Nevola®

Desvenlafaxine INN 50 mg & 100 mg Extended Release Tablet

COMPOSITION
Nevola® 50 mg tablet: Each Extended-Release tablet contains Desvenlafaxine Succinate INN equivalent to 50 mg of Desvenlafaxine.
Nevola® 100 mg tablet: Each Extended-Release tablet contains Desvenlafaxine Succinate INN equivalent to 100 mg of Desvenlafaxine.

CLINICAL PHARMACOLOGY
Nevola® (Desvenlafaxine) is a synthetic form of the isolated major active metabolite of Venlafaxine, and is categorized as a Serotonin-Norepinephrine Reuptake Inhibitor (SNRI). It works by blocking the transporter reuptake protein for key neurotransmitters affecting mood, thereby leaving more active neurotransmitters in the synapse. The neurotransmitters affected are Serotonin (5-hydroxytryptamine) and Norepinephrine (Noradrenaline). It is approximately 10 times more potent at inhibiting Serotonin uptake than Norepinephrine uptake.

MECHANISM OF ACTION
The exact mechanism of the antidepressive action of Desvenlafaxine is unknown, but is thought to be related to the potentiation of Serotonin and Norepinephrine in the central nervous system, through inhibition of their reuptake. Non-clinical studies have shown that Desvenlafaxine is a potent Serotonin and Norepinephrine Reuptake Inhibitor (SNRI).

PHARMACOKINETICS
The single-dose pharmacokinetics of Desvenlafaxine are linear and dose-proportional in a dose range of 50 to 400 mg/day. With once-daily dosing, steady-state plasma concentrations are achieved within approximately 4 to 5 days.

INDICATIONS
Nevola® is indicated for the treatment of Major Depressive Disorder (MDD).

CONTRAINDICATIONS
Hypersensitivity to Desvenlafaxine Succinate, Venlafaxine Hydrochloride or to any excipients in the **Nevola®** formulation.
The use of MAOIs (Mono Amine Oxidase Inhibitors) intended to treat psychiatric disorders with **Nevola®** or within 7 days of stopping the treatment with **Nevola®** is contraindicated. The use of **Nevola®** within 14 days of stopping MAOI intended to treat psychiatric disorders is also contraindicated.

WARNINGS AND PRECAUTIONS
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 they are taking antidepressant medications or not and this risk may persist until significant remission occurs. Pooled analysis of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents and young adults (aged 18 to 24) with Major Depressive Disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24.

USE IN PREGNANCY AND LACTATION
Pregnancy Category 'C'.
Nevola® should be used during pregnancy only if the potential benefits justify the potential risks to the fetus.
Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from **Nevola®** a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

DRUG-DRUG INTERACTION
Clinical studies have shown that Desvenlafaxine does not have a clinically relevant effect on CYP2D6 (e.g., Desipramine, Atomoxetine, Dextromethorphan, Metoprolol, Nebivolol, Perphenazine, Tolterodine) metabolism at the dose of 100 mg daily. Reduce the dose of these substrates by one-half if co-administered with 400 mg of Desvenlafaxine. Avoid use of Desvenlafaxine with other Desvenlafaxine-containing products or Venlafaxine products. The concomitant use of Desvenlafaxine with other Desvenlafaxine-containing products or Venlafaxine will increase Desvenlafaxine blood levels and increase dose-related adverse reactions. Like CNS-acting drugs, patients should be advised to avoid alcohol consumption while taking **Nevola®**.

SIDE-EFFECTS
Nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, dry mouth and specific male sexual function disorders.

DOSAGE AND ADMINISTRATION
The recommended dose for **Nevola®** (Desvenlafaxine Succinate) is 50 mg once daily, with or without food.
In clinical studies, doses of 50-400 mg/day were shown to be effective. When discontinuing therapy, gradual dose reduction is recommended whenever possible to minimize discontinuation symptoms. Desvenlafaxine Succinate should be taken at approximately the same time each day. Tablets must be swallowed whole with fluid and not divided, crushed, chewed, or dissolved.

USE IN SPECIFIC POPULATION
Dosage Adjustment in Renal Impairment: No dosage adjustment is necessary in patients with mild renal impairment. The recommended dose in patients with moderate renal impairment is 50 mg per day. The recommended dose in patients with severe renal impairment or End-Stage Renal Disease (ESRD) is maximum 50 mg every other day. Supplemental dose should not be given to patients after dialysis. The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.

Dosage Adjustment in Hepatic Impairment: The recommended dose in patients with hepatic impairment is 50 mg/day. Maximum 100 mg/day is not recommended.

MAINTENANCE/CONTINUATION/EXTENDED TREATMENT
It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacologic therapy. Patients should be periodically reassessed to determine the need for continued treatment.

STORAGE
Store in a cool and dry place, protected from light.

PRESENTATION
Nevola® 50 mg tablet: Each box containing 3x10's tablets in Alu-Alu blister pack.
Nevola® 100 mg tablet: Each box containing 2x10's tablets in Alu-Alu blister pack.

Manufactured by:
ZISKA PHARMA
Ziska Pharmaceuticals Ltd.
Gazipur, Bangladesh