xxxxxxxx-5343

ESCITALOPRAM

FELIZ S 10
FELIZ S 20

10 mg and 20 mg Film-Coated Tablet
Antidepressant

"Antidepressant increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders and those considering use of these agents must balance risk with the clinical need".

FORMULATION:
Each film-coated tablet contains:
Escitalopram (as Oxalate) ..... 10 mg / 20 mg

DESCRIPTION:
Escitalopram Oxalate is an orally administered selective serotonin reuptake inhibitor (SSRI). The chemical name of Escitalopram Oxalate is S(+)1-[3-(dimethyl amino) propyl]-1-(4-fluorophenyl)-1, 3-dihydro-5-isobenzofuran (oxalate salt). Its molecular formula is $C_{20}H_{21}FN_2O$ (Base) and $C_{20}H_{21}FN_2O.C_2H_2O_4$ (oxalate salt) and its molecular weight is 324.40 (base) and 414.42 (oxalate salt).
Escitalopram Oxalate (Feliz S 10) Film-Coated Tablet is a white to off white, round, binconvex, film-coated tablet, debossed with breakline on both sides, separating "11" and "36" on one side and "10" on other side.
Escitalopram Oxalate (Feliz S 20) Film-Coated Tablet is a white to off white, round, binconvex, film-coated tablet, debossed with breakline on both sides, separating "11" and "37" on one side and "20" on 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 resulting from its inhibition of CNS neuronal reuptake of serotonin (5-HT). 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-HT1-7) or other receptors including alpha-and beta-adrenergic, dopamine (D-1-5), histamine (H1-3), muscarinic (M-1-5) 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.

PHARMACOKINETIC:
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, the mean Tmax was 5+1.5 hours. Absorption of Escitalopram is not affected by food. The absolute bioavailability of citalopram is about 80% relative to an intravenous dose, and the volume of distribution of citalopram is about 12L/kg. Data specific to Escitalopram are unavailable. The binding of Escitalopram to human plasma proteins is approximately 56%.

Metabolism and Elimination:
Following oral administrations of Escitalopram, the fraction of drug recovered in the urine as Escitalopram and S-demethycitalopram (S-DCT) is about 8% and 10% respectively. The oral clearance of the Escitalopram is 600 mL/min, with approximately7% 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 Escitalopram metabolite S-DCT in plasma is approximately one-third that of Escitalopram. CYP3A4 and CYP2C19 are the primary isozymes involved in the demethylation of Escitalopram.

Population Subgroups:
Age Escitalopram AUC and half-life is increased by approximately 50% in elderly subjects, and Cmax is unchanged. 10mg is the recommended dose for elderly.

Gender:
There are no differences in AUC, Cmax and half-life between the male and female subjects so no adjustment of dosage on the basis of gender is needed.

Reduced renal function:
In patients with mild to moderate renal function impairment, oral clearance of citalopram was reduced by 17% compared to normal subjects. No adjustment of dosage for such patients is recommended. No information is available about the pharmacokinetics of Escitalopram in patients with severely reduced renal function (creatinine clearance <20mL/min).

Reduced Hepatic function:
Citalopram oral clearance was reduced by 37% and half life was doubled in patients with reduced hepatic function compared to normal subjects. 10 mg is recommended dose of Escitalopram for most hepatically impaired patients.

INDICATION:
Used for the management of generalised anxiety disorder, obsessive-compulsive disorder, panic disorder with or without agoraphobia, social phobia, and post- traumatic stress disorder.

DOSAGE AND METHOD OF ADMINISTRATION:

Initial Treatment: (Adults)
The recommended dose of Escitalopram is 10mg once daily. If the dose is increased to 20mg, this should occur after a minimum of one week. Escitalopram should be administered daily, in the morning or evening, with or without food.

Special Populations:
An initial dose of 5mg daily for the first two weeks of treatment is recommended dose for most elderly patients and patients with hepatic impairment. Depending on individual patient response, the dose may be increased to 10mg/day. No dosage adjustments are necessary for patients with mild or moderate renal impairment. Escitalopram should be used with caution in patients with severe renal impairment.

Maintenance Treatment:
Systematic evaluation of continuing Escitalopram 10 or 20 mg/day for periods of up to 36 weeks in patients with major depressive disorder who responded while taking Escitalopram during and 8-week acute treatment phase demonstrated a benefit of such maintenance treatment.

Panic disorder with or without agoraphobia:
An initial dose of 5mg is recommended for the first week before increasing the dose to 10mg daily. The dose may be increased up to a maximum of 20mg daily, dependent on individual patient response.

Switching Patients To or From a Monoamine Oxidase Inhibitor
At least 14 days should elapse between discontinuation of an MAOI and inhibition of Escitalopram before starting a MAOI.
Or as prescribed by the physician.

WITHDRAWAL:
Escitalopram should be withdrawn gradually to reduce the risk of withdrawal symptoms.

CONTRAINDICATIONS:
Monoamine oxidase inhibitors (MAOIs) Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated.
Pimozide Concomitant use in patients taking pimozide is contraindicated.
Hypersensitivity to escitalopram or citalopram Contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients of Escitalopram (Feliz S) film-coated tablet.

WARNING:
General:
Serotonin Syndrome The development of a potentially life-threatening serotonin syndrome has been reported with SNRIs and SSRIs, including escitalopram oxalate, alone but particularly with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination) seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome.
The concomitant use of escitalopram oxalate with MAOIs intended to treat psychiatric disorders is contraindicated. Treatment with escitalopram oxalate and any concomitant serotonergic agents, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.

Suicide
The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high risk patients should accompany initial drug therapy.

PRECAUTIONS

Hyponatremia
Several cases of hyponatremia or SIADH (syndrome of inappropriate antidiuretic hormone secretion) have been reported in association with racemic citalopram. All patients with these events have recovered with discontinuation of Escitalopram or citalopram and/or medical intervention.

Activation of Mania / Hypomania
Activation of mania / hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. Escitalopram should be used cautiously in patients with a history of mania.

Seizures
Escitalopram has not been systemically evaluated in patients with a seizure disorder. 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.

Use in Patients with Concomitant Illness
Caution is advisable in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Escitalopram has not been systematically evaluated tin patients with a recent history of myocardial infarction or unstable heart disease.
In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Escitalopram in hepatically impaired patients is 10 mg / day.

PREGNANCY AND LACTATION:
Pregnancy Category C
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.
Labor and Delivery: The effect of Escitalopram on labor and delivery in humans is unknown.
Nursing Mothers: There have been two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in associated with breast feeding from a citalopram treated mother; in one case, the infant was reported to recover completely upon discontinuation of citalopram by its mother and, in the second case, no follow up information was available. The decision whether to continue or discontinue either nursing or Escitalopram therapy should take into account the risks of citalopram 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.

DRUG INTERACTIONS:
CNS Drugs Due to CNS effects of Escitalopram, caution should be used when it is taken in combination with other centrally acting drugs.
Alcohol Although racemic citalopram did not potentiate the congnitive and motor effects of alcohol, the use of alcohol by patients taking Escitalopram is not recommended.
Lithium May enhance the serotonergic effects of Escitalopram, caution should be exercised when Escitalopram and lithium are co-administered.
Sumatriptan There have been rare reports of weakness, hyperreflexia and in-coordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment of sumatriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised.
Ketoconazole Combined administration of racemic citalopram (40mg), and Ketoconazole (200mg) decreased the Cmax, and AUC of Ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram.
CYP3A4 and - 2C19 inhibitors The metabolism of escitalopram is mainly mediated by CYP2C19 and CYP3A4 may also contribute to the metabolism although to a smaller extent. Co-administration of escitalopram with omeprazole 30 mg once daily (a CYP2C19 inhibitor) resulted in moderate (approximately 50%) increase in the plasma concentrations of escitalopram. Co-administration of escitalopram with cimetidine 400 mg twice daily (moderately potent general enzyme-inhibitor) resulted in a moderate (approximately 70%) increase in the plasma concentrations of escitalopram.
Thus, caution should be exercised when used concomitantly with CYP2C19 inhibitors (e.g. omeprazole, esomeprazole, fluvoxamine, lansoprazole, ticlopidine) or cimetidine. A reduction in the dose of escitalopram may be necessary based on monitoring of side-effects during concomitant treatment.
Drugs Metabolized by Cytochrome P4502D6 Escitalopram is an inhibitor of the enzyme CYP2D6. Caution is recommended when escitalopram is co-administered with medicinal products that are mainly metabolized by this enzyme, and that have a narrow therapeutic index, e.g. flecainide, propafenone and metoprolol (when used in cardiac failure), or some CNS acting medicinal products that are mainly metabolised by CYP2D6, e.g. antidepressants such as desipramine, clomipramine and nortriptyline or antipsychotics like risperidone, thioridazine and haloperidol. Dosage adjustment may be warranted. Co-administration with desipramine cases in a twofold increase in the plasma levels of desipramine.
Metoprolol Administration of 20 mg/day Escitalopram for 21 days resulted in a 50% increase in Cmax and 82% increase in AUC of the beta-adrenergic blocker Metoprolol (given in a single dose of 100 mg). Increased Metoprolol plasma levels have been associated with decreased cardio-selectivity. Co-administration of Escitalopram and Metoprolol had no clinically significant effects on blood pressure or heart rate. .

ADVERSE EFFECTS:
Adverse reactions are most frequent during the first or second week of treatment and usually decrease in intensity and frequency with continued treatment.

Tabulated list of adverse reactions
Adverse reactions known for SSRIs and also reported for escitalopram in either placebo-controlled clinical studies or as spontaneous post-marketing events are listed below by system organ class and frequency.
Frequencies are taken from clinical studies; they are not placebo-corrected. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), or not known (cannot be estimated from the available data).

System organ class	Frequency	Undesirable Effect
Blood and lymphatic system disorders	Not known	Thrombocytopenia
Immune system disorders	Rare	Anaphylactic reaction
Endocrine disorders	Not known	Inappropriate ADH secretion
Metabolism and nutrition disorders	Common	Decreased appetite, increased appetite, weight increased
	Uncommon	Weight decreased
	Not known	Hyponatraemia, anorexia[1]
Psychiatric disorders	Common	Anxiety, restlessness, abnormal dreams libido decreased Female: anorgasmia
	Uncommon	Bruxism, agitation, nervousness, panic attack, confusional state
	Rare	Aggression, depersonalisation, hallucination
	Not known	Mania, suicidal ideation, suicidal behaviour[2]
Nervous system disorders	Very common	Headache
	Common	Insomnia, somnolence, dizziness, paraesthesia, tremor
	Uncommon	Taste disturbance, sleep disorder, syncope
	Rare	Serotonin syndrome
	Not known	Dyskinesia, movement disorder, convulsion, psychomotor restlessness/akathisia[1]
Eye disorders	Uncommon	Mydriasis, visual disturbance
Ear and labyrinth disorders	Uncommon	Tinnitus
Cardiac disorders	Uncommon	Tachycardia
	Rare	Bradycardia
	Not known	Electrocardiogram QT prolonged Ventricular arrhythmia including torsade de pointes
Vascular disorders	Not known	Orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Common	Sinusitis, yawning
	Uncommon	Epistaxis
Gastrointestinal disorders	Very common	Nausea
	Common	Diarrhoea, constipation, vomiting, dry mouth
	Uncommon	Gastrointestinal haemorrhages (including rectal haemorrhage)
Hepatobiliary disorders	Not known	Hepatitis, liver function test abnormal
Skin and subcutaneous tissue disorders	Common	Sweating increased
	Uncommon	Urticaria, alopecia, rash, pruritus
	Not known	Ecchymosis, angioedemas
Musculoskeletal and connective tissue disorders	Common	Arthralgia, myalgia
Renal and urinary disorders	Not known	Urinary retention
Reproductive system and breast disorders	Common	Male: ejaculation disorder, impotence
	Uncommon	Female: metrorrhagia, menorrhagia
	Not known	Galactorrhoea
		Male: priapism
General disorders and administration site conditions	Common	Fatigue, pyrexia
	Uncommon	Oedema

[1] These events have been reported for the therapeutic class of SSRIs.
[2] Cases of suicidal ideation and suicidal behaviours have been reported during escitalopram therapy or early after treatment discontinuation.
"For Suspected Adverse Reaction, report to FDA: www.fda.gov.ph or to Torrent: www.torrentpharma.com".
Patient must seek medical attention immediately at the first sign of any adverse drug reaction shall appear.

OVERDOSAGE AND TREATMENT:
Symptoms most often accompanying ecitalopram overdose, alone or in combination with other drugs and/or alcohol, included convulsions, coma, dizziness, hypotension, insomnia, nausea, vomiting, sinus tachycardia, somnolence, and ECG changes (including QT prolongation and very rare cases of torsade de pointes). Acute renal failure has been very rarely reported accompanying overdose.
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 overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose.

STORAGE:
Store at temperatures not exceeding 30°C.
KEEP OUT OF REACH AND SIGHT OF CHILDREN.

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

AVAILABILITY:
Escitalopram Oxalate (FELIZ S 10) 10 mg Film- Coated Tablet Alu-Alu blister pack of 10's (Box of 100's)- DRP-3538
Escitalopram Oxalate (FELIZ S 20) 20 mg Film-Coated Tablet Alu-Alu blister pack of 10's (Box of 100's) - DRP-3539

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April 2017

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
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Imported and Distributed by :
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Makati City, PHILIPPINES

PRODUCT NAME	:	Feliz S	**COUNTRY :** Philippines	**LOCATION :** Chhatral	**Supersedes A/W No.:**	
ITEM / PACK	:	Insert	**NO. OF COLORS:** 1	**REMARK : Folded Size 30 mm**		
DESIGN STYLE	:	-	**PANTONE SHADE NOS.:**	**SUBSTRATE :**		
CODE	:	xxxxxxxx-5343	■ Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM)	:	150 x 370		Prepared By	**Pkg.Dev**			
ART WORK SIZE	:	S/S		Reviewed By	**Pkg.Dev**			
DATE	:	07-10-2017		Approved By	**Quality**			

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.