Nodep®

(Escitalopram)

نوڈیپ

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated tablet contains:
Escitalopram Oxalate equivalent to Escitalopram USP.... 5 mg
Escitalopram Oxalate equivalent to Escitalopram USP.... 10 mg
Escitalopram Oxalate equivalent to Escitalopram USP.... 20 mg

DESCRIPTION
Nodep (Escitalopram) 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 (dimethyl-amino) propyl] -1-(*p*-fluorophenyl)-5-phthalancarbonitrile. The molecular formula is $C_{20}H_{21}FN_2O \bullet C_2H_2O_4$ and the molecular weight is 414.40.

WARNINGS: SUICIDALITY AND ANTIDEPRESSANT DRUGS
Antidepressants are known to increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Escitalopram or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term data is not known to increase in the risk of suicidality with antidepressants in adults beyond age 24; a reduction in risk with antidepressants in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Escitalopram is not approved for use in pediatric patients less than 12 years of age.

CLINICAL INFORMATION
Indications
• ***Major Depressive Disorder***
Nodep (Escitalopram) is indicated for the acute and maintenance treatment of major depressive disorder in adults and in adolescents 12 to 17 years of age.
• ***Generalized Anxiety Disorder***
Nodep (Escitalopram) is indicated for the acute treatment of Generalized Anxiety Disorder (GAD) in adults.
• ***Panic disorder with or without agoraphobia***
Nodep (Escitalopram) is indicated for the treatment of panic disorder with or without agoraphobia.
• ***Social anxiety disorder (social phobia)***
Nodep (Escitalopram) is indicated for the treatment of social anxiety disorder (social phobia).
• ***Obsessive-compulsive disorder***
Nodep (Escitalopram) is indicated treatment of obsessive-compulsive disorder.

Dosage and Administration
Major Depressive Disorder
Initial Treatment
Adolescents
The recommended dose of Nodep (Escitalopram) is 10 mg once daily. If the dose is increased to 20 mg, this should occur after a minimum of three weeks.
Adults
The recommended dose of Nodep (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 Nodep (Escitalopram) 10 or 20 mg/day in adults patients with major depressive disorder who responded while taking Nodep (Escitalopram) during an 8-week, acute-treatment phase demonstrated a benefit of such maintenance treatment.
Nevertheless, the physician who elects to use Nodep (Escitalopram) for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient. Patients should be periodically reassessed to determine the need for maintenance treatment.
Generalized Anxiety Disorder
Initial Treatment
Adults
The recommended starting dose of Nodep (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
Generalized anxiety disorder is recognized as a chronic condition. The efficacy of Nodep (Escitalopram) in the treatment of GAD beyond 8 weeks is not known. The physician who elects to use Nodep (Escitalopram) for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.
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 (social phobia)
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 is known 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 behavioral therapy is not known. Pharmacotherapy is part of an overall therapeutic strategy.
Obsessive-Compulsive Disorder
Initial dosage is 10 mg once daily. Depending on the individual patient response, the dose may be increased to a maximum of 20 mg daily.
As OCD is a chronic disease, patients should be treated for a sufficient period to ensure that they are symptom free.
Treatment benefits and dose should be re-evaluated at regular intervals .
Dosage Adjustment
Hepatic Impairment
10 mg/day is the recommended dose for patients with hepatic impairment.
Renal Impairment
No dosage adjustment is necessary for patients with mild or moderate renal impairment. Nodep (Escitalopram) should be used with caution in patients with severe renal impairment.
Elderly
10 mg/day is the recommended dose for most elderly patients.
Discontinuation of Treatment with Nodep (Escitalopram)
Symptoms associated with discontinuation of Nodep (Escitalopram) and other SSRIs and SNRIs are known to occur. Patients should be monitored for these symptoms when discontinuing treatment. 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.
Switching a Patient To or From a Monoamine Oxidase Inhibitor (MAOI) Intended to Treat Psychiatric Disorders
At least 14 days should elapse between discontinuation of an MAOI intended to treat psychiatric disorders and initiation of therapy with Nodep (Escitalopram). Conversely, at least 14 days should be allowed after stopping Nodep (Escitalopram) before starting an MAOI intended to treat psychiatric disorders.
Administration Requirement
Nodep (Escitalopram) should be administered once daily, in the morning or evening, with or without food.

Contraindications
• ***Monoamine Oxidase Inhibitors (MAOIs)***
The use of MAOIs intended to treat psychiatric disorders with Escitalopram or within 14 days of stopping treatment with Escitalopram is contraindicated because of an increased risk of serotonin syndrome. The use of Escitalopram within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated.
Starting Escitalopram in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome.
• **Pimozide**
Concomitant use in patients taking Pimozide is contraindicated.
• **Hypersensitivity to Escitalopram or citalopram**
Escitalopram is contraindicated in patients with a hypersensitivity to Escitalopram or citalopram or any of the inactive ingredients.

Warnings and Precautions
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. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. Antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment.
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.
Screening Patients for Bipolar Disorder
A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Escitalopram is not approved for use in treating bipolar depression.
Serotonin Syndrome
The development of a potentially life-threatening serotonin syndrome is known to occur with SNRIs and SSRIs, including Escitalopram, alone but particularly with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines, 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). Patients should be monitored for the emergence of serotonin syndrome.
If concomitant use of Escitalopram with other serotonergic drugs including, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, buspirone, tryptophan, amphetamine and St. John's Wort is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases.
Treatment with Escitalopram and any concomitant serotonergic agents, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.
Seizures
Escitalopram is not known in patients with a seizure disorder. Convulsion is known to occur in association with Escitalopram treatment. 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.
Activation of Mania/Hypomania
Activation of mania/hypomania and hypomania are known to occur in patients treated with Escitalopram. As with all drugs effective in the treatment of major depressive disorder, Escitalopram should be used cautiously in patients with a history of mania.
Hyponatremia
Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Escitalopram and it is probably due to syndrome of inappropriate antidiuretic hormone secretion (SIADH), and is reversible when Escitalopram is discontinued. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who is otherwise volume depleted may be at greater risk. Discontinuation of Escitalopram should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.
Abnormal Bleeding
SSRIs and SNRIs, including Escitalopram, may increase the risk of bleeding events. Bleeding events related to SSRIs and SNRIs use are ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages. 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.
Interference with Cognitive and Motor Performance
Escitalopram 10 mg/day does not produce impairment of intellectual function or psychomotor 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.
Angle Closure Glaucoma
Angle Closure Glaucoma
The pupillary dilation that occurs following use of many antidepressant drugs including Escitalopram may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.
Use in Patients with Concomitant Illness
Caution is advisable in using Escitalopram in patients with diseases or conditions that produce altered metabolism or hemodynamic responses.
Escitalopram is not known in patients with a recent history of myocardial infarction or unstable heart disease.

Interactions

Triptans

If concomitant treatment of Escitalopram with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increase.

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 does not potentiate the cognitive and motor effects of alcohol, as with other psychotropic medications, the use of alcohol by patients taking Escitalopram is not recommended.

Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)

Concurrent use of an NSAID or aspirin may potentiate the risk of bleeding. Altered anticoagulant effects, including increased bleeding, are known to occur when SSRIs and SNRIs are co administered with warfarin. Patients receiving warfarin therapy should be carefully monitored Escitalopram is initiated or discontinued.

Cimetidine

Concomitant use with cimetidine is known to result in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown.

Digoxin

Concomitant use with digoxin does not significantly affect the pharmacokinetics of either citalopram or digoxin.

Lithium

Because lithium may enhance the serotonergic effects of Escitalopram, caution should be exercised when Escitalopram and lithium are co administered.

Pimozide and Citalopram

Racemic citalopram does not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known.

Sumatriptan

If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, Escitalopram) is clinically warranted, appropriate observation of the patient is advised.

Theophylline

The effect of theophylline on the pharmacokinetics of citalopram is not known.

Warfarin

Concomitant use does not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time is increased by 5%, the clinical significance of which is unknown.

Carbamazepine

Co administration does not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels are known to be 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 co administered.

Triazolam

Co administration does not significantly affect the pharmacokinetics of either citalopram or triazolam.

Ketoconazole

Co administration is known to decrease the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and does not significantly affect the pharmacokinetics of citalopram.

Ritonavir

Co administration does not affect the pharmacokinetics of either ritonavir or Escitalopram.

CYP3A4 and -2C19 Inhibitors

Co administration does not significantly affect the pharmacokinetics of Escitalopram. Because Escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease Escitalopram clearance.

Drugs Metabolized by Cytochrome P4502D6

Co administration, with Escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on Escitalopram metabolism. Caution is indicated in the co administration of Escitalopram and drugs metabolized by CYP2D6.

Metoprolol

Co administration may result in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels are known to be associated with decreased cardioselectivity. Co administration of Escitalopram and metoprolol has no clinically significant effects on blood pressure or heart rate.

Electroconvulsive Therapy (ECT)

No data is available on use of ECT and Escitalopram.

Pregnancy and Breastfeeding

Pregnancy Category C

There is insufficient data available for use in pregnant women, therefore, Escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Escitalopram is excreted in human breast milk. Caution should be exercised and breastfeeding infants should be observed for adverse reactions when Escitalopram is administered to a nursing woman.

Effects on ability to drive and use machines

Although Escitalopram is known not to affect intellectual function or psychomotor performance, any psychoactive medicinal product may impair judgment or skills. Patients should be cautioned about the potential risk of an influence on their ability to drive a car and operate machinery.

Adverse Reactions

Blood and Lymphatic System Disorders

Anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia purpura, leukopenia, thrombocytopenia.

Cardiac Disorders

Atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular arrhythmia, ventricular tachycardia.

Ear and labyrinth disorders

Vertigo

Endocrine Disorders

Diabetes mellitus, hyperprolactinemia, SIADH.

Eye Disorders

Angle closure glaucoma, diplopia, mydriasis, visual disturbance.

Gastrointestinal Disorder

Dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage.

General Disorders and Administration Site Conditions

Abnormal gait, asthenia, edema, fall, feeling abnormal, malaise. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis.

Immune System Disorders

Allergic reaction, anaphylaxis. Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, hypercholesterolemia, INR increased, prothrombin decreased.

Metabolism and Nutrition Disorders

Hyperglycemia, hypoglycemia, hypokalemia, hyponatremia.

Musculoskeletal and Connective Tissue Disorders

Muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis.

Nervous System Disorders:

Akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor.

Pregnancy, Puerperium and Perinatal Conditions

Spontaneous abortion.

Psychiatric Disorders

Acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion, depersonalization, depression aggravated, delirium, delusion, disorientation, feeling unreal, hallucinations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm or thoughts of self-harm, suicide attempt, suicidal ideation, suicidal tendency.

Renal and Urinary Disorders

Acute renal failure, dysuria, urinary retention.

Reproductive System and Breast Disorders

Menorrhagia, priapism. Respiratory.

Thoracic and Mediastinal Disorders

Dyspnea, epistaxis, pulmonary embolism, pulmonary hypertension of the newborn.

Skin and Subcutaneous Tissue Disorders

Alopecia, angioedema, dermatitis, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

Overdose

Overdoses of up to 600 mg, with no associated fatalities are known to occur. During clinical practice of Escitalopram, overdoses involving overdoses of over 1000 mg is known.

Symptoms

Most often accompanying Escitalopram 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 very rarely occur accompanying overdose.

Management

There is no specific antidote. Maintain airway, adequate oxygenation and respiratory function monitoring. Gastric lavage and the use of activated charcoal should be considered.

PHARMACOLOGICAL PROPERTIES

Pharmacokinetic group: antidepressants, selective serotonin reuptake inhibitors ATC-code: N 06 AB 10

Mechanism of action

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).

Pharmacokinetic properties

Absorption and Distribution

Following a single oral dose (20 mg 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% relative to an intravenous dose, and the volume of distribution of citalopram is about 12 L/kg. Data specific on 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 is known to be 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).

PHARMACEUTICAL INFORMATION

Shelf life

2 years

Special Precautions for storage

- Do not store above 30°C
- Protect from light and moisture.
- Keep out of the reach of children.

ہدایات:

۳۰°C سے زیادہ درجہ حرارت پر نہ رکھیں۔

دوا کو روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

To be sold on the prescription of a registered medical practitioner only.

صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

Nature and contents of container

Nodep (Escitalopram) 5 mg tablets are available in the blister pack of 14's (2 X 7's).

Nodep (Escitalopram) 10 mg tablets are available in the blister pack of 14's (2 X 7's).

Nodep (Escitalopram) 20 mg tablets are available in the blister pack of 14's (2 X 7's).

MANUFACTURED BY

ASPIN

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