SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT:

ESCIGRESS 5 (Escitalopram Tablets USP 5 mg)

Strength: 5 mg

Pharmaceutical form: Tablet

Yellow, round, biconvex film coated tablet plain on both sides.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each Film Coated Tablet Contains:
Escitalopram Oxalate USP
eq. to Escitalopram 5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM: Tablet

Yellow, round, biconvex film coated tablet plain on both sides.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Labelled indications include major depressive disorder (MDD) and generalized anxiety disorder (GAD).

4.2 Posology and method of administration:

Escitalopram should be administered once daily, in the morning or evening, with or without food.

Major Depressive Disorder:

Initial Treatment:

Adolescents: The recommended dose of Escitalopram is 10 mg once daily. A flexible-dose trial of Escitalopram (10 to 20 mg/day) demonstrated the effectiveness of Escitalopram. If the dose is increased to 20 mg, this should occur after a minimum of three weeks.

Adults: The recommended dose of Escitalopram is 10 mg once daily. If the dose is increased to 20 mg, this should occur after a minimum of one week.

Maintenance Treatment:

It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacological therapy beyond response to the acute episode. Systematic evaluation of continuing Escitalopram 10 or 20 mg/day in adults patients with major

depressive disorder who responded while taking Escitalopram during an 8-week, acute-treatment phase demonstrated a benefit of such maintenance treatment.

Generalized Anxiety Disorder:

Adults: The recommended starting dose of Escitalopram is 10 mg once daily. If the dose is increased to 20 mg, this should occur after a minimum of one week.

4.3 Contraindications:

Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated.

4.4 Special warnings and precautions for use:

WARNING:

Clinical Worsening and Suicide Risk:

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

Potential for Interaction with Monoamine Oxidase Inhibitors:

In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome.

Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms.

PRECAUTION:

General

Discontinuation of Treatment:
Patients should be monitored for the 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.

Abnormal Bleeding:
Patients should be cautioned about the risk of bleeding associated with the concomitant use of escitalopram and NSAIDs, aspirin, or other drugs that affect coagulation.

Hyponatremia:
Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death.

Use in Patients with Concomitant Illness:
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 racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of escitalopram in hepatically impaired patients is 10 mg/day.
Patients should be cautioned about the concomitant use of escitalopram and NSAIDs, aspirin, warfarin, or other drugs that affect coagulation since combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding.

4.5 Interaction with other medicinal products and other

forms of interaction: Serotonergic Drugs:
The concomitant use of escitalopram with other SSRIs, SNRIs or tryptophan is not
recommended.
Triptans: There have been rare post marketing reports of serotonin syndrome with use of an SSRI and a triptan.
CNS Drugs - Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally acting drugs.
Alcohol - Although escitalopram did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking escitalopram is not recommended.

Drugs That Interfere with Hemostasis:
Patients receiving warfarin therapy should be carefully monitored when escitalopram is initiated or discontinued.
Sumatriptan - There have been rare post marketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan.

Electroconvulsive Therapy (ECT) - There are no clinical studies of the combined use of ECT and escitalopram.
Carcinogenesis: The relevance of the findings to humans is unknown.
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.

Pregnancy-Nonteratogenic Effects

When treating a pregnant woman with escitalopram during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment.

Labor and Delivery

The effect of escitalopram on labor and delivery in humans is unknown.

Nursing Mothers

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 the pediatric population have not been established. Anyone considering the use of escitalopram in a child or adolescent must balance the potential risks with the clinical need.

4.6 Fertility, pregnancy, and lactation.

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.

Pregnancy-Nonteratogenic Effects

When treating a pregnant woman with escitalopram during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment.

Labor and Delivery

The effect of escitalopram on labor and delivery in humans is unknown.

Nursing Mothers

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.

4.7 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.

4.8 Undesirable effects

Adverse Events Associated with Discontinuation of Treatment:

The most commonly observed adverse events were insomnia,

ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence.

Dose Dependency of Adverse Events:

The potential dose dependency of common adverse events are diarrhea, nausea, mouth dryness, dizziness, insomnia, nasopharyngitis, and dyspepsia.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

Human Experience:

During the postmarketing evaluation of escitalopram, overdoses involving overdoses of over
1000 mg have been reported. As with other SSRIs, a fatal outcome in a patient who has taken an overdose of escitalopram has been rarely reported.

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.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Selective serotonin reuptake inhibitors
ATC code: N06AB10

5.1 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).

Escitalopram has no or very low affinity for serotonergic (5-HT1-7) or other receptors including alpha- and betaadrenergic, dopamine (D1-5), histamine (H1-3), muscarinic (M1-5), and benzodiazepine receptors. Escitalopram 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.

5.2 Pharmacokinetic properties

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 (20 mg tablet or solution) 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% relative toan intravenous dose, and the volume of distribution of citalopram is about 12 L/kg. 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 Sdemethylcitalopram (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 Sdidemethylcitalopram (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.

5.3 Preclinical safety data

Psychopharmacology
June 2003, Volume 167, Issue 4, pp 353–362
Escitalopram, the *S*-(+)-enantiomer of citalopram, is a selective serotonin reuptake inhibitor with potent effects in animal models predictive of antidepressant and anxiolytic activities
C. Sánchez, P. B. F. Bergqvist, L. T. Brennum, S. Gupta, S. Hogg, A. Larsen, O. Wiborg
Original Investigation
DOI: 10.1007/s00213-002-1364-z
Cite this article as:
Sánchez, C., Bergqvist, P.B.F., Brennum, L.T. et al. Psychopharmacology (2003) 167: 353. doi:10.1007/s00213-002-1364-z Abstract
Objective
The pharmacological profile of escitalopram, the *S*-(+)-enantiomer of citalopram, was studied and compared with citalopram and the *R*-(−)-enantiomer, *R*-citalopram.
Methods

Inhibition of the serotonin transporter (5-HTT) was studied in COS-1 cells expressing the human 5-HTT (h-5-HTT) and in rat brain synaptosomes. In vitro selectivity was studied relative to noradrenaline transporter (NAT) and dopamine transporter (DAT) function in rat brain synaptosomes, and affinities for other binding sites were determined. In vivo 5-HT activity was measured as inhibition of neuronal firing rate in rat dorsal raphe nucleus (DRN) and enhancement of 5-hydroxytryptophan (5-HTP)-induced behaviour (mouse and rat). Furthermore, studies were conducted in models of antidepressant (mouse forced-swim test), anxiolytic [foot-shock-induced ultrasonic vocalization (USV) in adult rats and mouse black and white box] and anti-aggressive activity (socially isolated mice).

Results

Escitalopram inhibited 5-HTT functions approximately 2 times more potently than citalopram and at least 40 times more potently than *R*-citalopram. Escitalopram showed insignificant activity at other monoamine transporters and 144 other binding sites. Escitalopram inhibited 5-HT neuronal firing in DRN and potentiated 5-HTP-induced behaviours more potently than citalopram; *R*-citalopram was inactive. Escitalopram and citalopram, but not R-citalopram, reduced forced swimming - induced immobility and facilitated exploratory behaviour in the black and white box. Escitalopram and citalopram inhibited USV potently; *R*-citalopram was several times less potent. Escitalopram, citalopram and *R*-citalopram inhibited aggressive behaviour weakly. Escitalopram and citalopram had very potent antiaggressive effects when co-administered with l-5-HTP.

Conclusion

Escitalopram is a very selective 5-HT reuptake inhibitor. It is more potent than its racemate citalopram and is effective in animal models predictive of antidepressant and anxiolytic activities.

Keywords

Escitalopram5-HT uptake inhibition Anxiety Depression Aggression Rodents

References

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2. Blier P, de Montigny C (1997) Current advances and trends in the treatment of depression. Trends Pharmacol Sci 15:220–226

3. Borsini F (1995) Role of the serotonergic system in the forced swimming test. Neurosci Biobehav Rev 19:377–395

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The number of granule cells in rat hippocampus is reduced after chronic mild stress and re-established after chronic escitalopram treatment

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Abstract
Stress and depression cause structural changes in the hippocampal formation. Some of these can be reversed by chronic antidepressant treatment. In the present study, we examined the changes in the total number of granule cells and the volume of the granule cell layer after exposing rats to chronic mild stress and chronic escitalopram treatment. Furthermore, we investigated which classes of immature granule cells are affected by stress and targeted by escitalopram. Rats were initially exposed to 2 weeks of CMS and 4 weeks of escitalopram treatment with concurrent exposure to stress. The behavioral changes, indicating a decrease in sensitivity to a reward, were assessed in terms of sucrose consumption. We found a significant 22.4% decrease in the total number of granule cells in the stressed rats. This decrease was reversed in the stressed escitalopram treated rats that responded to the treatment, but not in the rats that did not respond to escitalopram treatment. These changes were not followed by alterations in the volume of the granule cell layer. We also showed a differential regulation of dentate neurons, in different stages of development, by chronic stress and chronic escitalopram treatment. Our study shows that the anhedonia-like state in the CMS rats is associated with a reduced number of granule cells. We conclude that escitalopram acts on specific cellular targets during neuronal differentiation and that recovery from anhedonia-like behavior in rats may be the consequence of an escitalopram mediated increase in specific subtypes of immature dentate neurons.
Keywords
Chronic mild stress; Depression; Hippocampus; Escitalopram; Granule cells; Stereology

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients

Sr. No.	Name of Excipient
1.	Microcrystalline cellulose 102
2.	Silicified Microcrystalline Cellulose
3.	Purified Talc
4.	Croscarmellose Sodium
5.	Magnesium Stearate

6.	Hypromellose 15cps
7.	Ferric Oxide (Yellow)
8.	Polyethylene Glycol 6000
9.	Titanium Dioxide
10.	Isopropyl Alcohol
11.	Dichloromethane

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

24 months

6.4 Special precautions for storage:

Store at a temperature not exceeding 30°C. Protect from light and moisture.

6.5 Nature and contents of the container:

1) 10 tablets in a blister, 10 such blisters are packed in a primary carton along with the package insert.
2) 10 tablets in a blister, 3 such blisters are packed in a primary carton along with the package insert.
3) 10 tablets in a blister, 1 such blister is packed in a primary carton along with the package insert.
4) 10 tablets in a blister, 1 such blister is packed in a monocarton along with package insert. Such 10 monocartons are packed in an outer carton.

6.6 Special precautions for disposal <and other handling>:

Not applicable

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

MARKETING AUTHORIZATION HOLDER

La Renon Healthcare Pvt. Ltd
207-208, ISCON Elegance, Circle-P, Prahlad Nagar Cross Roads, S.G. Highway, Ahmedabad-380015, Gujarat, India.

Manufactured By:

Stanford Laboratories Pvt. Ltd.
(A subsidiary company of La Renon Healthcare Pvt. Ltd)
8, Industrial Area, Mehatpur, Dist. Una, (H.P.) 174315, India.

8. MARKETING AUTHORIZATION NUMBER:
H2021/CTD6189/2013ER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/September/2021

10. DATE OF REVISION OF THE TEXT:

31/03/2026