ESCITALOPRAM OXALATE

MORCET

10 mg Film-Coated Tablet

ANTIDEPRESSANT
(SELECTIVE SEROTONIN REUPTAKE INHIBITOR)

FORMULATION:
Each film-coated tablet contains:
Escitalopram (as oxalate).....10 mg

PRODUCT DESCRIPTION:
Light green-colored, biconvex round shaped, film-coated tablet, engraved SEARLE on one side and breakline on the other side.

PHARMACODYNAMICS:
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. Tolerance to a model of antidepressant effect in rats was not induced by long-term (up to 5 weeks) treatment with Escitalopram. Escitalopram has no or very low affinity for serotonergic (5-HT1-7) or other receptors including alpha-adrenergic and beta-adrenergic, dopamine (D1-5), histamine (H1-3), muscarinic (M1-5), and benzodiazepine receptors. Escitalopram also does not bind to, or has low affinity for, various ion channels including Na+, K+, Cl-, and Ca++ channels. 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 10-30 mg/day. Biotransformation of escitalopram is mainly hepatic with a mean terminal t½ of about 27-32 hrs. With once daily dosing, steady-state plasma concentrations are achieved within approximately 1 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. The tablet and the oral solution dosage forms of Escitalopram oxalate are bioequivalent.

INDICATIONS:
Treatment of depression, panic disorder with or without agoraphobia, generalized and social anxiety disorders, and obsessive-compulsive disorder.

DOSAGE AND ADMINISTRATION:
In the treatment of depression, generalized anxiety disorder, the usual dose is 10 mg once daily, may be increased after at least a week up to maximum of 20 mg once daily, if necessary.

Panic Disorder With or Without Agoraphobia: Initial Dose: 5 mg once daily, may be increased after a week to 10 mg once daily; further increases up to a maximum of 20 mg daily may be necessary in some patients.

Patients with Hepatic Impairment or Poor Metabolizers with Respect to the Cytochrome P450 Isoenzyme CYP2C19: Initial Dose: 5 mg daily, may be increased to 10 mg daily after 2 weeks depending on response.

Elderly: Initial treatment with ½ the usual recommended dose and a lower maximum dose should be considered in elderly patients. Patients with hepatic impairment or those who are poor metabolizers with respect to cytochrome P450 isoenzyme CYP2C19 should also receive an initial dose of 5 mg daily; the dose may be increased to 10 mg daily after 2 weeks or depending on response. Escitalopram should be withdrawn gradually to reduce the risk of withdrawal symptoms. Or as prescribed by the physician.

WARNINGS AND PRECAUTIONS:
Because of its epileptogenic effect, selective serotonin reuptake inhibitors (SSRIs) should be used with caution in patients with epilepsy or a history of such disorders (and should be avoided if the epilepsy is poorly controlled). Treatment should be stopped if seizures develop or when there is an increase in seizure frequency. Care is advised in patients receiving electroconvulsive therapy (ECT) as prolonged seizures have occurred rarely. SSRIs should also be used with caution in patients with cardiac disease or a history of bleeding disorders. Although SSRIs are preferred to tricyclics for the treatment of depression in patients with diabetes, that may alter glycemic control and therefore, caution is also warranted in diabetic subjects. SSRIs should also be used with caution in patients with angle-closure glaucoma.

FERTILITY, PREGNANCY AND LACTATION:
Pregnancy
For Escitalopram only, limited clinical data are available regarding exposed pregnancies.

Animal studies have shown reproductive toxicity. Escitalopram should not be used during pregnancy unless clearly necessary and only after careful consideration of the risk/benefit.

Neonates should be observed if maternal use of Escitalopram continues into the later stages of pregnancy, particularly in the third trimester. Abrupt discontinuation should be avoided during pregnancy.
The following symptoms may occur in the neonate after maternal SSRI/SNRI use in later stages of pregnancy: respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty sleeping. These symptoms could be due to either serotonergic effects or discontinuation symptoms. In a majority of instances the complications begin immediately or soon (<24 hours) after delivery.

Epidemiological data have suggested that the use of SSRIs in pregnancy, particularly in late pregnancy, may increase the risk of persistent pulmonary hypertension in the newborn (PPHN). The observed risk was approximately 5 cases per 1000 pregnancies. In the general population, 1 to 2 cases of PPHN per 1000 pregnancies occur.

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Lactation
It is expected that Escitalopram will be excreted into human milk.
Consequently, breastfeeding is not recommended during treatment.

Fertility
Animal data have shown that Escitalopram may affect sperm quality. Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.

ADVERSE DRUG REACTIONS:
Selective serotonin reuptake inhibitors are less sedating than tricyclic antidepressants (TCAs) and have fewer antimuscarinic and cardiotoxic effects. Adverse effects reported with SSRIs include dry mouth and gastrointestinal disturbances e.g., nausea, vomiting, dyspepsia, constipation and diarrhea. Anorexia and weight loss may also occur. Neurological adverse effects have included either anxiety, restlessness, nervousness, insomnia or drowsiness and fatigue; headache, tremor, dizziness, seizures, hallucinations, confusion, agitation, extrapyramidal effects, depersonalization, mania, panic attacks, sexual dysfunction and symptoms suggestive of a serotonin syndrome have occurred. Excessive sweating, pruritus, skin rashes, alopecia, photosensitivity and urticaria have been reported. Angioedema and anaphylactoid reactions have occurred.

DRUG INTERACTIONS:
Selective serotonin reuptake inhibitors interact with other drugs mainly as a result of its inhibitory activity on hepatic cytochrome P450 isoenzymes. Individual SSRIs do not all exhibit the same degree of inhibition nor react with the isoenzymes. The drugs inhibited by specific SSRIs depend on the isoenzyme affected.
As SSRIs have occasionally been associated with bleeding disorders and other effects on the blood, caution is advised when given with drugs known to affect platelet function.
Although different antidepressants have been used together under expert supervision in refractory cases of depression, severe adverse reactions including the serotonin syndrome may occur.

OVERDOSE AND TREATMENT:
Toxicity
Clinical data on escitalopram overdose are limited and many cases involve concomitant overdoses of other drugs. In the majority of cases mild or no symptoms have been reported. Fatal cases of escitalopram overdose have rarely been reported with Escitalopram alone; the majority of cases have involved overdose with concomitant medications. Doses between 400 mg and 800 mg of Escitalopram alone have been taken without any severe symptoms.

Symptoms
Symptoms seen in reported overdose of escitalopram include symptoms mainly related to the central nervous system (ranging from dizziness, tremor, and agitation to rare cases of serotonin syndrome, convulsion, and coma), the gastrointestinal system (nausea/vomiting), and the cardiovascular system (hypotension, tachycardia, QT interval prolongation, and arrhythmia) and electrolyte/fluid balance conditions (hypokalemia, hyponatremia).

Management
There is no specific antidote. Establish and maintain an airway, ensure adequate oxygenation and respiratory function. Gastric lavage and the use of activated charcoal should be considered. Gastric lavage should be carried out as soon as possible after oral ingestion. Cardiac and vital signs monitoring are recommended along with general symptomatic supportive measures.

ECG monitoring is advised in case of overdose in patients with congestive heart failure/bradyarrhythmias, in patients using concomitant medications that prolong the QT interval, or in patients with altered metabolism, e.g. liver impairment.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

AVAILABILITY:
Alu/Alu Blister Pack x 10's (Box of 30's)

DRP-3790
Date of First Authorization: June 6, 2012
Date of Revision of Package Insert: May 15, 2024

Manufactured by:
The Searle Company Limited
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Distributed by:
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