is voorgestel dat die effek van aripiprasool bewerkstellig word deur 'n kombinasie van aktiwiteit as gedeeltelike agonis op dopamien D2- en serotonien 5HT1a-reseptore en aktiwiteit as antagonis op serotonien 5HT2-reseptore.

Aripiprasool het *in vitro* hoë bindingsaffiniteit vir dopamien D2- en D3-, serotonien 5HT1a- en 5HT2a-reseptore getoon en matige affiniteit vir dopamien D4-, serotonien 5HT2C- en 5HT7-, alfa1-adrenergiese en histamien H1-reseptore. Aripiprasool vertoon ook matige bindingsaffiniteit aan plekke vir serotonienheropname en geen beduidende affiniteit vir muskariniese reseptore nie. Aripiprasool het as antagonis opgetree in diermodelle van dopamienergiese hiperaktiwiteit en as agonis in diermodelle van dopamienergiese hipoaktiwiteit. Interaksie met ander reseptore as dopamien en serotonien kan party van die ander kliniese effekte van aripiprasool verklaar.

5.2. Farmakokinetiese eienskappe
Absorpsie
Aripiprasool word na orale toediening van **ALEBON** goed geabsorbeer met piek konsentrasies in die plasma binne 3 - 5 uur na dosering. Aripiprasool ondergaan die minimum presistemiese metabolisme. Die absolute orale biobeskikbaarheid van aripiprasool uit die tabletformulering is 87 %. Die biobeskikbaarheid van aripiprasool word nie beduidend deur voedsel beïnvloed nie.

Verspreiding
Aripiprasool versprei wyd deur die liggaam met 'n oënskynlike volume van verdeling van 4,9 L/kg. Teen terapeutiese konsentrasies is meer as 99 % van die aripiprasool aan proteïene in die serum, hoofsaaklik albumien, gebind. Aripiprasool verander nie die farmakokinetika en farmakodinamika van hoogs proteïengebinde warfarien nie wat toon dat warfarien nie van die proteïene verplaas word nie.

Biotransformasie
Aripiprasool ondergaan die minimum presistemiese metabolisme. Aripiprasool word tot 'n groot mate deur die lewer gemetaboliseer, hoofsaaklik deur drie biotransformasieroetes: dehidrogenering, hidroksilering en N-alkilering. *In vitro*-studies het gevind dat CYP3A4- en CYP2D6-ensieme verantwoordelik is vir dehidrogenering en hidroksilering van aripiprasool en dat N-dealkilering deur CYP3A4 gekataliseer word. Aripiprasool is die belangrikste vorm van die middel in sistemiese sirkulasie. By gelykvlakke maak dehidro-aripiprasool, die aktiewe metaboliet, ongeveer 39 % van die AOK van aripiprasool in die plasma uit.

Uitskeiding
Die gemiddelde eliminasiehalfleeftyd van aripiprasool is ongeveer 75 uur met sterk metaboliseerders van CYP2D6 en ongeveer 146 uur met swak metaboliseerders van CYP2D6.

Na 'n enkele orale dosis van [14^C]-gemerkte aripiprasool is ongeveer 27 % en 60 % van die toegediende radioaktiwiteit in die urien en feses onderskeidelik gevind. Minder as 1 % van onveranderde aripiprasool is in die urien uitgeskei en ongeveer 18 % van die orale dosis is onveranderd in die feses gevind. Die totale opruiming van aripiprasool uit die liggaam is 0,7 mL/min/kg wat hoofsaaklik in die lewer geskied.

Lineariteit
Gelykvlakkonsentrasies word binne 14 dae bereik. Opbou van aripiprasool met 'n faktor 5 is voorspelbaar tydens veelvoudige dosering. By gelykvlakke is die farmakokinetika van aripiprasool direk eweredig aan die dosis. Daar is minimale diurnale variasie in die verspreiding van aripiprasool en sy aktiewe metaboliet, dehidro-aripiprasool. Dit is aangetoon dat hierdie belangrikste metaboliet in menslike plasma, dehidro-aripiprasool, soortgelyke affiniteit vir D2-reseptore as die moederverbinding het.

Spesiale populasies
Geslag
Die C_{maks} en AOK van aripiprasool en sy aktiewe metaboliet, dehidro-aripiprasool, is hoër in vrouens as in mans en die oënskynlike orale opruiming van aripiprasool is dienooreenkomstig laer in vroue. Hierdie verskille word egter grootliks verklaar deur verskille in liggaamsmassa tussen mans en vroue. Geen aanpassing in die dosis op grond van geslag word aanbeveel nie.

Rook
Populasie farmakokinetiese evaluering het geen bewyse van kliniese beduidende effekte van rook op die farmakokinetika van aripiprasool getoon nie. *In vitro*-studies met menslike lewerensieme toon dat aripiprasool nie 'n substraat vir CYP1A2 is nie en ook nie direkte glukuronidering ondergaan nie. Rook behoort dus nie 'n effek op die farmakokinetika van aripiprasool te hê nie. In ooreenstemming met hierdie *in vitro*-resultate het evaluering van die populasie farmakokinetika nie enige beduidende farmakokinetiese verskille tussen rokers en nierokers aangetoon nie. Geen aanpassing in die dosis op grond van rookstatus word aanbeveel nie.

Ras
Hoewel geen spesifieke farmakokinetiese studie gedoen is om die effek van ras op die verspreiding van aripiprasool te bestudeer nie, het evaluering van die populasie farmakokinetika geen getuienis van klinies beduidende effekte in die farmakokinetika van aripiprasool tussen rasse aangetoon nie. Geen aanpassing in die dosis op grond van ras word aanbeveel nie.

Swak nierfunksie
In pasiënte met erge swak nierfunksie (kreatinienopruiming < 30 mL/min) was die C_{maks} van aripiprasool (gegee as 'n enkele dosis van 15 mg) en dehidro-aripiprasool hoër, maar die AOK was laer vir aripiprasool en hoër vir dehidro-aripiprasool.
Die uitskeiding deur die niere van sowel onveranderde aripiprasool en dehidro-aripiprasool is minder as 1% van die dosis. Geen aanpassing in die dosis is nodig vir pasiënte met swak nierfunksie nie.

Swak lewerfunksie
In 'n studie met 'n enkele dosis (15 mg aripiprasool) aan proefpersone met verskillende grade lewersirrose (Child-Pugh Klasse A, B en C) was die AOK van aripiprasool vergeleke met dié van gesonde proefpersone hoër met ligte verswakte lewerfunksie, hoër met matige verswakte lewerfunksie en laer met erge verswakte lewerfunksie. Geen aanpassing in die dosis is vanweë hierdie effekte nodig nie.

Bejaarde pasiënte
In farmakokinetiese studies (met 'n enkele dosis van 15 mg aripiprasool) was die opruiming van aripiprasool laer in bejaardes (≥ 65 jaar) vergeleke met jonger volwasse proefpersone (18 tot 64 jaar).

Daar was egter geen waarneembare ouderdomseffek in die farmakokinetiese analise in die populasie van skisofreniese pasiënte nie. Dit lyk ook asof die farmakokinetika van aripiprasool na veelvoudige dosisse aan bejaarde pasiënte soortgelyk is as dié aangemeld in jong gesonde proefpersone. Geen aanpassing in die dosis is vir bejaarde pasiënte nodig nie (kyk afdeling 4.4).

Pediatriese populasie
Die farmakokinetika van aripiprasool en dehidro-aripiprasool in pediatriese pasiënte van 10 tot 17 jaar oud was soortgelyk aan dié in volwassenes na regstelling vir die verskille in liggaamsgewig.

5.3 Prekliniese veiligheidsdata
Dierestudies met rotte en konyne kon nie potensiële toksisiteit op die ontwikkeling van die fetus uitsluit nie.

6. FARMASEUTIESE BESONDERHEDE
6.1. Lys van hulpstowwe
Mikrokristallyne sellulose, hidroksipropielsellulose, laktosemonohidraat, magnesiumstearaat, mieliestysel en kolloïdale watervrye silika.
Daarbenewens bevat die 5 mg-tablet FD&C blue nr. 2 (KI Nr.: 73015).

6.2. Onverenigbaarhede
Nie toepaslik nie

6.3. Rakleeftyd
36 maande

6.4. Spesiale voorsorgmaatreëls vir bewaring
Bêre by of onder 25 °C.
Bêre in die oorspronklike houer totdat dit vir gebruik benodig word.

HOU BUITE BEREIK VAN KINDERS.

6.5. Aard en inhoud van die houer
Stulppakke:
30 tablette is verpak in aluminiumfolie/PVC-film stulpverpakkings. Elke karton bevat 3 stulpstroke met 10 tablette elk.

HDPE-houers:
30 tablette word verpak in 'n wit ondeursigtige HDPE-houer met 'n wit ondeursigtige polipropileenprop met watte, silikagelsakkie en rayon.
Nie alle pakke en pakgroottes word noodwendig bemark nie.

6.6. Spesiale voorsorgmaatreëls vir die wegdoen van gebruikte medisyne of afvalstowwe wat uit sodanige medisyne verkry word, en ander hantering van die produk
Geen spesiale vereistes nie.

7. HOUER VAN DIE REGISTRASIESERTIFIKAAT
AUROGEN SA (Edms) Bpk
Woodhillkantoorpark, Gebou 1, Eerste vloer
Phillip Engelbrechtlaan 53
Meyersdal Uitbr. 12, 1448
Johannesburg
Suid-Afrika

8. REGISTRASIENOMMER
ALEBON 5 mg: 47/2.6.5/1080
ALEBON 10 mg: 47/2.6.5/1081
ALEBON 15 mg: 47/2.6.5/1082

9. DATUM VAN EERSTE MAGTIGING
18 Mei 2021

P1528027

✂ DETACH BEFORE DISPENSING

SKEDULERINGSTATUS

S5

PASIËNTINLIGTINGSBLAD
ALEBON (5 mg/ 10 mg/ 15 mg)
Aripiprasool
(Bevat suiker: 76,00 mg/ 66,50 mg/ 99,75 mg laktosemonohidraat per tablet).

Lees hierdie hele blad noukeurig deur voordat u begin om ALEBON te drink.
- **Hou hierdie blad. Dit mag nodig wees dat u dit weer moet lees.**
- **As u nog enige vrae het, moet u u dokter, apteker of ander gesondheidsorgverskaffer vra.**
- **ALEBON is vir u persoonlik voorgeskryf en u moet nie u medisyne vir ander mense gee nie. Dit kan hulle skaad, selfs al is hulle simptome dieselfde as u s'n.**

Wat in hierdie blad is:
1. Wat ALEBON is en waarvoor dit gebruik word
2. Wat u moet weet voordat u ALEBON drink
3. Hoe om ALEBON te drink
4. Moontlike newe-effekte
5. Hoe om ALEBON te bêre
6. Inhoud van die pak en ander inligting

1. Wat ALEBON is en waarvoor dit gebruik word
ALEBON word gebruik vir die behandeling van volwassenes en adolessente van 18 jaar en ouer wat aan 'n siekte genaamd skisofrenie ly. Dit is 'n versteuring waardeur u gedagtes of ervarings uit voeling met die werklikheid lyk, soos om dinge wat nie daar is nie, te hoor of te sien, agterdogtigheid, verkeerde oortuigings, en u kan ongeorganiseerde spraak of gedrag ervaar en minder deelname aan daaglikse aktiwiteite hê. Mense met hierdie toestand kan ook depressief, skuldig, angstig of gespanne voel.

ALEBON word gebruik vir die behandeling van volwassenes wat ly aan 'n toestand met simptome soos om "hoog" te voel, wat oormatige hoeveelhede energie het, minder slaap as gewoonlik nodig het, baie vinnig praat met jaende idees en soms erge prikkelbaarheid. In volwassenes word ALEBON ook gebruik om te voorkom dat hierdie toestand terugkeer in pasiënte wat op behandeling met ALEBON gereageer het.

2. Wat u moet weet voordat u ALEBON drink
Moenie ALEBON drink nie:
- as u hipersensitief (allergies) vir aripiprasool of vir enige van die ander bestanddele van ALEBON is
- As u jonger as 18 jaar oud is.

Wees veral versigtig met ALEBON
- As u depressie vererger, of as u selfdoodgedagtes of -gedrag het, moet u u dokter dadelik kontak.
- As u 'n kardiovaskulêre siekte het (' n siekte van die hart en sirkulasie) of 'n familiegeskiedenis van hartsiektes, hartaanvalle, beroerte of abnormale bloeddruk.
- As u ly aan toestande wat die bloedvate en bloedtoevoer na die brein beïnvloed. As u situasies ervaar wat u aan lae bloeddruk (uitdroging) kan blootstel en as u behandeling ontvang met medisyne wat u bloeddruk verlaag.
- As tekens en simptome van laat diskinesie voorkom ('n toestand wat gekenmerk word deur herhalende, onwillekeurige bewegings, veral in die gesig). Tipes onwillekeurige bewegings sluit in: Grimas (gesigte trek), tongbewegings, lippe lek, lippe smak, vou van die lippe en oormatige oogknip.
- As u toestande ervaar wat kan bydra tot die verhoging van die liggaamstemperatuur, bv. hard oefen, blootstelling aan uiterste hitte, onderhewig aan uitdroging.
- As u krampe, spiersametrekkings, styfheid, trae beweging ervaar.
- As u simptome ervaar van 'n toestand genaamd kwaadaardige neuroleptiese sindroom, wat hoë koors, spierstyfheid, veranderde geestestatus en tekens van outonome onstabiliteit (onreëlmatige pols of bloeddruk, vinnige hartklop, sweet en abnormale hartklop) kan wees.
- As u toevalle (stuiptrekkings) het.
- As u aan demensieverwante psigose ly (as u agterkom dat u 'n afname in geheue, taal, probleemoplossing en ander denkvaardighede het) en as u ouer pasiënt is, aangesien u dokter u dalk meer noukeurig moet monitor.
- As u te veel suiker in die bloed het ('n siekte wat diabetes genoem word). 'n Siekte gekenmerk deur simptome soos oormatige dors, groot hoeveelhede urien, groter eetlus en voel swak of as u 'n familiegeskiedenis van diabetes, versteuring van die skildklier of pituïtêre adenoom het.
- As u agterkom dat u gewig optel, ongewone bewegings ontwikkel, slaperigheid ondervind wat met normale daaglikse aktiwiteite inmeng, sukkel om te sluk of allergiese simptome het.

Gebruik van ander medisyne saam met ALEBON

Sê altyd vir u gesondheidspraktisyn as u enige ander medisyne gebruik (waaronder aanvullende en tradisionele medisyne). Kyk Moenie ALEBON gebruik nie.

Sê vir u dokter as u medisyne gebruik om u bloeddruk te verlaag.
ALEBON kan die effek versterk van medisyne wat gebruik word om die bloeddruk te verlaag.
As u ALEBON saam met sekere medisyne gebruik, kan u dokter dalk u dosis van ALEBON verander.

Sê vir u dokter as u enige van die volgende medisynes drink of gebruik:
- Kinidien (vir die behandeling van onreëlmatige hartklop of malaria).
- Fluoksetien (om depressie te behandel) of paroksetien (om depressie of angs te behandel).
- Ketokonasool of itrakonasool (om fungusinfeksies te behandel).
- Sekere medisyne wat vir MIV gebruik word, byvoorbeeld efavirens of nevirapien en 'n klas MIV-medisyne genaamd MIV-proteaseremmers - vra u dokter of apteker gerus indien u nie seker is nie.
- karbaamasepien, fenitoïen of fenobarbitoon (om toevalle te voorkom).
- Sekere antibiotika soos rifampisien of rifabutien (om bakteriële infeksies te behandel).
- Sint Janskruid ('n kruiemiddel vir die behandeling van depressie).

Hierdie medisyne kan die risiko vir newe-effekte verhoog of die effek van ALEBON verlaag; as u enige ongewone simptoom kry as u enige van hierdie medisyne saam met ALEBON gebruik, moet u u dokter raadpleeg.

Swangerskap, borsvoeding en vrugbaarheid
ALEBON word in borsmelk uitgeskei. U moet nie borsvoed as u ALEBON drink nie.

As u swanger is, dink dat u swanger kan wees of beplan om swanger te raak, of as u u baba borsvoed, moet u u dokter, apteker of ander gesondheidskundige om advies raadpleeg voordat u ALEBON drink.

Die volgende simptome kan voorkom in pasgebore babas van moeders wat ALEBON in die laaste trimester (laaste drie maande van hul swangerskap) gebruik het: bewerasie, spierstyfheid en/of -swakheid, slaperigheid, agitasie, asemhalingsprobleme en probleme met voeding. As u baba enige van hierdie simptome ontwikkel, moet u moontlik u dokter skakel.

Motorbestuur en gebruik van masjinerie
Soos met ander antipsigotika moet gevaarlike masjiene, waaronder motorvoertuie, versigtig gebruik word totdat u redelik seker is dat aripiprasool u nie nadelig beïnvloed nie.

U kan duiselig, verward of lighoofdig voel en visieprobleme kan voorkom nadat u ALEBON gedrink het. As dit gebeur, moet u nie motor bestuur of enige gereedskap of masjiene gebruik nie. Vra vir u dokter as u nie seker is nie.

Belangrike inligting oor sommige van die bestanddele van ALEBON
ALEBON bevat laktose wat 'n tipe suiker is. Voordat u ALEBON drink, moet u dus u dokter om advies raadpleeg as u sommige suikers nie kan verdra nie.

3. Hoe om ALEBON te drink

Moenie medisyne wat vir u voorgeskryf is vir enige ander persoon gee nie. Gebruik ALEBON altyd presies soos wat u dokter vir u gesê het. Raadpleeg u dokter of apteker as u nie seker is nie.

U dokter sal vir u sê hoe lank u behandeling met ALEBON sal duur.

ALEBON moet heel met 'n halwe glas water afgesluk word. Moenie kou nie.

Skisofrenie
Die aanbevole aanvangsdosis van ALEBON is 10 of 15 mg/dag, met 'n instandhoudingsdosis van 15 mg/dag volgens 'n eenmalige skedule.

Bipolêre manie
Die aanbevole aanvangsdosis vir ALEBON is 15 mg/dag volgens 'n eenmalige skedule.

U dokter kan egter 'n laer of hoër dosis tot 'n maksimum van 30 mg een keer per dag voorskryf.

Sê vir u dokter of apteker as u die indruk het dat die effek van ALEBON te sterk of te swak is.

Probeer om die ALEBON-tablet elke dag op dieselfde tyd te drink.

Selfs as u beter voel, moet u nie ophou om die daaglikse dosis ALEBON te drink sonder om eers met u dokter te praat nie. U dokter sal vir u sê hoe lank u behandeling met ALEBON sal duur.

Gebruik van ALEBON saam met voedsel en drank
ALEBON kan met of sonder voedsel gedrink word.
Alkohol moet vermy word terwyl u ALEBON drink.

As u meer ALEBON gedrink het as wat u moes

As u besef dat u meer ALEBON gedrink het as wat u moes (of as iemand anders u ALEBON gedrink het), moet u u dokter of apteker dadelik raadpleeg. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of gifsentrum en neem die verpakking van ALEBON saam.

As u 'n dosis ALEBON oorgeslaan het
As u vergeet om 'n dosis te drink, drink dit sodra as wat u dit onthou, behalwe as dit bykans tyd vir u volgende dosis is. Moenie 'n dubbele dosis gebruik om vir vergete individuele dosisse op te maak nie.

4. Moontlike newe-effekte
ALEBON kan newe-effekte veroorsaak, hoewel nie almal dit kry nie.

Nie al die newe-effekte wat vir ALEBON aangemeld is, is in hierdie blad opgeneem nie. As u algemene gesondheidstoestand vererger of as u newe-effekte ervaar terwyl u ALEBON drink, moet u u dokter, apteker of ander gesondheidspraktisyn asseblief om advies raadpleeg.

Indien enige van die volgende voorkom, moet u ophou om ALEBON te drink en onmiddellik vir u dokter sê of na die ongevalle-afdeling van u naaste hospitaal gaan:
- Allergiese reaksie (bv. anafilaktiese reaksie, probleme met asemhaling of sluk, swelling, waaronder geswelde tong, geswelde gesig, erge jeuk of galbulte).

Hierdie is almal baie ernstige newe-effekte. As u dit ervaar, kan dit wees dat u 'n ernstige reaksie op ALEBON het. Dit mag wees dat u dringende mediese aandag of hospitalisasie nodig het.

Sê dadelik vir u dokter of gaan na die ongevalle-afdeling van u naaste hospitaal as u enige van die volgende opmerk:
- Neuroleptiese kwaadaardige sindroom (NKS): As u agterkom dat u hart vinniger as normaal of onreëlmatig klop, as u baie sweet, as u spiere styf is, kan u 'n ernstige toestand, genaamd neuroleptiese maligne sindroom (NKS), hê.
- Hiperglisemie (hoë bloedsuikervlakke) Verhogings in bloedsuikervlakke kan voorkom in mense wat ALEBON drink. Ekstreme hoë bloedsuikervlakke kan tot koma of die dood lei. Simptome van hoë bloedsuikervlakke tydens die gebruik van ALEBON is: polidipsie (voel baie dors), poliurie (moet meer as gewoonlik urineer), polifagie (oormatige eet) en swakheid
- Tardiewe diskinesie: gekenmerk deur uitsteek van die tong ('vlieë vang'), lek van lippe, suig, laterale kou, en 'n suur gesig trek
- Distonie: langdurige abnormale sametrekkings van spiergroepe kan gedurende die eerste paar dae van behandeling in vatbare individue voorkom. Simptome van distonie is onder meer krampe in die nekspiere, wat soms tot styfheid in die keel lei, slukprobleme, asemhalingsprobleme en/of uitsteek van die tong.
- Ortostatiese hipotensie (lae bloeddruk): lighoofdigheid of floute wanneer u te vinnig uit 'n sittende of lêende posisie opkom.
- Toevalle (konvulsies)

Hierdie is almal ernstige newe-effekte.
Dit mag wees dat u dringende mediese aandag nodig het.

Sê vir u dokter as u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:
- Onvermoë om te slaap (slapeloosheid), slaperigheid (lomerigheid), angs, rusteloosheid
- Hoofpyn, sedasie, duiseligheid
- Dowwe visie
- Naarheid, hardlywigheid, dispepsie (sooibrand), hipersekresie van speeksel, braking
- Moegheid

Newe-effekte wat minder dikwels voorkom:
- Hiperprolaktinemie (hoë vlakke van die hormoon prolaktien)
- Hiperglukemie (hoë vlakke suiker in die bloed)
- Depressie
- Hiperseksualiteit (aanhoudende of skielike toename in libido)
- Distonie (onwillekeurige spiersametrekkings wat herhalende of kronkelende bewegings veroorsaak)
- Diplopie (dubbelvisie)
- Tagikardie (vinnige polsslag)
- Hik
- Disfagie (probleme met sluk)
- Diarree

Onbekende frekwensie:
- Leukopenie ('n lae vlak van witbloedselle in die bloed, wat die vermoë om infeksie te beveg, kan belemmer)
- Neutropenie (lae vlak van neutrofiele. Neutrofiele is 'n tipe witbloedsel)
- Trombositopenie (lae bloedplaatjietelling. Plaatjies is kleurlose bloedselle wat help dat bloed stol)
- Allergiese reaksie
- Diabetiese hiperosmolêre koma (simptome sluit in tekens van uitdroging, swakheid, krampe in die bene, visieprobleme en 'n veranderde vlak van bewussyn)
- Diabetiese ketoasidose (oormatige dors, gereelde urinering, naarheid en braking, buikpyn, swakheid of moegheid, kortasemheid, asem met vrugtigeur en verwardheid)
- Hiponatremie (lae vlakke natrium in die bloed)
- Anoreksie
- Gewigsverlies
- Toename in gewig
- Selfdoodpoging, selfdoodgedagtes en suksesvolle selfdood
- Kompulsiewe dobbel
- Aggressie
- Agitasie
- Senuagtigheid
- Grand mal-stuiptrekkings (veroorsaak 'n verlies van bewussyn en hewige spiersametrekkings)
- Serotoniensindroom (simptome is onder meer hoë liggaamstemperatuur, agitasie, sterker reflekse, bewing, sweet, wye pupille en diarree)
- Spraakversteuring
- Okulogiriese krisis (onwillekeurige bewegings van die oogballe)
- Skielike onverklaarbare dood
- Torsades de pointes (abnormale hartritme wat tot skielike hartsterfte kan lei)
- Verlenging van QT-interval
- Ventrikulêre aritmieë
- Hartstilstand (skielike, onvervagte verlies aan hartfunksie, asemhaling en bewussyn)
- Bradikardie (stadige polsslag)
- Veneuse trombo-embolisme (bloedklont) - [waaronder longembolie (bloedklont in die slagaar in die long) en diep veneuse trombose]
- Hipertensie (hoë bloeddruk)
- Sinkopee (tydelike verlies van bewussyn)
- Longontsteking vanweë aspirasie (as u voedsel, maagsuur of speeksel in u longe inasem)
- Laringospasma (spasma van die stembande wat dit tydelik moeilik maak om te praat of asem te haal)
- Orofaringeale spasma
- Pankreatitis (ontsteekte pankreas. Simptome is onder meer die boonste buikpyn wat na die rug uitstraal; dit kan vererger word deur te eet, veral voedsel met baie vet. Geswelde en teer buik, naarheid en braking, koors en vinnige hartklop)
- Buikongemak
- Maagongemak
- Lewerversaking/hepatiese versaking (simptome sluit in naarheid, verlies aan eetlus, moegheid, diarree, geelsug, 'n geel kleur van die vel en oë, gewigsverlies, kneus of bloei maklik, jeuk en vogopbou in die bene
- Hepatitis (inflammasie van die lewer)
- Geelsug (geel verkleuring van die vel of oë)
- Hoër vlakke alanienaminotransferase (ALT)
- Hoër vlakke aspartaataminotransferase (AST)
- Hoër vlakke gammaglutamieltransferase (GGT)
- Hoër vlakke alkaliese fosfatase
- Veluitslag
- Fotosensitiwiteitsreaksies
- Alopesie (haarverlies van die kopvel of elders op die liggaam)
- Hiperhidrose (oormatige sweet)
- Rabdomiolise ('n afbreek van spierweefsel wat 'n skadelike proteïen in die bloed vrystel)
- Mialgie (pyn of krampe in 'n spier of 'n groep spiere)
- Spierstyfheid
- Urinêre inkontinensie (verlies aan blaasbeheer)
- Urienretensie
- Priapisme ('n langdurige ereksie van die penis, gewoonlik sonder seksuele opwinding)
- Versteuring van temperatuurregulering (gevaarlike lae liggaamstemperatuur of koors)
- Pyn in die borskas
- Perifere edeem (akkumulasie van vloeistof wat swelling veroorsaak)
- Hoër vlakke geglikosileerde hemoglobien
- Fluktuasie in bloedglukosevlakke
- Hoër vlakke kreatinienfosfokinase

As u enige newe-effekte opmerk wat nie in hierdie blad genoem word nie, moet u u dokter of apteker asseblief in kennis stel.

Aanmeld van newe-effekte
Praat met u dokter, apteker of verpleegkundige as u newe-effekte kry. Dit sluit alle moontlike newe-effekte in wat nie in hierdie blad gelys word nie. U kan newe-effekte ook via https://www.sahpra.org.za/Publications/Index/8 aanmeld. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van hierdie medisyne te gee.

5. Hoe om ALEBON te bêre
HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS.
Bêre by of onder 25 °C.
Bêre in die oorspronklike houer totdat dit vir gebruik benodig word.
Moenie in 'n badkamer bêre nie.
Moenie na die vervaldatum op die etiket gebruik nie.

Gee alle ongebruikte medisyne terug aan u apteker.
Ongebruikte medisyne moet nie in dreinering- of rioolstelsels (bv. toilette) gegooi word nie.

6. Inhoud van die pak en ander inligting
Wat ALEBON bevat
Die aktiewe bestanddeel is aripiprasool.
Elke tablet van ALEBON 5 mg bevat 5 mg aripiprasool.
Bevat suiker: 76,00 mg laktosemonohidraat.

Elke tablet van ALEBON 10 mg bevat 10 mg aripiprasool.
Bevat suiker: 66,50 mg laktosemonohidraat.

Elke tablet van ALEBON 15 mg bevat 15 mg aripiprasool.
Bevat suiker: 99,75 mg laktosemonohidraat.

Die ander bestanddele is mikrokristallyne sellulose, hidroksipropielsellulose, laktosemonohidraat, magnesiumstearaat, mieliestysel en kolloïdale watervrye silika.

Daarbenewens bevat die ALEBON 5 mg-tablet FD&C blue nr. 2 (KI Nr.: 73015).

Hoe ALEBON lyk en die inhoud van die pakkie
ALEBON 5 mg:
Blou, gemodifiseerde reghoekige onbedekte tablette met "62" op die een kant gedruk en "H" op die ander kant.

ALEBON 10 mg:
Wit, gemodifiseerde reghoekige onbedekte tablette met "63" op die een kant gedruk en "H" op die ander kant.

ALEBON 15 mg:
Wit, gemodifiseerde ronde onbedekte tablette met "64" op die een kant gedruk en "H" op die ander kant.

Stulppakke:
30 tablette is verpak in aluminiumfolie/PVC-film stulpverpakkings. Elke karton bevat 3 stulpstroke met 10 tablette elk.

HDPE-houers:
30 tablette word verpak in 'n wit ondeursigtige HDPE-houer met 'n wit ondeursigtige polipropileenprop met watte, silikagelsakkie en rayon.

Nie alle pakke en pakgroottes word noodwendig bemark nie.

NAAM, BESIGHEIDSADRES EN TELEFOONNOMMER VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT
AUROGEN SA (Edms) Bpk
Woodhillkantoorpark, Gebou 1, Eerste vloer
Phillip Engelbrechtlaan 53
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Registrasienommer:
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