

For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

TOLAZ DT

1. Generic Name

Olanzapine orally disintegrating tablets USP

2. Qualitative and quantitative composition

TOLAZ DT 2.5

Each uncoated tablet contains:

Olanzapine I.P. 2.5 mg

Excipients: MANNITOL, CROSPVIDONE, POWDAROME PINEAPPLE PREMIUM, MICROCRYSTALLINE CELLU, MAGNESIUM STEARATE

TOLAZ DT 5

Each uncoated tablet contains:

Olanzapine I.P. 5 mg

Colour: Lake of Sunset Yellow

Excipients: MANNITOL, CROSPVIDONE, COLLOIDAL SILICON DIOXIDE POWDAROME ORANGE PREMIUM, LAKE OF SUNSET YELLOW, MICROCRYSTALLINE CELLU, MAGNESIUM STEARATE

TOLAZ DT 7.5

Each uncoated tablet contains:

Olanzapine I.P. 7.5 mg

Excipients: MANNITOL, CROSPVIDONE, LAKE OF SUNSET YELLOW, ASPARTAME, MICROCRYSTALLINE CELLU, MAGNESIUM STEARATE

TOLAZ DT 10

Each uncoated tablet contains:

Olanzapine I.P. 10 mg

Colour: Lake of Sunset Yellow

Excipients: MANNITOL, CROSPVIDONE, LAKE OF SUNSET YELLOW, ASPARTAME, MICROCRYSTALLINE CELLU, MAGNESIUM STEARATE

3. Dosage form and strength

Dosage Form: Uncoated tablet

Strength: Olanzapine – 2.5 / 5/ 7.5 / 10 mg

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for treatment of schizophrenia in adults

4.2 Posology and method of administration

As directed by the Physician.

Adults

Schizophrenia

The recommended starting dose for Olanzapine Accord 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 Accord for treatment of manic episode, continue therapy for preventing recurrence at the same dose. If a new manic, mixed, or depressive episode occurs, Olanzapine Accord 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.

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

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.

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed Patients with known risk for narrow-angle glaucoma.

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.

Dementia-related psychosis and/or behavioural disturbances

Olanzapine is not recommended for use in patients with dementia-related psychosis and/or behavioural 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 4.4 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 ischaemic 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 (see section 4.8), 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 judgement.

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 creatinine 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 (see section 4.8). 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 utilised 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 Accord, 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 (see section 4.8). Lipid alterations should be managed as clinically appropriate, particularly in dyslipidemic patients and in patients with risk factors for the development of lipids disorders. Patients treated with any antipsychotic medicines, including Olanzapine Accord, should be monitored regularly for lipids in accordance with utilised 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] ≥ 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 antagonise 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 were 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. It is recommended that blood pressure is measured periodically in patients over 65 years.

Sudden cardiac death

In postmarketing 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.

4.5 Drugs interactions

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 (see section 4.2).

Inhibition of CYP1A2

Fluvoxamine, a specific CYP1A2 inhibitor, has been shown to significantly inhibit the metabolism of olanzapine. The mean increase in olanzapine C_{max} 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 (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 (eg, 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

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

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, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breast-feeding

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.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Because olanzapine may cause somnolence and dizziness, patients should be cautioned about operating machinery, including motor vehicles.

4.8 Undesirable effects

Summary of the safety profile

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 (see section 4.4), glucosuria, increased appetite, dizziness, akathisia, parkinsonism, leukopenia, neutropenia (see section 4.4), dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic aminotransferases (see section 4.4), rash, asthenia, fatigue pyrexia, arthralgia, increased alkaline phosphatase, high gamma glutamyltransferase, high uric acid, high creatine phosphokinase and oedema.

Tabulated list of adverse reactions

The following table lists the adverse reactions and laboratory investigations observed from spontaneous reporting and in clinical trials. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The frequency terms listed are defined as follows: Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$), not known (cannot be estimated from the data available).

Very common	Common	Uncommon	Rare	Not known
Blood and the lymphatic system disorders				
	Eosinophilia Leukopenia ¹⁰ Neutropenia ¹⁰		Thrombocytopenia ¹¹	
Immune system disorders				
		Hypersensitivity ¹		
Metabolism and nutrition disorders				
Weight gain ¹	Elevated cholesterol levels ^{2,3} Elevated glucose levels ⁴	Development or exacerbation of diabetes occasionally associated with ketoacidosis or coma, including	Hypothermia ¹²	

	Elevated triglyceride levels ^{2,5} Glucosuria Increased appetite	some fatal cases ¹¹		
Nervous system disorders				
Somnolence	Dizziness Akathisia ⁶ Parkinsonism ⁶ Dyskinesia ⁶	Seizures where in most cases a history of seizures or risk factors for seizures were reported ¹¹ Dystonia (including oculogyration) ¹¹ Tardive dyskinesia ¹¹ Amnesia ⁹ Dysarthria Stuttering ¹¹ Restless legs syndrome ¹¹	Neuroleptic malignant syndrome Discontinuation symptoms ^{7,12}	
Cardiac disorders				
		Bradycardia QTc prolongation	Ventricular tachycardia/fibrillation, sudden death ¹¹	
Vascular disorders				
Orthostatic hypotension ¹⁰		Thromboembolism (including pulmonary embolism and deep vein thrombosis)		
Respiratory, thoracic and mediastinal disorders				
		Epistaxis ⁹		
Gastro-intestinal disorders				

	Mild, transient anticholinergic effects including constipation and dry mouth	Abdominal distension ⁹ Salivary hypersecretion ¹¹	Pancreatitis ¹¹	
Hepato-biliary disorders				
	Transient, asymptomatic elevations of hepatic aminotransferases (ALT, AST), especially in early treatment (see section 4.4)		Hepatitis (including hepatocellular, cholestatic or mixed liver injury) ¹¹	
Skin and subcutaneous tissue disorders				
	Rash	Photosensitivity reaction, Alopecia		Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
Musculoskeletal and connective tissue disorders				
	Arthralgia ⁹		Rhabdomyolysis ¹¹	
Renal and urinary disorders				
		Urinary incontinence, urinary retention Urinary hesitation ¹¹		
Pregnancy, puerperium and perinatal conditions				
				Drug withdrawal syndrome neonatal
Reproductive system and breast disorders				

	Erectile dysfunction in males Decreased libido in males and females	Amenorrhea Breast enlargement Galactorrhea in females Gynaecomastia/breast enlargement in males	Priapism ¹²	
General disorders and administration site conditions				
	Asthenia, Fatigue, Oedema Pyrexia ¹⁰			
Investigations				
Elevated plasma prolactin levels ⁸	Increased alkaline phosphatase ¹⁰ High creatine phosphokinase ¹¹ High Gamma Glutamyltransferase ¹⁰ High Uric Acid ¹⁰	Increased total bilirubin		

¹Clinically 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).

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

³Observed 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 ($\geq 5.17 - < 6.2$ mmol/l) to high (≥ 6.2 mmol/l) were very common.

⁴Observed 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 ($\geq 5.56 - < 7$ mmol/l) to high (≥ 7 mmol/l) were very common.

⁵Observed 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.

⁶In 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 can-not be concluded at present that olanzapine produces less tardive dyskinesia and/or other tardive extrapyramidal syndromes.

⁷Acute 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.

⁹Adverse event identified from clinical trials in the Olanzapine Integrated Database.

¹⁰As assessed by measured values from clinical trials in the Olanzapine Integrated Database.

¹¹Adverse event identified from spontaneous post-marketing reporting with frequency determined utilising the Olanzapine Integrated Database.

¹²Adverse event identified from spontaneous post-marketing reporting with frequency estimated at the upper limit of the 95% confidence interval utilising 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 (see section 4.4). 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 ($\geq 10\%$) 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 $\geq 7\%$ 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 $\geq 7\%$ 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.

The following table summarizes the adverse reactions reported with a greater frequency in adolescent patients (aged 13-17 years) than in adult patients or adverse reactions only identified during short-term clinical trials in adolescent patients. Clinically significant weight gain ($\geq 7\%$) appears to occur more frequently in the adolescent population compared to adults with comparable exposures. The magnitude of weight gain and the proportion of adolescent patients who had clinically significant weight gain were greater with long-term exposure (at least 24 weeks) than with short-term exposure.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The frequency terms listed are defined as follows: Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$).

<p>Metabolism and nutrition disorders</p> <p><i>Very common:</i> Weight gain¹³, elevated triglyceride levels¹⁴, increased appetite.</p> <p><i>Common:</i> Elevated cholesterol levels¹⁵</p>
<p>Nervous system disorders</p> <p><i>Very common:</i> Sedation (including: hypersomnia, lethargy, somnolence).</p>
<p>Gastro-intestinal disorders</p> <p><i>Common:</i> Dry mouth</p>
<p>Hepato-biliary disorders</p> <p><i>Very common:</i> Elevations of hepatic aminotransferases (ALT/AST; see section 4.4).</p>
<p>Investigations</p> <p><i>Very common:</i> Decreased total bilirubin, increased GGT, elevated plasma prolactin levels¹⁶.</p>

¹³ Following short term treatment (median duration 22 days), weight gain $\geq 7\%$ of baseline body weight (kg) was very common (40.6%), $\geq 15\%$ of baseline body weight was common (7.1%) and $\geq 25\%$ was common (2.5%). With long-term exposure (at least 24 weeks), 89.4% gained $\geq 7\%$, 55.3% gained $\geq 15\%$ and 29.1% gained $\geq 25\%$ of their baseline body weight.

¹⁴ Observed for fasting normal levels at baseline (< 1.016 mmol/l) which increased to high (\geq 1.467 mmol/l) and changes in fasting triglycerides from borderline at baseline (\geq 1.016 mmol/l - < 1.467 mmol/l) to high (\geq 1.467 mmol/l).

¹⁵ Changes in total fasting cholesterol levels from normal at baseline (< 4.39 mmol/l) to high (\geq 5.17 mmol/l) were observed commonly. Changes in total fasting cholesterol levels from borderline at baseline (\geq 4.39 - < 5.17 mmol/l) to high (\geq 5.17 mmol/l) were very common.

¹⁶ Elevated plasma prolactin levels were reported in 47.4% of adolescent patients.

Reporting of suspected adverse reactions

If you get any 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 directly via any point of contact of Torrent Pharma available at: https://torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine

4.9 Overdose

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 2 g 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 (ie, 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.

5. Pharmacological properties

5.1 Mechanism of Action

Olanzapine is an antipsychotic, antimanic, and mood stabilising agent that demonstrates a broad pharmacologic profile across a number of receptor systems.

5.2 Pharmacodynamic properties

Pharmacotherapeutic group: psycholeptics, diazepines, oxazepines, thiazepines and oxepines.

ATC code: N05A H03

In reported preclinical studies, olanzapine exhibited a range of receptor affinities ($K_i < 100\text{nM}$) for serotonin 5HT_{2A/2C}, 5HT₃, 5HT₆; dopamine D₁, D₂, D₃, D₄, D₅; cholinergic muscarinic receptors M₁-M₅; α_1 adrenergic; and histamine H₁ receptors. Animal behavioural 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 5HT₂ than D₂ activity in 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 reported single oral dose (10mg) Positron Emission Tomography (PET) study in healthy volunteers, olanzapine produced a higher 5HT_{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.

Clinical efficacy

In reported two of two placebo- and two of three comparator-controlled trials with over 2,900 schizophrenic patients presenting with both positive and negative symptoms, Olanzapine was associated with statistically significantly greater improvements in negative as well as positive symptoms.

In a reported multinational, double-blind, comparative study of schizophrenia, schizoaffective and related disorders, which included 1,481 patients with varying degrees of associated depressive symptoms (baseline mean of 16.6 on the Montgomery-Asberg Depression Rating Scale), a prospective secondary analysis of baseline to endpoint mood score change demonstrated a statistically significant improvement ($P = 0.001$) favouring Olanzapine (-6.0) versus haloperidol (-3.1).

In patients with a manic or mixed episode of bipolar disorder, olanzapine demonstrated superior efficacy to placebo and valproate semisodium (divalproex) in reduction of manic symptoms over 3 weeks. Olanzapine also demonstrated comparable efficacy results to haloperidol in terms of the proportion of patients in symptomatic remission from mania and depression at 6 and 12 weeks. In a co-therapy study of patients treated with lithium or valproate for a minimum of 2 weeks, the addition of olanzapine 10mg (co-therapy with lithium or valproate) resulted in a greater reduction in symptoms of mania than lithium or valproate monotherapy after 6 weeks.

In a reported 12-month recurrence prevention study in manic episode patients who achieved remission on olanzapine and were then randomised to olanzapine or placebo,

olanzapine demonstrated statistically significant superiority over placebo on the primary endpoint of bipolar recurrence. Olanzapine also showed a statistically significant advantage over placebo in terms of preventing either recurrence into mania or recurrence into depression.

In a reported second 12-month recurrence prevention study in manic episode patients who achieved remission with a combination of olanzapine and lithium and were then randomised to olanzapine or lithium alone, olanzapine was statistically non-inferior to lithium on the primary endpoint of bipolar recurrence (olanzapine 30.0%, lithium 38.3%; $p = 0.055$).

In an 18-month co-therapy study in manic or mixed episode patients stabilised with olanzapine plus a mood stabiliser (lithium or valproate), long-term olanzapine co-therapy with lithium or valproate was not statistically significantly superior to lithium or valproate alone in delaying bipolar recurrence, defined according to syndromic (diagnostic) criteria.

Paediatric population

In reported controlled efficacy data in adolescents (ages 13 to 17 years) are limited to short-term studies in schizophrenia (6 weeks) and mania associated with bipolar I disorder (3 weeks), involving less than 200 adolescents. Olanzapine was used as a flexible dose starting with 2.5 and ranging up to 20 mg/day. During treatment with olanzapine, adolescents gained significantly more weight compared with adults. The magnitude of changes in fasting total cholesterol, LDL cholesterol, triglycerides, and prolactin were greater in adolescents than in adults. There are no controlled data on maintenance of effect or long-term safety. Information on long term safety is primarily limited to open-label, uncontrolled data.

5.3 Pharmacokinetic properties

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 α 1-acid-glycoprotein.

Metabolism

Olanzapine is metabolised 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.

Excretion

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 hours) 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 hours) 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).

Hepatic impairment

A small study of the effect of impaired liver function in 6 subjects with clinically significant (Childs Pugh Classification A (n = 5) and B (n = 1)) cirrhosis revealed little effect on the pharmacokinetics of orally administered olanzapine (2.5 – 7.5 mg single dose): Subjects with mild to moderate hepatic dysfunction had slightly increased systemic clearance and faster elimination half-time compared to subjects with no hepatic dysfunction (n = 3). There were more smokers among subjects with cirrhosis (4/6; 67 %) than among subjects with no hepatic dysfunction (0/3; 0 %).

Renal impairment

In renally impaired patients (creatinine clearance <10ml/min) versus healthy subjects, there was no significant difference in mean elimination half-life (37.7 versus 32.4 hours) or clearance (21.2 versus 25.0 l/hr). A mass balance study showed that approximately 57% of radio labelled olanzapine appeared in urine, principally as metabolites.

Smokers

In reported non-smoking versus smoking subjects (males and females), the mean elimination half-life was prolonged (38.6 versus 30.4 hours) and the clearance was reduced (18.6 versus 27.7 l/hr).

The plasma clearance of olanzapine is lower in elderly versus young subjects, in females versus males, and in non-smokers versus smokers. However, the magnitude of the impact of age, gender, or smoking on olanzapine clearance and half-life is small in comparison to the overall variability between individuals.

In a reported study of Caucasians, Japanese, and Chinese subjects, there were no differences in the pharmacokinetic parameters among the three populations.

Paediatric population

Adolescents (ages 13 to 17 years): The pharmacokinetics of olanzapine are similar between adolescents and adults. In clinical studies, the average olanzapine exposure was approximately 27% higher in adolescents. Demographic differences between the adolescents and adults include a lower average body weight and fewer adolescents were smokers. Such factors possibly contribute to the higher average exposure observed in adolescents.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Acute (Single-Dose) Toxicity

Signs of oral toxicity in rodents were characteristic of potent neuroleptic compounds: hypoactivity, coma, tremors, clonic convulsions, salivation, and depressed weight gain. The median lethal doses were approximately 210mg/kg (mice) and 175mg/kg (rats). Dogs tolerated single oral doses up to 100mg/kg without mortality. Clinical signs included sedation, ataxia, tremors, increased heart rate, laboured respiration, miosis, and anorexia. In monkeys, single oral doses up to 100mg/kg resulted in prostration and, at higher doses, semi-consciousness.

Repeated-Dose Toxicity

In reported studies up to 3 months duration in mice and up to 1 year in rats and dogs, the predominant effects were CNS depression, anticholinergic effects, and peripheral haematological disorders. Tolerance developed to the CNS depression. Growth parameters were decreased at high doses. Reversible effects consistent with elevated prolactin in rats included decreased weights of ovaries and uterus and morphologic changes in vaginal epithelium and in mammary gland.

Haematologic toxicity

Effects on haematology parameters were found in each species, including dose-related reductions in circulating leukocytes in mice and non-specific reductions of circulating leukocytes in rats; however, no evidence of bone marrow cytotoxicity was found. Reversible neutropenia, thrombocytopenia, or anaemia developed in a few dogs treated with 8 or 10mg/kg/day (total olanzapine exposure [AUC] is 12- to 15-fold greater than that of a man given a 12mg dose). In cytopenic dogs, there were no adverse effects on progenitor and proliferating cells in the bone marrow.

Reproductive Toxicity

Olanzapine had no teratogenic effects. Sedation affected mating performance of male rats. Estrous cycles were affected at doses of 1.1mg/kg (3-times the maximum human dose) and reproduction parameters were influenced in rats given 3mg/kg (9- times the maximum human dose). In the offspring of rats given olanzapine, delays in foetal development and transient decreases in offspring activity levels were seen.

Mutagenicity

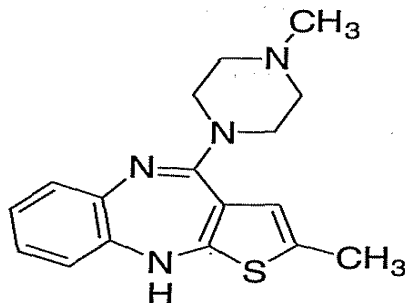
Olanzapine was not mutagenic or clastogenic in a full range of standard tests, which included bacterial mutation tests and in vitro and in vivo mammalian tests.

Carcinogenicity

Based on the reported results of studies in mice and rats, it was concluded that Olanzapine is not carcinogenic.

7. Description

Olanzapine is 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine. Having molecular formula C₁₇H₂₀N₄S and molecular weight 312.4. The chemical structure is:



8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable.

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

TOLAZ-DT 2.5/5/7.5/10 mg is available in blister of 10 tablets.

8.4 Storage and handing instructions

STORE AT A TEMPERATURE NOT EXCEEDING 30 °C, PROTECTED FROM LIGHT AND MOISTURE.

Keep all medicines out of reach of children.

9. Patient Counselling Information

Package leaflet: Information for the user
TOLAZ DT
Olanzapine orally disintegrating tablets USP

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

9.1 What TOLAZ DT is and what it is used for

9.2 What you need to know before you use TOLAZ DT

9.3 How to use TOLAZ DT Possible side effects

9.4 How to store TOLAZ DT

9.5 Contents of the pack and other information

9.1 What TOLAZ DT is and what it is used for

Olanzapine tablets contains the active substance olanzapine. Olanzapine tablets belongs to a group of medicines called antipsychotics and is used to treat the following conditions:

- Schizophrenia, a disease with symptoms such as hearing, seeing or sensing things which are not there, mistaken beliefs, unusual suspiciousness, and becoming withdrawn. People with this disease may also feel depressed, anxious or tense.
- Moderate to severe manic episodes, a condition with symptoms of excitement or euphoria.

Olanzapine tablets has been shown to prevent recurrence of these symptoms in patients with bipolar disorder whose manic episode has responded to olanzapine treatment.

9.2 What you need to know before you use TOLAZ DT**Do Not take TOLAZ DT tablets if:**

- If you are allergic (hypersensitive) to olanzapine or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may be recognized as a rash, itching, a swollen face, swollen lips or shortness of breath. If this has happened to you, tell your doctor.
- If you have been previously diagnosed with eye problems such as certain kinds of glaucoma (increased pressure in the eye).

Warnings and precautions

Talk to your doctor or pharmacist before you take Olanzapine tablets

- The use of Olanzapine tablets in elderly patients with dementia is not recommended as it may have serious side effects.
- Medicines of this type may cause unusual movements mainly of the face or tongue. If this happens after you have been given Olanzapine tablets tell your doctor.
- Very rarely, medicines of this type cause a combination of fever, faster breathing, sweating, muscle stiffness and drowsiness or sleepiness. If this happens, contact your doctor at once.
- Weight gain has been seen in patients taking Olanzapine tablets. You and your doctor should check your weight regularly. Consider referral to a dietician or help with a diet plan if necessary.
- High blood sugar and high levels of fat (triglycerides and cholesterol) have been seen in patients taking Olanzapine tablets. Your doctor should do blood tests to check blood sugar and certain fat levels before you start taking Olanzapine tablets and regularly during treatment.
- Tell the doctor if you or someone else in your family has a history of blood clots, as medicines like these have been associated with the formation of blood clots.

If you suffer from any of the following illnesses tell your doctor as soon as possible:

- Stroke or “mini” stroke (temporary symptoms of stroke)
- Parkinson’s disease
- Prostate problems
- A blocked intestine (Paralytic ileus)
- Liver or kidney disease
- Blood disorders
- Heart disease
- Diabetes
- Seizures
- If you know that you may have salt depletion as a result of prolonged severe diarrhea and vomiting (being sick) or usage of diuretics (water tablets)

If you suffer from dementia, you or your carer/relative should tell your doctor if you have ever had a stroke or "mini" stroke.

As a routine precaution, if you are over 65 years your blood pressure may be monitored by your doctor

Children and adolescents

Olanzapine tablets is not for patients who are under 18 years.

Other medicines and Olanzapine tablets

Only take other medicines while you are on Olanzapine tablets if your doctor tells you that you can. You might feel drowsy if Olanzapine tablets is taken in combination with antidepressants or medicines taken for anxiety or to help you sleep (tranquillisers).

Tell your doctor if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor if you are taking:

- medicines for Parkinson's disease.
- carbamazepine (an anti-epileptic and mood stabiliser), fluvoxamine (an antidepressant) or ciprofloxacin (an antibiotic) - it may be necessary to change your Olanzapine Tablets dose.

Olanzapine tablets with alcohol

Do not drink any alcohol if you have been given Olanzapine tablets as together with alcohol it may make you feel drowsy.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. You should not be given this medicine when breast-feeding, as small amounts of Olanzapine tablets can pass into breast milk.

The following symptoms may occur in newborn babies, of mothers that have used Olanzapine tablets 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

There is a risk of feeling drowsy when you are given Olanzapine tablets. If this happens do not drive or operate any tools or machines. Tell your doctor.

9.3 How to use TOLAZ DT

Always take Olanzapine tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how many Olanzapine tablets to take and how long you should continue to take them. The daily dose of Olanzapine tablets is between 5 and 20 mg. Consult your doctor if your symptoms return but do not stop taking Olanzapine tablets unless your doctor tells you to.

You should take your Olanzapine tablets once a day following the advice of your doctor. Try to take your tablets at the same time each day. It does not matter whether you take them with or without food. Olanzapine coated tablets are for oral use. You should swallow the Olanzapine tablets whole with water.

If you take more TOLAZ DT Tablets than you should

Patients who have taken more Olanzapine tablets than they should, have experienced the following symptoms: rapid beating of the heart, agitation/aggressiveness, problems with speech, unusual movements (especially of the face or tongue) and reduced level of

consciousness. Other symptoms may be: acute confusion, seizures (epilepsy), coma, a combination of fever, faster breathing, sweating, muscle stiffness and drowsiness or sleepiness, slowing of the breathing rate, aspiration, high blood pressure or low blood pressure, abnormal rhythms of the heart. Contact your doctor or hospital straight away if you experience any of the above symptoms. Show the doctor your pack of tablets.

If you forget to take TOLAZ DT Tablets

- Take your tablets as soon as you remember. Do not take two doses in one day.

If you stop taking TOLAZ DT tablets

Do not stop taking your tablets just because you feel better. It is important that you carry on taking Olanzapine tablets for as long as your doctor tells you.

If you suddenly stop taking Olanzapine tablets, symptoms such as sweating, unable to sleep, tremor, anxiety or nausea and vomiting might occur. Your doctor may suggest you to reduce the dose gradually before stopping treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately if you have:

- unusual movement (a common side effect that may affect up to 1 in 10 people) mainly of the face or tongue;
- blood clots in the veins (an uncommon side effect that may affect up to 1 in 100 people) especially in the legs (symptoms include swelling, pain, and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately;

A combination of fever, faster breathing, sweating, muscle stiffness and drowsiness or sleepiness (the frequency of this side effect cannot be estimated from the available data).

Very common side effects (may affect more than 1 in 10 people) include weight gain, sleepiness; and increases in levels of prolactin in the blood. In the early stages of treatment, some people may feel dizzy or faint (with a slow heart rate), especially when getting up from a lying or sitting position. This will usually pass on its own but if it does not, tell your doctor.

Common side effects (may affect up to 1 in 10 people) include changes in the levels of some blood cells, circulating fats and early in treatment, temporary increases in liver enzymes; increases in the level of sugars in the blood and urine; increases in levels of uric acid and creatine phosphokinase in the blood; feeling more hungry; dizziness; restlessness; tremor; unusual movements(dyskinesias); constipation; dry mouth; rash; loss of strength; extreme tiredness; water retention leading to swelling of the hands, ankles or feet; fever; joint pain; and sexual dysfunctions such as decreased libido in males and females or erectile dysfunction in males.

Uncommon side effects (may affect up to 1 in 100 people) include hypersensitivity (e.g. swelling in the mouth and throat, itching, rash); diabetes or the worsening of diabetes, occasionally associated with ketoacidosis (ketones in the blood and urine) or coma; seizures, usually associated with a history of seizures (epilepsy); muscle stiffness or spasms (including eye movements); restless legs syndrome; problems with speech; stuttering; slow heart rate; sensitivity to sunlight; bleeding from the nose; abdominal distension; drooling; memory loss or forgetfulness; urinary incontinence; lack of ability to urinate; hair loss; absence or decrease in menstrual periods; and changes in breasts in males and females such as an abnormal production of breast milk or abnormal growth.

Rare side effects (may affect up to 1 in 1000 people) include lowering of normal body temperature; abnormal rhythms of the heart; sudden unexplained death; inflammation of the pancreas causing severe stomach pain, fever and sickness; liver disease appearing as yellowing of the skin and white parts of the eyes; muscle disease presenting as unexplained aches and pains; and prolonged and/or painful erection.

Very rare side effects include serious allergic reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS appears initially as flu-like symptoms with a rash on the face and then with an extended rash, high temperature, enlarged lymph nodes, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia).

While taking olanzapine, elderly patients with dementia may suffer from stroke, pneumonia, urinary incontinence, falls, extreme tiredness, visual hallucinations, a rise in body temperature, redness of the skin and have trouble walking. Some fatal cases have been reported in this particular group of patients.

In patients with Parkinson's disease Olanzapine tablets may worsen the symptoms.

Reporting of suspected adverse reactions

If you get any 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 directly via any point of contact of Torrent Pharma available at: https://torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine

9.5 How to store TOLAZ DT

STORE AT A TEMPERATURE NOT EXCEEDING 30 °C, PROTECTED FROM LIGHT AND MOISTURE.

Keep all medicines out of reach of children.

9.6 Contents of the pack and other information What

TOLAZ DT contains:

The active substance is Olanzapine Tablets.

TOLAZ-DT 2.5/5/7.5/10 mg is available in blister of 15 tablets.

10. Details of manufacturer

Manufactured by:

Torrent pharmaceutical. Pvt.ltd.

32 No. middle camp, NH-10

East district, Gangtok, Sikkim-737 135.

or

Windlas Biotech Limited (Plant-IV)

Plot No. 183 & 192,

Mohabewala Industrial Area,

Dehradun-248 110 (Uttarakhand)

11. Details of permission or licence number with date

Mfg Lic No M/563/2010 date: 06 dec 2021

or

Windlas Biotech Limited (Plant-IV)

Mfg Lic No. 47/UA/2009

12. Date of revision

APRIL-2022

MARKETED BY



TORRENT PHARMACEUTICALS LTD.

IN/ TOLAZ DT /APRIL-2022/03/PI