

SILDENAFIL TABLETS IP 50 mg & 100 mg

Vega 50 / 100

Composition:

Each film coated tablet contains:

Sildenafil Citrate IP

Equivalent to Sildenafil 100 mg and 50 mg

Excipients q.s.

Colour: Indigo Carmine & Titanium Dioxide IP

Therapeutic indications:

Sildenafil is indicated in adult of men with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance. In order for sildenafil to be effective, sexual stimulation is required.

Dosage:-

Posology and method of administration:

Use in adults:

The recommended dose is 50mg taken as needed approximately one hour before sexual activity. Based on efficacy and tolerability, the dose may be increased to 100mg or decreased to 25mg. The maximum recommended dose is 100mg. The maximum recommended dosing frequency is once per day. If sildenafil is taken with food, the onset of activity may be delayed compared to the fasted state.

Special populations

Elderly patients

Dosage adjustments are not required in elderly patients (≥65 years old).

Patients with renal impairment:

The dosing recommendations described in 'Use in adults' apply to patients with mild to moderate renal impairment (creatinine clearance = 30 - 80 ml/min). Since sildenafil clearance is reduced in patients with severe renal impairment (creatinine clearance <30 ml/min) a 25mg dose should be considered. Based on efficacy and tolerability, the dose may be increased step-wise to 50mg up to 100mg as necessary.

Patients with hepatic impairment: Since sildenafil clearance is reduced in patients with hepatic impairment (e.g. cirrhosis) a 25mg dose should be considered. Based on efficacy and tolerability, the dose may be increased step-wise to 50mg up to 100mg as necessary.

Paediatric population

Sildenafil is not indicated for individuals below 18 years of age.

Use in patients taking other medicinal products:

With the exception of ritonavir for which co-administration with sildenafil is not advised starting dose of 25mg should be considered in patients receiving concomitant treatment with CYP3A4 inhibitors. In order to minimize the potential of developing postural hypotension in patients receiving alpha-blocker treatment, patients should be stabilised on alpha-blocker therapy prior to initiating sildenafil treatment. In addition, initiation of sildenafil at a dose of 25mg should be considered.

Interaction with other medicinal products and other forms of interaction:

Hypersensitivity to the active substance or to any of the excipients listed in formulation. Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway, sildenafil was shown to potentiate the hypotensive effects of nitrates, and its co-administration with nitric oxide donors (such as amyl nitrite) or nitrates in any form is therefore contraindicated. Agents for the treatment of erectile dysfunction, including sildenafil, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure). Sildenafil is contraindicated in patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure. The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: severe hepatic impairment, hypotension (blood pressure <90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients has genetic disorders of retinal phosphodiesterases).

Special warnings and precaution:

A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes, before pharmacological treatment is considered.

Cardiovascular risk factors

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. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Prior to prescribing sildenafil, physicians should carefully consider whether their patients with certain underlying conditions could be adversely affected by such vasodilatory effects, especially in combination with sexual activity. Sildenafil potentiates the hypotensive effect of nitrates. Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular haemorrhage, transient ischemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of sildenafil. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of sildenafil without sexual activity. It is not possible to determine whether these events are related directly to these factors or to other factors.

Priapism

Agents for the treatment of erectile dysfunction, including sildenafil, should 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).

Concomitant use with other treatments for erectile dysfunction

The safety and efficacy of combinations of sildenafil with other treatments for erectile dysfunction have not been studied. Therefore the use of such combinations is not recommended.

Effects on vision

Cases of visual defects have been reported spontaneously in connection with the intake of sildenafil and other PDE5 inhibitors. Cases of non-arteritic anterior ischaemic optic neuropathy, a rare condition, have been reported spontaneously and in an observational study in connection with the intake of sildenafil and other PDE5 inhibitors. Patients should be advised that in the event of any sudden visual defect, they should stop taking sildenafil and consult a physician immediately.

Concomitant use with ritonavir

Co-administration of sildenafil with ritonavir is not advised.

Concomitant use with alpha-blockers

Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing. In order to minimize the potential for developing postural hypotension, patients should be hemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25mg should be considered. In addition, physicians should advise patients what to do in the event of postural hypotensive symptoms.

Effect on bleeding

Studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside in vitro. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore sildenafil should be administered to these patients only after careful benefit-risk assessment.

Women

Sildenafil is not indicated for use by women.

Fertility, pregnancy and lactation:

Sildenafil is not indicated for use by women.

Pharmacology:**Mechanism of action:**

Sildenafil is an oral therapy for erectile dysfunction. In the natural setting, i.e. with sexual stimulation, it restores impaired erectile function by increasing blood flow to the penis. The physiological mechanism responsible for erection of the penis involves the release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. Nitric oxide then activates the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), producing smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood.

Pharmacodynamic properties:

Studies in vitro have shown that sildenafil is selective for PDE5, which is involved in the erection process. Its effect is more potent on PDE5 than on other known phosphodiesterases. There is a 10-fold selectivity over PDE6 which is involved in the photo transduction pathway in the retina. At maximum recommended doses, there is an 80-fold selectivity over PDE1, and over 700-fold over PDE2, 3, 4, 7, 8, 9, 10 and 11. In particular, sildenafil has greater than 4,000-fold selectivity for PDE5 over PDE3, the cAMP-specific phosphodiesterase isoform involved in the control of cardiac contractility.

Pharmacokinetic properties:**Absorption:**

Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. The mean absolute oral bioavailability is 41% (range 25-63%). After oral dosing of sildenafil AUC and C_{max} increase in proportion with dose over the recommended dose range (25-100mg). When sildenafil is taken with food, the rate of absorption is reduced with a mean delay in max of 60 minutes and a mean reduction in C_{max} of 29%.

Distribution:

The mean steady state volume of distribution (V_d) for sildenafil is 105 l, indicating distribution into the tissues. After a single oral dose of 100mg, the mean maximum total plasma concentration of sildenafil is approximately 440 mg/ml (CV 40%). Since sildenafil (and its major circulating N-desmethyl metabolite) is 96% bound to plasma proteins, this results in the mean maximum free plasma concentration for sildenafil of 18 mg/ml (38 mg). Protein binding is independent of total drug concentrations. In healthy volunteers receiving sildenafil (100mg single dose), less than 0.0002% (average 188 mg) of the administered dose was present in ejaculate 90 minutes after dosing.

Overdose:

In single dose volunteer studies of doses up to 800mg, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing, dizziness, dyspepsia, nasal congestion, altered vision) was increased. In cases of overdose, standard supportive measures should be adopted as required. Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

Storage : Store protected from moisture
Keep out of reach of children.

Presentation: 1 x 4 Tablets.

Signature

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