Cytochrome P450 substrates— Tadalafil is not expected to cause clinically s

2 (e.g., theophyline) — Tadalafii (10 mg once per day) had no significant effect on the etics of theophyline. When tadalafi was administered to subjects taking theophyline, a small (35 bests per minute) of the increase in heart rate associated with theophyline was observed. CYP2C9 (e.g., warfarin) — Tadalafil (10 mg and 20 mg once per day) had no significant effect on sure (AUC) to S-warfarin or R-warfarin, nor did tadalafil affect changes in prothrombin time induced

CYP3A (e.g., mickacolam, lovastarin or bosentan) — Tadalatil (10 mg and 20 mg once per day) had no significant effect on exposure (AUC) to midsacolam or lovastatin. Tadalatil (40 mg once per day) had no clinically significant effect on exposure (AUC and C_{mistal}) of bosentan, a substrate of CYP2C9 and CYP3A, or its mataballist.

Aspirin — Tadakafii (10 mg and 20 mg once per day) did not potentiate the increase in bleeding time caused by aspirin

P-ghypoprotein (e.g., dipoxin) — Coadministration of tadalafil (40 mg once per day) for 10 days did not have a significant effect on the steady-state pharmacoleinetics of digoxin (0.25 mg/day) in healthy subjects. Combined oral contraceptives— At steady-state, tadalatil (40 mg once per day) increased ethinyl estradiol exposure (AID) by 28% and c_{max} by 70% relative to oral contraceptive administered with placebo. There uses no circulticate data-fat to dataful for invancementary. Antacids—Simultaneous administration of a matacid (magnesium hydroxids/aluminum tydroxids) and tadadril (10 mg) reduced the apparent rate of absorption of tadalafili without altering exposure (ADC) to datalafil.

H2 antagonists (e.g., nizatidine) — An increase in gastric pH resulting from no significant effect on tadalati (10 mg) pharmacokinetics.

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14.3 Reproductive Tailcology Studies

All Reproductive Tailcology Studies

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All Reproduction shades have been preferred in risk and mixe at spoopers up to 17 times to MARIO.

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CLINICAL STUDIES Tadalatil for Pulmonary Arterial Hypertension

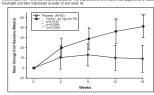
14.1 Tedalatili for Pulmonary Arterial Hypertension
A madimized, double-blief, if a laveis placebo-controlled study was conducted
pulmonary afterial hypertension, defined as a resting mean pulmorary areby pressure
pulmonary afterial hypertension, defined as a resting mean pulmorary areby pressure
Wood satists via replication, and a resting a resting a resting to the study and
Wood satists via replication. Allowed basicipuum dieneary inclusion
be desiring up to 125 mg whose daily and chronic anticoapsistion. The use of proceducition of
prosphoridestream intimizer, or other chronic Partitionarions were not permitted.

prospinosestrate intention," of order crimiter. For missing the state of permission.

Solitication were characterised by a final permission of the state of the permission of the state of

The control of the co

om baseline at week 16 in 6-MWD (see Figure 1). In o-adjusted mean change increase in 6-MWD was 33 provement in 6-MWD was apparent at 8 weeks of



patients taking only in 6-MWD was 44

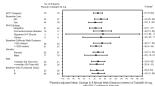
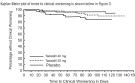


Figure 2: Placebo-adjusted Mean Change in 6-Minute Walk Distance (meters) of Tadalatil Tablets 40 mg

nical worsening (defined as death, lung transplantation, atrial septostomy, hospitalization PAH, initiation of new PAH therapy [prostacyclin or analog, endothelin receptor ord, or worsening WHO functional class) in the diadalati tablets 40 mg group compared ad the groups that used lower doses of tadalatifit tablets.





ents (N+357) from the placebo-controlled study entered a long-term extension study. Of these, its have been treated with tadalafil for at least 6 months and 182 for 1 year (median exposure 356

us a counter group, uses data must be interpreted cautiously.

How Supplied

Tadslarf tablets USP, 20 mg are white colour, capsule shaped, biconvex, filmwith T15' on one side and 'ff' on the other side. They are supplied as follows:

les of 30 tablets NDC 31722-647-30 on of 100 (10x10) unit-dose tablets NDC 31722-647-31

Storage htms at 20°C to 25°C (68°F to 77°F); [see USP Controlled Room

- out of reach of children. ENT COUNSELING INFORMATION FDA-Approved Patient Labeling (Pat Inform patients of contraindicatio stimulators.
- inform patients that tadalaffi is also marketed as CIALIS for erectile dysfunction (ED) and for the signs and symptoms of benign prostatic hyperplasia (BPH). Advise polients taking tadalaffi tablets not to take CIALIS or other PDES inhibitors. Advise patients to seek immediate medical attention in the event of a sudden loss of vision in one or both eyes while taking badaloff tablets. Such an event may be a sign of MAION.
- Advise patients to seek prompt medical attention in the event of sudden decrease or loss of hearing while taking tadalaff tablets. These events may be accompanied by tinnitus and dizziness.



PATIENT INFORMATION Tadalafil (ta-DAL-a-fil) Tablets, USP

Read this patient information before you start taking tadalafil tablets and each time you get a refill. There may be new information his information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about tadalafil tablets?

Never take tadalafil tablets with any nitrate or guanylate cyclase stimulator medicines:

- Your blood pressure could drop quickly to an unsafe level
- You could get dizzy, faint and even have a heart attack or stroke.

Nitrates include:

- Medicines that treat chest pain (angina)
- Nitroglycerin in any form including tablets, patches, sprays, and ointments
- Other nitrate medicines (isosorbide mononitrate or dinitrate)
- Street drugs that are inhaled, called "poppers" (amyl nitrate butyl nitrate or nitrite)

Counylate or inititle)
Guanylate cyclase stimulators include:
Riocipuat (Adempas®) a medicine that treats pulmonary arterial hypertension and chronic-thromboembolic pulmonary hypertension

hypertension
Ask your healthcare provider or pharmacist if you are not sure if
you take a nitrate or guanylate cyclase stimulator medicine.
What are tadalafil tablets?
Tadalafil tablet is a prescription medicine used to treat pulmonary
arterial hypertension (PAH, high blood pressure in your lungs) to
improve your ability oexercise.
It is not known if tadalafil tablet is safe or effective in children.
Who should not take tadalafil tablets?
Do not take tadalafil tablets?
If you

Do not take tadalafil tablets if you

- o not take raudain unders in your take any medicines called nitrates. use recreational drugs called "poppers" like amyl nitrate, butyl nitrate or nitrate to raitrate to a called guanylate cyclase stimulators
- are allergic to tadalafil or any other ingredient in tadalafil tablets.
 See "What are the ingredients in tadalafil tablets?" at the end of this leaflet.
 See "What is the most important information I should know about tadalafil tablets?"

What should I tell my healthcare provider before taking tadalafil tablets?

- tablets?
 Before taking tadalafil tablets, tell your healthcare provider about all of your medical conditions, including if you:

 are allergic to tadalafil tablets or Calis or any of its ingredients. See the end of this leaflet for a complete list of ingredients in tadalafit tablets.

 have pulmonary veno-occlusive disease (PVOD)

 have heart profilems such as canding chest pain), heart
- have heart problems such as angina (chest pain), heart failure, irregular heartbeats, or have had a heart attack have low blood pressure or high blood pressure that is not
- have had a stroke
- have liver problems
- have kidney problems or get dialysis have stomach ulcers
- have retinitis pigmentosa, a rare genetic eve disease have ever had any sudden vision loss, including any damage to your optic nerve or NAION.
- have ever had hearing problems such as ringing in the ears, dizziness, or loss of hearing
- ears, uccuress, or uss or nearing have a deformed penis shape or Peyronie's disease have had an erection that lasted more than 4 hours have blood cell problems such as sickle cell anemia, multiple myeloma, or leukemia
- are pregnant or planning to become pregnant. It is not known if tadalafil tablets will harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breast feed. It is not known if tadalafil passes into your breast milk. You and your healthcare provider should decide if you will take tadalafil tablets or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Tadalafil tablets and other medicines may affect each other.

Especially tell your healthcare provider if you take any of these medicines:

- cines:

 nitrates or guanylate cyclase stimulators (see "What is
 the most important information I should know about
 tadafalli tablets?")
 anti-hypertensives, used to treat high blood pressure. Your
 blood pressure could suddenly drop. You could get dizzy
- or faint alpha blockers, used to treat prostate disease and high
- blood pressure. Your blood pressure could suddenly drop You could get dizzy or faint.
- protease inhibitors, used to treat HIV infection, such as ritonavir (Norvir®, Kaletra®) ketoconazole (Extina®, Xolegel®, Ketozole®, Nizoral A-D®, Nizoral®) itraconazole (Sporanox®)
- erythromycin (several brand names exist. Please consult your healthcare provider to determine if you are taking this medicine) rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®)
- bosentan (Tracleer®)
 - phenobarbital, phenytoin (Dilantin®), carbamazepine (Tegretol®)
- CIALIS® or other medicines or treatments for erectile dysfunction (impotence).
- dysfunction (impotence). Tadalafil table is also marketed as CIALIS for the treatment of male erectile dysfunction (ED, impotence) and for the signs and symptoms of benign prostatic hyperplasia (BPH, enlarged prostate). Do not take both tadalafil tablets and CIALIS. Do not take tadalafil tablets and other medicines or treatments for erectile dysfunction.

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure. Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take tadalafil tablets?

- Take tadalafil tablets exactly as your healthcare provider tells
- you.

 Take tadalafil tablets at the same time every day. You should take both tablets at the same time, one after the other, every day. Do not split your dose.

 Tadalafil tablets can be taken with or without food.

- radiatini ladiuetis can be taken with or without food.
 Do not change your dose or stop taking tadalafit lablets without speaking to your healthcare provider.
 If you take too much tadalafit lablets, call your healthcare provider or go to an emergency department right away.

 What should I avoid white taking tadalafit lablets?

 Do not have more than A a lock-contribute district.

Do not have more than 4 alcohol-containing drinks in a short period of time while you take tadalafil tablets. Drinking too much alcohol can lower your blood pressure. You could get dizzy or

What are the possible side effects of tadalafil tablets? The following side effects were reported rarely in patients taking tadalafil:

- Decreased eyesight or loss of vision in one or both eyes (NAION). If you notice a sudden decrease or loss of vision in one or both eyes, contact a healthcare provider right away.
- one or both eyes, contact a healthcare provider right away.

 Sudden decrease or loss of hearing, sometimes with ringing in the ears and dizziness. If you notice a sudden decrease or loss of hearing, contact a healthcare provider right away.

 In men, an erection that lasts more than 4 hours (with or without pain). Talk to your healthcare provider or go to the emergency department right away. An erection that lasts more than 4 hours must be treated as soon as possible or you can have lasting damage to your penis, including the inability to have erections.

 See "What is the most important information I should know about datailall tablets?"

The most common side effects with tadalafil tablets include:

- headache
- muscle pain
- getting red or hot in the face (flushing)
- nausea pain in the arms, legs, or back

pain in the arms, legs, or back
 upset stomach
 stuffy or congested nose
 stuffy or congested nose
 Tell your healthcare provider about any side effect that bothers
you or does not go away.
 These are not all the possible side effects of tadalafil tablets.
 For more information, ask your healthcare provider or
pharmacist. Call your doctor for medical advice about side
effects. You may report side effects to FDA at 1-004-PDA-1086.

How Should I Store Tadalafil Tablets?

Store tadalafil tablets at room temperature between 68°F to 77°F (20°C to 25°C)

Keep tadalafil tablets and all medicines out of the reach of

Continued.

General Information about the safe and effective use of tadalafil tablets tablets
Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use tadalafil tablets for a condition for which it was not prescribed. Do not give tadalafil tablets to other people, even if they have the same symptoms you have. It may harm them.

symptoms vin forwar in ray narm tram primise patient information leaflet summarizes the most important information about tadalafil tablets. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about tadalafil tablets are five for the fact of the control of the

For more information, call 1-866-495-1995.

What Are The Ingredients In Tadalafil Tablets?

what Are Tie Ingrequentus in rapadami rabules? Active Ingredient tadalafil, USP Inactive Ingredients: colloidal silicon dioxide, copovidone, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyoxyl 40 hydrogenated castor oil, talc, titanium dioxide, and friacetin. Rx only

*The brands listed are trademarks of their respective owners and are not trademarks of Hetero Labs Limited. The makers of these brands are not affiliated with and do not endorse Hetero Labs Limited or its products.

Patient Information available at http://camberpharma.com/medication-guides



Manufactured for: Camber Pharmaceutic Piscataway, NJ 08854 iticals. Inc

By: **HETERO™** Hetern I abs Limited Jeedimetla, Hyderabad - 500 055, India

Revised: 01/2019