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Tadalafil Tablets USP

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TADALAFIL TABLETS safely and effectively. See full prescribing information for TADALAFIL TABLETS.

TADALAFIL tablets, for oral use

Initial U.S. Approval: 2003

---------- RECENT MAJOR CHANGES ----------

Warnings and Precautions (5.4) 05/2017

---------- INDICATIONS AND USAGE ----------

Tadalafil tablet is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of:

- erectile dysfunction (ED) (1.1)
- the signs and symptoms of benign prostatic hyperplasia (BPH) (1.2)
- ED and the signs and symptoms of BPH (ED/BPH) (1.3)

If tadalafil tablets are used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks (1.4).

---------- DOSAGE AND ADMINISTRATION ----------

- *Tadalafil tablets for use as needed:*
- ED: Starting dose: 10 mg as needed prior to sexual activity. Increase to 20 mg or decrease to 5 mg based upon efficacy/tolerability. Improves erectile function compared to placebo up to 36 hours post dose. Not to be taken more than once per day (2.1).
- *Tadalafil tablets for once daily use:*
- ED: 2.5 mg taken once daily, without regard to timing of sexual activity. May increase to 5 mg based upon efficacy and tolerability (2.2).
- BPH: 5 mg, taken at approximately the same time every day (2.3)
- ED and BPH: 5 mg, taken at approximately the same time every day (2.3, 2.4).
- Tadalafil tablets may be taken without regard to food (2.5).

---------- DOSAGE FORMS AND STRENGTHS ----------

Tablets: 2.5 mg, 5 mg, 10 mg, 20 mg (3).

---------- CONTRAINDICATIONS ----------

- Administration of tadalafil tablets to patients using any form of organic nitrate is contraindicated. Tadalafil tablets were shown to potentiate the hypotensive effect of nitrates (4.1).
- History of known serious hypersensitivity reaction to tadalafil tablets or ADCIRCA® (4.2)
- Administration with guanylate cyclase (GC) stimulators, such as, riociguat (4.3)

---------- WARNINGS AND PRECAUTIONS ----------

- Patients should not use tadalafil tablets if sex is inadvisable due to cardiovascular status (5.1).
- Use of tadalafil tablets with alpha-blockers, antihypertensives or substantial amounts of alcohol (≥5 units) may lead to hypotension (5.6, 5.9).
- Tadalafil tablets are not recommended in combination with alpha-blockers for the treatment of BPH because efficacy of the combination has not been adequately studied and because of the risk of blood pressure lowering. Caution is advised when tadalafil tablets are used as a treatment for ED in men taking alpha-blockers. (2.7, 5.6, 7.1, 12.2).
- Patients should seek emergency treatment if an erection lasts >4 hours. Use tadalafil tablets with caution in patients predisposed to priapism (5.3).
- Patients should stop tadalafil tablets and seek medical care if a sudden loss of vision occurs in one or both eyes, which could be a sign of non-arteritic anterior ischemic optic neuropathy (NAION). Tadalafil tablets should be used with caution, and only when the anticipated benefits outweigh the risks, in patients with a history of NAION. Patients with a "crowded" optic disc may also be at an increased risk of NAION (5.4, 6.2).
- Patients should stop tadalafil tablets and seek prompt medical attention in the event of sudden decrease or loss of hearing (5.5).
- Prior to initiating treatment with tadalafil tablets for BPH, consideration should be given to other urological conditions that may cause similar symptoms (5.14).

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (≥2%) include headache, dyspepsia, back pain, myalgia, nasal congestion, flushing, and pain in limb (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Umedica Laboratories USA Inc. at 1-855-288-5777 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Tadalafil tablets can potentiate the hypotensive effects of nitrates, alpha-blockers, antihypertensives or alcohol (7.1).
- CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) increase tadalafil tablets exposure (2.7, 5.10, 7.2) requiring dose adjustment:
  - Tadalafil tablets for use as needed: no more than 10 mg every 72 hours
  - Tadalafil tablets for once daily use: dose not to exceed 2.5 mg
- CYP3A4 inducers (e.g. rifampin) decrease tadalafil tablets exposure (7.2).

---------- USE IN SPECIFIC POPULATIONS ----------

Hepatic Impairment (2.6, 5.8, 8.6):

- Mild or Moderate: Dosage adjustment may be needed.
- Severe: Use is not recommended.

Renal Impairment (2.6, 5.7, 8.7):

- Patients with creatinine clearance 30 to 50 mL/min: Dosage adjustment may be needed.
- Patients with creatinine clearance less than 30 mL/min or on hemodialysis: For use as needed: Dose should not exceed 5 mg every 72 hours. Once daily use is not recommended.

See 17 for PATIENT COUNSELING INFORMATION and FDA- approved patient labeling

Revised: 04/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Erectile Dysfunction

Tadalafil tablets are indicated for the treatment of erectile dysfunction (ED).

1.2 Benign Prostatic Hyperplasia

Tadalafil tablets are indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

1.3 Erectile Dysfunction and Benign Prostatic Hyperplasia

Tadalafil tablets are indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

1.4 Limitation of Use

If tadalafil tablets are used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of tadalafil tablets decreases from 4 weeks until 26 weeks, and the incremental benefit of tadalafil tablets beyond 26 weeks is unknown *[see Clinical Studies (14.3)]*.

2 DOSAGE AND ADMINISTRATION

Do not split Tadalafil tablets; entire dose should be taken.

2.1 Tadalafil tablets for use as Needed for Erectile Dysfunction

- The recommended starting dose of tadalafil tablets 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.
- Tadalafil tablets for use as needed was shown to improve erectile function compared to placebo up to 36 hours following dosing. Therefore, when planning patients on optimal use of tadalafil tablets, this should be taken into consideration.

2.2 Tadalafil tablets for Once Daily Use for Erectile Dysfunction

The recommended starting dose of tadalafil tablets for once daily use is 2.5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.

The tadalafil tablets dose for once daily use may be increased to 5 mg, based on efficacy and tolerability.

2.3 Tadalafil tablets for Once Daily Use for Benign Prostatic Hyperplasia

- The recommended dose of tadalafil tablets for once daily use is 5 mg, taken at approximately the same time every day.
- When therapy for BPH is initiated with tadalafil tablets and finasteride, the recommended dose of tadalafil tablets for once daily use is 5 mg, taken at approximately the same time every day for up to 26 weeks.

2.4 Tadalafil tablets for Once Daily Use for Erectile Dysfunction and Benign Prostatic Hyperplasia

The recommended dose of tadalafil tablets for once daily use is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.

2.5 Use with Food

Tadalafil tablets may be taken without regard to food.

2.6 Use in Specific Populations

Renal Impairment

Tadalafil tablets for Use as Needed

- Creatinine clearance 30 to 50 mL/min: A starting dose of 5 mg not more than once per day is recommended, and the maximum dose is 10 mg not more than once in every 48 hours.
- Creatinine clearance less than 30 mL/min or on hemodialysis: The dose is 5 mg not more than once in every 72 hours *[see Warnings and Precautions (5.7) and Use in Specific Populations (8.7)]*.

Tadalafil tablets for Once Daily Use

Erectile Dysfunction

- Creatinine clearance less than 30 mL/min or on hemodialysis: Tadalafil tablets dose for once daily use is not recommended *[see Warnings and Precautions (5.7) and Use in Specific Populations (8.7)]*.

Benign Prostatic Hyperplasia and Erectile Dysfunction/Benign Prostatic Hyperplasia

- Creatinine clearance 30 to 50 mL/min: A starting dose of 2.5 mg is recommended. An increase to 5 mg may be considered based on individual response.
- Creatinine clearance less than 30 mL/min or on hemodialysis: Tadalafil tablets for once daily use is not recommended *[see Warnings and Precautions (5.7) and Use in Specific Populations (8.7)]*.

Hepatic Impairment

Tadalafil tablets for Use as Needed

- Mild or moderate (Child Pugh Class A or B): The dose should not exceed 10 mg once per day. The use of tadalafil tablets once per day has not been extensively evaluated in patients with hepatic impairment and therefore, caution is advised.
- Severe (Child Pugh Class C): The use of tadalafil tablets is not recommended *[see Warnings and Precautions (5.8) and Use in Specific Populations (8.6)]*.

Tadalafil tablets for Once Daily Use

- Mild or moderate (Child Pugh Class A or B): Tadalafil tablets for once daily use has not been extensively evaluated in patients with hepatic impairment. Therefore, caution is advised if tadalafil tablets for once daily use is prescribed to these patients.
- Severe (Child Pugh Class C): The use of tadalafil tablets is not recommended *[see Warnings and Precautions (5.8) and Use in Specific Populations (8.6)]*.

2.7 Concomitant Medications

Nitrates

Concomitant use of nitrates in any form is contraindicated *[see Contraindications (4.1)]*.

Alpha-Blockers

ED — When tadalafil tablets are coadministered with an alpha-blocker in patients being treated for ED, patients should be stable on alpha-blocker therapy prior to initiating treatment, and tadalafil tablets should be initiated at the lowest recommended dose *[see Warnings and Precautions (5.6), Drug Interactions (7.1), and Clinical Pharmacology (12.2)]*.

BPH — Tadalafil tablets are not recommended for use in combination with alpha-blockers for the treatment of BPH *[see Warnings and Precautions (5.6), Drug Interactions (7.1), and Clinical Pharmacology (12.2)]*.

CYP3A4 Inhibitors

Tadalafil tablets for Use as Needed — For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose of tadalafil tablets is 10 mg, not to exceed once every 72 hours *[see Warnings and Precautions (5.10) and Drug Interactions (7.2)]*.

Tadalafil tablets for Once Daily Use — For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose is 2.5 mg *[see Warnings and Precautions (5.10) and Drug Interactions (7.2)]*.

3 DOSAGE FORMS AND STRENGTHS

Four strengths of almond-shaped tablets are available in different sizes and yellow color.

2.5 mg tablets debossed with "TAD"

5 mg tablets debossed with "T5"

10 mg tablets debossed with "T10"

20 mg tablets debossed with "T20"

4 CONTRAINDICATIONS

4.1 Nitrates

Administration of tadalafil tablets to patients who are using any form of organic nitrate, either regularly and/or intermittently, is contraindicated. In clinical pharmacology studies, tadalafil tablets were shown to potentiate the hypotensive effect of nitrates *[see Clinical Pharmacology (12.2)]*.

4.2 Hypersensitivity Reactions

Tadalafil tablets are contraindicated in patients with a known serious hypersensitivity to tadalafil (tadalafil tablets or ADCIRCA®). Hypersensitivity reactions have been reported, including Stevens-Johnson syndrome and exfoliative dermatitis *[see Adverse Reactions (6.2)]*.

4.3 Concomitant Guanylate Cyclase (GC) Stimulators

Do not use tadalafil tablets in patients who are using a GC stimulator, such as riociguat. PDE5 inhibitors, including tadalafil tablets may potentiate the hypotensive effects of GC stimulators.

5 WARNINGS AND PRECAUTIONS

Evaluation of erectile dysfunction and BPH should include an appropriate medical assessment to identify potential underlying causes, as well as treatment options.

Before prescribing tadalafil tablets, it is important to note the following:

5.1 Cardiovascular

Physicians should consider the cardiovascular status of their patients, since there is a degree of cardiac risk associated with sexual activity. Therefore, treatments for erectile dysfunction, including tadalafil tablets, should not be used in men for whom sexual activity is inadvisable as a result of their underlying cardiovascular status.

Patients who experience symptoms upon initiation of sexual activity should be advised to refrain from further sexual activity and seek immediate medical attention.

Physicians should discuss with patients the appropriate action in the event that they experience anginal chest pain requiring nitroglycerin following intake of tadalafil tablets. In such a patient, the use of tadalafil tablets where nitrate administration is deemed medically necessary for a life-threatening situation, at least 48 hours should have elapsed after the last dose of tadalafil tablets before nitrate administration is considered. In such circumstances, nitrates should still only be administered under close medical supervision with appropriate hemodynamic monitoring. Therefore, patients who experience anginal chest pain after taking tadalafil tablets should seek immediate medical attention *[see Contraindications (4.1) and Patient Counseling Information (17.1)]*.

Patients with left ventricular outflow obstruction, (e.g., aortic stenosis and idiopathic hypertrophic subaortic stenosis) can be sensitive to the action of vasodilators, including PDE5 inhibitors.

The following groups of patients with cardiovascular disease were not included in clinical safety and efficacy trials for tadalafil tablets, and therefore, no further information is available. tadalafil tablets are not recommended for the following groups of patients:

- 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, hypertension (<90/50 mm Hg), or uncontrolled hypertension
- stroke within the last 6 months.

As with other PDE5 inhibitors, tadalafil has mild systemic vasodilatory properties that may result in transient decreases in blood pressure. In a clinical pharmacology study, tadalafil 20 mg was shown to have an additive decrease in supine blood pressure, relative to placebo, of 1.6/0.8 mm Hg in healthy subjects *[see Clinical Pharmacology (12.2)]*. While this effect should not be of consequence in most patients taking tadalafil tablets, physicians should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects. Patients with severely impaired autonomic control of blood pressure may be particularly sensitive to the actions of vasodilators, including PDE5 inhibitors.

5.2 Potential for Drug Interactions When Taking Tadalafil tablets for Once Daily Use

Physicians should be aware that tadalafil tablets for once daily use provides continuous plasma tadalafil levels and should consider this when evaluating the potential for interactions with medications (e.g., nitrates, alpha-blockers, antihypertensives and potent inhibitors of CYP3A4) and with substantial consumption of alcohol *[see Drug Interactions (7.1, 7.2, 7.3)]*.

5.3 Prolonged Erection

There have been rare reports of prolonged erections greater than 4 hours and priapism (painful erections greater than 6 hours in duration) for this class of compounds. Priapism, if not treated promptly, can result in irreversible damage to the erectile tissue. Patients who have an erection lasting greater than 4 hours, whether painful or not, should seek emergency medical attention.

Tadalafil tablets should be used with caution in patients who have 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).

5.4 Effects on the Eye

Physicians should advise patients to stop use of all phosphodiesterase type 5 (PDE5) inhibitors, including tadalafil tablets, and seek medical attention in the event of a sudden loss of vision in one or both eyes. Such an event may be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), a rare condition but a cause of decreased vision, including permanent loss of vision. that has been reported rarely postmarketing in temporal association with the use of all PDE5 inhibitors. Based on published literature, the annual incidence of NAION is 2.5-11.8 cases per 100,000 in males aged ≥50.

An observational case-crossover study evaluated the risk of NAION when PDE5 inhibitor use, as a class, occurred immediately before NAION onset (within 5 half-lives), compared to PDE5 inhibitor use in a prior time period. The results suggest an approximate 2-fold increase in the risk of NAION, with a risk estimate of 2.15 (95% CI 1.06, 4.34). A similar study reported a consistent result, with a risk estimate of 2.27 (95% CI 0.99, 5.20). Other risk factors for NAION, such as the presence of "crowded" optic disc, may have contributed to the occurrence of NAION in these studies.

Neither the rare postmarketing reports, nor the association of PDE5 inhibitor use and NAION in the observational studies, substantiate a causal relationship between PDE5 inhibitor use and NAION *[see Adverse Reactions (6.2)]*.

Physicians should consider whether their patients with underlying NAION risk factors could be adversely affected by use of PDE5 inhibitors. Individuals who have already experienced NAION are at increased risk of NAION recurrence. Therefore, PDE5 inhibitors, including tadalafil tablets, should be used with caution in these patients and only when the anticipated benefits outweigh the risks. Individuals with "crowded" optic disc are also considered at greater risk for NAION compared to the general population; however, routine screening is not in support screening of prospective users of PDE5 inhibitors, including tadalafil tablets, for this uncommon condition.

Patients with known hereditary degenerative retinal disorders, including retinitis pigmentosa, were not included in the clinical trials, and use in these patients is not recommended.

5.5 Sudden Hearing Loss

Physicians should advise patients to stop taking PDE5 inhibitors, including tadalafil tablets, and seek prompt medical attention in the event of sudden decrease or loss of hearing. These events, which may be accompanied by tinnitus and dizziness, have been reported in temporal association to the intake of PDE5 inhibitors, including tadalafil tablets. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors *[see Adverse Reactions (6.1, 6.2)]*.

5.6 Alpha-blockers and Antihypertensives

Physicians should discuss with patients the potential for tadalafil tablets to augment the blood-pressure-lowering effect of alpha-blockers and antihypertensive medications *[see Drug Interactions (7.1) and Clinical Pharmacology (12.2)]*.

Caution is advised when PDE5 inhibitors are coadministered with alpha-blockers. PDE5 inhibitors, including tadalafil tablets, and alpha-adrenergic blocking agents are both vasodilators with blood-pressure-lowering effects. When vasodilators are used in combination, an additive effect on blood pressure may be anticipated. In some patients, concomitant use of these two drug classes can lower blood pressure significantly *[see Drug Interactions (7.1) and Clinical Pharmacology (12.2)]*, which may lead to symptomatic hypotension (e.g., fainting). Consideration should be given to the following:

ED

- Patients should be stable on alpha-blocker therapy prior to initiating a PDE5 inhibitor. Patients who demonstrate hemodynamic instability on alpha-blocker therapy alone are at increased risk of symptomatic hypotension with concomitant use of PDE5 inhibitors.
- In those patients who are stable on alpha-blocker therapy, PDE5 inhibitors should be initiated at the lowest recommended dose.
- In those patients already taking an optimized dose of PDE5 inhibitor, alpha-blocker therapy should be initiated at the lowest dose. Stepwise increase in alpha-blocker dose may be associated with further additional postural hypotension, but not with additional PDE5 inhibitor dose.
- Safety of combined use of PDE5 inhibitors and alpha-blockers may be affected by other variables, including intravascular volume depletion and other antihypertensive drugs, *[see Dosage and Administration (2.7) and Drug Interactions (7.1)]*.

BPH

- The efficacy of the coadministration of an alpha-blocker and tadalafil tablets for the treatment of BPH has not been adequately studied, and due to the potential vasodilatory effects of combined use resulting in blood pressure lowering, the coordination of tadalafil tablets and alpha-blockers is not recommended for the treatment of BPH. *[see Dosage and Administration (2.7), Drug Interactions (7.1), and Clinical Pharmacology (12.2)]*.
- Patients on alpha-blocker therapy for BPH should discontinue their alpha-blocker at least one day prior to starting tadalafil tablets for once daily use for the treatment of BPH.

5.7 Renal Impairment

Tadalafil tablets for Use as Needed

Tadalafil tablets should be limited to 5 mg not more than once in every 72 hours in patients with creatinine clearance less than 30 mL/min or end-stage renal disease on hemodialysis. The starting dose of tadalafil tablets in patients with creatinine clearance 30 – 50 mL/min should be 5 mg not more than once per day, and the maximum dose should be limited to 10 mg not more than once in every 48 hours. *[see Use in Specific Populations (8.7)]*.

Tadalafil tablets for Once Daily Use

ED

Due to increased tadalafil exposure (AUC), limited clinical experience, and the lack of ability to influence clearance by dialysis, tadalafil tablets for once daily use is not recommended in patients with creatinine clearance less than 30 mL/min *[see Use in Specific Populations (8.7)]*.

BPH and ED/BPH

Due to increased tadalafil exposure (AUC), limited clinical experience, and the lack of ability to influence clearance by dialysis, tadalafil tablets for once daily use is not recommended in patients with creatinine clearance less than 30 mL/min. In patients with creatinine clearance 30 – 50 mL/min, start dosing at 2.5 mg once daily, and increase the dose to 5 mg once daily based upon individual response *[see Dosage and Administration (2.6), Use in Specific Populations (8.7), and Clinical Pharmacology (12.3)]*.

5.8 Hepatic Impairment

Tadalafil tablets for Use as Needed

In patients with mild or moderate hepatic impairment, the dose of tadalafil tablets should not exceed 10 mg. Because of insufficient information in patients with severe hepatic impairment, use of tadalafil tablets in this group is not recommended *[see Use in Specific Populations (8.6)]*.

Tadalafil tablets for Once Daily Use

Tadalafil tablets for once daily use has not been extensively evaluated in patients with mild or moderate hepatic impairment. Therefore, caution is advised if tadalafil tablets for once daily use is prescribed to these patients. Because of insufficient information in patients with severe hepatic impairment, use of tadalafil tablets in this group is not recommended *[see Use in Specific Populations (8.6)]*.

5.9 Alcohol

Patients should be made aware that both alcohol and tadalafil tablets, a PDE5 inhibitor, act as mild vasodilators. When mild vasodilators are taken in combination, blood-pressure-lowering effects of each individual compound may be increased. Therefore, physicians should inform patients that substantial consumption of alcohol (e.g., 5 units or greater) in combination with tadalafil tablets can increase the potential for orthostatic signs and symptoms, including increase in heart rate, decrease in standing blood pressure, dizziness, and headache *[see Clinical Pharmacology (12.2)]*.

5.10 Concomitant Use of Potent Inhibitors of Cytochrome P450 3A4 (CYP3A4)

Tadalafil tablets are metabolized predominantly by CYP3A4 in the liver. The dose of tadalafil tablets for use as needed should be limited to 10 mg no more than once every 72 hours in patients taking potent inhibitors of CYP3A4 such as ritonavir, ketoconazole, and itraconazole *[see Drug Interactions (7.2)]*. In patients taking potent inhibitors of CYP3A4 chronically, the dose of tadalafil tablets for once daily use is 2.5 mg *[see Dosage and Administration (2.7)]*.

5.11 Combination With Other PDE5 Inhibitors or Erectile Dysfunction Therapies

The safety and efficacy of combinations of tadalafil tablets and other PDE5 inhibitors or treatments for erectile dysfunction have not been studied. Inform patients not to take tadalafil tablets with other PDE5 inhibitors, including ADCIRCA.

5.12 Effects on Bleeding

In vitro studies have shown that tadalafil is a selective inhibitor of PDE5. PDE5 is found in platelets. When administered in combination with aspirin, tadalafil 20 mg did not prolong bleeding time, relative to aspirin alone. Tadalafil tablets have not been administered to patients with bleeding disorders or peptic ulcer disease. Tadalafil tablets should be given to patients with these conditions only if the potential benefit is deemed to outweigh the risk. Safety assessment and caution.

5.13 Consideration in Patients About Sexually Transmitted Diseases

The use of tadalafil tablets offers no protection against sexually transmitted diseases. Counseling patients about the protective measures necessary to guard against sexually transmitted diseases, including Human Immunodeficiency Virus (HIV) should be considered.

5.14 Consideration of Other Urological Conditions Prior to Initiating Treatment for BPH

Prior to initiating treatment with tadalafil tablets for BPH, consideration should be given to other urological conditions that may cause similar symptoms. In addition, prostate cancer and BPH may coexist.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Tadalafil was administered to over 9000 men during clinical trials worldwide. In trials of tadalafil tablets for once daily use, a total of 1434, 962, and 115 were treated for at least 6 months, 1 year, and 2 years, respectively. If tadalafil tablets for use as needed, over 1300 and 1000 subjects were treated for at least 6 months and 1 year respectively.

Table 1: Treatment-Emergent Adverse Reactions Reported by ≥2% of Patients Treated with tadalafil tablets (10 or 20 mg) and More Frequent on Drug than Placebo in the Eight Primary Placebo-Controlled Clinical Studies (Including a Study in Patients with Diabetes) for tadalafil tablets for use as Needed

Adverse Reaction	Placebo (N=4078)	Tadalafil 5 mg (N=151)	Tadalafil 10 mg (N=394)	Tadalafil 20 mg (N=635)
Headache	5%	11%	11%	15%
Dyspepsia	1%	4%	8%	10%
Back pain	2%	3%	3%	6%
Myalgia	1%	1%	4%	3%
Nasal congestion	1%	2%	3%	3%
Flushing*	1%	2%	3%	3%
Pain in limb	1%	1%	3%	3%

*The term flushing includes: facial flushing and flushing

Tadalafil tablets for Once Daily Use for ED

In three placebo-controlled clinical trials of 12 or 24 weeks duration, age was 58 years (range 21 to 82) and the discontinuation rate due to adverse events in patients treated with tadalafil was 3.2%, compared to 2.8% in placebo- treated patients.

The following adverse reactions were reported *(see Table 2)* in clinical trials of 12 weeks duration:

Table 2: Treatment-Emergent Adverse Reactions Reported by ≥2% of Patients Treated with Tadalafil tablets for Once Daily Use (2.5 or 5 mg) and More Frequent on Drug than Placebo in the Three Primary Placebo-Controlled Phase 3 Clinical Studies (Including a Study in Patients with Diabetes) for Tadalafil tablets for Once Daily Use for ED

Adverse Reaction	Placebo (N=248)	Tadalafil 2.5 mg (N=196)	Tadalafil 5 mg (N=304)
Headache	5%	3%	6%
Dyspepsia	2%	4%	5%
Nasopharyngitis	2%	4%	4%
Back pain	1%	3%	3%
Upper respiratory tract infection	1%	3%	3%
Flushing	1%	1%	3%
Myalgia	1%	2%	2%
Cough	0%	4%	2%
Diarrhea	0%	2%	2%
Nasal congestion	0%	2%	2%
Pain in extremity	0%	1%	2%
Urinary tract infection	0%	2%	0%
Gastroesophageal reflux disease	0%	2%	1%
Abdominal pain	0%	2%	1%

The following adverse reactions were reported *(see Table 3)* over 24 weeks treatment duration in one placebo-controlled clinical study:

Table 3: Treatment-Emergent Adverse Reactions Reported by ≥2% of Patients Treated with Tadalafil tablets for Once Daily Use (2.5 mg) and More Frequent on Drug than Placebo in One Placebo-Controlled Clinical Study of 24 Weeks Treatment Duration for Tadalafil tablets for Once Daily Use for ED

Adverse Reaction	Placebo (N=364)	Tadalafil 2.5 mg (N=181)	Tadalafil 5 mg (N=97)
Nasopharyngitis	5%	6%	6%
Gastroenteritis	2%	3%	3%
Back pain	3%	5%	2%
Upper respiratory tract infection	1%	3%	4%
Dyspepsia	1%	4%	1%
Gastroesophageal reflux disease	0%	3%	2%
Myalgia	2%	4%	1%
Hypertension	0%	1%	3%
Nasal congestion	0%	2%	4%

Tadalafil tablets for Once Daily Use for BPH and for ED and BPH

In three placebo-controlled clinical trials of 12 weeks duration, two in patients with BPH and one in patients with ED and BPH, the mean age was 63 years (range 44 to 92) and the discontinuation rate due to adverse events in patients treated with tadalafil was 3.6% compared to 1.6% in placebo-treated patients. Adverse reactions leading to discontinuation reported by at least 2 tadalafil tablets treated patients were: upper abdominal pain, dyspepsia and myalgia. The following adverse reactions were reported *(see Table 4)*.

Table 4: Treatment-Emergent Adverse Reactions Reported by ≥1% of Patients Treated with Tadalafil tablets for Once Daily Use (5 mg) and More Frequent on Drug than Placebo in Three Placebo-Controlled Clinical Studies of 12 Weeks Treatment Duration, Including Two Studies for tadalafil tablets for Once Daily Use for BPH and One Study for ED and BPH

Adverse Reaction	Placebo (N=576)	Tadalafil 5 mg (N=585)
Headache	2.3%	4.1%
Dyspepsia	0.2%	2.4%
Back pain	1.4%	2.4%
Nasopharyngitis	1.6%	2.1%
Diarrhea	1.0%	1.4%
Pain in extremity	0.3%	1.4%
Myalgia	0.3%	1.2%
Dizziness	0.5%	1.0%

Additional, less frequent adverse reactions (<1%) reported in the controlled clinical trials of tadalafil tablets for BPH or ED and BPH included: gastroesophageal reflux disease, upper abdominal pain, nausea, vomiting, arthralgia, and muscle spasm.

Back pain or myalgia was reported at incidence rates described in Tables 1 through 4. In tadalafil clinical pharmacology trials, back pain or myalgia generally occurred 12 to 24 hours after dosing and typically resolved within 48 hours. The back pain/myalgia associated with tadalafil treatment was characterized by diffuse bilateral lower lumbar, gluteal, thigh, or thoracolumbar muscular discomfort and was exacerbated by recumbency.

In general, pain was reported as mild or moderate in severity and resolved without medical treatment, but severe back pain was reported with a low frequency (<5% of all reports). When medical treatment was necessary, acetaminophen or non-steroidal anti-inflammatory drugs were generally effective; however, in a small percentage of subjects who required treatment, a mild narcotic (e.g., codeine) was used. Overall, approximately 0.5% of all subjects treated with tadalafil tablets for on demand use discontinued treatment as a consequence of back pain/myalgia. In the 1-year open label extension study, back pain and myalgia were reported in 5.5% and 1.3% of patients, respectively. Clinical laboratory testing, including measures for inflammation, muscle injury, or renal damage revealed no evidence of medically significant underlying pathology. Incidence rates for tadalafil tablets for once daily use for ED, BPH and BPH/ED are described in Tables 2, 3 and 4. In studies of tadalafil tablets for once daily use, adverse reactions of back pain and myalgia were generally mild or moderate with a discontinuation rate of <1% across all indications.

Across placebo-controlled studies with tadalafil tablets for use as needed for ED, diarrhea was reported more frequently (4% overall and 2% in patients 65 years of age and older who were treated with tadalafil tablets (2.5% of patients) *[see Use in Specific Populations (8.5)]*.

Across all studies with any tadalafil tablets dose, reports of changes in color vision were rare (<0.1% of patients). The following adverse reactions were identified as isolated reports; less frequent events (<2%) reported in controlled clinical trials of tadalafil tablets for once daily use or use as needed. A causal relationship of these events to tadalafil tablets is uncertain. Excluded from this list are those events that were minor, those with no plausible relation to drug use, and reports too imprecise to be meaningful.

Body as a Whole — hypersensitivity reactions

Cardiovascular — angina pectoris, chest pain, hypotension, myocardial infarction, postural hypotension, palpitations, syncope, tachycardia

Digestive — abnormal liver function tests, dry mouth, dysphagia, esophagitis, gastritis, GGTP increased, loose stools, nausea, upper abdominal pain, vomiting, gastroesophageal reflux disease, hemorrhoidal hemorrhage, rectal hemorrhage

Musculoskeletal — arthralgia, neck pain

Nervous — dizziness, hypesthesia, incoordination, paresthesia, somnolence, vertigo

Renal and Urinary — renal impairment

Respiratory — dyspnea, epistaxis, pharyngitis

Skin and Appendages — pruritus, rash, sweating

Ophthalmologic — blurred vision, changes in color vision, conjunctivitis (including conjunctival hyperemia), eye pain, lacrimation increase, swelling of eyelids

Otologic — sudden decrease or loss of hearing, tinnitus

Urogenital — priapism *[see Warnings and Precautions (5.3)]*.

7 DRUG INTERACTIONS

7.1 Potential for Pharmacodynamic Interactions with Tadalafil tablets

Nitrates — Administration of tadalafil tablets to patients who are using any form of organic nitrate, is contraindicated. In clinical pharmacology studies, tadalafil tablets were shown to potentiate the hypotensive effect of nitrates. In a patient who has taken tadalafil tablets, where nitrate administration is deemed medically necessary for a life-threatening situation, at least 48 hours should elapse after the last dose of tadalafil tablets before nitrate administration is considered. In such circumstances, nitrates should only be administered under close medical supervision with appropriate hemodynamic monitoring. Therefore, pat