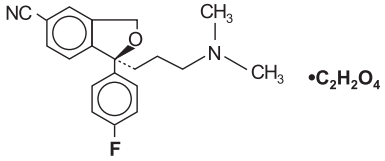
E-Dynapram

(Escitalopram) Tablets USP

Composition:
Each film coated tablet contains:
Escitalopram 10mg
(As Escitalopram Oxalate)
Finished Product Specs.: USP.

Description:
E-DYNAPRAM (escitalopram oxalate) is an orally administered selective serotonin reuptake inhibitor (SSRI). Escitalopram is the pure S-enantiomer (single isomer) of the racemic bicyclic phthalane derivative citalopram. Escitalopram oxalate is designated S-(+)-1-[3-(dimethylamino)propyl]-1-(p-fluorophenyl)-5-phthalancarbonitrile oxalate with the following structural formula:



PHARMACOLOGICAL PROPERTIES:
Pharmacodynamic Properties:
The mechanism of antidepressant action of Escitalopram, the S-enantiomer of racemic citalopram, is presumed to be linked to potentiation of serotonergic activity in the central nervous system (CNS) resulting from its inhibition of CNS neuronal reuptake of serotonin (5-HT). In vitro and in vivo studies in animals suggest that Escitalopram is a highly selective serotonin reuptake inhibitor (SSRI) with minimal effects on norepinephrine and dopamine neuronal reuptake. Escitalopram is at least 100-fold more potent than the R-enantiomer with respect to inhibition of 5-HT reuptake and inhibition of 5-HT neuronal firing rate. Escitalopram has no or very low affinity for serotonergic ($5\text{-HT}_{1\text{-}7}$) or other receptors including α and β adrenergic, dopamine ($D_{1\text{-}5}$), histamine ($H_{1\text{-}3}$), muscarinic ($M_{1\text{-}5}$), and benzodiazepine receptors. Antagonism of muscarinic, histaminergic, and adrenergic receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular side effects of other psychotropic drugs.

Pharmacokinetics:
The single and multiple-dose pharmacokinetics of Escitalopram are linear and dose proportional in a dose range of 10 to 30 mg/day. Biotransformation of Escitalopram is mainly hepatic; with a mean terminal half-life of about 27-32 hours. With once daily dosing, steady state plasma concentrations are achieved within approximately one week. At steady state, the extent of accumulation of Escitalopram in plasma in young healthy subjects was 2.2-2.5 times the plasma concentrations observed after a single dose.

Absorption and Distribution:
Following a single oral dose (20mg tablet) of Escitalopram, peak blood levels occur at about 5 hours. Absorption of Escitalopram is not affected by food.
The absolute bioavailability of citalopram is about 80%. The volume of distribution of citalopram is about 12L/kg. Data specific on Escitalopram are unavailable.
The binding of Escitalopram to human plasma proteins is approximately 56%.

Metabolism and Elimination:
Following oral administration of Escitalopram, the fraction of drug recovered in the urine as Escitalopram and S-demethylcitalopram (S-DCT) is about 8% and 10%, respectively. The oral clearance of Escitalopram is 600 mL/min, with approximately 7% of that due to renal clearance. Escitalopram is metabolized to S-DCT and S-didemethylcitalopram (S-DDCT). In humans, unchanged Escitalopram is the predominant compound in plasma. At steady state, the concentration of the Escitalopram metabolite S-DCT in plasma is approximately one - third that of Escitalopram. The level of S-DDCT was not detectable in most subjects. *In vitro* studies show that Escitalopram is at least 7 and 27 times more potent than S-DCT and S-DDCT, respectively, in the inhibition of serotonin reuptake, suggesting that the metabolites of Escitalopram do not contribute significantly to the antidepressant actions of Escitalopram. S-DCT and S-DDCT also have no or very low affinity for serotonergic ($5\text{-HT}_{1\text{-}7}$) or other receptors including alpha- and beta- adrenergic, dopamine ($D_{1\text{-}5}$), histamine ($H_{1\text{-}3}$), muscarinic ($M_{1\text{-}5}$), and benzodiazepine receptors. S-DCT and S-DDCT also do not bind to various ion channels including Na^+, K^+, Cl^-, and Ca^{++} channels.
In vitro studies using human liver microsomes indicated that CYP3A4 and CYP2C19 are the primary isozymes involved in the N-demethylation of Escitalopram.

INDICATIONS AND USAGE
Major Depressive Disorder:
E-DYNAPRAM (Escitalopram) is indicated for the treatment of major depressive disorder.
A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least five of the following nine symptoms: depressed mood, loss of Interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt or suicidal ideation.
The efficacy of ***E-DYNAPRAM*** in hospitalized patients with major depressive disorders has not been adequately studied. Nevertheless, the physician who elects to use ***E-DYNAPRAM*** for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Generalized Anxiety Disorder:
E-DYNAPRAM is indicated for the treatment of Generalized Anxiety Disorder (GAD). Generalized Anxiety Disorder (DSM-IV) is characterized by excessive anxiety and worry (apprehensive expectation) that is persistent for at least 6 months and which the person finds difficult to control. It must be associated with at least 3 of the following symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance. The efficacy of ***E-DYNAPRAM*** in the long-term treatment of GAD, that is, for more than 8 weeks, has not been systematically evaluated. The physician who elects to use ***E-DYNAPRAM*** for extended periods should periodically re- evaluate the long-term usefulness of the drug for the individual patient.

Panic Disorder:
E-DYNAPRAM is also used for the treatment of panic disorder. This disease is characterized by patients developing unexpected attacks of intense panic or anxiety when faced with particular situations or due to the fear of experiencing new attacks. Precisely what triggers the attacks varies from patient to patient. The attacks recur when the patient faces the same situation again.

DOSAGE AND ADMINISTRATION
Major Depressive Disorder:
Initial Treatment
The recommended dose of ***E-DYNAPRAM*** is 10mg once daily. The dose is increased to 20mg, after a minimum of one week.
E-DYNAPRAM should be administered once daily, in the morning or evening, with or without food.
Maintenance Treatment.
It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacological therapy beyond response for the acute episode. Patients should be periodically reassessed to determine the need for maintenance treatment.

Generalized Anxiety Disorder:
Initial Treatment
The recommended starting dose of ***E-DYNAPRAM*** is 10mg once daily. The dose is increased to 20mg after a minimum of one week. ***E-DYNAPRAM*** should be administered once daily, in the morning or evening, with or without food.

Maintenance Treatment
Generalized anxiety Disorder recognized as a chronic condition. The physician who elects to use ***E-DYNAPRAM*** for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Panic Disorder:
The starting dose is 5mg per day for the first week before increasing the dose to 10-15mg per day. The dose may be increased to a maximum of 20mg per day. Patient who are prone to panic attacks may actually experience a temporary period of heightened anxiety after starting treatment which generally resolves during the first 1-2 weeks. Therefore, a low starting dose is recommended in panic disorder.

Elderly Patients:
The usual starting dose is 5mg per day. It is recommended that the maximum dose is kept below 20mg.

Hepatic Impairment:
It is recommended that patients with liver disease receive an initial dose of 5mg daily for the first two weeks. The dose may be increase to 10mg daily.

Renal impairment:
No dosage adjustment is necessary for patients with mild or moderate renal impairment. ***E-DYNAPRAM*** should be used with caution in patients with severe renal impairment.

Children and adolescents (<18 years):
E-DYNAPRAM should not be given to children or adolescents.

Switching Patients To or From a Monoamine Oxidase Inhibitor:
At least 14 days should elapse between discontinuation of an MAOI and initiation of ***E-DYNAPRAM*** therapy. Similarly, at least 14 days should be allowed after stopping ***E-DYNAPRAM*** before starting an MAOI.

CONTRAINDICATIONS:
Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated. Escitalopram is contraindicated in patients with a hypersensitivity to Escitalopram or citalopram or any of the inactive ingredients in Escitalopram.

WARNINGS:
There has been a long standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients. Therefore, all patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality and unusual changes in behaviour, especially during the initial few months of a course of drug therapy, or at times of dose change, either increase or decrease.

PRECAUTIONS:
General
Discontinuation of Treatment with Escitalopram:
Patients should be monitored for these symptoms when discontinuing treatment with Escitalopram. 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.

Hyponatremia
Hyponatremia and SIADH have been reported as seen in association with other marketed drugs effective in the treatment of major depressive disorder.

Activation of Mania/Hypomania
As with all drugs effective in the treatment of major depressive disorder, Escitalopram should be used cautiously in patients with a history of mania.

Seizures
Like other drugs effective in the treatment of major depressive disorder, Escitalopram should be introduced with care in patients with a history of seizure disorder.

Interference with Cognitive and Motor Performance
Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Escitalopram therapy does not affect their ability to engage in such activities.

Use in Patients with Concomitant illness
Clinical experience with Escitalopram in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Escitalopram in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Escitalopram has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease.
In subjects with hepatic impairment, clearance of recemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Escitalopram in hepatically impaired patients is 10mg/day.
Escitalopram is extensively metabolized, therefore, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Escitalopram, however, it should be used with caution in such patients.

Concomitant Administration with Racemic Citalopram
Escitalopram is the active isomer of racemic citalopram, the two agents should not be co- administered.

Drug Interactions:
CNS Drugs-Given the primary CNS effects of Escitalopram, caution should be used when it is taken in combination with other centrally acting drugs. As with other psychotropic medications, the use of alcohol by patients taking Escitalopram is not recommended.

Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin)
Serotonin release by platelets plays an important role in hemostasis. Use of psychotropic drugs interfere with serotonin reuptake and upper gastrointestinal bleeding may occur with their concurrent use with NSAID or aspirin. Thus, patients should be cautioned about the use of such drugs concurrently with Escitalopram.

Lithium-Lithium may enhance the serotonergic effects of Escitalopram, caution should be exercised when Escitalopram and lithium are coadministered. MAO Inhibitors. It is recommended that Escitalopram should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Escitalopram before starting an MAOI.
Digoxin-Combined administration of citalopram and digoxin (single dose of 1mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin.
Warfarin-Prothrombin time was increased by 5%, the clinical significance of which is unknown. Theophylline-combined administration of citalopram and the theophylline (single dose of 300mg) did not affect the pharmacokinetics of theophylline. The effect of theopylline on the pharmacokinetics of citalopram was not evaluated.Sumatriptan-if concomitant treatment with sumatriptan and an SSRI (eg, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, Escitalopram) is clinically warrented, appropriate observation of the patient is advised.
Carbamazepine-Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the Clearance of Escitalopram should be considered if the two drugs are coadministered.
Triazolam-Combined administration of racemic citalopram (titrated to 40mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25mg) does not significantly affects the pharmacokinetics of either citalopram or triazolam.
Ketoconazole Combined administration of racemic citalopram (40mg) and ketoconazole (200mg), a potent CYP3A4 inhibitor, decreases the Cmax and AUC of ketoconazole by 21 % and 10%, respectively, and does not significantly affect the pharmacokinetics of citalopram.
Metoprolol-increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Escitalopram and metoprolol had no clinically significant effects on blood pressure or heart rate.

Pregnancy:
There are no adequate and well-controlled studies in pregnant women; therefore, Escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:
The decision whether to continue or discontinue either nursing or Escitalopram therapy should take into account the risks of Escitalopram exposure for the infant and the benefits of Escitalopram treatment for the mother.

Pediatric Use:
Safety and effectiveness in pediatric patients have not been established.

UNDESIRABLE EFFECTS:
Escitalopram is usually well tolerated, the undesirable events that can occur include insomnia, changes in sexual functions, nausea, sweating increased, fatigue, and somnolence.

Physical and Psychological Dependence:
Physicians should carefully evaluate Escitalopram patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behaviour).

OVERDOSAGE:
Human Experience
There were reports of Escitalopram overdose involving doses of up to 600mg with no associated fatalities. All patients recovered and no symptoms associated with the overdoses were reported. In clinical trials of racemic citalopram, there were no reports of fatalities during citalopram overdoses up to 2000mg.
Symptoms most often accompanying citalopram overdose, alone or in combination with other drugs and/or alcohol, include dizziness, sweating, nausea, vomiting, somnolence, sinus tachycardia, and convulsions. Rarely, symptoms include amnesia, confusion, coma, hyperventilation, cyanosis, rhabdomyolysis, and ECG changes.

Management of Overdose:
Establish and maintain an airway to ensure adequate ventilation and oxygenation. Gastric evacuation by lavage and use of activated charcoal should be considered. Careful observation and cardiac and vital sign monitoring are recommended, along with general symptomatic and supportive care. Due to the large volume of distribution of Escitalopram, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. There are no specific antidotes for Escitalopram. In managing over dosage, consider the possibility of multiple-drug involvement.

Availability:
E-DYNAPRAM 10mg tablet: Pack of 10 Tablets.

Storage Conditions:
- Store below 30ºC.
- Protect from heat, light and moisture.
- Use only on medical advice.
- For oral use only.

Keep all medicines out of the reach of children.

Manufactured by :
Indus Pharma (Pvt.) Ltd.
65/27, Korangi Industrial Area,
Karachi-74900, Pakistan.

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