

**Size: 240 (L) x 350 (H) mm**

**Folding size: 30 x 90 mm**

**Carton size: 46 x 22 x 106 mm**

↓ Front

BB

# OLANZAPINE

OLAN™

10 mg Film-Coated Tablet  
ATYPICAL ANTIPSYCHOTIC

**PRODUCT NAME:**  
OLAN

**NAME AND STRENGTH:**  
Olanzapine Film-Coated Tablet 10 mg

**PHARMACOLOGIC CATEGORY:**  
ATYPICAL ANTIPSYCHOTIC

**PRODUCT DESCRIPTION:**  
Light yellow coloured, circular, biconvex film coated tablets with a breakline on one surface.

**FORMULATION/COMPOSITION:**  
Each film-coated tablet contains:  
Olanzapine ..... 10 mg

## PHARMACODYNAMICS/PHARMACOKINETICS:

### Pharmacodynamics:

Olanzapine has a higher affinity for 5-HT2A serotonin receptors than D2 dopamine receptors, which is a common property of all atypical antipsychotics, aside from the benzamine antipsychotics such as Aripiprazole. Olanzapine also had the highest affinity of any second-generation antipsychotic towards the P-glycoprotein in one *in vitro* study. P-glycoprotein transports a number of drugs across a number of different biological membranes including the blood-brain barrier, which could mean that less brain exposure to olanzapine results from this interaction with the P-glycoprotein.

### Pharmacokinetics:

#### Absorption

Olanzapine is well absorbed after oral administration, reaching peak plasma concentrations within 5 to 8 hours. The absorption is not affected by food. Absolute oral bioavailability relative to intravenous administration has not been determined.

#### Distribution

The plasma protein binding of olanzapine was about 93 % over the concentration range of about 7 to about 1000 ng/ml. Olanzapine is bound predominantly to albumin and  $\alpha_1$ -acid-glycoprotein.

#### Biotransformation

Olanzapine is metabolized in the liver by conjugative and oxidative pathways. The major circulating metabolite is the 10-N-glucuronide, which does not pass the blood brain barrier. Cytochromes P450- CYP1A2 and P450-CYP2D6 contribute to the formation of the N-desmethyl and 2-hydroxymethyl metabolites, both exhibited significantly less *in vivo* pharmacological activity than olanzapine in animal studies. The predominant pharmacologic activity is from the parent olanzapine.

#### Elimination

After oral administration, the mean terminal elimination half-life of olanzapine in healthy subjects varied on the basis of age and gender. In healthy elderly (65 and over) versus non-elderly subjects, the mean elimination half-life was prolonged (51.8 versus 33.8 hr) and the clearance was reduced (17.5 versus 18.2 l/hr). The pharmacokinetic variability observed in the elderly is within the range for the non-elderly. In 44 patients with schizophrenia > 65 years of age, dosing from 5 to 20mg/day was not associated with any distinguishing profile of adverse events.

In female versus male subjects the mean elimination half life was somewhat prolonged (36.7 versus 32.3 hr) and the clearance was reduced (18.9 versus 27.3 l/hr). However, olanzapine (5-20mg) demonstrated a comparable safety profile in female (n=467) as in male patients (n=869).

## INDICATIONS:

### Adults

Olanzapine is indicated for the treatment of schizophrenia.

Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response.

Olanzapine is indicated for the treatment of moderate to severe manic episode.

In patients whose mania episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.

## DOSAGE AND MODEL ROUTE OF ADMINISTRATION:

### Posology

#### Adults

Schizophrenia: The recommended starting dose for olanzapine is 10mg/day.

Manic episode: The starting dose is 15mg as a single daily dose in monotherapy or 10mg daily in combination therapy.

Preventing recurrence in bipolar disorder: The recommended starting dose is 10mg/day. For patients who have been receiving olanzapine for treatment of manic episode, therapy for preventing recurrence should be continued at the same dose. If a new manic, mixed, or depressive episode occurs, olanzapine treatment should be continued (with dose optimization as needed), with supplementary therapy to treat mood symptoms, as clinically indicated.

During treatment for schizophrenia, manic episode and recurrence prevention in bipolar disorder, daily dosage may subsequently be adjusted on the basis of individual clinical status within the range 5-20mg/day. An increase to a dose greater than the recommended starting dose is advised only after appropriate clinical reassessment and should generally occur at intervals of not less than 24 hours.

### Special populations

#### Elderly patients

A lower starting dose (5mg/day) is not routinely indicated but should be considered for those 65 and over when clinical factors warrant.

#### Patients with renal and/or hepatic impairment

A lower starting dose (5mg) should be considered for such patients. In cases of moderate hepatic insufficiency (cirrhosis, Child-Pugh Class A or B), the starting dose should be 5mg and only increased with caution.

#### Smokers

The starting dose and dose range need not be routinely altered for non-smokers relative to smokers. The metabolism of olanzapine may be induced by smoking. Clinical monitoring is recommended and an increase of olanzapine dose may be considered if necessary.

When more than one factor is present which might result in slower metabolism (female gender, geriatric age, non-smoking status), consideration should be given to decreasing the starting dose. Dose escalation, when indicated, should be conservative in such patients.

#### Pediatric population

Olanzapine is not recommended for use in children and adolescents below 18 years of age due to a lack of data on safety and efficacy. A greater magnitude of weight gain, lipid and prolactin alterations has been reported in short term studies of adolescent patients than in studies of adult patients.

#### Method of administration

Olanzapine can be given without regards for meals as absorption is not affected by food. Gradual tapering of the dose should be considered when discontinuing olanzapine.

## CONTRAINDICATIONS & PRECAUTION(S), WARNING(S):

Hypersensitivity to the active substance(s) or to any of the excipients. Patients with known risk of narrow-angle glaucoma

## PRECAUTIONS & WARNINGS:

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.

#### Dementia-related psychosis and/or behavioral disturbances

Olanzapine is not recommended for use in patients with dementia-related psychosis and/or behavioral disturbances because of an increase in mortality and the risk of cerebrovascular accident. In placebo-controlled clinical trials (6-12 weeks duration) of elderly patients (mean age 78 years) with dementia-related psychosis and/or disturbed behaviours, there was a 2-fold increase in the incidence of death in olanzapine-treated patients compared to patients treated with placebo (3.5% vs. 1.5%, respectively). The higher incidence of death was not associated with olanzapine dose (mean daily dose 4.4mg) or duration of treatment. Risk factors that may predispose this patient population to increased mortality include age > 65 years, dysphagia, sedation, malnutrition and dehydration, pulmonary conditions (e.g., pneumonia, with or without aspiration), or concomitant use of benzodiazepines. However, the incidence of death was higher in olanzapine-treated than in placebo-treated patients independent of these risk factors. In the same clinical trials, cerebrovascular adverse events (CVAE e.g., stroke, transient ischemic attack), including fatalities, were reported. There was a 3-fold increase in CVAE in patients treated with olanzapine compared to patients treated with placebo (1.3% vs. 0.4%, respectively). All olanzapine- and placebo-treated patients who experienced a cerebrovascular event had pre-existing risk factors. Age > 75 years and vascular/mixed type dementia were identified as risk factors for CVAE in association with olanzapine treatment. The efficacy of olanzapine was not established in these trials.

#### Parkinson's disease

The use of olanzapine in the treatment of dopamine agonist associated psychosis in patients with Parkinson's disease is not recommended. In clinical trials, worsening of Parkinsonian symptomatology and hallucinations were reported very commonly and more frequently than with placebo, and olanzapine was not more effective than placebo in the treatment of psychotic symptoms. In these trials, patients were initially required to be stable on the lowest effective dose of anti-Parkinsonian medicinal products (dopamine agonist) and to remain on the same anti-Parkinsonian medicinal products and dosages throughout the study. Olanzapine was started at 2.5mg/day and titrated to a maximum of 15mg/day based on investigator judgment.

#### Neuroleptic Malignant Syndrome (NMS)

NMS is a potentially life-threatening condition associated with antipsychotic medicinal products. Rare cases reported as NMS have also been received in association with olanzapine. 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 fever without additional clinical manifestations of NMS, all antipsychotic medicines, including olanzapine must be discontinued.

#### Hyperglycaemia and diabetes

Hyperglycaemia and/or development or exacerbation of diabetes occasionally associated with ketoacidosis or coma has been reported uncommonly, including some fatal cases. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in accordance with utilized antipsychotic guidelines, e.g. measuring of blood glucose at baseline, 12 weeks after starting olanzapine treatment and annually thereafter. Patients treated with any antipsychotic medicines, including olanzapine film-coated tablets, should be observed for signs and symptoms of Hyperglycaemia (such as polydipsia, polyuria, polyphagia, and weakness) and patients with diabetes mellitus or with risk factors for diabetes mellitus should be monitored regularly for worsening of glucose control. Weight should be monitored regularly, e.g. at baseline, 4, 8 and 12 weeks after starting olanzapine treatment and quarterly thereafter.

#### Lipid alterations

Undesirable alterations in lipids have been observed in olanzapine-treated patients in placebo-controlled clinical trials. Lipid alterations should be managed as clinically appropriate, particularly in dyslipidaemia patients and in patients with risk factors for the development of lipids disorders. Patients treated with any antipsychotic medicines, including olanzapine film-coated tablets, should be monitored regularly for lipids in accordance with utilized antipsychotic guidelines, e.g. at baseline, 12 weeks after starting olanzapine treatment and every 5 years thereafter.

#### Anticholinergic activity

While olanzapine demonstrated anticholinergic activity *in vitro*, experience during the clinical trials revealed a low incidence of related events. However, as clinical experience with olanzapine in patients with concomitant illness is limited, caution is advised when prescribing for patients with prostatic hypertrophy, or paralytic ileus and related conditions.

#### Hepatic function

Transient, asymptomatic elevations of hepatic aminotransferases, ALT, AST have been seen commonly, especially in early treatment. Caution should be exercised and follow-up organized in patients with elevated ALT and/or AST, in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic medicines. In cases where hepatitis (including hepatocellular, cholestatic or mixed liver injury) has been diagnosed, olanzapine treatment should be discontinued.

#### Neutropenia

Caution should be exercised in patients with low leukocyte and/or neutrophil counts for any reason, in patients receiving medicines known to cause neutropenia, in patients with a history of drug-induced bone marrow depression/toxicity, in patients with bone marrow depression caused by concomitant illness, radiation therapy or chemotherapy and in patients with hypereosinophilic conditions or with myeloproliferative disease. Neutropenia has been reported commonly when olanzapine and valproate are used concomitantly.

#### Discontinuation of treatment

Acute symptoms such as sweating, insomnia, tremor, anxiety, nausea, or vomiting have been reported rarely ( $\geq 0.01\%$  and  $< 0.1\%$ ) when olanzapine is stopped abruptly.

#### QT interval

In clinical trials, clinically meaningful QTc prolongations (Fridericia QT correction [QTcF]  $\geq 500$  milliseconds [msec] at any time post baseline in patients with baseline QTcF  $< 500$  msec) were uncommon (0.1% to 1%) in patients treated with olanzapine, with no significant differences in associated cardiac events compared to placebo. However, caution should be exercised when olanzapine is prescribed with medicines known to increase QTc interval, especially in the elderly, in patients with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalaemia or hypomagnesaemia.

#### Thromboembolism

Temporal association of olanzapine treatment and venous thromboembolism has been reported uncommonly ( $\geq 0.1\%$  and  $< 1\%$ ). A causal relationship between the occurrence of venous thromboembolism and treatment with olanzapine has not been established. However, since patients with schizophrenia often present with acquired risk factors for venous thromboembolism all possible risk factors of VTE e.g. immobilisation of patients, should be identified and preventive measures undertaken.

#### General CNS activity

Given the primary CNS effects of olanzapine, caution should be used when it is taken in combination with other centrally acting medicines and alcohol. As it exhibits *in vitro* dopamine antagonism, olanzapine may antagonize the effects of direct and indirect dopamine agonists.

#### Seizures

Olanzapine should be used cautiously in patients who have a history of seizures or are subject to factors which may lower the seizure threshold. Seizures have been reported to occur uncommonly in patients when treated with olanzapine. In most of these cases, a history of seizures or risk factors for seizures was reported.

#### Tardive Dyskinesia

In comparator studies of one year or less duration, olanzapine was associated with a statistically significant lower incidence of treatment emergent dyskinesias. However the risk of tardive dyskinesia increases with long term exposure, and therefore if signs or symptoms of tardive dyskinesia appear in a patient on olanzapine, a dose reduction or discontinuation should be considered. These symptoms can temporally deteriorate or even arise after discontinuation of treatment.

#### Postural hypotension

Postural hypotension was infrequently observed in the elderly in olanzapine clinical trials. It is recommended that blood pressure is measured periodically in patients over 65 years.

#### Sudden cardiac death

In post marketing reports with olanzapine, the event of sudden cardiac death has been reported in patients with olanzapine. In a retrospective observational cohort study, the risk of presumed sudden cardiac death in patients treated with 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 a pooled analysis.

#### Paediatric population

Olanzapine is not indicated for use in the treatment of children and adolescents. Studies in patients aged 13-17 years showed various adverse reactions, including weight gain, changes in metabolic parameters and increases in prolactin levels.

#### Lactose

Olanzapine Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

## PREGNANCY AND LACTATION:

### Pregnancy

There are no adequate and well-controlled studies in pregnant women. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with olanzapine. Nevertheless, because human experience is limited, olanzapine should be used in pregnancy only if the potential benefit justifies the potential risk to the foetus.

New born infants exposed to antipsychotics (including olanzapine) 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-borns should be monitored carefully.

#### Lactation

In a study in breast-feeding, healthy women, olanzapine was excreted in breast milk. Mean infant exposure (mg/kg) at steady state was estimated to be 1.8% of the maternal olanzapine dose (mg/kg). Patients should be advised not to breast feed an infant if they are taking olanzapine.

#### Fertility

Effects on fertility are unknown

## INTERACTIONS:

#### Paediatric population

Interaction studies have only been performed in adults.

#### Potential interactions affecting olanzapine

Since olanzapine is metabolised by CYP1A2, substances that can specifically induce or inhibit this isoenzyme may affect the pharmacokinetics of olanzapine.

#### Induction of CYP1A2

The metabolism of olanzapine may be induced by smoking and carbamazepine, which may lead to reduced olanzapine concentrations. Only slight to moderate increase in olanzapine clearance has been observed. The clinical consequences are likely to be limited, but clinical monitoring is recommended and an increase of olanzapine dose may be considered if necessary.

#### Inhibition of CYP1A2

Fluvoxamine, a specific CYP1A2 inhibitor, has been shown to significantly inhibit the metabolism of olanzapine. The mean increase in olanzapine Cmax following fluvoxamine was 54% in female non-smokers and 77% in male smokers. The mean increase in olanzapine AUC was 52% and 108% respectively. A lower starting dose of olanzapine should be considered in patients who are using fluvoxamine or any other CYP1A2 inhibitors, such as ciprofloxacin. A decrease

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in the dose of olanzapine should be considered if treatment with an inhibitor of CYP1A2 is initiated.  
**Decreased bioavailability**  
 Activated charcoal reduces the bioavailability of oral olanzapine by 50 to 60% and should be taken at least 2 hours before or after olanzapine.  
 Fluoxetine (a CYP2D6 inhibitor), single doses of antacid (aluminium, magnesium) or cimetidine have not been found to significantly affect the pharmacokinetics of olanzapine.  
**Potential for olanzapine to affect other medicinal products**  
 Olanzapine may antagonise the effects of direct and indirect dopamine agonists.  
 Olanzapine does not inhibit the main CYP450 isoenzymes *in vitro* (e.g. 1A2, 2D6, 2C9, 2C19, 3A4). Thus no particular interaction is expected as verified through *in vivo* studies where no inhibition of metabolism of the following active substances was found: tricyclic antidepressant (representing mostly CYP2D6 pathway), warfarin (CYP2C9), theophylline (CYP1A2) or diazepam (CYP3A4 and 2C19). Olanzapine showed no interaction when co-administered with lithium or biperiden.

Therapeutic monitoring of valproate plasma levels did not indicate that valproate dosage adjustment is required after the introduction of concomitant olanzapine.  
**General CNS activity**  
 Caution should be exercised in patients who consume alcohol or receive medicinal products that can cause central nervous system depression.  
 The concomitant use of olanzapine with anti-Parkinsonian medicinal products in patients with Parkinson's disease and dementia is not recommended.  
**QTc interval**  
 Caution should be used if olanzapine is being administered concomitantly with medicinal products known to increase QTc interval.

**ADVERSE EFFECTS:****Adults**

The most frequently (seen in ≥ 1% of patients) reported adverse reactions associated with the use of olanzapine in clinical trials were somnolence, weight gain, eosinophilia, elevated prolactin, cholesterol, glucose and triglyceride levels, glycosuria, increased appetite, dizziness, akathisia, parkinsonism, leukopenia, neutropenia, dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic aminotransferases, rash, asthenia, fatigue, pyrexia, arthralgia, increased alkaline phosphatase, high gamma glutamyl transferase, high uric acid, high creatine phosphokinase and oedema.

Very common	Common	Uncommon	Rare	Not known
<b>Blood and the lymphatic system disorders</b>				
	Eosinophilia Leukopenia <sup>10</sup> Neutropenia <sup>10</sup>		Thrombocytopenia <sup>11</sup>	
<b>Immune system disorders</b>				
		Hypersensitivity <sup>11</sup>		
<b>Metabolism and nutrition disorders</b>				
Weight gain <sup>1</sup>	Elevated cholesterol levels <sup>4,3</sup> Elevated glucose levels <sup>4</sup> Elevated triglyceride levels <sup>4,5</sup> Glycosuria Increased appetite	Development or exacerbation of diabetes occasionally associated with ketoacidosis or coma, including some fatal cases	Hypothermia <sup>12</sup>	
<b>Nervous system disorders</b>				
Somnolence	Dizziness Akathisia <sup>6</sup> Parkinsonism <sup>6</sup> Dyskinesia <sup>6</sup>	Seizures where in most cases a history of seizures or risk factors for seizures were reported <sup>11</sup> Dystonia (including oculogyration) Tardive dyskinesia Amnesia <sup>9</sup> Dysarthria	Neuroleptic malignant syndrome Discontinuation symptoms <sup>12</sup>	
<b>Cardiac disorders</b>				
		Bradycardia QT <sub>c</sub> prolongation	Ventricular tachycardia/fibrillation, sudden death	
<b>Vascular disorders</b>				
Orthostatic hypotension <sup>10</sup>		Venous thromboembolism (including pulmonary embolism and deep vein thrombosis)		
<b>Respiratory, thoracic and mediastinal disorders</b>				
		Epistaxis <sup>9</sup>		
<b>Gastrointestinal disorders</b>				
	Mild, transient anticholinergic effects including constipation and dry mouth	Abdominal distension <sup>9</sup>	Pancreatitis <sup>11</sup>	
<b>Hepato-biliary disorders</b>				
	Transient, asymptomatic elevations of hepatic aminotransferases (ALT, AST), especially in early treatment		Hepatitis (including hepatocellular, cholestatic or mixed liver injury) <sup>11</sup>	
<b>Skin and subcutaneous tissue disorders</b>				
	Rash	Photosensitivity reaction Alopecia		
<b>Musculoskeletal and connective tissue disorders</b>				
	Arthralgia <sup>9</sup>		Rhabdomyolysis <sup>11</sup>	
<b>Renal and urinary disorders</b>				
		Urinary incontinence, urinary retention Urinary hesitation <sup>11</sup>		
<b>Pregnancy, puerperium and perinatal conditions</b>				
			Drug withdrawal syndrome neonatal	
<b>Reproductive system and breast disorders</b>				
	Erectile dysfunction in males Decreased libido in males and females	Amenorrhea Breast enlargement Galactorrhea in females Gynaecomastia/breast enlargement in males	Priapism <sup>12</sup>	
<b>General disorders and administration site conditions</b>				
	Asthenia Fatigue Oedema Pyrexia <sup>10</sup>			
<b>Investigations</b>				

Elevated plasma prolactin levels <sup>9</sup>	Increased alkaline phosphatase <sup>10</sup> High creatine phosphokinase <sup>11</sup> High Gamma glutamyltransferase <sup>10</sup> High uric acid <sup>10</sup>	Increased total bilirubin	
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<sup>1</sup>Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Following short-term treatment (median duration 47 days), weight gain ≥ 7% of baseline body weight was very common (22.2 %); ≥ 15 % was common (4.2 %); and ≥ 25 % was uncommon (0.8 %). Patients gaining ≥ 7 %, ≥ 15 % and ≥ 25 % of their baseline body weight with long-term exposure (at least 48 weeks) were very common (64.4 %, 31.7 % and 12.3 % respectively).

<sup>2</sup>Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline.

<sup>3</sup>Observed for fasting normal levels at baseline (< 5.17 mmol/l) which increased to high (≥ 6.2 mmol/l). Changes in total fasting cholesterol levels from borderline at baseline (≥ 5.17 - < 6.2 mmol/l) to high (≥ 6.2 mmol/l) were very common.

<sup>4</sup>Observed for fasting normal levels at baseline (< 5.56 mmol/l) which increased to high (≥ 7 mmol/l). Changes in fasting glucose from borderline at baseline (≥ 5.56 - < 7 mmol/l) to high (≥ 7 mmol/l) were very common.

<sup>5</sup>Observed for fasting normal levels at baseline (< 1.69 mmol/l) which increased to high (≥ 2.26 mmol/l). Changes in fasting triglycerides from borderline at baseline (≥ 1.69 mmol/l - < 2.26 mmol/l) to high (≥ 2.26 mmol/l) were very common.

<sup>6</sup>In clinical trials, the incidence of Parkinsonism and dystonia in olanzapine-treated patients was numerically higher, but not statistically significantly different from placebo. Olanzapine-treated patients had a lower incidence of Parkinsonism, akathisia and dystonia compared with titrated doses of haloperidol. In the absence of detailed information on the pre-existing history of individual acute and tardive extrapyramidal movement disorders, it cannot be concluded at present that olanzapine produces less tardive dyskinesia and/or other tardive extrapyramidal syndromes.

<sup>7</sup>Acute symptoms such as sweating, insomnia, tremor, anxiety, nausea and vomiting have been reported when olanzapine is stopped abruptly.

<sup>8</sup>In clinical trials of up to 12 weeks, plasma prolactin concentrations exceeded the upper limit of normal range in approximately 30% of olanzapine-treated patients with normal baseline prolactin value. In the majority of these patients the elevations were generally mild, and remained below two times the upper limit of normal range.

<sup>9</sup>Adverse event identified from clinical trials in the Olanzapine Integrated Database.

<sup>10</sup>As assessed by measured values from clinical trials in the Olanzapine Integrated Database.

<sup>11</sup>Adverse event identified from spontaneous post-marketing reporting with frequency determined utilizing the Olanzapine Integrated Database.

<sup>12</sup>Adverse event identified from spontaneous post-marketing reporting with frequency estimated at the upper limit of the 95% confidence interval utilizing the Olanzapine Integrated Database.

**Long-term exposure (at least 48 weeks)**  
The proportion of patients who had adverse, clinically significant changes in weight gain, glucose, total/LDL/HDL cholesterol or triglycerides increased over time. In adult patients who completed 9-12 months of therapy, the rate of increase in mean blood glucose slowed after approximately 6 months.

**Additional information on special populations**

In clinical trials in elderly patients with dementia, olanzapine treatment was associated with a higher incidence of death and cerebrovascular adverse reactions compared to placebo. Very common adverse reactions associated with the use of olanzapine in this patient group were abnormal gait and falls. Pneumonia, increased body temperature, lethargy, erythema, visual hallucinations and urinary incontinence were observed commonly.

In clinical trials in patients with drug-induced (dopamine agonist) psychosis associated with Parkinson's disease, worsening of Parkinsonian symptomatology and hallucinations were reported very commonly and more frequently than with placebo.

In one clinical trial in patients with bipolar mania, valproate combination therapy with olanzapine resulted in an incidence of neutropenia of 4.1%; a potential contributing factor could be high plasma valproate levels. Olanzapine administered with lithium or valproate resulted in increased levels (≥10%) of tremor, dry mouth, increased appetite, and weight gain. Speech disorder was also reported commonly. During treatment with olanzapine in combination with lithium or divalproex, an increase of ≥ 7% from baseline body weight occurred in 17.4% of patients during acute treatment (up to 6 weeks). Long-term olanzapine treatment (up to 12 months) for recurrence prevention in patients with bipolar disorder was associated with an increase of ≥7% from baseline body weight in 39.9% of patients.

**Paediatric population**

Olanzapine is not indicated for the treatment of children and adolescent patients below 18 years. Although no clinical studies designed to compare adolescents to adults have been conducted, data from the adolescent trials were compared to those of the adult trials.

**OVERDOSE AND TREATMENT:****- Symptoms**

Very common symptoms in overdose (>10% incidence) include tachycardia, agitation/aggressiveness, dysarthria, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma.

Other medically significant sequelae of overdose include delirium, convulsion, coma, possible neuroleptic malignant syndrome, respiratory depression, aspiration, hypertension or hypotension, cardiac arrhythmias (< 2% of overdose cases) and cardiopulmonary arrest. Fatal outcomes have been reported for acute overdoses as low as 450mg but survival has also been reported following acute overdose of approximately 2g of oral olanzapine.

**- Treatment**

There is no specific antidote for olanzapine. Induction of emesis is not recommended. Standard procedures for management of overdose may be indicated (i.e. gastric lavage, administration of activated charcoal). The concomitant administration of activated charcoal was shown to reduce the oral bioavailability of olanzapine by 50 to 60%.

Symptomatic treatment and monitoring of vital organ function should be instituted according to clinical presentation, including treatment of hypotension and circulatory collapse and support of respiratory function. Do not use epinephrine, dopamine, or other sympathomimetic agents with beta-agonist activity since beta stimulation may worsen hypotension. Cardiovascular monitoring is necessary to detect possible arrhythmias. Close medical supervision and monitoring should continue until the patient recovers.

**STORAGE CONDITION:**

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

**DOSAGE FORMS AND PACKAGING AVAILABLE:**

Olanzapine Tablets 10 mg (Olan-10) are packed in Alu-Alu Blister Pack of 10's (Box of 20's and 100's)

**INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):**

Not Applicable

**NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:****Marketing Authorization Holder**

Brown & Bur PHILIPPINES INC  
U-501, 5/F, SEDCCO 1 Bldg., 120 Rada cor., Legaspi Sts., Legaspi Village, Makati City, Philippines

**NAME AND ADDRESS OF MANUFACTURER:****MICRO LABS LIMITED**

92 SIPOT INDUSTRIAL COMPLEX,  
HOSUR-633 126 (T.N), INDIA

**CAUTION STATEMENT:**

FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION .

**ADR REPORTING STATEMENT:**

FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph

Seek medical attention immediately at the first sign of Adverse Drug Reaction.

**REGISTRATION NUMBER:**

DRP-7196

**DATE OF FIRST AUTHORIZATION:**

28 JUNE 2012

**DATE OF REVISION OF PACKAGE INSERT:**

Feb. 2017

EXG-ML01I-

350 mm

240 mm

MICRO LABS LIMITED, BANGALORE, INDIA						
1	Product Name	Olan		Colours Used		
2	Strength	10 mg		■ BLACK		
3	Component	Leaflet				
4	Category	Export - Philippines				
5	Dimension	240 x 350 mm				
6	Artwork Code	EXG-ML01I-				
7	Pharma Code	N/A				
8	Reason for Change	New Artwork		<small>Colours not for Printing ■ Keylines</small>		
		Prepared by (DTP)	Checked by (PD)	Approved by		
Sign				Head CQA	Head Production/ Packing (Site)	
Date		19-11-2021		Head QC (Site)	Head QA (Site)	