VI.2 Elements for a Public Summary

<PRODUCT NAME> 5 mg tablets
<PRODUCT NAME> 10 mg tablets
<PRODUCT NAME> 15 mg tablets
<PRODUCT NAME> 30 mg tablets
<PRODUCT NAME> 10 mg orodispersible tablets
<PRODUCT NAME> 15 mg orodispersible tablets

VI.2.1 Overview of disease epidemiology

Schizophrenia
Schizophrenia is a chronic (ongoing) mental illness that commonly manifests with difficulties distinguishing between reality and imagination. Common symptoms include disorganised thinking and speech, hallucinations (hearing or seeing things that are not there), suspiciousness, false beliefs (delusion) and abnormal social behaviour. Schizophrenia affects approximately 0.7% of adults, and is more prevalent among men. Onset is common during young adulthood in males and approximately 5 years later in women. Schizophrenia occurs across the globe, but incidence rates vary significantly between countries.
Genetic factors such as a family history of schizophrenia may play a role in the development of the disease; higher parental age, birth complications, maternal infections during pregnancy and cannabis use are other risks discussed in the medical literature.
Treatment usually comprises a combination of psychosocial interventions and pharmaceutical therapy, with antipsychotics as first line treatment. With appropriate treatment, most cases of schizophrenia can be adequately managed. Schizophrenia is generally not progressive.

Bipolar I disorder (manic episodes)
Bipolar I disorder (BPI) is a mental illness characterised by alternating periods of normal or depressed mood, and abnormally elevated or irritable mood with heightened activity (manic episodes). During manic episodes, patients may need less sleep, are highly talkative, have delusions of grandeur, flight of ideas and are easily distractible. BPI affects both genders equally and usually develops around the age of 21 years on average, but can occur at any stage of life. Globally, 0.6% of the population are affected by BPI, with incidence increasing in recent years. Genetic, environmental and biochemical factors, as well as personality traits are thought contribute to its manifestation.
Both psychological and pharmaceutical therapies are employed. Manic episodes are commonly treated with antipsychotics, with the exact drug dependent on the type of the episode. Patients with BPI may also receive mood stabilisers to manage other phases or specific symptoms of their disease.

VI.2.2 Summary of treatment benefits

ARIPIPRAZOLE is one of a group of medicines called antipsychotics.
It is used to treat adults and adolescents aged 15 years and older who suffer from a disease characterised by symptoms such as hearing, seeing or sensing things which are not there, suspiciousness, mistaken beliefs, incoherent speech and behaviour and emotional flatness. People with this condition may also feel depressed, guilty, anxious or tense.

ARIPIPRAZOLE is used to treat adults and adolescents aged 13 years and older 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 it also prevents this condition from returning in patients who have responded to the treatment with ARIPIPRAZOLE.

VI.2.3 Unknowns relating to treatment benefits

None identified.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Movement disorders (Extrapyramidal syndrome (EPS), including tardive dyskinesia)	In clinical trials, there were uncommon reports of abnormal involuntary movements (dyskinesia) in patients receiving aripiprazole. These symptoms can worsen over time or even only become apparent after treatment has been stopped. An inability to sit still (akathisia) and tremors (parkinsonism) were observed clinical trials of aripiprazole in paediatric patients. Extrapyramidal symptoms of varying severity, including tremor, high or low muscle tension, have been observed in neonates whose mothers had used antipsychotics (including aripiprazole) during the third trimester of pregnancy Consequently, newborns should be monitored carefully.	Tell your doctor if you develop unusual movement disorders while receiving <PRODUCT NAME>; they may decrease your dose or even discontinue treatment altogether. They may also choose to monitor your symptoms more closely. Movement disorders can also develop after therapy has been stopped. Tell your doctor if you develop abnormal muscle or movement symptoms; they will advise you on the best course of action. If you experience any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in the package leaflet.
Severe nerve disorder due to certain drugs (Neuroleptic Malignant Syndrome (NMS))	Neuroleptic Malignant Syndrome (NMS) is a potentially fatal symptom complex associated with antipsychotic medicinal products, including rare cases during treatment with aripiprazole. Symptoms of NMS are: high fever (hyperpyrexia), stiff muscles, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, fast heartbeat, sweating and abnormal heart rhythm). Other symptoms	Tell your doctor immediately if you suffer from muscle stiffness or inflexibility with high fever, sweating, altered mental status, or very rapid or irregular heartbeat. If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fever without additional clinical manifestations of NMS, all antipsychotic medicinal products, including

	may include rhabdomyolysis (a serious condition resulting from the breakdown of muscle tissue), and acute kidney failure.	aripiprazole, must be discontinued.

Potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Epileptic fits (Seizures*)	Uncommon cases of seizure were reported during treatment with aripiprazole in clinical trials. Therefore, aripiprazole should be used with caution in patients who have a history of seizure disorder or have conditions associated with seizures.
High blood sugar or diabetes (Hyperglycaemia/diabetes*)	High blood sugar (hyperglycaemia), in some cases associated with severe complications or fatality, has been reported in patients treated with atypical antipsychotic agents, including aripiprazole. Patients with obesity and a family history of diabetes are at increased risk of severe complications. The frequency for these events to occur cannot be estimated from the available data. However, no significant differences in the incidence rates of hyperglycaemia-related adverse reactions (including diabetes) or laboratory values between aripiprazole and placebo were identified in clinical studies.
Suicidal thoughts and behaviours (Suicide-related events*)	Thoughts of suicide, suicide attempt and suicide have been observed since the product has been marketed. The frequency of these events is unknown. **Immediately** talk to your doctor if you have thoughts or feelings about harming yourself; these thoughts may be caused by the drug.
Low blood pressure when getting up (Orthostatic hypotension*)	Sudden changes in blood pressure that can lead to feeling dizzy, especially when getting up from a lying or sitting position, have occurred in up to 1 in 100 people treated with aripiprazole have been observed
Dysbalance in blood fat levels (Dyslipidaemia*)	In a pooled analysis on lipid parameters from placebo-controlled clinical trials in adults, aripiprazole has not been shown to induce clinically relevant alterations in levels of total cholesterol, triglycerides, HDL and LDL. However, an impact of aripiprazole on blood fat levels cannot be fully excluded.
Weight gain	Weight gain has been observed in patients treated with aripiprazole. If you notice you are gaining weight, please tell your doctor.
Tiredness and sleepiness (Somnolence/fatigue)	Sleepiness and tiredness were very common (greater than 1 in 10 patients) in children and adolescents aged 13 years and older during treatment with aripiprazole. Consult your doctor if you are concerned about excessive sleepiness or if it severely impacts on your daily functioning; they will advise you on the best course of action.

Problems related to the heart and blood vessels (Cardiovascular-related disorders)	Antipsychotics have been associated with formation of blood clots, and heart attacks have been observed in up to 1 in 100 patients treated with <PRODUCT NAME>. Talk to your doctor before taking <PRODUCT NAME> if you suffer from Cardiovascular diseases, family history of cardiovascular disease, stroke or "mini" stroke or abnormal blood pressure.
Abnormal conduction of your heart on ECG (Conduction abnormalities)	In clinical trials of aripiprazole, the incidence of QT prolongation (a specific part of the heart beat process) was comparable to placebo. As with other antipsychotics, aripiprazole should be used with caution in patients with a family history of QT prolongation.
Abnormal growth (Growth)	There is a risk of growth abnormalities in patients treated with aripiprazole.
Low levels of the hormone prolactin in patients under 18 (Low prolactin in paediatric patients)	Low prolactin levels during aripiprazole therapy have been observed in paediatric patients with irritability associated with autistic disorder, schizophrenia and bipolar disorder. In the first group (irritability associated with autism), pooled analysis of three trials in patients aged 6 to 17 years showed low serum prolactin levels in 58.7% of aripiprazole-treated females and 86.6% of aripiprazole-treated males. In the pooled adolescent schizophrenia population (13-17 years) with exposure up to 2 years, incidence of low serum prolactin levels was 29.5% in females and 48.3% in males. In the paediatric bipolar population (10-17 years) with exposure up to 30 weeks, incidence of low serum prolactin levels was 28.0% in females and 53.3% in males.
Swallowing problems (mainly in patients with schizophrenia) (Dysphagia (predominantly applies to schizophrenia population))	Swallowing difficulties can be a symptom of dystonia, which is a known risk of the class of antipsychotics, but can also occur on its own during treatment with aripiprazole.
Intolerance to milk sugar (Lactose intolerance)	The colouring used in preparing <PRODUCT NAME> contains lactose. This may affect patients with inherent lactose intolerance.
Patients that also suffer from attention-deficit-hyperactivity disorder (ADHD) (ADHD comorbidity)	Even though Bipolar I Disorder and ADHD frequently occur in the same patients, very limited safety data are available on concomitant use of aripiprazole and stimulants; therefore, extreme caution should be taken when these drugs are co-administered.

Drug interactions	<PRODUCT NAME> may increase the effect of medicines used to lower the blood pressure. Taking <PRODUCT NAME> with some medicines may require adjustments of the <PRODUCT NAME> dose; these include • Medicines to correct heart rhythm • Antidepressants or herbal remedy used to treat depression and anxiety • Antifungal agents • Certain medicines to treat HIV infection • Anticonvulsants used to treat epilepsy Medicines that increase the level of serotonin will increase the risk of side effects when taken at the same time as aripiprazole. These include: triptans, tramadol, tryptophan, SSRIs (such as paroxetine and fluoxetine), tricyclics (such as clomipramine, amitriptyline), pethidine, St John's Wort and venlafaxine.
Higher mortality and stroke rate in elderly patients with dementia (Increased mortality and CVA in elderly patients with dementia)	In elderly patients with dementia, more fatal cases have been reported while taking aripiprazole. In addition, cases of stroke or "mini" stroke have been reported.
Excessive gambling (Pathological gambling)	Excessive gambling has been reported in 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. The frequency of this reaction cannot be estimated.
A combination of symptoms associated with too much of the neurotransmitter serotonin (Serotonin syndrome)	Serotonin syndrome is a reaction that may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles. Serotonin syndrome has been reported in patients treated with aripiprazole, especially in combination with other drugs affecting the serotonin syndrome. The frequency of this reaction is unknown.
Liver disorders (Hepatic adverse events)	Liver failure, inflammation of the liver, yellowing of the skin and white part of eyes, and abnormal liver test values have been reported since the marketing of aripiprazole.

***** Important potential risks

Missing information

Risk	What is known
Safety in pregnancy and lactation	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. Neonates 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, newborns should be monitored carefully. Aripiprazole is excreted in human breast milk. Patients should be advised not to breast feed if they are taking aripiprazole.
Safety in paediatrics	Younger patients are at increased risk of experiencing adverse events associated with aripiprazole. Therefore, aripiprazole is not recommended for use in children and adolescents below 13 years of age

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.