

## **VI.2 Elements for a public summary**

### ***VI.2.1 Overview of disease epidemiology***

Olanzapine is an antipsychotic medicine that is used in patients with schizophrenia, a mental illness with a number of symptoms, including disorganised thinking and speech, hallucinations, suspiciousness and delusions (mistaken beliefs). It is also effective in maintaining improvement in patients who have responded to an initial course of treatment. Olanzapine is also used to treat moderate to severe manic episodes (extremely high mood) in adults. It can also be used to prevent the recurrence of these episodes (when symptoms come back) in adults with bipolar disorder (a mental illness causing alternating periods of high mood and depression) who have responded to an initial course of treatment.

Estimates of the risk of developing schizophrenia averaged approximately 0.72%. The rate ratio for males:females was 1.4:1.

Bipolar disorder in its broadest sense has a community lifetime prevalence of 4%. Race, ethnicity, and gender have no effect on prevalence rates, but women are more likely to experience rapid cycling, mixed states, depressive episodes, and bipolar II disorder than men.

### **VI.2.2 Summary of treatment benefits**

Olanzapine is an antipsychotic medicine. As for other antipsychotic agents, the exact mechanism of action of olanzapine is unknown, but it attaches to several receptors on the surface of nerve cells in the brain, and disrupts signals transmitted between brain cells by 'neurotransmitters', chemicals that allow nerve cells to communicate with each other. It is known as an 'atypical' antipsychotic because it is different from the older antipsychotic medicines that have been available since the 1950s.

It is considered that olanzapine's beneficial effect is due to it blocking receptors for the neurotransmitters 5-hydroxytryptamine (also called serotonin) and dopamine. Since these neurotransmitters are involved in schizophrenia and bipolar disorder, olanzapine helps to normalise the activity of the brain, reducing the symptoms of these diseases.

Based on the available data from clinical studies and clinical experience of several years, olanzapine represents an effective drug in the treatment of schizophrenia, bipolar disorder and moderate to severe manic episodes.

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, olanzapine can be considered effective in the approved indications and generally well tolerated.

### **VI.2.3 Unknowns relating to treatment benefits**

Not applicable.

### **VI.2.4 Summary of safety concerns**

#### **Important identified risks**

| <b>Risk</b>   | <b>What is known</b>   | <b>Preventability</b>   |
|---|--|---|
| Weight gain   | Increase in body weight has been reported which may be a predisposing factor for increases in the level of sugars in the blood and/or development or worsening of diabetes.<br>Weight gain is a very common side effect which may affect and more than 1 in 10 people and feeling more hungry is a common side effect of olanzapine which may affect up to 1 in 10 people. | <ul style="list-style-type: none"><li>• Talk to your doctor or pharmacist before you take olanzapine. You and your doctor should check your weight regularly.</li><li>• Tell your doctor if you are feeling more hungry than usual.</li><li>• Tell your doctor immediately if you experience weight gain.</li><li>• Referral to a dietician or help with a diet plan if necessary should be considered.</li></ul> |
| Glucose dysregulation<br>( <i>Impaired regulation of the level of sugars in the blood</i> ) | High blood sugar has been seen in patients taking this medicine. Increases in the level of sugars in the blood and urine may affect up to 1 in 10 people and/or development or worsening of diabetes occasionally associated with ketoacidosis (ketones in the blood and urine) or coma has been reported uncommonly (in up to 1 in  | <ul style="list-style-type: none"><li>• If you suffer from diabetes tell your doctor as soon as possible.</li><li>• Talk to your doctor or pharmacist before you take olanzapine.</li><li>• Your doctor should do blood tests to check blood sugar and certain fat levels before you start taking olanzapine and regularly during treatment.</li><li>• If you get any side effects, talk to</li></ul>             |

| Risk   | What is known   | Preventability   |
|--|---|--|
|  | 100 people). In some cases, a prior increase in body weight has been reported which may be a predisposing factor.<br>The proportion of patients who had significant changes in level of sugars in the blood increased during the course of treatment.                         | your doctor or pharmacist.   |
| Dyslipidaemia<br>(changes in the levels of circulating fats) | Changes in the levels of circulating fats have been seen in patients taking this medicine and may affect up to 1 in 10 people.<br>The proportion of patients who had significant high levels of fat (triglycerides and cholesterol) increased during the course of treatment. | <ul style="list-style-type: none"> <li>• Talk to your doctor or pharmacist before you take olanzapine.</li> <li>• Your doctor should do blood tests to check blood sugar and certain fat levels before you start taking olanzapine and regularly during treatment.</li> <li>• If you get any side effects, talk to your doctor or pharmacist.</li> </ul> |

### Important potential risks

| Risk  | What is known (Including reason why it is considered a potential risk)  |
|---|---|
| Increased risk of cardiac death (presumed sudden cardiac death)<br>(sudden death) | The event of sudden unexplained death has been reported rarely in patients with olanzapine (in up to 1 in 1000 people). The risk of presumed sudden cardiac death in patients treated with antipsychotic drugs (such as olanzapine) was approximately twice the risk in patients not using antipsychotics. In the study, the risk of olanzapine was comparable to the risk of atypical antipsychotics included in analysis. |

#### VI.2.5 Summary of risk minimisation measures by safety concern

No additional risk minimisation measures are proposed.

#### VI.2.6 Planned post authorisation development plan

Not applicable.

#### VI.2.7 Summary of changes to the risk management plan over time

| Version | Date        | Safety Concerns   | Comment |
|---------|-------------|---|---------|
| 1.0     | 13 Nov 2013 | <b>Important identified risks (all indications/populations)</b><br>Extrapyrimal symptoms (akathisia, parkinsonism, dyskinesia, tardive dyskinesia)<br>Somnolence<br>Hyperglycemia and diabetes mellitus | NA      |

| Version | Date        | Safety Concerns  | Comment   |
|---------|-------------|--|---|
|         |             | <p>Weight gain and increased appetite<br/> Lipid changes (includes decreased HDLs/increased LDLs)<br/> Orthostatic hypotension<br/> Hepatitis, jaundice and increased serum aminotransferases<br/> Withdrawal (discontinuation) symptoms<br/> Neuroleptic malignant syndrome<br/> Thromboembolism<br/> Seizure<br/> Blood disorders (neutropenia, eosinophilia, thrombocytopenia, leukopenia)<br/> Anticholinergic activity<br/> Hypersensitivity</p> <p><b>Important identified risks for special populations or indications</b></p> <p>Use in dopamine agonist associated psychosis in patients with Parkinson's disease<br/> Use in patients with narrow-angle glaucoma<br/> Increased mortality and risk of cerebrovascular adverse events in elderly patients with dementia-related psychosis and/or behavioural disturbances</p> <p><b>Important potential risks seen with other drugs in the antipsychotic class (all indications/populations)</b></p> <p>QT prolongation<br/> Sudden cardiac death<br/> General CNS effects in combination with other centrally acting medicines and alcohol</p> <p><b>Important potential risks for special populations</b></p> <p>Use of olanzapine in patients with hepatic impairment<br/> Use of olanzapine in elderly patients<br/> Use of olanzapine in pregnant women (third trimester) patients</p> <p><b>Missing information</b></p> <p>Use of olanzapine in pregnant women (first and second trimester)<br/> Use of olanzapine in lactating women</p> |   |
| 1.1     | 21 Jul 2014 | <p><b>Important Identified Risks</b></p> <ul style="list-style-type: none"> <li>• Weight gain</li> <li>• Glucose dysregulation</li> <li>• Dyslipidaemia</li> </ul> <p><b>Important Potential Risks</b></p> <ul style="list-style-type: none"> <li>• Increased risk of cardiac death (presumed sudden cardiac death)</li> </ul> <p><b>Missing Information</b></p> <p>None</p>   | The safety concerns were updated according to EPAR for Zyprexa/Zyprexa Velotab (EMA/33437 5/2014; dated 25 April 2014). |