Front

Olabex™

(Olanzapine + Fluoxetine)

Capsule

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COMPOSITION:
Olabex 3/25 Capsule:
Each capsule contains:
Olanzapine ..... 3 mg.
Fluoxetine (as HCl) ..... 25 mg.

Product Specs.: USP

Olabex 6/25 Capsule:
Each capsule contains:
Olanzapine ..... 6 mg.
Fluoxetine (as HCl) ..... 25 mg.

Product Specs.: USP

WARNING
SUICIDAL THOUGHTS AND BEHAVIORS AND INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

- Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. This drug is not approved for use in children less than 10 years of age. Monitor for worsening and emergence of suicidal thoughts and behaviors.
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. This drug is not approved for the treatment of patients with dementia-related psychosis.

DESCRIPTION:
Olabex (olanzapine and fluoxetine HCl capsules) combines olanzapine and fluoxetine hydrochloride. Olanzapine belongs to the thienobenzodiazepine class. Fluoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI).

CLINICAL PHARMACOLOGY:
Mechanism of action:
Although the exact mechanism of **Olabex** is unknown, it has been proposed that the activation of 3 monoaminergic neural systems (serotonin, norepinephrine, and dopamine) is responsible for its enhanced antidepressant effect.
Pharmacodynamics:
Olanzapine binds with high affinity to the following receptors: Serotonin 5HT2A/2C, 5HT6 (K_i=4, 11, and 5 nM, respectively), dopamine D1-4 (K_i=11 to 31 nM), histamine H_1 (K_i=7 nM), and adrenergic α1 receptors (Ki=19 nM). Olanzapine is an antagonist with moderate affinity binding for serotonin 5HT3 (K_i=57 nM) and muscarinic M_1-5 (K_i=73, 96, 132, 32, and 48 nM, respectively). Olanzapine binds weakly to GABAA, BZD, and β-adrenergic receptors (K_i>10 μM). Fluoxetine is an inhibitor of the serotonin transporter and is a weak inhibitor of the norepinephrine and dopamine transporters. Antagonism at receptors other than dopamine and 5HT2 may explain some of the other therapeutic and side effects of olanzapine. Olanzapine's antagonism of muscarinic M_{1-5} receptors may explain its anticholinergic-like effects. The antagonism of histamine H_1 receptors by olanzapine may explain the somnolence observed with this drug. The antagonism of α1-adrenergic receptors by olanzapine may explain the orthostatic hypotension observed with this drug. Fluoxetine has relatively low affinity for muscarinic, α1-adrenergic, and histamine H_1 receptors.
Pharmacokinetics: The overall steady-state plasma concentrations of olanzapine and fluoxetine when given as the combination in the therapeutic dose ranges were comparable with those typically attained with each of the monotherapies.
Absorption and bioavailability:
Olabex — Following a single oral 12-mg/50-mg dose of **Olabex**, peak plasma concentration is achieved at 4 and 6 hours, respectively. It is unlikely that there would be a significant food effect on the bioavailability of **Olabex**.
Olanzapine — Olanzapine is well absorbed and reaches peak concentration approximately 6 hours following an oral dose. Food does not affect the rate or extent of olanzapine absorption when olanzapine is given alone. It is eliminated extensively by first pass metabolism.
Fluoxetine — Following a single dose, peak plasma concentrations are observed after 6 to 8 hours. Food does not appear to affect the systemic bioavailability of fluoxetine, although it may delay its absorption by 1 to 2 hours.
Distribution:
Olabex — The in vitro binding to human plasma proteins of olanzapine and fluoxetine in combination is similar to the binding of the individual components.
Olanzapine — 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 α1-acid glycoprotein.
Fluoxetine — Over the concentration range from 200 to 1000 ng/mL, approximately 94.5% of fluoxetine is bound in vitro to human serum proteins, including albumin and α1-glycoprotein.
Metabolism and elimination:
Olabex — Olabex therapy yielded steady-state concentrations of norfluoxetine similar to those seen with fluoxetine in the therapeutic dose range.
Olanzapine — Its half-life ranges from 21 to 54 hours (5th to 95th percentile; mean of 30 hr). Administration of olanzapine once daily leads to steady-state concentrations in about 1 week that are approximately twice the concentrations after single doses.
Fluoxetine — Fluoxetine is extensively metabolized in the liver to its only identified active metabolite, norfluoxetine, via the CYP2D6 pathway. A number of unidentified metabolites exist. The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney.

INDICATIONS AND USAGE:
Depressive episodes associated with bipolar I Disorder: **Olabex** is indicated for the acute treatment of depressive episodes associated with Bipolar I Disorder in adults.
Treatment resistant depression: **Olabex** 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).

DOSAGE AND ADMINISTRATION:
Depressive episodes associated with bipolar I Disorder:
Adults — Administer **Olabex** once daily in the evening, generally beginning with the 6 mg/25 mg (mg olanzapine/mg equivalent fluoxetine) capsule. Make dosage adjustments, if indicated, according to efficacy and tolerability. The safety of doses above 18 mg of olanzapine and 75 mg of fluoxetine has not been evaluated in adult clinical studies. Periodically reexamine the need for continued pharmacotherapy.
Children and Adolescents (10 to 17 years of age) — Administer **Olabex** once daily in the evening, generally beginning with the 3 mg/25 mg capsule, without regard to meals, with a recommended target dose within the approved dosing range (6/25; 6/50; 12/50 mg). The safety of doses above 12 mg of olanzapine and 50 mg of fluoxetine has not been evaluated in pediatric clinical studies. Periodically reexamine the need for continued pharmacotherapy.
Treatment resistant depression: Administer **Olabex** once daily in the evening, generally beginning with the 6 mg/25 mg capsule. Adjust dosage, if indicated, according to efficacy and tolerability. The safety of doses above 18 mg/75 mg has not been evaluated in clinical studies. Periodically reexamine the need for continued pharmacotherapy. Safety and efficacy of Olabex for treatment resistant depression in patients under 18 years of age have not been established.
Specific populations: Start **Olabex** at 3 mg/25 mg or 6 mg/25 mg in patients with a predisposition to hypotensive reactions, patients with hepatic impairment, or patients who exhibit a combination of factors that may slow the metabolism of **Olabex** (female gender, geriatric age, nonsmoking status) or those patients who may be pharmacodynamically sensitive to olanzapine. Titrate slowly and adjust dosage as needed in patients who exhibit a combination of factors that may slow metabolism.
Treatment of pregnant women during the third trimester: When treating pregnant women with fluoxetine, a component of **Olabex**, during the third trimester, the physician should carefully consider the potential risks and potential benefits of treatment. Neonates exposed to SNRIs or SSRIs late in the third trimester have developed complications requiring prolonged hospitalizations, respiratory support, and tube feeding. The physician may consider using a lower dose in the third trimester.
Discontinuation of treatment with Olabex: Symptoms associated with discontinuation of fluoxetine, a component of **Olabex**, SNRIs, and SSRIs, have been reported.

CONTRAINDICATIONS:
The use of Olabex is contraindicated with the following:
- Monoamine Oxidase Inhibitors (MAOI)
- Pimozide
- Thioridazine

WARNINGS AND PRECAUTIONS:
Clinical worsening and suicide risk: Patients with Major Depressive Disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide.
All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Families and caregivers of patients being treated with antidepressants for Major Depressive Disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.
Prescriptions for **Olabex** should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose. It should be noted that **Olabex** is not approved for use in treating any indications in the pediatric population.
Elderly patients with dementia-related psychosis:
Increased Mortality — Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. **Olabex** is not approved for the treatment of patients with dementia-related psychosis.
Cerebrovascular Adverse Events (CVAE), Including Stroke — Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. Olanzapine and **Olabex** are not approved for the treatment of patients with dementia-related psychosis.
Neuroleptic malignant syndrome (NMS): A potentially fatal symptom complex sometimes referred to as 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). 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. There is no general agreement about specific pharmacological treatment regimens for NMS. If after recovering from NMS, a patient requires treatment with an antipsychotic, the patient should be carefully monitored, since recurrences of NMS have been reported.
Drug reaction with eosinophilia and systemic symptoms (DRESS): DRESS can occur with **Olabe**x. Features of DRESS may include rash, fever, swollen glands and other internal organ involvement such as liver, kidney, lung and heart. DRESS is sometimes fatal.
Hyperglycemia: Physicians should consider the risks and benefits when prescribing **Olabex** to patients with an established diagnosis of diabetes mellitus, or having borderline increased blood glucose level (fasting 100-126 mg/dL, non-fasting 140-200 mg/dL). Patients taking **Olabex** should be monitored regularly for worsening of glucose control.
Hyperlipidemia: Undesirable alterations in lipids have been observed with **Olabex** use. Clinical monitoring, including baseline and periodic follow-up lipid evaluations in patients using it, is recommended. Clinically meaningful, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed. Clinically meaningful increases in total cholesterol have also been seen with use.
Weight gain: Potential consequences of weight gain should be considered prior to initiation of therapy; regular monitoring of weight is required.
Serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions: Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of **Olabex** with MAOIs intended to treat depression is contraindicated. If concomitant treatment of **Olabex** with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of **Olabex** with serotonin precursors (such as tryptophan) is not recommended. Treatment with **Olabex** and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately, if the above reactions occur, supportive symptomatic treatment should be initiated.
Allergic reactions and rash: The majority of the cases of rash and/or urticaria were mild. Most patients improved promptly with discontinuation of fluoxetine and/or adjunctive treatment with antihistamines or steroids.
Activation of mania/hypomania: Prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for Bipolar Disorder; such screening should include a detailed psychiatric history, including a family history of suicide, Bipolar Disorder, and depression. It should be noted that **Olabex** is approved for the acute treatment of depressive episodes associated with Bipolar I Disorder.
Tardive dyskinesia: A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. **Olabex** should be prescribed in a manner that is most likely to minimize the risk of tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear in a patient on **Olabex**, drug discontinuation should be considered. However, some patients may require treatment with **Olabex** despite the presence of the syndrome. The need for continued treatment should be reassessed periodically.
Orthostatic hypotension: **Olabex** may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia and, in some patients, syncope, especially during the initial dose-titration period.
Leukopenia, Neutropenia, and agranulocytosis:
Class Effect — Events of leukopenia/neutropenia have been reported temporally related to antipsychotic agents. Patients with a history of a clinically significant low WBC or drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of therapy.
Seizures: **Olabex** 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. **Olabex** is not approved for the treatment of patients with Alzheimer's disease. Conditions that lower the seizure threshold may be more prevalent in a population of ≥65 years of age.
Abnormal bleeding: SNRIs and SSRIs, including fluoxetine, may increase the risk of bleeding reactions. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anti-coagulants may add to this risk. Patients should be cautioned about the risk of bleeding associated with the concomitant use of **Olabex** and NSAIDs, aspirin, or other drugs that affect coagulation.
Hyponatremia: Hyponatremia has been reported during treatment with SNRIs and SSRIs, including fluoxetine and **Olabex**. Elderly patients may be at greater risk of developing hyponatremia with SNRIs and SSRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk. Discontinuation of **Olabex** should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.
Potential for cognitive and motor impairment: Sedation-related adverse reactions were commonly reported. As with any CNS-active drug, **Olabex** has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that **Olabex** therapy does not affect them adversely.
Falls: **Olabex** may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and recurrently for patients on long- term antipsychotic therapy.
Body temperature regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic drugs. Appropriate care is advised when prescribing.
Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, **Olabex** elevates prolactin levels, and a modest elevation persists during administration. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male subjects.
Concomitant use of olanzapine and fluoxetine products: Caution should be exercised when prescribing these medications concomitantly with **Olabex**.
Long elimination half-life of fluoxetine: Because of the long elimination half-lives of fluoxetine and its major active metabolite, changes in dose will not be fully reflected in plasma for several weeks, affecting both strategies for titration to final dose and withdrawal from treatment. This is of potential consequence when drug discontinuation is required or when drugs are prescribed that might interact with fluoxetine and norfluoxetine following the discontinuation of fluoxetine.
Discontinuation of treatment with Olabex: Patients should be monitored for these symptoms when discontinuing treatment with fluoxetine. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate. Plasma fluoxetine and norfluoxetine concentration decrease gradually at the conclusion of therapy, which may minimize the risk of discontinuation symptoms with this drug.
Laboratory tests: Fasting blood glucose testing and lipid profile at the beginning of, and periodically during treatment is recommended.

ADVERSE REACTIONS:
Reactions are classified by body system using the following definitions: frequent adverse reactions are those occurring in at least 1/100 patients; infrequent adverse reactions are those occurring in 1/100 to 1/1000 patients; and rare reactions are those occurring in fewer than 1/1000 patients.
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:* gastritis, gastroenteritis, nausea and vomiting, peptic ulcer; *Rare:* GI hemorrhage, intestinal obstruction, liver fatty deposit, pancreatitis.
Hemic and Lymphatic System — *Frequent:* ecchymosis; *Infrequent:* anemia, thrombocytopenia; *Rare:* leukopenia, purpura.
Metabolic and Nutritional — *Frequent:* generalized edema, weight loss; *Rare:* bilirubinemia, creatinine increased, gout.
Musculoskeletal System — *Rare:* osteoporosis.
Nervous System — *Frequent:* amnesia; *Infrequent:* ataxia, buccoglossal syndrome, coma, dysarthria, emotional lability, euphoria, hypokinesia, movement disorder, myoclonus; *Rare:* hyperkinesia, libido increased, withdrawal syndrome.
Respiratory System — I*nfrequent:* epistaxis, yawn; *Rare:* laryngismus.
Skin and Appendages — *Infrequent:* alopecia, dry skin, pruritis; *Rare:* exfoliative dermatitis.
Special Senses — *Frequent:* taste perversion; Infrequent: abnormality of accommodation, dry eyes.
Urogenital System — *Frequent:* breast pain, menorrhagia, urinary frequency, urinary incontinence; *Infrequent:* amenorrhea, female lactation, hypomenorrhea, metrorrhagia, urinary retention, urinary urgency, urination impaired; *Rare:* breast engorgement.
Adverse reactions reported since market introduction that were temporally (but not necessarily causally) related to **Olabex** therapy include the following: rhabdomyolysis and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis).

DRUG INTERACTIONS:
The drug-drug interactions sections of fluoxetine and olanzapine are applicable to **Olabex**. As with all drugs, the potential for interaction by a variety of mechanisms (e.g., pharmacodynamic, pharmacokinetic drug inhibition or enhancement, etc.) is a possibility.
Monoamine oxidase inhibitors (MAOI): **Olabex** should not be used in combination with an MAOI, or within a minimum of 14 days of discontinuing therapy with an MAOI.
CNS Acting drugs: Caution is advised if the concomitant administration of **Olabex** and other CNS-active drugs is required.
Serotonergic drugs: Based on the mechanism of action of SNRIs and SSRIs, including **Olabex**, and the potential for serotonin syndrome, caution is advised when **Olabex** is co-administered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort. The concomitant use of **Olabex** with SNRIs, SSRIs, or tryptophan is not recommended.
Triptans: There have been rare post-marketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of **Olabex** with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.
Tryptophan: Concomitant use with tryptophan is not recommended.
Drugs that Interfere with Hemostasis (e.g., NSAIDs, Aspirin, Warfarin): Altered anticoagulant effects, including increased bleeding, have been reported when SNRIs or SSRIs are co-administered with Aspirin, warfarin.
Potential for other drugs to affect Olabex:
Benzodiazepines — Co-administration of diazepam with olanzapine potentiated the orthostatic hypotension observed with olanzapine.
Inducers of 1A2 — Carbamazepine therapy (200 mg BID) causes an approximate 50% increase in the clearance of olanzapine. Higher daily doses of carbamazepine may cause an even greater increase in olanzapine clearance.
Inhibitors of CYP1A2 — Fluvoxamine decreases the clearance of olanzapine. This results in a mean increase in olanzapine. C_{max} following fluvoxamine administration of 54% in female nonsmokers and 77% in male smokers. The mean increase in olanzapine AUC is 52% and 108%, respectively. Lower doses of the olanzapine component of **Olabex** should be considered in patients receiving concomitant treatment with fluvoxamine.
The Effect of Other Drugs on Olanzapine — Fluoxetine, an inhibitor of CYP2D6, decreases olanzapine clearance a small amount
Potential for Olabex to affect other drugs:
Pimozide — Concomitant use of fluoxetine and pimozide is contraindicated.
Carbamazepine — Patients on stable doses of carbamazepine have developed elevated plasma anticonvulsant concentrations and clinical anticonvulsant toxicity following initiation of concomitant fluoxetine treatment.
Alcohol — The coadministration of ethanol with **Olabex** may potentiate sedation and orthostatic hypotension.
Thioridazine — Thioridazine should not be administered with **Olabex** or administered within a minimum of 5 weeks after discontinuation of **Olabex**. Thioridazine administration produces a dose-related prolongation of the QTc interval, which is associated with serious ventricular arrhythmias, such as torsades de pointes-type arrhythmias and sudden death. This risk is expected to increase with fluoxetine-induced inhibition of thioridazine metabolism.
Antihypertensive Agents — Because of the potential for olanzapine to induce hypotension, **Olabex** may enhance the effects of certain antihypertensive agents.
Levodopa and Dopamine Agonists — The olanzapine component of **Olabex** may antagonize the effects of levodopa and dopamine agonists.
Benzodiazepines — When concurrently administered with fluoxetine, the half-life of diazepam may be prolonged in some patients. Co-administration of alprazolam and fluoxetine has resulted in increased alprazolam plasma concentrations and in further psychomotor performance decrement due to increased alprazolam levels.
Clozapine — Elevation of blood levels of clozapine has been observed in patients receiving concomitant fluoxetine.
Haloperidol — Elevation of blood levels of haloperidol has been observed in patients receiving concomitant fluoxetine.
Phenytoin — Patients on stable doses of phenytoin have developed elevated plasma levels of phenytoin with clinical phenytoin toxicity following initiation of concomitant fluoxetine.
Lithium —Lithium levels should be monitored in patients taking O**Olabex** concomitantly with lithium.

USE IN SPECIFIC POPULATIONS:
Pregnancy: SSRI use, particularly later in pregnancy, may increase the risk for persistent pulmonary hypertension and symptoms of poor adaptation (respiratory distress, temperature instability, feeding difficulty, hypotonia, irritability, tremor) in the neonate. Olanzapine may cause extrapyramidal symptoms and/or withdrawal symptoms in neonates with third trimester exposure.
Nursing mothers:
OLABEX — Because of the potential for serious adverse reactions in nursing infants from OLABEX, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. It is recommended that women not breast-feed when receiving **Olabex**.
Olanzapine —It is recommended that women receiving olanzapine should not breast-feed.
Fluoxetine — Fluoxetine is excreted in human breast milk.
Females and males of reproductive potential:
Infertility:
Females: Based on the pharmacologic action of olanzapine (dopamine D2 receptor blockade), treatment with **Olabex** may result in an increase in serum prolactin levels, which may lead to a reversible reduction in fertility in females of reproductive potential.
Pediatric use:
Olabex — The safety and efficacy of **Olabex** in patients 10 to 17 years of age has been established for the acute treatment of Depressive Episodes Associated with Bipolar I Disorder. The types of adverse events observed with **Olabex** in children and adolescents were generally similar to those observed in adults. However, the magnitude and frequency of some changes were greater in children and adolescents than adults. These included increases in lipids, hepatic enzymes, and prolactin, as well as increases in the QT interval. Anyone considering the use of **Olabex** in a child or adolescent must balance the potential risks with the clinical need. Safety and efficacy of **Olabex** for treatment resistant depression in patients under 18 years of age have not been established.
Olanzapine — Safety and effectiveness of olanzapine in children <13 years of age have not been established.
Fluoxetine — Significant toxicity, including myotoxicity, long-term neurobehavioral and reproductive toxicity, and impaired bone development, has been observed following exposure of juvenile animals to fluoxetine. Some of these effects occurred at clinically relevant exposures.
Geriatric use:
Olabex — In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
Olanzapine — Olanzapine is not approved for the treatment of patients with dementia-related psychosis. Also, 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.
Fluoxetine — SNRIs and SSRIs, including **Olabex**, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse reaction.
Hepatic impairment: A lower or less frequent dose of the fluoxetine-component of **Olabex** should be used in patients with cirrhosis. Caution is advised when using **Olabex** in patients with diseases or conditions that could affect its metabolism.

DRUG ABUSE AND DEPENDENCE:
Dependence: **Olabex**, as with fluoxetine and olanzapine, has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. Physicians should carefully evaluate patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of **Olabex** (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

OVERDOSAGE:
OLABEX — An overdose of combination therapy is defined as confirmed or suspected ingestion of a dose of >20 mg olanzapine in combination with a dose of >80 mg fluoxetine. Adverse reactions associated with these reports included somnolence (sedation), impaired consciousness (coma), impaired neurologic function (ataxia, confusion, convulsions, dysarthria), arrhythmias, lethargy, essential tremor, agitation, acute psychosis, hypotension, hypertension, and aggression. Fatalities have been confounded by exposure to additional substances including alcohol, thioridazine, oxycodone, and propoxyphene.
Olanzapine — In symptomatic patients, symptoms with ≥ 10% incidence included agitation/aggressiveness, dysarthria, tachycardia, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Among less commonly reported symptoms were the following potentially medically serious reactions: aspiration, cardiopulmonary arrest, cardiac arrhythmias (such as supraventricular tachycardia as well as a patient that experienced sinus pause with spontaneous resumption of normal rhythm), delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypertension, and hypotension.
Fluoxetine — Patients experienced sequelae after overdose, including abnormal accommodation, abnormal gait, confusion, unresponsiveness, nervousness, pulmonary dysfunction, vertigo, tremor, elevated blood pressure, impotence, movement disorder, and hypomania. The remaining 206 patients had an unknown outcome. The most common signs and symptoms associated with non-fatal overdose were seizures, somnolence, nausea, tachycardia, and vomiting. Other important adverse reactions reported with fluoxetine overdose (single or multiple drugs) included coma, delirium, ECG abnormalities (such as QT-interval prolongation and ventricular tachycardia, including torsades de pointes-type arrhythmias), hypotension, mania, neuroleptic malignant syndrome-like reactions, pyrexia, stupor, and syncope.

Management of overdose: In managing overdose, the possibility of multiple drug involvement should be considered. In case of acute overdose, establish and maintain an airway and ensure adequate ventilation, which may include intubation. Induction of emesis is not recommended as the possibility of obtundation, seizures, or dystonic reactions of the head and neck following overdose may create a risk for aspiration. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. A specific precaution involves patients who are taking or have recently taken **Olabex** and may have ingested excessive quantities of a TCA (tricyclic antidepressant). In such cases, accumulation of the parent TCA and/or an active metabolite may increase the possibility of serious sequelae and extend the time needed for close medical observation. Due to the large volume of distribution of olanzapine and fluoxetine, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidote for either fluoxetine or olanzapine overdose is known. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. Do not use epinephrine, dopamine, or other sympathomimetics with **β**-agonist activity, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blockade. The physician should consider contacting a poison control center for additional information on the treatment of any overdose.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Olabex 3/25 Capsule	:	Pack of 2 x 7 capsules.
Olabex 6/25 Capsule	:	Pack of 2 x 7 capsules.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
WnsFeild Pharmaceuticals.
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FOR FURTHER INFORMATION PLEASE CONTACT:

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