OXETINE®

DESCRIPTION

OXETINE is the trade name of Fluoxetine Hydrochloride, an antidepressant and an antiobsessional agent.
Each **OXETINE 20** Coated Tablet contains Fluoxetine 20mg as Fluoxetine Hydrochloride.

CHEMISTRY

Fluoxetine Hydrochloride is: (±)-*N*-Methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride.

CLINICAL PHARMACOLOGY

OXETINE is a potent and selective inhibitor of serotonin uptake in the central nervous system (CNS), with no effect on norepinephrine. **OXETINE** potentiates the pharmacologic effects of serotonin via preventing its inactivation. Consequently, 5-HT receptors are desensitized or downregulated after chronic administration of **OXETINE**. **OXETINE** does not directly interact with serotonergic, muscarinic, cholenergic, histaminergic H , or alpha-adrenergic receptors. This high-selectivity of **OXETINE** makes it unique among other currently available serotonin-facilitating antidepressants. Fluoxetine is well absorbed with a small first-pass effect. Food does not affect the extent of absorption, although the rate may be slightly decreased. Onset of action is after 1 to 4 weeks.

INDICATIONS

- ❑ Treatment of mental depression: **OXETINE** is indicated for the treatment of major depressive disorder.
- ❑ Treatment of obsessive-compulsive disorder: **OXETINE** is used to relieve symptoms of obsessive-compulsive disorder.
- ❑ Treatment of bulimia nervosa: **OXETINE** is indicated for the treatment of binge-eating and vomiting behaviours in patients with moderate to severe bulimia nervosa.
- ❑ **OXETINE** is also indicated for the treatment of the premenstrual dysphoric disorder (PMDD).

DOSAGE

Usual adult dose

- ❑ Depression or obsessive-compulsive disorder: initially 20mg Fluoxetine a day as a single morning dose. The dose may be increased by 20mg a day at weekly intervals after several weeks of treatment, as needed and tolerated.
- ❑ Bulimia nervosa: 60 mg/day as a single morning dose.
- ❑ premenstrual dysphoric disorder (PMDD):
  - Initial treatment: 20 mg/day
  - Maintenance: Efficacy of **OXETINE** is maintained up to 6 months at 20 mg/day dosage, patients should be periodically reassessed to determine need for continued treatment.
- ❑ Usual adult prescribing limits: 80mg a day.

Notes

- ❑ It is recommended that doses over 20mg a day be taken in two divided doses, in the morning and at noon.
- ❑ A lower dose or less frequent dosage should be exercised in patients with hepatic impairment, in elderly, and in patients with concurrent disease or on multiple concurrent medications.
- ❑ Because of the long elimination half lives of Fluoxetine (2-3 days) and its active metabolite, norfluoxetine (7 - 9 days), dosing changes are not reflected in plasma for several weeks.
- ❑ **OXETINE** may be taken with food to lessen possible stomach upset.
- ❑ Dosage adjustments for renal impairment are not usually necessary with **OXETINE**.

ADVERSE EFFECTS

- ❑ More frequent effects: Anxiety and nervousness, diarrhea, drowsiness, headache, increased sweating, insomnia, nausea.
- ❑ Less frequent effects: Abnormal dreams, changes in taste or vision, chest pain, trouble in breathing, joint or muscle pain, skin rash, hives or itching, chills or fever, constipation, cough, decreased appetite or weight loss, decrease in concentration, decreased sexual drive or ability, dizziness or lightheadedness, dryness of mouth, fast or irregular heartbeat, feeling of warmth or heat, flushing or redness of skin, frequent urination, increased appetite, menstrual pain, stuffy nose, tiredness or weakness, tremor, vomiting, stomach cramps, gas, or pain.

USE IN PREGNANCY

There are no adequate and controlled studies to date in humans. Fluoxetine is not teratogenic in rodents, but is fetotoxic in rats. Risk benefit should be considered before using Fluoxetine in pregnant women. The prolonged elimination of the drug and its active metabolite from the body after discontinuance of therapy should be considered when a woman of child bearing potential receiving Fluoxetine plans to become pregnant. FDA Pregnancy Category C.

USE IN LACTATION

Fluoxetine and its metabolites distribute into human milk. This has been reported to adversely effect an infant in one case resulting in sleep disorders, crying and gastrointestinal adverse effects. Therefore, Fluoxetine should not be used in nursing women, and women should be advised to notify their physician if they plan to breast-feed. The slow elimination of Fluoxetine and norfluoxetine after discontinuance should be considered.

INTERFERENCE WITH CLINICAL AND LABORATORY TESTS

Not documented.

DRUG INTERACTIONS

- ❑ Fluoxetine may potentiate concurrently given CNS depression-producing medication or alcohol.
- ❑ Caution in concurrent use of highly protein-bound drugs, especially anticoagulants, or digitalis or digitoxin, because of possible displacement by Fluoxetine.
- ❑ Caution and close monitoring are suggested when anticonvalsants (phenytoin and carbamazepine) are used concurrently with Fluoxetine because of risk of elevated anticonvulsant plasma levels and risk of toxicity.
- ❑ A potentially lethal hyperserotonergic state may occur as the result of combining a serotonergic agent such as Fluoxetine with monoamine oxidase (MAO) inhibitors including furazolidine, procarbazine, and selegiline (see Contraindications).
- ❑ Tryptophan concurrent use may potentiate agitation, restlessness, and gastrointestinal problems.

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- ❑ May need to reduce the dose of tricyclic antidepressants, maprotiline, or trazodone by about 50% because plasma concentrations may be doubled.
- ❑ Diazepam half life may be prolonged by Fluoxetine.
- ❑ Lithium concentrations may be altered by Fluoxetine leading to toxicity. Lithium concentrations should be monitored.
- ❑ Patients should be observed for interaction when Fluoxetine is administered with sumatriptan or with antipsychotics (e.g., haloperidol, clozapine, pimozide).
- ❑ Fluoxetine inhibits P450IID6 isoenzyme activity. This results in possibility for toxicity with thioridazone when given concomitantly with Fluoxetine (see contraindications). Doses of other drugs metabolized by P450IID6 (e.g., vinblastine, tricyclic antidepressants) may need reduction.

CONTRAINDICATIONS

- ❑ Hypersensitivity to Fluoxetine.
- ❑ Patients receiving or having recently received (i.e., within 2 weeks), monoamine oxidase (MAO) inhibitors or thiaridazone therapy. At least 5 weeks should be allowed after stopping Fluoxetine before starting a MAO inhibitors or thiaridazone.

WARNINGS

Risk-benefit must be considered when the following medical problems exist:

- ❑ Hepatic or renal function impairment: lower doses or less frequent dosing is recommended because metabolism, or possibly excretion, is delayed.
- ❑ Discontinue Fluoxetine in patients who develop a rash, or other possibly allergic phenomena for which an alternative etiology cannot be identified, since systemic effect, possibly related to vasculitis, have occurred in such patients.
- ❑ Glycemic control may be altered in Diabetes mellitus.
- ❑ Seizures may be induced by Fluoxetine in patients with history of seizure disorders, debilitated patients, or patients taking multiple CNS-active medications.

OVERDOSE

Limited information is available on the acute toxicity of Fluoxetine. Possible effects include agitation and restlessness, hypomania, severe nausea and vomiting, and seizures. Treatment is essentially symptomatic and supportive, possibly including administration of activated charcoal with sorbitol, maintaining respiratory and cardiac function and body temperature, and ECG monitoring. Administer an anticonvulsant, e.g. diazepam, if necessary for seizure control. Fluoxetine and norfluoxetine are not substantially removed by hemodialysis.

PRECAUTIONS

- ❑ Careful supervision of depressed patients with suicidal tendencies is recommended especially during early treatment phase prior to peak effectiveness of Fluoxetine. Prescribing the smaller number of tablets necessary for good patient management is recommended to prevent overdosing.
- ❑ There have been recent anecdotal reports of few cases of suicidal ideation occurring in patients on Fluoxetine therapy; patients who have previously been treated with other antidepressants, or who develop intense fatigues, hypersomnia, or restlessness on Fluoxetine therapy may be at greatest risk.
- ❑ Fluoxetine may possibly cause drowsiness, impairment of judgment, thinking or motor skills. Caution when driving or doing jobs requiring alertness.
- ❑ Safety and efficacy have not been established in pediatrics.

HOW SUPPLIED

- ❑ Boxes of 10 blistered tablets of **OXETINE 20** Tablets.
- ❑ Boxes of 20 blistered tablets of **OXETINE 20** Tablets.
- ❑ Boxes of 30 blistered tablets of **OXETINE 20** Tablets.
- ❑ Hospital packs of different presentations.

Store away from children, at a temperature between 15°-30° C, protected from light.
Do not use after the expiry date shown on the package.

THIS IS A MEDICAMENT

- ❑ A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- ❑ Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who dispensed the medicament.
- ❑ The doctor and the pharmacist are experts in medicine.
- ❑ Do not by yourself interrupt the period of treatment prescribed for you.
- ❑ Do not repeat the same prescription without consulting your doctor.
- ❑ Keep medicaments out of the reach of children.

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COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

Prescribing Information Available Upon Request

THE JORDANIAN PHARMACEUTICAL MANUFACTURING CO. (P.L.C)
JPM *P.O. BOX 94, NAOR 11710, JORDAN*