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FDA Approves Addition to CIALIS® (tadalafil) Product Label

Study Data Shows Cialis 5 mg Initiated with Finasteride Provides Significantly Greater Improvements in Urinary Symptoms of Benign Prostatic Hyperplasia than Placebo with Finasteride

INDIANAPOLIS, Oct. 25, 2013 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the U.S. Food and Drug Administration (FDA) approved a product label addition for CIALIS to include data from a 26-week study that showed CIALIS 5 mg for once daily use started in combination with finasteride significantly improved the signs and symptoms of benign prostatic hyperplasia (BPH) as early as 4 weeks, compared to placebo with finasteride, in men with BPH and an enlarged prostate. The combination of CIALIS and finasteride initiated for BPH therapy is recommended for up to 26 weeks because the incremental benefit of CIALIS decreases from 4 weeks until 26 weeks, and the incremental benefit of CIALIS beyond 26 weeks is unknown.

CIALIS is approved by the FDA to treat erectile dysfunction (ED), the signs and symptoms of BPH, and both ED and the signs and symptoms of BPH (ED+BPH). Finasteride is a type II 5 alpha-reductase inhibitor (5-ARI) approved by the FDA for the treatment of BPH in men with an enlarged prostate.

"Urinary symptom improvement with 5-ARI therapy can take 6 to 12 months," said Claus Roehrborn, MD, chairman, Department of Urology, The University of Texas Southwestern Medical Center. "These data demonstrate that the combination of CIALIS 5 mg for once daily use with finasteride leads to symptom improvement as early as four weeks in men with BPH and an enlarged prostate. This means that CIALIS 5 mg for once daily use can be an effective option for early symptom relief when started in combination with finasteride."

The primary endpoint of the study - changes in total International Prostate Symptom Score (IPSS) at 12 weeks - demonstrated that symptom improvement in patients starting BPH treatment with CIALIS 5 mg for once daily use and finasteride was greater than those starting with placebo and finasteride (-5.2 vs. -3.8; $P = .001$). Key secondary endpoints demonstrated that improvements in IPSS occurred at the first scheduled observation at week 4 (-4.0 vs. -2.3; $P < .001$) and continued through week 26.

It is important to note that CIALIS is not to be taken with medicines called "nitrates" such as isosorbide dinitrate or isosorbide mononitrate which are often prescribed for chest pain; or with recreational drugs called "poppers" like amyl or butyl nitrite, as the combination may cause an unsafe drop in blood pressure; or if allergic to CIALIS or ADCIRCA® (tadalafil), or any of its ingredients. Anyone who experiences any symptoms of an allergic reaction, such as rash, hives, swelling of the lips, tongue or throat, or difficulty breathing or swallowing, should call a healthcare provider or get help right away.

In a subgroup of patients with BPH who were also sexually active and had ED at baseline, CIALIS initiated with finasteride significantly improved erectile function, as measured by the International Index of Erectile Dysfunction—Erectile Function Domain, compared to placebo with finasteride. These results were evident at 4 weeks (3.7 vs. -1.1; $P < .001$), 12 weeks (4.7 vs. 0.6; $P < .001$) and 26 weeks (4.7 vs. 0.0; $P < .001$).

About the Study

The randomized, double-blind, placebo-controlled, 26-week trial assessed the efficacy and safety of CIALIS 5 mg for once daily use or placebo co-administered with finasteride 5 mg in 696 men aged 45 years and older (mean age 64) with an IPSS of at least 13, a urine flow rate (Qmax) of 4 milliliters per second (mL/sec) to 15 mL/sec and a prostate volume at least 30 mL. The study was conducted at 70 sites in 13 countries.[1]

The primary measure was the IPSS, a questionnaire evaluating lower urinary tract symptoms occurring during the preceding month where lower scores indicate less severe symptoms. The pre-specified secondary measure was the International Index of Erectile Function-Erectile Function Domain (IIEF-EF), a questionnaire evaluating erectile function where higher scores indicate better erectile function.

Results from the Phase 3b study — Study H6D-CR-LVIW — have been accepted for publication in *The Journal of Urology* and are available now online at <http://dx.doi.org/10.1016/j.juro.2013.09.059>.

About BPH and ED

Benign prostatic hyperplasia (BPH) is a condition where the prostate enlarges, which can cause urinary symptoms like needing

to go urgently and frequently.

ED is a condition where the penis does not fill with enough blood to harden and expand when a man is sexually excited, or when he cannot keep an erection.

BPH and ED are conditions that may occur in the same patient. Several studies have shown that many men with ED also experience the symptoms of BPH.[2][3],[4]

About CIALIS

CIALIS is indicated for the treatment of men with erectile dysfunction (ED), men with the signs and symptoms of benign prostatic hyperplasia (BPH), and men with both ED and the signs and symptoms of BPH. CIALIS is not for women or children. If CIALIS is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks.

Important Safety Information for CIALIS® (tadalafil) tablets

What Is The Most Important Information I Should Know About CIALIS?

Do not take CIALIS if you:

- **take medicines called "nitrates"** such as isosorbide dinitrate or isosorbide mononitrate which are often prescribed for chest pain as the combination may cause an unsafe drop in blood pressure
- use recreational drugs called "poppers" like amyl nitrite and butyl nitrite
- **are allergic to CIALIS or Adcirca® (tadalafil), or any of its ingredients.** Call your healthcare provider or get help right away if you experience any symptoms of an allergic reaction, such as **rash**, **hives**, swelling of the lips, tongue or throat, or difficulty breathing or swallowing

After taking a single tablet, some of the active ingredient of CIALIS remains in your body for more than 2 days. The active ingredient can remain longer if you have problems with your kidneys or liver, or you are taking certain other medications.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex. Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease.

What Should I Tell My Healthcare Provider Before Taking CIALIS?

CIALIS is not right for everyone. Only your healthcare provider and you can decide if CIALIS is right for you. Ask your healthcare provider if your heart is healthy enough for you to have sexual activity. You should not take CIALIS if your healthcare provider has told you not to have sexual activity because of your health problems. Before taking CIALIS, tell your healthcare provider about all your medical problems, particularly if you have or ever had:

- **heart problems** such as chest pain (angina), heart failure, irregular heartbeats, or have had a heart attack
- **high or low blood pressure** or have high blood pressure that is not controlled
- **stroke**
- **liver or kidney problems or require dialysis**
- **retinitis pigmentosa**, a rare genetic (runs in families) eye disease
- **severe vision loss, including a condition called NAION**
- **stomach ulcers or a bleeding problem**
- **a deformed penis shape** or Peyronie's disease
- **an erection that lasted more than 4 hours**
- **blood cell problems** such as sickle cell anemia, multiple myeloma, or leukemia

Can Other Medicines Affect CIALIS?

Tell your healthcare provider about all the medicines you take especially if you take:

- medicines called "nitrates" which are often prescribed for chest pain
- alpha-blockers often prescribed for prostate problems
- blood pressure medications
- medicines for HIV or some types of oral antifungal medications
- some types of antibiotics such as clarithromycin, telithromycin, erythromycin (several brand names exist, please contact your healthcare provider to determine if you are taking this medicine)
- other medicines or treatments for erectile dysfunction (ED)
- CIALIS is also marketed as Adcirca for the treatment of pulmonary arterial hypertension. Do not take both CIALIS and Adcirca. Do not take sildenafil citrate (Revatio®)* with CIALIS.

What Should I Avoid While Taking CIALIS?

- Do not use other ED medicines or ED treatments while taking CIALIS.
- Do not drink too much alcohol when taking CIALIS (for example, 5 glasses of wine or 5 shots of whiskey). Drinking too much alcohol can increase your chances of getting a headache or getting dizzy, increasing your heart rate, or lowering your blood pressure.

What Are The Possible Side Effects Of CIALIS?

The most common side effects with CIALIS are: headache, indigestion, back pain, muscle aches, flushing, and stuffy or runny nose. These side effects usually go away after a few hours. Men who get back pain and muscle aches usually get it 12 to 24 hours after taking CIALIS. Back pain and muscle aches usually go away within 2 days. Call your healthcare provider if you get any side effect that bothers you or one that does not go away.

Uncommon but serious side effects include:

An erection that won't go away: If you get an erection lasting more than 4 hours, seek immediate medical help to avoid long-term injury.

In rare instances, men taking prescription ED tablets, including CIALIS, reported a sudden decrease or loss of vision or hearing (sometimes with ringing in the ears and dizziness). It's not possible to determine if these events are related directly to the ED tablets or to other factors. If you have a sudden decrease or loss of vision or hearing, stop taking any ED tablet, including CIALIS and call a healthcare provider right away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

CIALIS does not:

- cure ED
- increase a man's sexual desire
- protect a man or his partner from sexually transmitted diseases, including HIV
- serve as a male form of birth control

CIALIS is available by prescription only. For additional information, talk to your doctor and see full Patient Information at <http://pi.lilly.com/us/cialis-ppi.pdf> and Prescribing Information at <http://pi.lilly.com/us/cialis-pi.pdf>, or visit www.cialis.com for more information.

* The brand listed is a trademark of its respective owner and is not a trademark of Eli Lilly and Company. The maker of this brand is not affiliated with and does not endorse Eli Lilly and Company or its products.

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About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs.

This press release contains forward-looking statements about the use of Cialis for the treatment of BPH and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development, commercialization, and regulatory review. There is no guarantee that the product will receive additional regulatory approvals. There is also no guarantee that the product will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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[2] Rosen R, Altwein J, Boyle P, Roger SK, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol. 2003;44(6):637-649.

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[4] Gacci M, et al. Critical analysis of the relationship between sexual dysfunctions and lower urinary tract symptoms due to benign prostatic hyperplasia. In press. Eur Urol 2011; doi:10.1016/j.eururo.2011.06.037.

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