OXEPIN

(Fluoxetine + Olanzapine) USP

CAPSULES
25mg + 6mg
25mg + 3mg

COMPOSITION

Oxepin 25mg+6mg

Each capsule contains:

Fluoxetine (as HCl) USP.....25mg

Olanzapine USP.....6mg

Oxepin 25mg+3mg

Each capsule contains:

Fluoxetine (as HCl) USP.....25mg

Olanzapine USP.....3mg

DESCRIPTION

OXEPIN (Fluoxetine HCl and Olanzapine) Capsule combines an atypical antipsychotic and a selective serotonin reuptake inhibitor, Fluoxetine HCl and Olanzapine. Olanzapine belongs to thienobenzodiazepine class. Fluoxetine HCl is a Selective Serotonin Reuptake Inhibitor (SSRI).

MECHANISM OF ACTION

Although the exact mechanism of Fluoxetine HCl and Olanzapine is unknown, it has been proposed that the activation of 3 monoaminergic neural systems (norepinephrine) is responsible for its enhanced effect. In animal studies, Fluoxetine HCl and Olanzapine combination has been shown to produce synergistic increase in norepinephrine and dopamine release in the prefrontal cortex compared with either component alone, as well as increases in serotonin.

PHARMACODYNAMICS

Olanzapine binds with high affinity to the following receptors: serotonin $5HT_2$ and $5HT_6$, dopamine D_{1-4}, histamine H_1 receptor and adrenergic α1 receptors. Olanzapine is an antagonist with moderate affinity binding for serotonin $5HT_3$ and muscarinic M_{1-5}. Olanzapine binds weakly to GABA, BZD, and β-adrenergic receptors. Fluoxetine is an inhibitor of the serotonin transporter and is a weak inhibitor of the norepinephrine and dopamine transporters.

PHARMACOKINETICS

ABSORPTION AND BIO-AVAILABILITY: Olanzapine: It is well absorbed and reaches peak concentration approximately in 6 hours following an oral dose. Food does not affect the rate or extent of Olanzapine absorption. It is metabolized extensively by first pass effect with approximately 40% of the dose metabolized before reaching the systemic circulation. **Fluoxetine:** Following a single oral 40mg dose, peak plasma concentrations of Fluoxetine from 15 to 55ng/ml are observed after 6 to 8 hours. Food does not appear to affect the systemic bio-availability of Fluoxetine, although it may delay its absorption by 1 to 2 hours; which is probably not clinically significant. Distribution: The in-vitro binding to human plasma proteins of Fluoxetine HCl and Olanzapine in combination is similar to the binding of the individual components. **Olanzapine**: It is extensively distributed throughout the body with a volume of distribution of approximately 1000L. It is 93% bound to plasma proteins over the concentration range of 7 to 1100ng/ml, binding primarily to albumin and α1-acid glycoprotein. **Fluoxetine:** Over the concentration range from 200 to 1000ng/ml, approximately 94.5% of Fluoxetine is bound in vitro to human serum proteins, including albumin and α-glycoprotein.

METABOLISM AND ELIMINATION

Fluoxetine HCl and Olanzapine therapy yields steady state concentrations of nor-fluoxetine similar to those with Fluoxetine in the therapeutic dose range. Olanzapine displays linear pharmacokinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours.

SPECIFIC POPULATIONS

GERIATRIC: Based on the individual pharmacokinetic profiles of Fluoxetine HCl and Olanzapine, the pharmacokinetics of Fluoxetine HCl and Olanzapine Capsules may be altered in geriatric patients. Caution should be exercised in dosing the elderly, especially if there are other factors that might-additively influence drug metabolism and/or pharmacodynamic sensitivity.

RENAL IMPAIRMENT: The pharmacokinetics of Fluoxetine HCl and Olanzapine has not been studied in patients with renal impairment. However, individual pharmacokinetics of Fluoxetine HCl and Olanzapine do not differ significantly in patients with renal impairment. Fluoxetine HCl and Olanzapine Capsules dosing adjustment based upon renal impairment is not routinely required.

HEPATIC IMPAIRMENT: Based on the individual pharmacokinetic profiles of Fluoxetine HCl and Olanzapine, the pharmacokinetics of Fluoxetine HCl and Olanzapine Capsules may be altered in patients with hepatic impairment. The lowest starting dose should be considered for patients with hepatic impairment.

INDICATIONS

DEPRESSIVE EPISODES ASSOCIATED WITH BIPOLAR I DISORDER: OXEPIN (Fluoxetine HCl and Olanzapine) Capsule is indicated for the acute treatment of depressive episodes associated with Bipolar I Disorder in adults.

TREATMENT RESISTANT DEPRESSION: OXEPIN (Fluoxetine HCl and Olanzapine) Capsule is indicated for the acute treatment of Treatment Resistant Depression (Major Depressive Disorder in adults who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode).

CONTRA-INDICATIONS

Fluoxetine HCl and Olanzapine Capsule is contra-indicated, if patient is hypersensitive to active substances and any of its excipients.

DOSAGE AND ADMINISTRATION

DEPRESSIVE EPISODES ASSOCIATED WITH BIPOLAR I DISORDER: OXEPIN (Fluoxetine HCl and Olanzapine) Capsule should be administered once daily in the evening, generally beginning with the 25mg/6mg capsule. While food has no appreciable effect on the absorption of Fluoxetine HCl and Olanzapine Capsule given individually, the effect of food on the absorption of Fluoxetine HCl and Olanzapine Capsule has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with OXEPIN (Fluoxetine HCl and Olanzapine) Capsule in a dose range of Olanzapine 6mg to 12mg and Fluoxetine 25mg to 50mg.

The safety of doses above 75mg/18mg has not been evaluated in clinical studies. It is generally accepted that Bipolar I Disorder, including the depressive episodes associated with Bipolar I Disorder, is a chronic illness requiring chronic treatment. The physician should periodically re-examine the need for continued pharmacotherapy.

TREATMENT RESISTANT DEPRESSION: OXEPIN (Fluoxetine HCl and Olanzapine) Capsule should be administered once daily in the evening, generally beginning with the 25mg/6mg capsule. While food has no appreciable effect on the absorption of Fluoxetine HCl and Olanzapine given individually, the effect of food on the absorption of OXEPIN (Fluoxetine HCl and Olanzapine) Capsule has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with OXEPIN (Fluoxetine HCl and Olanzapine) Capsule in a dose range of Olanzapine 6mg to 18mg and Fluoxetine 25mg to 50mg. The safety of doses above 75mg/18mg has not been evaluated in clinical studies. It is generally accepted that Treatment Resistant Depression (Major Depressive Disorder in adult patients who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode) is a chronic illness requiring chronic treatment. The physician should periodically re-examine the need for continued pharmacotherapy.

USE IN SPECIFIC POPULATIONS: The starting dose of OXEPIN (Fluoxetine HCl and Olanzapine) Capsule 25mg/6mg should be used for patients with a predisposition to reactions, patients with hepatic impairment, or patients who exhibit a combination of factors that may slow the metabolism of OXEPIN (Fluoxetine HCl and Olanzapine) Capsule (female gender, geriatric age, nonsmoking status) or those patients who may be pharmacodynamically sensitive to Olanzapine. Dosing modification may be necessary in patients who exhibit a combination of factors that may slow metabolism. When indicated, dose escalation should be performed with caution in these patients. OXEPIN (Fluoxetine HCl and Olanzapine) Capsule has not been systematically studied in patients >65 years of age or in patients <18 years of age.

PREGNANCY: Category C
Fluoxetine HCl and Olanzapine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, taking into account the risk of untreated Bipolar I Depression or Treatment Resistant Depression.

SIDE EFFECTS
Commonly observed adverse reactions in short-term controlled-studies including depressive episodes associated with bipolar/disorder and treatment resistant depression: SEXUAL DYSFUNCTION: In the pool of controlled Fluoxetine HCl and Olanzapine studies in patients with Bipolar depression, there were higher rates of the treatment-emergent adverse reactions decreased and abnormal in the Fluoxetine HCl and Olanzapine group than in the placebo group. Sexual dysfunction, including priapism has been reported with all SSRIs.

BODY AS A WHOLE: Frequent: chills, neck rigidity, photosensitivity reaction; Rare: death.

CARDIOVASCULAR SYSTEM: Frequent: vasodilatation; Infrequent: QT-interval prolonged.

DIGESTIVE SYSTEM: Frequent: diarrhea; Infrequent: nausea and vomiting; Rare: gastrointestinal hemorrhage, liver fatty deposits.

NERVOUS SYSTEM: Infrequent: buccoglossal syndrome, coma, depersonalization, emotional hypokinesia, movement disorder; Rare: hyperkinesia, libido increased, withdrawal syndrome.

DRUG INTERACTIONS
MONO AMINE OXIDASE INHIBITORS (MAOIs): Fluoxetine HCl and Olanzapine should not be used in combination with MAOIs or within a minimum of 14 days of discontinuing therapy with MAOIs. There have been reports of serious, sometimes fatal reactions (including rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delerium and coma) in patients receiving Fluoxetine in combination with an MAOIs and in patients who have recently, discontinued Fluoxetine and are then started on MAOIs.

CNS ACTING DRUGS: Caution is advised if the concomitant administration of Fluoxetine HCl and Olanzapine and other CNS active drugs is required. In evaluating individual cases, consideration should be given to use lower initial doses of the concomitantly administered drugs, using conservative titration schedules, and monitoring of clinical status.

OVERDOSE MANAGEMENT
No specific antidote for either Fluoxetine or Olanzapine overdose is known. Treatment should be supportive and symptomatic.

BLACK-BOX WARNING

SUICIDALITY: Incr. risk of suicidality in children, adolescents and young adults w/ major depressive or other psychiatric disorders esp. during 1st months of tx w/ antidepressants vs. placebo; weigh risk vs. benefit; In short-term studies of antidepressants vs. placebo, suicidality risk not incr. in pts >24 y and risk decr. in pts 65 y and older; observe all pts for clinical worsening, suicidality, or unusual behavior changes; advise families and caregivers of need for close observation and communication w/ prescriber; not approved in pts <10 yo
DEMENTIA-RELATED PSYCHOSIS: not approved for dementia-related psychosis; incr. mortality risk in elderly dementia pts on conventional or atypical antipsychotics; most deaths due to cardiovascular or infectious events; extent to which incr. mortality attributed to antipsychotic vs. some pt characteristic(s) not clear

INSTRUCTIONS
Store at 15-30°C. Protect from heat, light & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION
OXEPIN 25mg + 6mg & 25mg + 3mg capsules are available in the blister packs of 2x7's.

اوگزیپن (فلوآکسیٹین+اولینزاپین) یو ایس پی کیپسول

خوراک: دوا ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: دوا کو **15-30°** سینٹی گریڈ پر رکھیں۔
گرمی، روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
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