Lepinza 10mg
(Olanzapine)
Lepinza 5mg
(Olanzapine)

لیپنزا ۱۰ ملی گرام
(اولیانزاپین)
لیپنزا ۵ ملی گرام
(اولیانزاپین)

COMPOSITION:
Each film coated tablet contains Olanzapine.....5mg
Each film coated tablet contains Olanzapine.....10mg

DESCRIPTION:
Lepinza (Olanzapine) is a psychotropic agent that belongs_to the thienobenzodiazepine class The chemical designation is 2-methyl-4-(4-methyl-l-piiperazlnyl)-l0H-thieno [2, 3-b] [l_ 5] bcnzodiazepine. The molecular formula is _Cl7H20N4S, and its molecular weight is 312.44.

PHARMACOLOGY:
Olanzapine is a selective mono'minergic antagonist with high affinity binding to 'the following receptors: serotonin 5HT2 A/2C. 5HT6 dopamine Dl-4. histamine Hl. and adrenergic alpha 1 receptors. Qlanzapine is an antagonist with moderate affinity binding for serotonin 5HT3 and.muscarinic Ml-5. Olanzapine is well absorbed and reaches peak concentration in approximately 6 hours following an oral dose. lt is eliminated extensively by first pass metabolism. with approximately. 40% of the dose metabolized before 'reaching the systemic circulation. Food does not affcct the rate or extent oi Olanzapine absorption. lts half life ranges from 21 to 54 hours, and apparent plasma clearance' ranges from ,l2 to 47 L/hr. Plastna concentrations. hallf-lifc and clearance ol Olanzapine may vary between individuals on the basis of smoking status, gender, and age. Olanzapinc is extensively distributedthroughout the body, with a volume of distributin of approximately 1000L. It is 93% bound to plasma proteins over the concentration range of 7 to .1 l00mg/ml. binding primarily to albumin and alphal acid glycgoprotein. Appiuximntely 57% and 30% of the dose was recovered in the urine and feces, respectively. After multiple dosing, the major circulating metabolites were the l0-N-glueoronide, present at steady state at 44% of the concentration of Olanzapine. Direct glucuronidation and cytochrome P450 (CYP) mediated oxidation are thc.primary metabolic pathways for Olanzapine.

INDICATION:
Schizophrenian: Lepinza is indicated for the treatment of schizophrenia.
Bipolar Disorder: Acute Monotherapy: Lepinza is indicated for the treatment of acute mixed of manic episodes associated with Bipolar disorder

CONTRAINDICATIONS:
Lepinza is contraindicated in patients with a known hypersensitivity to thc products. *Possible adverse effects:* Dental pain & flue syndrome, hypotension, flatulence. inereased salivation & thirst, diabetes mellitus, joint stiffness & twitching, abnormal dreams, amnesia. delusions, emotional liability. euphoria, manic reaction. paresthesia & schizophrenic reaction, dyspcnea. sweating, conjunctivitis, vaginitis.

Overdosage symptoms with l0% incidence included agitation/aggressiveness, dysarthria, tachycardia, varions cxtrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. ln case of acute overdosagc, establish and maintain an airway and ensure adequate oxygenation and ventilation, which rnay includc intuhations. Gastric lavage (after intubation, if patients are unconscious) and administration of activated charcoal together with a laxative should be considercd.

Storage Condition:
Store in a cool dry place and dark place between l5-30C. Keep all medicine out of the reach of children.

Presentation
Lcpinza l0mg Tablet is available in alu alu blister packing containing (lxl0's).
Lepinza 5mg Tablet is available in alu alu blister packing containing (lxl0's).

Manufactured by:
NEXUS
Nexus Pharma (Pvt.) Ltd.
Plot No. 4/19 - 436, Sector 21,
Korangi Industrial Area, Karachi

Marketed by:
ORGANIC Pharmaceuticals

DRUG INTERATIONS:
Given the primary CNS effects of Olanzapinc, caution should be used when Olanzapinc 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. Olanzapinc may antagonize the effects of levodopa and dopamine antagonists.
The effect of other drug on Olanzapine Agents that induce CYP_1A_2 or glucuronyl transfersae enzymes, such as omeprazole and rifampin, may cause an increase in Olanzapine clearance. Inhibitors of CYP_1A_2 could potentially inhibit Olanzapine clearance. Although Olanzapine is metabolized by multiple enzyme systems, indication or inhibition of single enzyme may appreciably after Olanzapinc clearance. Therefore a dose increase (for induction) or a dosage decrease (for inhibition) may need to be considered with specific drugs.
Charcoal: the administration of activated charcoal (lg) reduced the Cmax and AUC of oral Olanzapine by about 60%. As peak Olanzapine levels are not typically obtained until about 6 hours after dosing. charcoal may be a useful treatment for Olanzapine overdose.
*Cimetidine & antacids:*Single doses of cimetidinc (800mg) or aluminum-and magnesium-containing antacids did not affect the over bioavailability ofOlanzapine. This increase is likely due to the fact that carbamazepine is a potent inducer of CYP l A2 activity.
Ethanol: Ethanol (45 mg/70kg single dose) did not have an affect on Olanzapine pharmacokinetities. Fluoxetine: Fluoxetine (50 mg single dose or 60mg daily for 8 days) cause a single small (mean l6%) increase in the maximum concentration of Olanzapine and a small (mean 16%) decrease in Olanzapine clcarance. Fluvoxamine: Fluvoxaine, a CYPIA2 inhibitor, decreases the clearance of Olanzapine. This results in a mean increasein Olanzapine Cmax following fluvoxaminc of 54% in female nonsmokers and 77% in male smokers. The mean increase in Olirnzapine AUC is 52% and l08% respectively. Warfarin: Warfarin (20mg single dose) did not affect Olanzapine pharmacokinetics. Effects of Olanzapine on other drugs: Olanzapine has little potential to inhibit CYPlA2, CYP2C9, CYP2Cl9. CYP2D6 and CYP3A. Thus Olanzapine is unlikely to cause clinically important drug. interaction mediated by these enzymes. Lithium: Multiple doses of Olanzapine (l0mg for 8 days) did not influence the kinetics of lithium. Therefore, concomitant Olanzapine administration does not require dosage adjustrment of lithium. Valproate: Concomitant Olanzapine administration does not require dosage adjustment of valproate. Single doses of Olanzapine did not affect the pharmacokinetics of imipraminc or its active metabolie desipramine, and warfarin. Multiule doses of Olanzapine did not influence the kinetics of diazepam and its active methabolite N-desmethyldiazepam. ethanol or biperiden. However the co-adiministration of either diazepam or ethanol with Olanzapine potentiated the orthostatic hypotcnsion observed with Olanzapine. Multiple doses of Olanzapine did not. affect the pharmacokinetics of theophyline or its metabolites.
WARNING: General: *Heodynamic Effects:* Olanzapine ay induce orthostatic hypotension associated with dizziness, tachycardia and is some patients syncope. especially during the initial dose-titration period, probably reflecting its alpha adrenergic antagonistic properties. Seizures: Olanzapine should be used cautiously in patients with history seizures or with condition that potentially lower the seizure threshold. e.g:, Alzheimer's dementia. Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, Olanzapine elevates prolacting levels and a modest elevation persist during chronic administration Transminase Elevations: Caution should be exercised in patient with signs of'symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic function reserves, and in patient with are being treated with potentially hcpatotoxic drugs.
Potential for cognitive and mother impairment: Since Olanzapine has the potential to impairment judgment, thinking, or mother- skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that olaznapine therapy does not affect them adversely. Body Temperature Regulations: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Dysphagia. Esophageal dysmotility and aspiration have been associated with antipsychotic drugs use Suicide. The possibility of a suicide attempt is inherent in schizophrenia and in bioploar disorder and close supervision of high-risk patients should accompany drug therapy. Increased Mortality in Elderly Patient with Dementia-Related Psychosis: Elderly patient with dementia related psychosis treated with antipsycliotic drug are at an increase risk of death. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. Pregnancy: The drug should be used during pregnancy only if thepotential justifies the potential risk to the fetus Nursing mothers: it is recommended that women reecving olanzapine should not breast-feed. Pediatric Use: safety and effectiveness in pediatric patient have not been established.

DOSAGE AND ADMINISTRATION:
Schizophrenia: Lepinza Tablets should be administered on a once-a-day schedule without reg-ard to meals, generally beginning with 5 to l0mg initially, with a target dose of l0mg/day with several days. Further dosage adjustments for approximately l week in the typical patient. When dosage adjustments, are necessary, dose increment/decrements of 5mg QD are recommended. The recommended starting dosing 5mg in paticnts who are debilitated, who have a predisposition to hypertensive reactions, who otherwise exhibit a combination of factors that may result in slower metabolism of olaznapine (e.g. nonsmoking female patient 65 years of age) or who may be more pharmacodynamically sensitive to olaznapine. When indicated, dose esealation should be performed with caution in these patients. Bipolar disorder: Monotherapy: Lepinza Tablets should be administered on a once a day schedule without regard to meals, generally beginning with 10 or 15mg. Dosage adjustments, if indicated, should generally occur at intervals of not less than 24 hours. When dosage adjustments are necessary, dose increment/decrements of 5mg QD are recommended. Maintenance monotherapy: The usual maintenance dose for bipoloart patients on montherapy with Lepinza tablets is5 to 20mg / day. The physician who elects to use Lepinza tablet for extended period should periodically re-evaluated the long term usefulness of the drug of the individual patient. Combination therapy with lithium or valproate: When administered in combination with lithium or valproate, dosing of Lepinza tablets should generally being with l0mg once a day without regard to meals.
Special instruction to the physician: