

(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. Patients should be advised not to breast-feed an infant if they are taking Olanzapine.

DRUG INTERACTIONS:

Induction of CYP1A2:

The metabolism of Olanzapine may be induced by smoking and carbamazepine, which may lead to reduced Olanzapine concentrations.

Inhibition of CYP1A2:

Fluvoxamine, a specific CYP1A2 inhibitor, has been shown to significantly inhibit the metabolism of Olanzapine.

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.

Potential for Olanzapine to affect other medicinal products:

Olanzapine may antagonise the effects of direct and indirect dopamine agonists.

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.

ADVERSE REACTIONS:

The most frequently reported adverse reactions associated with the use of Olanzapine were somnolence, weight gain, eosinophilia, elevated prolactin, cholesterol, glucose and triglyceride levels, glucosuria, increased appetite, dizziness, akathisia, parkinsonism, leukopenia, neutropenia, dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic aminotransferases, rash, asthenia, fatigue pyrexia, arthralgia, increased alkaline phosphatase, high gamma glutamyltransferase, high uric acid, high creatine phosphokinase and oedema.

INSTRUCTIONS:

Store below 30°C. Protect from heat, light & moisture. Keep out of the reach of children.

PRESENTATION:

Schizap (Olanzapine) tablets 5mg and 10mg are available in pack of 10's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر رکھیں۔

صرف رجمزڈ ڈاکٹر کے نسخے پر فروخت کریں۔

بچوں کی پہنچ سے دور رکھیں۔

Note: Product contains lactose.

نوٹ: پروڈکٹ میں لاکٹوز شامل ہے۔

Manufactured by:

Platinum
Pharmaceuticals (Pvt.) Ltd.
A-20, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

QAR No. AW 21-0838

SCHIZAP

(Olanzapine)

5mg & 10 mg Tablets

شیزاپ

(اولینزاپین)

۵ ملی گرام / ۱۰ ملی گرام گولیاں

Composition:

Each film coated tablet contains:

Olanzapine 5 mg

Product Complies U.S.P. Specs.

Olanzapine 10 mg

Product Complies U.S.P. Specs.

DESCRIPTION:

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

INDICATIONS:

Schizap (Olanzapine) is used to treat symptoms of schizophrenia and related psychotic disorders as well as those of bipolar disorder.

CONTRA-INDICATIONS:

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

PHARMACOLOGY:

Mechanism of Action:

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 (5HT₂) antagonism.

PHARMACOKINETICS:

Absorption:

Schizap (Olanzapine) is well absorbed after oral administration, reaching peak plasma concentrations within 5 to 8 hours. The absorption is not affected by food.

Distribution:

The plasma protein binding of Olanzapine was about 93% over the concentration range of about 7 to about 1000ng/ml. Olanzapine is bound predominantly to albumin and α 1-acid-glycoprotein.

Metabolism:

Schizap (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 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 as in male patients.

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).

Smokers:

In smoking subjects with mild hepatic dysfunction, mean elimination half-life (39.3 hours) was prolonged and clearance (18.0 l/hr) was reduced analogous to non-smoking healthy subjects (48.8 hours and 14.1 l/hr, respectively). In 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).

Paediatric population:

Adolescents (ages 13 to 17 years): The pharmacokinetics of Olanzapine is similar between adolescents and adults.

DOSAGE AND ADMINISTRATION:

Adults:

Schizophrenia

The recommended starting dose for Schizap (Olanzapine) is 10mg/day.

Manic episode:

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

Preventing recurrence in bipolar disorder:

The recommended starting dose is 10mg/day. For treatment of manic episode, continue therapy for preventing recurrence at the same dose. If a new manic, mixed, or depressive episode occurs, Schizap 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. Schizap can be given without regard for meals as absorption is not affected by food. Gradual tapering of the dose should be considered when discontinuing Schizap.

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 Schizap may be induced by smoking. Clinical monitoring is recommended and an increase of Schizap 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: Not recommended.

OVERDOSE:

Signs and Symptoms: Very common symptoms in overdose (> 10% incidence) include tachycardia, agitation/aggressiveness, dysarthria, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Other medically significant sequelae of overdose include delirium, convulsion, coma, possible neuroleptic malignant syndrome, respiratory depression, aspiration, hypertension or hypotension, cardiac arrhythmias (<2% of overdose cases), and cardiopulmonary arrest. Fatal outcomes have been reported for acute overdoses as low as 450mg, but survival has also been reported following acute overdose of approximately 2g of oral Olanzapine.

Management: There is no specific antidote for Olanzapine. Induction of emesis is not recommended. Standard procedures for management of overdose may be indicated

(i.e., gastric lavage, administration of activated charcoal). The concomitant administration of activated charcoal was shown to reduce the oral bioavailability of Olanzapine by 50 to 60%. Symptomatic treatment and monitoring of vital organ function should be instituted according to clinical presentation, including treatment of hypotension and circulatory collapse and support of respiratory function. Do not use epinephrine, dopamine, or other sympathomimetic agents with beta-agonist activity, since beta stimulation may worsen hypotension. Cardiovascular monitoring is necessary to detect possible arrhythmias. Close medical supervision and monitoring should continue until the patient recovers.

WARNING AND PRECAUTIONS:

Schizap (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. • The use of Olanzapine in the treatment of dopamine agonist associated psychosis in patients with Parkinson's disease is not recommended. • 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. 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. • 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, 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. • 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. • 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 cases where hepatitis (including hepatocellular, cholestatic or mixed liver injury) has been diagnosed, Olanzapine treatment should be discontinued. • Caution should be exercised in patients with low leukocyte and/or neutrophil counts for any reason. Neutropenia has been reported commonly when Olanzapine and valproate are used concomitantly. • Acute symptoms such as sweating, insomnia, tremor, anxiety, nausea, or vomiting have been reported rarely when Olanzapine is stopped abruptly. • 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. • 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. • Given the primary CNS effects of Olanzapine, caution should be used when it is taken in combination with other centrally acting medicines and alcohol. • Olanzapine should be used cautiously in patients who have a history of seizures or are subject to factors which may lower the seizure threshold. • Olanzapine has found to be associated with a statistically significant lower incidence of treatment emergent dyskinesia. • 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. • The risk of presumed sudden cardiac death in patients treated with Olanzapine was found to be approximately twice the risk in patients not using antipsychotics.

PREGNANCY AND LACTATION:

Pregnancy:

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