CITALIN®

℞
Escitalopram Tablets USP 5/10 mg

COMPOSITION:
CITALIN® 5
Each Film Coated Tablet Contains:
Escitalopram Oxalate USP
Eq. to Escitalopram..... 5 mg
Excipients q.s.
Colour: Yellow Oxide of Iron & Titanium Dioxide BP

CITALIN® 10
Each Film Coated Tablet Contains:
Escitalopram Oxalate USP
Eq. to Escitalopram.....10 mg
Excipients q.s.
Colour: Titanium Dioxide BP

DESCRIPTION:
CITALIN® 5/10 contains Escitalopram Oxalate for the treatment of major depressive episodes.

PHARMACODYNAMICS:
Pharmacotherapeutic group: antidepressants, selective serotonin reuptake inhibitors
ATC-code: N 06 AB 10
Mechanism of action
Escitalopram is a selective inhibitor of serotonin (5-HT) re-uptake with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter, with a 1000 fold lower affinity.
Escitalopram has no or low affinity for a number of receptors including 5-HT1A, 5-HT2, DA D1 and D2 receptors, α1-, α2-, β-adrenoceptors, histamine H1, muscarine cholinergic,benzodiazepine, and opioid receptors.
The inhibition of 5-HT re-uptake is the only likely mechanism of action explaining the pharmacological and clinical effects of escitalopram.

PHARMACOKINETICS:
Absorption
Absorption is almost complete and independent of food intake. (Mean time to maximum concentration (mean Tmax) is 4 hours after multiple dosing).
As with racemic citalopram, the absolute bioavailability of escitalopram is expected to be about 80%.
Distribution
The apparent volume of distribution (Vd,β/F) after oral administration is about 12 to 26 L/kg. The plasma protein binding is below 80% for escitalopram and its main metabolites.
Biotransformation
Escitalopram is metabolised in the liver to the demethylated and didemethylated metabolites. Both of these are pharmacologically active. Alternatively, the nitrogen may be oxidised to form the N-oxide metabolite. Both parent substance and metabolites are partly excreted as glucuronides. After multiple dosing the mean concentrations of the demethyl and didemethyl metabolites are usually 28-31% and <5%, respectively, of the escitalopram concentration. Biotransformation of escitalopram to the demethylated metabolite is mediated primarily by CYP2C19. Some contribution by the enzymes CYP3A4 and CYP2D6 is possible.
Elimination
The elimination half-life ($t_{½}$ β) after multiple dosing is about 30 hours and the oral plasma clearance (Cl_{oral}) is about 0.6 L/min. The major metabolites have a significantly longer half-life. Escitalopram and major metabolites are assumed to be eliminated by both the hepatic (metabolic) and the renal routes, with the major part of the dose excreted as metabolites in the urine.

THERAPEUTIC INDICATIONS:
Treatment of major depressive episodes.
Treatment of panic disorder with or without agoraphobia.
Treatment of social anxiety disorder (social phobia).
Treatment of generalised anxiety disorder.
Treatment of obsessive-compulsive disorder.

POSOLOGY AND METHOD OF ADMINISTRATION:
Posology
Safety of daily doses above 20 mg has not been demonstrated.
Major depressive episodes:
Usual dosage is 10 mg once daily. Depending on individual patient response, the dose may be increased to a maximum of 20 mg daily.
Usually 2-4 weeks are necessary to obtain antidepressant response. After the symptoms resolve, treatment for at least 6 months is required for consolidation of the response.
Panic disorder with or without agoraphobia:
An initial dose of 5 mg is recommended for the first week before increasing the dose to 10 mg daily. The dose may be further increased, up to a maximum of 20 mg daily, dependent on individual patient response.
Maximum effectiveness is reached after about 3 months. The treatment lasts several months.
Social anxiety disorder:
Usual dosage is 10 mg once daily. Usually 2-4 weeks are necessary to obtain symptom relief. The dose may subsequently, depending on individual patient response, be decreased to 5 mg or increased to a maximum of 20 mg daily.
Social anxiety disorder is a disease with a chronic course, and treatment for 12 weeks is recommended to consolidate response. Long-term treatment of responders has been studied for 6 months and can be considered on an individual basis to prevent relapse; treatment benefits should be re-evaluated at regular intervals.
Social anxiety disorder is a well-defined diagnostic terminology of a specific disorder, which should not be confounded with excessive shyness. Pharmacotherapy is only indicated if the disorder interferes significantly with professional and social activities.
The place of this treatment compared to cognitive behavioural therapy has not been assessed. Pharmacotherapy is part of an overall therapeutic strategy.
Reduced hepatic function:
An initial dose of 5 mg daily for the first two weeks of treatment is recommended in patients with mild or moderate hepatic impairment. Depending on individual patient response, the dose may be increased to 10 mg daily. Caution and extra careful dose titration is advised in patients with severely reduced hepatic function.

Method of administration
CITALIN® 5/10 is administered as a single daily dose and may be taken with or without food.

CONTRAINDICATION:
Hypersensitivity to the active substance or to any of the excipients
Concomitant treatment with non-selective, irreversible monoamine oxidase inhibitors (MAO-inhibitors) is contraindicated due to the risk of serotonin syndrome with agitation, tremor, hyperthermia etc.
The combination of escitalopram with reversible MAO-A inhibitors (e.g. moclobemide) or the reversible non-selective MAO-inhibitor linezolid is contraindicated due to the risk of onset of a serotonin syndrome .
Escitalopram is contraindicated in patients with known QT interval prolongation or congenital long QT syndrome.
Escitalopram is contraindicated together with medicinal products that are known to prolong the QT interval .

SPECIAL WARNING AND PRECAUTION FOR USE:
The following special warnings and precautions apply to the therapeutic class of SSRIs (Selective Serotonin Re-uptake Inhibitors).
Paediatric population
CITALIN® 5/10 should not be used in the treatment of paediatric population. Suicide related behaviours (suicide attempt and suicidal thoughts), and hostility (predominately aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among the paediatric population treated with antidepressants compared to those treated with placebo. If, based on clinical need, a decision to treat is nevertheless taken, the patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long-term safety data in the paediatric population concerning growth, maturation and cognitive and behavioural development are lacking.
Seizures
scitalopram should be discontinued if a patient develops seizures for the first time, or if there is an increase in seizure frequency (in patients with a previous diagnosis of epilepsy). SSRIs should be avoided in patients with unstable epilepsy, and patients with controlled epilepsy should be closely monitored.
Mania
SSRIs should be used with caution in patients with a history of mania/hypomania. SSRIs should be discontinued in any patient entering a manic phase.
Diabetes
In patients with diabetes, treatment with an SSRI may alter glycaemic control (hypoglycaemia or hyperglycaemia). Insulin and/or oral hypoglycaemic dosage may need to be adjusted.
Coronary heart disease
Due to limited clinical experience, caution is advised in patients with coronary heart disease.
ECT (electroconvulsive therapy):
There is limited clinical experience of concurrent administration of SSRIs and ECT, therefore caution is advisable

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Pharmacodynamic interactions :
Contraindicated combinations:
Irreversible non-selective MAOIs:
Cases of serious reactions have been reported in patients receiving an SSRI in combination with a non-selective, irreversible monoamine oxidase inhibitor (MAOI), and in patients who have recently discontinued SSRI treatment and have been started on such MAOI treatment. In some cases, the patient developed serotonin syndrome .
Escitalopram is contraindicated in combination with non-selective, irreversible MAOIs. Escitalopram may be started 14 days after discontinuing treatment with an irreversible MAOI. At least 7 days should elapse after discontinuing escitalopram treatment, before starting a non-selective, irreversible MAOI.
Reversible, selective MAO-A inhibitor (moclobemide):
Due to the risk of serotonin syndrome, the combination of escitalopram with a MAO-A inhibitor such as moclobemide is contraindicated .If the combination proves necessary, it should be started at the minimum recommended dosage and clinical monitoring should be reinforced.
Reversible, non-selective MAO-inhibitor (linezolid):
The antibiotic linezolid is a reversible non-selective MAO-inhibitor and should not be given to patients treated with escitalopram. If the combination proves necessary, it should be given with minimum dosages and under close clinical monitoring .
Irreversible, selective MAO-B inhibitor (selegiline):
In combination with selegiline (irreversible MAO-B inhibitor), caution is required due to the risk of developing serotonin syndrome. Selegiline doses up to 10 mg/day have been safely co-administered with racemic citalopram.
QT interval prolongation:
Pharmacokinetic and pharmacodynamic studies of escitalopram combined with other medicinal products that prolong the QT interval have not been performed. An additive effect of escitalopram and these medicinal products cannot be excluded. Therefore, co-administration of escitalopram with medicinal products that prolong the QT interval, such as Class IA and III antiarrhythmics, antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial agents (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarial treatment particularly halofantrine), certain antihistamines (e.g. astemizole, hydroxyzine, mizolastine), is contraindicated.
Combinations requiring precautions for use:
Serotonergic medicinal products:
Co-administration with serotonergic medicinal products (e.g. tramadol, sumatriptan and other triptans) may lead to serotonin syndrome.
Medicinal products lowering the seizure threshold:
SSRIs can lower the seizure threshold. Caution is advised when concomitantly using other medicinal products capable of lowering the seizure threshold (e.g antidepressants (tricyclics, SSRIs), neuroleptics (phenothiazines, thioxanthenes and butyrophenones), mefloquin, bupropion and tramadol).
Lithium, tryptophan:
There have been reports of enhanced effects when SSRIs have been given together with lithium or tryptophan, therefore concomitant use of SSRIs with these medicinal products should be undertaken with caution.
Alcohol:
No pharmacodynamic or pharmacokinetic interactions are expected between escitalopram and alcohol. However, as with other psychotropic medicinal products, the combination with alcohol is not advisable.
Pharmacokinetic interactions:
Influence of other medicinal products on the pharmacokinetics of escitalopram
The metabolism of escitalopram is mainly mediated by CYP2C19. CYP3A4 and CYP2D6 may also contribute to the metabolism although to a smaller extent. The metabolism of the major metabolite S-DCT (demethylated escitalopram) seems to be partly catalysed by CYP2D6.
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. Caution is advised when administering escitalopram in combination with cimetidine. Dose adjustment may be warranted.
Thus, caution should be exercised when used concomitantly with CYP2C19 inhibitors (e.g. omeprazole, esomeprazole, fluconazole, fluvoxamine, lansoprazole, ticlopidine) or cimetidine. A reduction in the dose of escitalopram may be necessary based on monitoring of side-effects during concomitant treatment .
Effect of escitalopram on the pharmacokinetics of other medicinal products
Escitalopram is an inhibitor of the enzyme CYP2D6. Caution is recommended when escitalopram is co-administered with medicinal products that are mainly metabolised 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 or metoprolol resulted in both cases in a twofold increase in the plasma levels of these two CYP2D6 substrates.
In vitro studies have demonstrated that escitalopram may also cause weak inhibition of CYP2C19. Caution is recommended with concomitant use of medicinal products that are metabolised by CYP2C19.

PREGNACY AND LACTATION
Pregnancy
For escitalopram only limited clinical data are available regarding exposed pregnancies.
Animal studies have shown reproductive toxicity . CITALIN® 5/10 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 CITALIN® 5/10 continues into the later stages of pregnancy, particularly in the third trimester. Abrupt discontinuation should be avoided during pregnancy.
Breast-feeding
It is expected that escitalopram will be excreted into human milk.
Consequently, breast-feeding is not recommended during treatment.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Although escitalopram has been shown not to affect intellectual function or psychomotor performance, any psychoactive medicinal product may impair judgement or skills. Patients should be cautioned about the potential risk of an influence on their ability to drive a car and operate machinery.

UNDESIRABLE 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
QT interval prolongation
Cases of QT interval prolongation and ventricular arrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT interval prolongation or other cardiac diseases.
Class effects
Epidemiological studies, mainly conducted in patients 50 years of age and older, show an increased risk of bone fractures in patients receiving SSRIs and TCAs. The mechanism leading to this risk is unknown.
Discontinuation symptoms seen when stopping treatment
Discontinuation of SSRIs/SNRIs (particularly when abrupt) commonly leads to discontinuation symptoms. Dizziness, sensory disturbances (including paraesthesia and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances are the most commonly reported reactions. Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when escitalopram treatment is no longer required, gradual discontinuation by dose tapering should be carried out .
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

OVERDOSE:
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 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 (hypokalaemia, hyponatraemia).
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.

INCOMPATIBILITY:
Not applicable.

SHELF LIFE:
36 months

PACKAGING:
10 Tablets are packed in Alu-Alu Blister & such 3 Blister are packed in printed carton along with pack insert.

STORAGE CONDITION:
Stored at a temperature not exceeding 30°C. Protect from light and moisture.
Keep the medicine out of reach of children.

Marketed by:

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