

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

Folding size: 30 x 175 mm

Carton size: 46 x 22 x 106 mm

Front

BB

OLANZAPINE

OLAN ODT

5 mg & 10 mg Orodispersible Tablet

ANTIPSYCHOTIC

PRODUCT NAME:

Olanzapine Orodispersible Tablets

NAME AND STRENGTH OF ACTIVE INGREDIENT(s):

Olanzapine Orodispersible Tablets 5/10mg.

PRODUCT DESCRIPTION:

Pale yellow to yellow colored, circular shaped, flat faced beveled edge, Orodispersible tablet, with breakline on one face and plain on other face. Tablet may contain few yellow colored specks of active pharmaceutical ingredient.

FORMULATION/COMPOSITION:

Each Orodispersible tablet contains:

Olanzapine USP.....5 mg / 10 mg

PHARMACODYNAMICS / PHARMACOKINETICS:

PHARMACODYNAMICS:

Olanzapine is an antipsychotic, antimanic and mood stabilizing agent that demonstrates a broad pharmacologic profile across a number of receptor systems. In preclinical studies, olanzapine exhibited a range of receptor affinities ($K_i < 100 \text{ nM}$) for serotonin 5 HT_{2A/2C}, 5 HT₃, 5 HT₆; dopamine D₁, D₂, D₃, D₄, D₅; cholinergic muscarinic receptors M_{1-M₅}; α₁ adrenergic; and histamine H₁ receptors. Animal behavioral studies with olanzapine indicated 5HT, dopamine, and cholinergic antagonism, consistent with the receptor-binding profile. Olanzapine demonstrated a greater *in vitro* affinity for serotonin 5HT₂ than dopamine D₂ receptors and greater 5 HT₂ than D₂ activity *in vivo* models. Electrophysiological studies demonstrated that olanzapine selectively reduced the firing of mesolimbic (A₁₀) dopaminergic neurons, while having little effect on the striatal (A₉) pathways involved in motor function. Olanzapine reduced a conditioned avoidance response, a test indicative of antipsychotic activity, at doses below those producing catalepsy, an effect indicative of motor side-effects. Unlike some other antipsychotic agents, olanzapine increases responding in an "anxiolytic" test. In a single oral dose (10 mg) Positron Emission Tomography (PET) study in healthy volunteers, olanzapine produced a higher 5 HT_{2A} than dopamine D₂ receptor occupancy. In addition, a Single Photon Emission Computed Tomography (SPECT) imaging study in schizophrenic patients revealed that olanzapine-responsive patients had lower striatal D₂ occupancy than some other antipsychotic- and Risperidone-responsive patients, while being comparable to clozapine-responsive patients.

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 α₁-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 20 mg/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 hrs) and the clearance was reduced (18.9 versus 27.3 l/hr). However, olanzapine (5-20 mg) demonstrated a comparable safety profile in female (n=467) as in male patients (n=869).

INDICATION:

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 manic 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:

Preventing recurrence in bipolar disorder: The recommended starting dose is 10 mg/day. For patients who have been receiving olanzapine for treatment of manic episode, continue therapy for preventing recurrence 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- 20 mg/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.

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.

Olanzapine Orodispersible Tablet should be placed in the mouth, where it will rapidly disperse in saliva, so it can be easily swallowed. Removal of the intact Orodispersible tablet from the mouth is difficult. Since the Orodispersible tablet is fragile, it should be taken immediately on opening the blister. Alternatively, it may be dispersed in a full glass of water or other suitable beverage (orange juice, apple juice, milk or coffee) immediately before administration.

Olanzapine Orodispersible tablet is bioequivalent to olanzapine coated tablets, with a similar rate and extent of absorption. It has the same dosage and frequency of administration as olanzapine coated tablets. Olanzapine Orodispersible tablets may be used as an alternative to olanzapine coated tablets.

Paediatric 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.

Elderly patients

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

Gender

The starting dose and dose range need not be routinely altered for female patients relative to male patients.

Smokers

The starting dose and dose range need not be routinely altered for non-smokers relative to smokers. 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. In cases where dose increments of 2.5 mg are considered necessary, Olanzapine coated tablets should be used.

Mode of Administration

Adults

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

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

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

Hypersensitivity to the active substance or to any of the excipients. Patients with known risk of narrow-angle glaucoma 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 approved for the treatment of dementia-related psychosis and/or behavioral disturbances and is not recommended for use in this particular group of patients 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 behaviors, 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 4.4 mg) 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 2.5 mg/day and titrated to a maximum of 15 mg/day based on investigator judgment.

Neuroleptic Malignant Syndrome (NMS): NMS is a potentially life-threatening condition associated with antipsychotic medicinal product. 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.

Hyperglycemia and diabetes: Hyperglycemia and/or development or exacerbation of diabetes occasionally associated with ketoacidosis or coma has been reported rarely, 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 agents, including Olanzapine, should be observed for signs and symptoms of hyperglycemia (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 dyslipidemia patients and in patients with risk factors for the development of lipids disorders. Patients treated with any antipsychotic agents, including Olanzapine, 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 very rarely (< 0.01%) when olanzapine is stopped abruptly.

QT interval? In clinical trials, clinically meaningful QTc prolongations (Fridericia QT correction [QTcF] ≥ 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, as with other antipsychotics, 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, hypokalemia or hypomagnesemia.

Thromboembolism: Temporal association of olanzapine treatment and venous thromboembolism has been reported uncommonly (≥ 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. immobilization 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 rarely 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 dyskinesia. 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. As with other antipsychotics, 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.

350 mm

240 mm

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Folding size: 30 x 175 mm

Carton size: 46 x 22 x 106 mm

Back

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. Long-term outcomes associated with these events have not been studied and remain unknown.

Phenylalanine: Olanzapine Orosoluble tablet contains aspartame, which is a source of phenylalanine. May be harmful for people with phenylketonuria.

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.

Neonates 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, hypertension, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns 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.

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 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 (aluminum, magnesium) or cimetidine have not been found to significantly affect the pharmacokinetics of olanzapine.

Potential for olanzapine to affect other medicinal products

Olanzapine may antagonize the effects of direct and indirect dopamine agonists. Olanzapine does not inhibit the main CYP450 isoenzyme *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 $\geq 1\%$ 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, Glucosuria, increased appetite, dizziness, akathisia, parkinsonism, dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic aminotransferases, rash, asthenia, fatigue and oedema.

Very common	Common	Uncommon	Not known
Blood and the lymphatic system disorders			
	Eosinophilia	Leukopenia Neutropenia	Thrombocytopenia
Immune system disorders			
			Allergic reaction
Metabolism and nutrition disorders			
Weight gain ¹	Elevated cholesterol levels ^{2,3} Elevated glucose levels ⁴ Elevated triglyceride levels ^{2,5} Glucosuria Increased appetite		Development or exacerbation of diabetes occasionally associated with ketoacidosis or coma, including some fatal cases Hypothermia
Nervous system disorders			
Somnolence	Dizziness Akathisia Parkinsonism Dyskinesia		Seizures where in most cases a history of seizures or risk factors for seizures were reported Neuroleptic malignant syndrome Dystonia (including oculogyration) Tardive dyskinesia Discontinuation symptoms ⁷
Cardiac disorders			
		Bradycardia QTc prolongation	Ventricular tachycardia/fibrillation, sudden death
Vascular disorders			
	Orthostatic hypotension	Thromboembolism (including pulmonary embolism and deep vein thrombosis)	
Gastrointestinal disorders			
	Mild, transient anticholinergic effects including constipation and dry mouth		Pancreatitis

Hepato-biliary disorders			
	Transient, asymptomatic elevations of hepatic aminotransferases (ALT, AST), especially in early treatment		Hepatitis (including hepatocellular, cholestatic or mixed liver injury)

1. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Following short term treatment (median duration 47 days), weight gain $\geq 7\%$ of baseline body weight was very common (22.2 %), $\geq 15\%$ was common (4.2 %) and $\geq 25\%$ was uncommon (0.8 %). Patients gaining $\geq 7\%$, $\geq 15\%$ and $\geq 25\%$ of their baseline body weight with long-term exposure (at least 48 weeks) were very common (64.4%, 31.7% and 12.3% respectively).
2. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline.
3. Observed for fasting normal levels at baseline ($< 5.17 \text{ mmol/l}$) which increased to high ($\geq 6.2 \text{ mmol/l}$). Changes in total fasting cholesterol levels from borderline at baseline ($\geq 5.17 - < 6.2 \text{ mmol/l}$) to high ($\geq 6.2 \text{ mmol/l}$) were very common.
4. Observed for fasting normal levels at baseline ($< 5.56 \text{ mmol/l}$) which increased to high ($\geq 7 \text{ mmol/l}$). Changes in fasting glucose from borderline at baseline ($\geq 5.56 - < 7 \text{ mmol/l}$) to high ($\geq 7 \text{ mmol/l}$) were very common.
5. Observed for fasting normal levels at baseline ($< 1.69 \text{ mmol/l}$) which increased to high ($\geq 2.26 \text{ mmol/l}$). Changes in fasting triglycerides from borderline at baseline ($\geq 1.69 \text{ mmol/l} - < 2.26 \text{ mmol/l}$) to high ($\geq 2.26 \text{ mmol/l}$) were very common.
6. 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.
7. Acute symptoms such as sweating, insomnia, tremor, anxiety, nausea and vomiting have been reported when olanzapine is stopped abruptly.
8. 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.
9. Adverse event identified from clinical trials in the Olanzapine Integrated Database.
10. As assessed by measured values from clinical trials in the Olanzapine Integrated Database.
11. Adverse event identified from spontaneous post-marketing reporting with frequency determined utilizing the Olanzapine Integrated Database.
12. 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.

OVERDOSE AND TREATMENT:

Signs and 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 450 mg but survival has also been reported following acute overdose of approximately 2 g of oral olanzapine.

Management: 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 Orosoluble Tablets 5 mg/10 mg (Olan ODT – 5/10) are packed in Alu-Alu Blister pack of 10's (Box of 30)

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

Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:

Marketing Authorization Holder

BROWN & BURK PHILS., INC.
U-501, 5/F SEDCO 1 Bldg., 120 Rada cor.
Legaspi Sts., Legaspi Village, Makati, Metro Manila

NAME AND ADDRESS OF MANUFACTURER:

MICRO LABS LIMITED
92, Sipcot Industrial Complex,
Hosur-635 126 (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:

OLAN ODT 5 mg : DRP-9846
OLAN ODT 10 mg : DRP-9666

DATE OF FIRST AUTHORIZATION:

-

DATE OF REVISION OF PACKAGE INSERT:

July 2017

EXG-ML01I-1714/A

350 mm

240 mm

MICRO LABS LIMITED, BANGALORE, INDIA					
1	Product Name	Olan ODT			<u>Colours Used</u>
2	Strength	5 mg & 10 mg			 BLACK
3	Component	Leaflet			
4	Category	Export - Philippines			
5	Dimension	240 (L) x 350 (H) mm			
6	Artwork Code	EXG-ML01I-1714/A			
7	Pharma Code	N/A			
8	Reason for Change	Olan ODT 5 mg Reg. No. inserted and from Antipsychotics to Antipsychotic			<u>Colours not for Printing</u>  Keylines
		Prepared by (DTP)	Checked by (PD)	Approved by	
Sign	Kanthalraju L.			Head CQA	Head Production/ Packing (Site)
Date	10-01-2022			Head QC (Site)	Head QA (Site)