For the use only of a Registered Medical Practioner or a Hospital or Laboratory.

Vardenafil Tablets

SAVITRA

COMPOSITION:

SAVITRA-10

Composition:

Each film coated tablet contains :

Vardenafil Hydrochloride Equivalent to Vardenafil	10 mg
Excipients	q.s.

Colour : Yellow Oxide of Iron and Titanium Dioxide

SAVITRA-20

Composition:

Each film coated tablet contains:

Vardenafil Hydrochloride Trihydrate Eq. to Vardenafil	20 mg
Excipients	q.s.

Colours: Iron Oxide Yellow NF and Iron Oxide Red NF

CHEMISTRY: Piperazine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-ethyl-, monohydrochloride.

CATEGORY: Phosphodiesterase-5 (PDE5) inhibitor

PHARMACOLOGY:

PHARMACODYNAMICS:

The monohydrochloride salt of vardenafil is a selective inhibitor of cyclic guanosine monophosphate (cGMP) - specific phosphodiesterase type 5 (PGE5). Penile erection is a hemodynamic process initiated by the relaxation of smooth muscle in the corpus cavernosum and its associated arterioles. During sexual stimulation, nitric oxide is released from nerve endings and endothelial cells in the corpus cavernosum. Nitric oxide activates the enzyme guanylate cyclase resulting in increased synthesis of cyclic guanosine monophosphate (cGMP) in the smooth muscle cells of the corpus cavernosum. The cGMP in turn triggers smooth muscle relaxation, allowing increased blood flow into the penis, resulting in erection. The tissue concentration of cGMP is regulated by both the rates of synthesis and degradation via phosphodiesterases (PDEs). The most abundant PDE in the human corpus cavernosum is the cGMP-specific phosphodiesterase type 5 (PDE5); therefore, the inhibition of PDE5 enhances erectile function by increasing the amount of cGMP. Because sexual stimulation is required to initiate the local release of nitric oxide, the inhibition of PDE5 has no effect in the absence of sexual stimulation. Vardenafil thus potentiates the natural response to sexual stimulation. Vardenafil causes a penile erection which is dependent upon endogenous nitric oxide synthesis and is potentiated by nitric oxide donors.

PHARMACOKINETICS:

Absorption:

Vardenafil is rapidly absorbed after oral administration. C_{max} is reached as early as 15 minutes, in 90% of the time Cmax is reached within 30 to 120 minutes of oral dosing in the fasted state.

Distribution:

The mean steady-state volume of distribution (Vss) for vardenafil is 208 L, indicating extensive tissue distribution.

Vardenafil and its major circulating metabolite, M1, are highly bound to plasma proteins (about 95% for parent drug and M1). This protein binding is reversible and independent of total drug concentrations.

Metabolism:

Vardenafil is metabolized predominantly by the hepatic enzyme CYP3A4, with contribution from the CYP3A5 and CYP2C isoforms. The major circulating metabolite, M1. The plasma concentration of M1 is approximately 26% that of the parent compound. M1 accounts for approximately 7% of total pharmacologic activity.

Excretion:

The total body clearance of vardenafil is 56 L/h, and the terminal half-life of vardenafil and its primary metabolite (M1) is approximately 4-5 hours. After oral administration, vardenafil is excreted as metabolites predominantly in the feces (approximately 91-95% of administered oral dose) and to a lesser extent in the urine (approximately 2-6% of administered oral dose).

Special populations:

Renal insufficiency

No dose adjustment is needed in patients with impaired renal function.

The pharmacokinetics of vardenafil has not been studied in patients requiring dialysis and vardenafil tablets should not be used in this situation.

Hepatic impairment

In patients with mild to moderate hepatic impairment (Child-Pugh A and B), vardenafil clearance was reduced in proportion to the degree of hepatic impairment.

The pharmacokinetics of vardenafil has not been studied in patients with severe hepatic impairment (Child-Pugh C). Vardenafil tablets should not be used in this population.

INDICATIONS:

Vardenafil is indicated for the treatment of erectile dysfunction.

DOSAGE AND ADMINISTRATION:

For most patients, the recommended starting dose of vardenafil tablets is 10 mg, taken orally approximately 60 minutes before sexual activity.

The dose may be increased to a maximum recommended dose of 20 mg or decreased to 5 mg based on efficacy and side effects.

The maximum recommended dosing frequency is once per day. Vardenafil tablets can be taken with or without food. Sexual stimulation is required for a response to treatment.

Geriatrics: A starting dose of 5 mg vardenafil tablets should be considered in patients 65 years of age

Children (from birth to 18 years): Vardenafil tablets are not indicated for use in children.

CONTRAINDICATIONS:

Patients with known hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS:

WARNINGS

Cardiovascular Disease

Prior to initiating any treatment for erectile dysfunction, physicians should consider the cardiovascular status of their patients, since there is a degree of cardiac risk associated with sexual activity. Vardenafil has vasodilator properties which may result in mild and transient decreases in blood pressure.

Other Pre-existing Medical Conditions

Agents for the treatment of erectile dysfunction should generally be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease) or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia).

The safety and efficacy of combinations of vardenafil with other treatments for erectile dysfunction (including other PDE5 inhibitors) have not been studied. Therefore the use of such combinations is not recommended.

PRECAUTIONS:

The evaluation of erectile dysfunction should include a determination of potential underlying causes, a medical assessment, and the identification of appropriate treatment.

Use with alpha-blockers

Caution is advised when PDE5 inhibitors are co-administered with alpha blockers. PDE5 inhibitors, including vardenafil tablets and alpha-adrenergic blocking agents are both vasodilators with blood-pressure lowering effects.

INTERACTIONS:

Macrolide Antibiotics

When used in combination with erythromycin or clarithromycin, a maximum vardenafil dose of 5 mg should not be exceeded.

Potent CYP 3A4 inhibitors

Ketoconazole

Vardenafil tablets must not be taken with dosages of ketoconazole higher than 200 mg.

Indinavir

Concomitant use of indinavir and vardenafil is contraindicated.

Ritonavir

Ritonavir significantly prolonged the half-life of vardenafil to 25.7 hours. Concomitant use with ritonavir is contraindicated.

Other CYP 3A4 Inhibitors

A maximum dose of vardenafil tablets 5 mg should not be exceeded if used in combination with ketoconazole, itraconazole, erythromycin or clarithromycin.

Nitrates, Nitric Oxide Donors
There is limited information on the potential hypotensive effects of vardenafil when given in combination with nitrates.

PREGNANCY AND LACTATION:
Use in pregnancy (Category B3):
Vardenafil is not indicated for use by women. There are no studies of vardenafil in pregnant women.

LACTATION
Vardenafil is not indicated for use by women. There are no human data on the excretion of vardenafil into breast milk or on the safety of vardenafil exposure in infants.

Effect to Drive & Use the Machine:
Patients should be aware of how they react to vardenafil before driving or operating machinery. Due to the vasodilatory properties of PDE 5 inhibitors, concomitant use with alpha-blockers, may contribute to dizziness.

ADVERSE DRUG REACTIONS:
Vardenafil was generally very well tolerated. Adverse events were generally transient and mild to moderate in nature.

OVERDOSAGE:
In cases of overdose, standard supportive measures should be taken as required. Renal dialysis is not expected to accelerate clearance because vardenafil is highly bound to plasma proteins and is not significantly eliminated in the urine.

PRESENTATION: Blister of 10 Tablets.

STORAGE: Store in a dry place below 30°C. Protect from light.
Keep out of reach of children.

LAST UPDATE: July 2015.

Manufactured by:
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