xxxxxxxx-8883

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

TOLANZ

(Olanzapine Orodispersible Tablet 5 mg / 10 mg)

COMPOSITION

TOLANZ 5

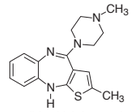
Each uncoated orodispersible tablet contains:
Olanzapine……...5 mg.

TOLANZ 10

Each uncoated orodispersible tablet contains:
Olanzapine……...10 mg.

DESCRIPTION

Olanzapine is a psychotropic agent that belongs to the thienobenzodiazepine class. The chemical designation is 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5] benzodiazepine. It has a molecular weight of 312.44. The molecular formula is $C_{17}H_{20}N_4S$ and the chemical structure is:



Olanzapine is a yellow crystalline solid, which is practically insoluble in water.
Olanzapine orodispersible tablets begins disintegrating in the mouth within seconds, allowing its contents to be subsequently swallowed with or without liquid.

CLINICAL PHARMACOLOGY

Pharmacodynamics:
Olanzapine is a selective monoaminergic antagonist with high affinity binding to the following receptors: serotonin $5HT_{2A/2C}$ (K_i=4 and 11 nM, respectively), dopamine $D_{1\text{-}4}$ (Ki=11-31 nM), muscarinic $M_{1\text{-}5}$ (Ki=1.9-25 nM), histamine H_1 (K_i=7 nM), and adrenergic α1 receptors (K_i=19 nM). Olanzapine binds weakly to $GABA_A$, Benzodiazepine (BZD), and β adrenergic receptors (K_i>10 μM). The mechanism of action of olanzapine, as with other drugs having efficacy in schizophrenia, is unknown. However, it has been proposed that this drug's efficacy in schizophrenia is mediated through a combination of dopamine and serotonin type 2 ($5HT_2$) antagonism. The mechanism of action of olanzapine in the treatment of acute manic episodes associated with Bipolar I Disorder is unknown.
Antagonism at receptors other than dopamine and $5HT_2$ with similar receptor affinities may explain some of the other therapeutic and side effects of olanzapine. Olanzapine's antagonism of muscarinic $M_{1\text{-}5}$ receptors may explain its anticholinergic effects. Olanzapine's antagonism of histamine H_1 receptors may explain the somnolence observed with this drug. Olanzapine's antagonism of adrenergic α_1 receptors may explain the orthostatic hypotension observed with this drug.

Pharmacokinetics

Olanzapine is well absorbed and reaches peak concentrations in approximately 6 hours following an oral dose. It is eliminated extensively by first pass metabolism, with approximately 40% of the dose metabolized before reaching the systemic circulation. Food does not affect the rate or extent of olanzapine absorption.
Pharmacokinetic studies showed that olanzapine tablets and olanzapine orodispersible tablets are bioequivalent.
Olanzapine displays linear kinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours (5th to 95th percentile; mean of 30 hr), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th percentile; mean of 25 L/hr).
Administration of olanzapine once daily leads to steady-state concentrations in about one week that are approximately twice the concentrations after single doses. Plasma concentrations, half-life, and clearance of olanzapine may vary between individuals on the basis of smoking status, gender, and age.
Olanzapine is extensively distributed throughout the body, with a volume of distribution of approximately 1000 L. It is 93% bound to plasma proteins over the concentration range of 7 to 1100 ng/mL, binding primarily to albumin and γ1-acid glycoprotein.

Metabolism and Elimination

Following a single oral dose of 14C labeled olanzapine, only 7% of the dose of olanzapine is reported to be excreted in the urine as unchanged drug, indicating that olanzapine is highly metabolized. Approximately 57% and 30% of the dose is recovered in the urine and feces, respectively. In the plasma, olanzapine accounts for only 12% of the AUC for total radioactivity, indicating significant exposure to metabolites. The major circulating metabolites are the 10-N-glucuronide, present at steady state at 44% of the concentration of olanzapine, and 4´-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed. Direct glucuronidation and cytochrome P450 (CYP) mediated oxidation are the primary metabolic pathways for olanzapine.

Special Populations

Renal Impairment - Because olanzapine is highly metabolized before excretion and only 7% of the drug is excreted unchanged, renal dysfunction alone is unlikely to have a major impact on the pharmacokinetics of olanzapine. Olanzapine is not removed by dialysis. The effect of renal impairment on metabolite elimination has not been studied.
Hepatic Impairment - Although the presence of hepatic impairment may be expected to reduce the clearance of olanzapine, the effect of impaired liver function on the pharmacokinetics of olanzapine in subjects with clinically significant (Childs Pugh Classification A and B) cirrhosis is not established.
Age - The mean elimination half-life of olanzapine has been reported to be 1.5 times greater in elderly (>65 years) than in non-elderly subjects (≤65 years). Caution should be used in dosing the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity.
Smoking Status – Olanzapine clearance is about 40% higher in smokers than in non-smokers, although dosage modifications are not routinely recommended.
Combined Effects - The combined effects of age, smoking, and gender could lead to substantial pharmacokinetic differences in populations. Dosing modification may be necessary in patients who exhibit a combination of factors that may result in slower metabolism of olanzapine.

INDICATIONS AND USAGE

Schizophrenia

Olanzapine indicated for the treatment of schizophrenia.

Bipolar Disorder

Acute Monotherapy – Olanzapine is indicated for the treatment of acute mixed or manic episodes associated with Bipolar I Disorder.
Maintenance Monotherapy - The benefit of maintaining bipolar patients on monotherapy with Olanzapine after achieving a responder status for an average duration of two weeks was demonstrated in a clinical study. The physician who elects to use olanzapine orodispersible form for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual.
Combination Therapy - The combination of olanzapine with lithium or valproate is indicate for the short-term treatment of acute manic episodes associated with Bipolar I Disorder.

CONTRAINDICATIONS

Olanzapine is contraindicated in patients with a known hypersensitivity to the product.

WARNINGS

Hyperglycaemia and Diabetes Mellitus — Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. The relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood.
Patients with an established diagnosis of diabetes mellitus who are started on atypical Anti-psychotics should be monitored regularly for worsening of glucose control. Fasting blood glucose testing at the beginning of treatment and periodically during treatment is recommended in patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes). Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, it is reported that hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.
Elderly Patients with Dementia-Related Psychosis - Olanzapine is not approved for the treatment of patients with dementia-related psychosis. A predisposition towards increased mortality is reported in the elderly patients with dementia-related psychosis. Risk factors that may predispose this patient population to increased mortality when treated with olanzapine include age >80 years, sedation, concomitant use of benzodiazepines or presence of pulmonary conditions (e.g., pneumonia, with or without aspiration).
Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia - Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, are reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.
Neuroleptic Malignant Syndrome (NMS) - NMS has been reported in association with administration of antipsychotic drugs, including 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.
The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.
If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.
Tardive Dyskinesia - Although the prevalence of tardive dyskinesia appears to be highest among the elderly, especially elderly women, it is difficult to predict at the inception of therapy, which patients are likely to develop the syndrome.
Olanzapine should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients (1) who suffer from a chronic illness that is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.
If signs and symptoms of tardive dyskinesia appear in a patient on olanzapine, drug discontinuation should be considered. However, some patients may require treatment with olanzapine despite the presence of the syndrome.

PRECAUTIONS

General

Hemodynamic Effects - Olanzapine may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α1-adrenergic antagonistic properties.
With olanzapine therapy, the risk of orthostatic hypotension and syncope may be minimized by initiating therapy with 5 mg QD. A more gradual titration to the target dose should be considered if hypotension occurs.
Olanzapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) where the occurrence of syncope, or hypotension and/or bradycardia might put the patient at increased medical risk. Olanzapine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease.
Caution is necessary in patients who receive treatment with other drugs having effects that can induce hypotension, bradycardia, respiratory or central nervous system depression. Concomitant administration of intramuscular olanzapine and parenteral benzodiazepine has not been studied and is therefore not recommended. If use of intramuscular olanzapine in combination with parenteral benzodiazepines is considered, careful evaluation of clinical status for excessive sedation and cardiorespiratory depression is recommended.
Seizures - Rarely, seizures have been reported to occur in olanzapine-treated patients. Olanzapine should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia.
Hyperprolactinemia - As with other drugs that antagonize dopamine D2 receptors, olanzapine elevates prolactin levels, and a modest elevation persists during chronic administration. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds, the clinical significance of elevated serum prolactin levels is unknown for most patients.
Transaminase Elevations - Transient, asymptomatic elevations of hepatic transaminases, ALT, AST have been seen commonly, especially in early oral treatment. Rare reports of hepatitis have been reported. Caution should be exercised 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 drugs. In the event of elevated ALT and/or AST during treatment, periodic assessment is recommended and dose reduction should be considered.
Potential for Cognitive and Motor Impairment - Since olanzapine has the potential to cause somnolence, impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that olanzapine therapy does not affect them adversely.
Body Temperature Regulation - Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing olanzapine for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.
Dysphagia - Oesophageal dysmotility and aspiration have been associated with antipsychotic drug use. Olanzapine and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.
Suicide - The possibility of a suicide attempt is inherent in schizophrenia and in bipolar disorder, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for olanzapine should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.
Use in Patients with Concomitant Illness - Clinical experience with olanzapine in patients with certain concomitant systemic illnesses is limited.
Olanzapine use has been associated with constipation, dry mouth, and tachycardia, all adverse events possibly related to cholinergic antagonism. Such adverse events do not usually require drug discontinuation, but olanzapine should be used with caution in patients with clinically significant prostatic hypertrophy, narrow angle glaucoma, or a history of paralytic ileus.
As with other CNS-active drugs, olanzapine should be used with caution in elderly patients with dementia. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Laboratory Tests

Periodic assessment of transaminases is recommended in patients with significant hepatic disease.

Drug Interactions

The risks of using olanzapine orodispersible tablets with other drugs have not been extensively evaluated. The potential drug interactions are mentioned below
Given the primary CNS effects of olanzapine, caution should be used when olanzapine is taken in combination with other centrally acting drugs and alcohol. Because of its potential for inducing hypotension, olanzapine may enhance the effects of certain antihypertensive agents.
Olanzapine may antagonize the effects of levodopa and dopamine agonists.
The Effect of Other Drugs on Olanzapine - Agents that induce CYP1A2 or glucuronyl transferase enzymes, such as omeprazole and rifampin, may cause an increase in olanzapine clearance. Inhibitors of CYP1A2 could potentially inhibit olanzapine clearance. Although olanzapine is metabolized by multiple enzyme systems, induction or inhibition of a single enzyme may appreciably alter olanzapine clearance. Therefore, a dosage increase (for induction) or a dosage decrease (for inhibition) may need to be considered with specific drugs.
Cimetidine and Antacids - Single doses of cimetidine (800 mg) or aluminium and magnesium containing antacids does not affect the oral bioavailability of olanzapine.
Carbamazepine - Carbamazepine therapy (200 mg bid) causes an approximately 50% increase in the clearance of olanzapine. This increase is likely due to the fact that carbamazepine is a potent inducer of CYP1A2 activity. Higher daily doses of carbamazepine may cause an even greater increase in olanzapine clearance.
Ethanol - Ethanol (45 mg/70 kg single dose) does not have an effect on olanzapine pharmacokinetics.
Fluoxetine - Fluoxetine causes a small increase in the maximum concentration of olanzapine and a small decrease in olanzapine clearance. The magnitude of the impact of this factor is small in comparison to the overall variability between individuals, and therefore dose modification is not routinely recommended.
Fluvoxamine - Fluvoxamine, a CYP1A2 inhibitor, decreases the clearance of olanzapine resulting in an increase in olanzapine Cmax and AUC. Lower doses of olanzapine should be considered in patients receiving concomitant treatment with fluvoxamine.
Effect of Olanzapine on Other Drugs - In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by these enzymes.
Lithium - Concomitant olanzapine administration does not require dosage adjustment of lithium.
Valproate - Concomitant olanzapine administration does not require dosage adjustment of valproate.
Single doses of olanzapine have not been reported to affect the pharmacokinetics of imipramine or its active metabolite desipramine, and warfarin. Multiple doses of olanzapine have not been reported to influence the kinetics of diazepam and its active metabolite N-desmethyldiazepam, theophylline or its metabolites, ethanol, or biperiden. However, the co-administration of either diazepam or ethanol with olanzapine has been reported to potentiate the orthostatic hypotension observed with olanzapine.

Carcinogenesis, Mutagenesis, Impairment of Fertility

An increase in mammary gland neoplasms has been reported in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin mediated. The relevance for human risk of the finding of prolactin mediated endocrine tumours in rodents is unknown.
Mutagenesis - No evidence of mutagenic potential for olanzapine has been reported in standard tests.
Impairment of Fertility - Rodent studies suggest that olanzapine may produce a delay in ovulation.

Pregnancy

Olanzapine falls under Pregnancy Category C. Olanzapine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Labor and Delivery

Oral administration of olanzapine to pregnant rats has been reported to result in prolonged gestation and an increased incidence of stillbirths. The effect of olanzapine on labour and delivery in humans is unknown.

Nursing Mothers

It is recommended that women receiving olanzapine should not breast-feed.

Paediatric Use

Safety and effectiveness in paediatric patients have not been established.

Geriatric Use

In patients with schizophrenia, no indication of any different tolerability of olanzapine in the elderly compared to younger patients has been reported. Olanzapine should be used with caution in elderly patients with dementia. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. The presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine should lead to consideration of a lower starting dose for any geriatric patient.

ADVERSE REACTIONS

Adverse event occurring at an incidence of 2% or more among oral olanzapine treated patients.
Body as a whole: Accidental injury, asthenia, fever, back pain, chest pain.
Cardiovascular system: Postural hypotension, tachycardia, hypertension.
Digestive system: Dry mouth, constipation, dyspepsia, vomiting, increased appetite
Metabolic and nutritional disorders: Weight gain, peripheral edema
Musculoskeletal system: Extremity pain, joint pain.
Nervous system: Somnolence, insomnia, dizziness, abnormal gait, tremor, akathisia, hypertonia, articulation impairment.
Respiratory system: Rhinitis, cough increased, pharyngitis
Special senses: Amblyopia
Urogenital system: Urinary incontinence, Urinary tract infection
Incidence equal to or less than that of placebo: abdominal pain, agitation, anorexia, anxiety, apathy, confusion, depression, diarrhea, dysmenorrhea, hallucinations, headache, hostility, hyperkinesias, myalgia, nausea, nervousness, paranoid reaction, personality disorder, rash, thinking abnormal, weight loss.

Other Adverse Events Observed During the Clinical Trials of Olanzapine

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients.
Body as a Whole - frequent: dental pain and flu syndrome; Infrequent: abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, and suicide attempt; Rare: chills and fever, hangover effect, and sudden death.
Cardiovascular System - Frequent: hypotension; Infrequent: atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, and ventricular extrasystoles; Rare: arteritis, heart failure, and pulmonary embolus.
Digestive System - Frequent: flatulence, increased salivation, and thirst; Infrequent: dysphagia, esophagitis, faecal impaction, faecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, and tooth caries; Rare: aphthous stomatitis, enteritis, eructation, oesophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, and tongue discoloration.
Endocrine System - Infrequent: diabetes mellitus; Rare: diabetic acidosis and goitre.
Hemic and Lymphatic System - Infrequent: anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, and thrombocytopenia; Rare: normocytic anemia and thrombocythemia.
Metabolic and Nutritional Disorders - Infrequent: acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, and upper extremity edema; Rare: gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, and water intoxication.
Musculoskeletal System - Frequent: joint stiffness and twitching; Infrequent: arthritis, arthrosis, leg cramps, and myasthenia; Rare: bone pain, bursitis, myopathy, osteoporosis, and rheumatoid arthritis.
Nervous System - Frequent: abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, and schizophrenic reaction; Infrequent: akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, and withdrawal syndrome; Rare: circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, and tobacco misuse.
Respiratory System - Frequent: dyspnea; Infrequent: apnoea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, and voice alteration; Rare: atelectasis, hiccup, hypoventilation, lung edema, and stridor.
Skin and Appendages - Frequent: sweating; Infrequent: alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, and vesiculobullous rash; Rare: hirsutism and pustular rash.
Special Senses - Frequent: conjunctivitis; Infrequent: abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, and tinnitus; Rare: corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, and pigment deposits lens.
Urogenital System - Frequent: vaginitis; Infrequent: abnormal ejaculation, amenorrhea, breast pain, cystitis, decreased menstruation, dysuria, female lactation, glycosuria, gynecomastia, hematuria, impotence, increased menstruation, menorrhagia, metrorrhagia, polyuria, premenstrual syndrome, pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged, and vaginal hemorrhage; Rare: albuminuria, breast enlargement, mastitis, and oliguria.

DOSAGE AND ADMINISTRATION

Schizophrenia

Usual Dose - Olanzapine Orodispersible tablet should be administered on a once-a-day schedule without regard to meals, generally beginning with 5 to 10 mg initially, with a target dose of 10 mg/day within several days. Further dosage adjustments, if indicated, should generally occur at intervals of not less than 1 week, since steady state for olanzapine would not be achieved for approximately 1 week in the typical patient. When dosage adjustments are necessary, dose increments/decrements of 5 mg QD are recommended.
In clinical trials, doses above 10 mg/day have not been demonstrated to be more efficacious than the 10 mg/day dose. An increase to a dose greater than the target dose of 10 mg/day (i.e., to a dose of 15 mg/day or greater) is recommended only after clinical assessment. The safety of doses above 20 mg/day has not been evaluated in clinical studies.
Dosing in Special Populations - The recommended starting dose is 5 mg in patients who are debilitated, who have a predisposition to hypotensive reactions, who otherwise exhibit a combination of factors that may result in slower metabolism of olanzapine (e.g., nonsmoking female patients ≥65 years of age), or who may be more pharmacodynamically sensitive to olanzapine. When indicated, dose escalation should be performed with caution in these patients.
Maintenance Treatment - The effectiveness of Olanzapine Orodispersible tablet, 10 mg/day to 20 mg/day, in maintaining treatment response in schizophrenic patients has been demonstrated in a clinical trial. Who had been stable on olanzapine for approximately 8 weeks and were then followed for a period of up to 8 months. Patients should be periodically reassessed to determine the need for maintenance treatment with appropriate dose.

Bipolar Disorder

Usual Monotherapy Dose - Olanzapine should be administered on a once-a-day schedule without regard to meals, generally beginning with 10 or 15 mg. The safety of doses above 20 mg/day has not been evaluated in clinical trials. Dosage adjustments, if indicated, should generally occur at intervals of not less than 24 hours, reflecting the procedures in the placebo-controlled trials. When dosage adjustments are necessary, dose increments/decrements of 5 mg QD are recommended.
Maintenance Monotherapy - The benefit of maintaining bipolar patients on monotherapy with olanzapine orodispersible tablet at a dose of 5 to 10 mg/day, after achieving a responder status for an average duration of two weeks, was demonstrated in a controlled trial.
Bipolar Mania Usual Dose in Combination with Lithium or Valproate - When administered in combination with lithium or valproate, olanzapine orodispersible tablet dosing should generally begin with 10 mg once a day without regard to meals.
Short-term (6 weeks) anti-manic efficacy of olanzapine has been demonstrated in a dose range of 5 mg to 20 mg/day in clinical trials. The safety of doses above 20 mg/day has not been evaluated in clinical trials.
Administration: 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.

STORAGE

Store below 30°C.
Keep out of reach of children.

EXPIRY DATE

Do not use later than the date of expiry.

PRESENTATION

Olanzapine Orodispersible Tablets 5 mg & 10 mg are available in Alu-Alu blister of 7 & 10 tablets.

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.