120x180mm

Fildil™
(Tadalafil)

Highnoon

COMPOSITION
Fildil 2.5mg Tablet: Each film-coated tablet contains: Tadalafil 2.5mg
Fildil 5mg Tablet: Each film-coated tablet contains: Tadalafil 5mg
Fildil 10mg Tablet: Each film-coated tablet contains: Tadalafil 10mg
Fildil 20mg Tablet: Each film-coated tablet contains: Tadalafil 20mg

DESCRIPTION
Tadalafil is an inhibitor of phosphodiesterase type 5 (PDE5).

MECHANISM OF ACTION
Tadalafil is an inhibitor of phosphodiesterase type 5 (PDE5), the enzyme responsible for the degradation of cyclic guanosine monophosphate (cGMP). Pulmonary arterial hypertension is associated with impaired release of nitric oxide by the vascular endothelium and consequent reduction of cGMP concentrations in the pulmonary vascular smooth muscle. PDE5 is the predominant phosphodiesterase in the pulmonary vasculature. Inhibition of PDE5 by tadalafil increases the concentrations of cGMP resulting in relaxation of pulmonary vascular smooth muscle cells and vasodilation of the pulmonary vascular bed.
Penile erection during sexual stimulation is caused by increased penile blood flow resulting from the relaxation of penile arteries and corpus cavernosal smooth muscle. This response is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cGMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum. The inhibition of phosphodiesterase type 5 (PDE5) enhances erectile function by increasing the amount of cGMP. Tadalafil inhibits PDE5. Because sexual stimulation is required to initiate the local release of nitric oxide, the inhibition of PDE5 by tadalafil has no effect in the absence of sexual stimulation.
The effect of PDE5 inhibition on cGMP concentration in the corpus cavernosum and pulmonary arteries is also observed in the smooth muscle of the prostate, the bladder and their vascular supply. The mechanism for reducing BPH symptoms has not been established.

PHARMACOKINETICS
Tadalafil is well absorbed after an oral dose, peak plasma concentration occurs within 2 hours; the rate and extent of absorption are not affected by food. Tadalafil is widely distributed into tissues and is about 94% bound to plasma proteins. It is metabolized in the liver mainly by the cytochrome P450 isoenzyme CYP3A4. The major metabolite, the methyl catechol glucuronide, is inactive. The mean half-life of tadalafil is about 17.5 hours. Tadalafil is excreted, mainly as metabolites, in the faeces (61% of the dose), and to a lesser extent in the urine (36 % of the dose). Clearance may be reduced in the elderly and in patients with renal impairment.

INDICATIONS AND USAGE
It is indicated;
- Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability.
- Treatment of erectile dysfunction (ED)
- Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH)
- Treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use
If it is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Tadalafil decreases from 4 weeks until 26 weeks, and the incremental benefit of Tadalafil beyond 26 weeks is unknown.

DOSAGE AND ADMINISTRATION
Pulmonary arterial hypertension: The recommended dose is 40 mg taken once daily with or without food.
Use as needed for erectile dysfunction: The recommended starting dose of Tadalafil for use as needed in most patients is 10 mg, taken prior to anticipated sexual activity. The dose may be increased to 20 mg or decreased to 5 mg, based on individual efficacy and tolerability. The maximum recommended dosing frequency is once per day in most patients. It may improve erectile function up to 36 hours.
Once daily use for erectile dysfunction: The recommended starting dose of Tadalafil for once daily use is 2.5 mg, taken at approximately the same time every day, without regard to timing of sexual activity. Dose may be increased to 5mg based on individual efficacy and tolerability.
Once daily use for benign prostatic hyperplasia: 5mg once daily taken at approximately the same time every day. When therapy for BPH is initiated with Tadalafil and finasteride, the recommended dose of Tadalafil for once daily use is 5 mg, taken at approximately the same time every day for up to 26 weeks.
Once daily use for erectile dysfunction and benign prostatic hyperplasia: The recommended dose of Tadalafil for once daily use is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.
Tadalafil may be taken without regard to food. Dose adjustments are not required in elderly patients. Dose adjustments are not required in patients with mild to moderate renal impairment. For patients with severe renal impairment, 10 mg is the maximum recommended dose. Once-a-day dosing of 2.5 or 5 is not recommended in patients with severe renal impairment
In men with hepatic impairment, the treatment of erectile dysfunction using on-demand Tadalafil the recommended dose is 10 mg taken prior to anticipated sexual activity and with or without food. There is limited clinical data on the safety of Tadalafil in patients with severe hepatic impairment (Child-Pugh Class C); if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician. There are no available data about the administration of doses higher than 10 mg of tadalafil to patients with hepatic impairment.
Once-a-day dosing both for the treatment of erectile dysfunction and benign prostatic hyperplasia has not been evaluated in patients with hepatic impairment; therefore, if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.
Dose adjustments are not required in diabetic patients.

CONTRAINDICATIONS
- It is contraindicated in patients who are using any form of organic nitrate, either regularly or intermittently. Do not use nitrates within 48 hours of the last dose of Tadalafil. It potentiates the hypotensive effect of nitrates.
- Coadministration of Concomitant Guanylate Cyclase GC stimulators such as riociguat with Tadalafil is contraindicated. It may potentiate the hypotensive effects of GC stimulators.
- It is contraindicated in patients with a known serious hypersensitivity to tadalafil. Hypersensitivity reactions have been reported, including Stevens-Johnson syndrome and exfoliative dermatitis.
- It is contraindicated in patients with myocardial infarction within the last 90 days, unstable angina or angina occurring during sexual intercourse, New York Heart Association Class 2 or greater heart failure in the last 6 months, uncontrolled arrhythmias, hypotension (< 90/50 mm Hg), or uncontrolled hypertension, a stroke within the last 6 month, cardiac disease for whom sexual activity is inadvisable, 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.

ADVERSE REACTIONS
The reported adverse events are; hypotension, visual loss, hearing loss, priapism, hypersensitivity reactions, angioedema, headache, dizziness, stroke (including haemorrhagic events), syncope, transient ischaemic attacks, migraine, seizures, transient amnesia, blurred vision, sensations described as eye pain, visual field defect, swelling of eyelids, conjunctival hyperaemia, non-arteritic anterior ischaemic optic neuropathy (naion), retinal vascular occlusion, central serous chorioretinopathy, tinnitus, sudden hearing loss, tachycardia, palpitations, myocardial infarction, unstable angina pectoris, ventricular arrhythmia, flushing, hypotension, hypertension, nasal congestion, nasopharyngitis, dyspnoea, epistaxis, respiratory tract infection (upper and lower), dyspepsia, abdominal pain, vomiting, nausea, gastro-oesophageal reflux, rash, urticaria, Stevens-Johnson Syndrome, exfoliative dermatitis, hyperhydrosis (sweating), back pain, myalgia, pain in extremity, haematuria, prolonged erections, priapism, penile haemorrhage, haematospermia, chest pain, peripheral oedema, fatigue, facial oedema and sudden cardiac death.

120x180mm

DRUG INTERACTIONS
- Administration of nitrates within 48 hours after the last dose of Tadalafil is contraindicated.
- When vasodilators are used in combination, an additive effect on blood pressure may be anticipated.
- Small reductions in blood pressure occurred following coadministration of tadalafil with antihypertensive agents: amlodipine, angiotensin II receptor blockers, bendroflumethiazide, enalapril, and metoprolol.
- When mild vasodilators are taken in combination, blood-pressure-lowering effects of each individual compound may be increased. Substantial consumption of alcohol (e.g., 5 units or greater) in combination with Tadalafil can increase the potential for orthostatic signs and symptoms, including increase in heart rate, decrease in standing blood pressure, dizziness, and headache. Tadalafil (10 mg or 20 mg) did not affect alcohol plasma concentrations and alcohol did not affect tadalafil plasma concentrations.
- CYP3A Inhibitors/Inducers: Ritonavir initially inhibits and later induces CYP3A, the enzyme involved in the metabolism of tadalafil. At steady state of ritonavir (about 1 week), the exposure to tadalafil is similar as in the absence of ritonavir.
- Potent Inhibitors of CYP3A; Tadalafil is metabolized predominantly by CYP3A in the liver. In patients taking potent inhibitors of CYP3A such as ketoconazole, and itraconazole, avoid use of Tadalafil.
- Potent Inducers of CYP3A; for patients chronically taking potent inducers of CYP3A, such as rifampicin, avoid use of Tadalafil.

WARNINGS AND PRECAUTIONS
- Tadalafil has vasodilatory properties that may result in transient decreases in blood pressure. Prior to prescribing Tadalafil, carefully consider whether patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects. Patients with preexisting hypotension, with autonomic dysfunction, with left ventricular outflow obstruction, may be particularly sensitive to the actions of vasodilators.
- Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD). Since there are no clinical data on administration of Tadalafil to patients with veno-occlusive disease, its administration to such patients is not recommended. Should signs of pulmonary oedema occur when Tadalafil is administered, the possibility of associated PVOD should be considered.
- When used to treat erectile dysfunction, non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported with the use of phosphodiesterase type 5 (PDE-5) inhibitors, including tadalafil. Most, but not all, of these patients had underlying anatomic or vascular risk factors for development of NAION, including but not necessarily limited to: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidaemia, and smoking.
- Patients with known hereditary degenerative retinal disorders, including retinitis pigmentosa have not been studied and use in these patients is not recommended.
- Cases of sudden decrease or loss of hearing, which may be accompanied by tinnitus and dizziness, have been reported in patients taking tadalafil. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors.
- The safety and efficacy of Tadalafil with another PDE5 inhibitor has not been studied and its should not be taken with other PDE5 inhibitors.
- There have been reports of prolonged erections greater than 4 hours and priapism (painful erections greater than 6 hours in duration) for this class of compounds. Patients with conditions that might predispose them to priapism (such as sickle cell anemia, multiple myeloma, or leukemia), or in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis, or Peyronie's disease) are at an increased risk. Priapism, if not treated promptly, can result in irreversible damage to the erectile tissue. Patients who have an erection lasting greater than 4 hours require medical attention.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are limited data from the use of tadalafil in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. As a precautionary measure, it is preferable to avoid the use of Tadalafil during pregnancy.

Breastfeeding
Data in animals have shown excretion of tadalafil in milk. A risk to the suckling child cannot be excluded. Tadalafil should not be used during breast feeding.

Effects on ability to drive and use machines
Tadalafil has negligible influence on the ability to drive or use machines. Although the frequency of reports of dizziness in placebo and tadalafil arms in clinical trials was similar, patients should be aware of how they react to Tadalafil before driving or using machines.

Paediatric Use
Safety and effectiveness in paediatric patients have not been established.

Geriatric Use
No overall differences in safety were observed between subjects over 65 years of age compared to younger subjects or those over 75 years of age. No dose adjustment is warranted based on age alone; however, a greater sensitivity to medications in some older individuals should be considered.

OVERDOSAGE
Single doses of up to 500 mg have been given to healthy subjects, and multiple daily doses up to 100 mg have been given to patients. Adverse events were similar to those seen at lower doses. In cases of overdose, standard supportive measures should be adopted as required. Haemodialysis contributes negligibly to tadalafil elimination.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
Fildil 2.5mg Tablets: Alu. PVC. Blister Pack of 1 x 10's.
Fildil 5mg Tablets: Alu. PVC. Blister Pack of 1 x 10's.
Fildil 10mg Tablets: Alu. PVC. Blister Pack of 1 x 10's.
Fildil 20mg Tablets: Alu. PVC. Blister Pack of 1 x 10's.

فلڈل™
(ٹڈالافل)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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