Front

Tadala

(Tadalafil)

Tablet

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COMPOSITION:
TADALA Tablet 5 mg:
Each film coated tablet contains:
Tadalafil ..... 5 mg.

Product Specs.: USP

TADALA Tablet 10 mg:
Each film coated tablet contains:
Tadalafil ..... 10 mg.

Product Specs.: USP

TADALA Tablet 20 mg:
Each film coated tablet contains:
Tadalafil ..... 20 mg.

Product Specs.: USP

Pharmacological Properties:
Pharmacotherapeutic group: Urologicals, Drugs used in erectile dysfunction.
ATC code: G04BE08.

Mechanism of action:
Tadalafil is a selective, reversible inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5). When sexual stimulation causes the local release of nitric oxide, inhibition of PDE5 by tadalafil produces increased levels of cGMP in the corpus cavernosum. This results in smooth muscle relaxation and inflow of blood into the penile tissues, thereby producing an erection. Tadalafil has no effect in the absence of sexual stimulation.

Pharmacokinetic properties:
Absorption: Tadalafil is readily absorbed after oral administration and the mean maximum observed plasma concentration (C_{max}) is achieved at a median time of 2 hours after dosing. The rate and extent of absorption of tadalafil are not influenced by food, tadalafil may be taken with or without food.
The mean volume of distribution is approximately 63l, indicating that Tadalafil is distributed into tissues. At therapeutic concentrations, 94% of tadalafil in plasma is bound in proteins.
Biotransformation: Tadalafil is predominantly metabolised by the cytochrome P450 (CYP) 3A4 isoform. The major circulating metabolite is the methylcatechol glucuronide.
Elimination: The mean oral clearance for tadalafil is 2.5l/h and the mean half-life is 17.5 hours in healthy subjects. Tadalafil is excreted predominantly as inactive metabolites, mainly in the faeces (61%) and to a lesser extent in the urine (36%).

INDICATIONS:
Treatment of erectile dysfunction in adult males.
In order for Tadalafil to be effective, sexual stimulation is required.
Tadalafil is not indicated for use by women.
Posology:
Adult men: In general, the recommended dose is 10 mg taken prior to anticipated sexual activity and with or without food. In those patients in whom Tadalafil 10 mg does not produce an adequate effect, 20 mg might be tried. It may be taken at least 30 minutes prior to sexual activity. The maximum dose frequency is once per day. Tadalafil 10mg and 20 mg is intended for use prior to anticipated sexual activity and it is not recommended for continuous daily use. In patients who anticipate a frequent use of Tadalafil (i.e., at least twice weekly) a once daily regimen with the lowest doses of Tadalafil might be considered suitable, based on patient choice and the physician's judgement. The appropriateness of continued use of the daily regimen should be reassessed periodically.
Special Populations:
Elderly men: Dose adjustments are not required in elderly patients.
Renal impairment: 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 tadalafil is not recommended in patients with severe renal impairment.
Hepatic impairment: The recommended dose of Tadalafil 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.
Diabetes: Dose adjustments are not required in diabetic patients.
Paediatric population: Not recommended for under 18 years of age.

METHOD OF ADMINISTRATION:
For oral use only.

CONTRAINDICATIONS:
Hypersensitivity to the active substance or to any of the excipients:
Tadalafil was shown to augment the hypotensive effects of nitrates. This is thought to result from the combined effects of nitrates and tadalafil on the nitric oxide/cGMP pathway. Therefore, administration of Tadalafil to patients who are using any form of organic nitrate is contraindicated.
Tadalafil, must not be used in men with cardiac disease for whom sexual activity is inadvisable. Physicians should consider the potential cardiac risk of sexual activity in patients with pre-existing cardiovascular disease.
The use of tadalafil is therefore contraindicated in the following:
- Patients with myocardial infarction within the last 90 days.
- Patients with unstable angina or angina occurring during sexual intercourse.
- Patients with New York Heart Association class 2 or greater heart failure in the last 6 months.
- Patients with uncontrolled arrhythmias, hypotension (<90/50mmHg), or uncontrolled hypertension.
- Patients with a stroke within the last 6 months.

Tadalafil 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 co-administration of PDE5 inhibitors, including tadalafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension.

WARNINGS & PRECAUTIONS:
Before treatment with Tadalafil: A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes, before pharmacological treatment is considered. 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. Tadalafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. The evaluation of erectile dysfunction should include a determination of potential underlying causes and the identification of appropriate treatment following an appropriate medical assessment. It is not known if Tadalafil is effective in patients who have undergone pelvic surgery or radical non-nerve-sparing prostatectomy.
Cardiovascular: Serious cardiovascular events, including myocardial infarction, sudden cardiac death, unstable angina pectoris, ventricular arrhythmia, stroke, transient ischaemic attacks, chest pain, palpitations and tachycardia, have been reported.
In patients who are taking alpha1 blockers, concomitant administration of Tadalafil may lead to symptomatic hypotension in some patients. The combination of tadalafil and doxazosin is not recommended.
Vision: Visual defects and cases of NAION have been reported in connection with the intake of Tadalafil and other PDE5 inhibitors. The patient should be advised that in case of sudden visual defect, he should stop taking Tadalafil and consult a physician immediately.
Decreased or sudden hearing loss: Cases of sudden hearing loss have been reported after the use of tadalafil. Patients should be advised to stop taking tadalafil and seek prompt medical attention in the event of sudden decrease or loss of hearing.
Hepatic impairment: There is limited clinical data on the safety of single-dose administration of Tadalafil in patients with severe hepatic insufficiency (Child-Pugh class C). If Tadalafil is prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.
Priapism and anatomical deformation of the penis: Patients who experience erections lasting 4 hours or more should be instructed to seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency may result. Tadalafil, 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).
Use with CYP3A4 inhibitors: Caution should be exercised when prescribing Tadalafil to patients using potent CYP3A4 inhibitors (ritonavir, saquinavir, ketoconazole, itraconazole, and erythromycin), as increased tadalafil exposure (AUC) has been observed if the medicinal products are combined.
Tadalafil and other treatments for erectile dysfunction: The safety and efficacy of combinations of Tadalafil and other PDE5 inhibitors or other treatments for erectile dysfunction have not been studied. The patients should be informed not to take Tadalafil in such combinations.

INTERACTIONS WITH OTHER DRUGS & MEDICATIONS:
Cytochrome P450 inhibitors: Tadalafil is principally metabolised by CYP3A4. When using potent CYP3A4 inhibitors (ritonavir, saquinavir, ketoconazole, itraconazole, and erythromycin), an increased tadalafil exposure (AUC) has been observed if the medicinal products are combined.
Although specific interactions have not been studied, other protease inhibitors, such as saquinavir, and other CYP3A4 inhibitors, such as erythromycin, clarithromycin, itraconazole, and grapefruit juice, should be co-administered with caution, as they would be expected to increase plasma concentrations of tadalafil Consequently, the incidence of the adverse reactions listed in section 4.8 might be increased.
Cytochrome P450 inducers: A CYP3A4 inducer, rifampicin can reduce exposure can be anticipated to decrease the efficacy of tadalafil; Other inducers of CYP3A4, such as phenobarbital, phenytoin, and carbamazepine, may also decrease plasma concentrations of tadalafil.
Nitrates: Tadalafil (5 mg, 10 mg and 20 mg) was shown to augment the hypotensive effects of nitrates. Therefore, administration of Tadalafil to patients who are using any form of organic nitrate is contraindicated
Anti-hypertensives (including calcium channel blockers): The co-administration of doxazosin (4 and 8 mg daily) and tadalafil (5 mg daily dose and 20 mg as a single dose) increases the blood pressure-lowering effect of this alpha-blocker in a significant manner. This effect lasts at least twelve hours and may be symptomatic, including syncope. Therefore, this combination is not recommended. Caution should be exercised when using tadalafil in patients treated with any alpha-blockers, and notably in the elderly. Appropriate clinical advice should be given to patients regarding a possible decrease in blood pressure when they are treated with antihypertensive medicinal products.
Riociguat: An additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. Concomitant use of riociguat with PDE5 inhibitors, including tadalafil, is contraindicated.
5- alpha reductase inhibitors: Caution should be exercised when tadalafil is co-administered with 5-ARIs.
Fertility: Tadalafil is not indicated for use by women.

ADVERSE EFFECTS:
The most commonly reported adverse reactions in patients taking Tadalafil for the treatment of erectile dysfunction were headache, dyspepsia, back pain and myalgia, in which the incidences increase with increasing dose of Tadalafil. The adverse reactions reported were transient, and generally mild or moderate. The majority of headaches reported with Tadalafil once-a-day dosing are experienced within the first 10 to 30 days of starting treatment.
The table below lists the adverse reactions for Tadalafil:
Frequency convention: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

Very common	Common	Uncommon	Rare
Immune system disorders			
		Hypersensitivity reactions	Angioedema
Nervous system disorders			
	Headache	Dizziness	Stroke (including haemorrhagic events), Syncope, Transient ischaemic attacks, Migraine, Seizures, Transient amnesia
Eye disorders			
		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
Ear and labyrinth disorders			
		Tinnitus	Sudden hearing loss
Cardiac disorders[1]			
		Tachycardia, Palpitations	Myocardial infarction, Unstable angina pectoris, Ventricular arrhythmia
Vascular disorders			
		Flushing	Hypotension, Hypertension
Respiratory, thoracic and mediastinal disorders			
	Nasal congestion	Dyspnoea, Epistaxis	
Gastrointestinal disorders			
	Dyspepsia	Abdominal pain, Vomiting, Nausea, Gastro-oesophageal reflux	
Skin and subcutaneous tissue disorders			
		Rash	Urticaria, Stevens-Johnson syndrome, Exfoliative dermatitis, Hyperhydrosis (sweating)
Renal and urinary disorders			
		Haematuria	
Musculoskeletal, connective tissue and bone disorders			
	Back pain, Myalgia, Pain in extremity		
Reproductive system and breast disorders			
		Prolonged erections	Priapism, Penile haemorrhage, Haematospermia
General disorders and administration site conditions			
		Chest pain1, Peripheral oedema, Fatigue	Facial oedema2, Sudden cardiac death

OVERDOSE:
In cases of overdose, standard supportive measures should be adopted, as required. Haemodialysis contributes negligibly to tadalafil elimination.

INSTRUCTIONS:
– Store below 30ºC.
– Protect from heat, sunlight & moisture.
– Keep out of the reach of children.
– To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
TADALA Tablet 5 mg : Pack of 1 x 4 tablets.
TADALA Tablet 10 mg : Pack of 1 x 4 tablets.
TADALA Tablet 20 mg : Pack of 1 x 4 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
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FOR FURTHER INFORMATION PLEASE CONTACT:

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