



New Study Evaluates Cialis® in parallel with Tamsulosin in Men with Signs and Symptoms Suggestive of Benign Prostatic Hyperplasia

Phase III study met primary endpoint

INDIANAPOLIS, Feb. 7, 2012 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that a Phase III study, published online by *European Urology*, showed both Cialis® (tadalafil) and tamsulosin significantly improved scores on the International Prostate Symptom Score (IPSS), compared to placebo, in men with signs and symptoms suggestive of benign prostatic hyperplasia (BPH). Cialis improved erectile dysfunction (ED) in those men who had both signs and symptoms of BPH and ED. The study also showed that maximum urinary flow rate increased significantly versus placebo with both Cialis and tamsulosin. This is the first international, placebo-controlled study evaluating Cialis in parallel with tamsulosin (as an active control) for signs and symptoms of BPH in the same population.

"We are very pleased with the results of this study," said Brad Woodward, M.D., senior medical director for Eli Lilly and Company. "Lilly is committed to research that can help us advance our understanding of ED and BPH — two conditions that affect millions of men worldwide."

Cialis for daily use is approved to treat ED, the signs and symptoms of BPH, and ED and the signs and symptoms of BPH in men who have both conditions (ED+BPH).

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 Addirca® (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.

About the Study

The randomized, double-blind, placebo-controlled, parallel-group, 12-week trial, conducted in 44 urology centers in 10 countries, assessed the efficacy and safety of Cialis 5 mg for daily use in parallel with tamsulosin 0.4 mg in men aged 45 years and older with signs and symptoms of BPH.

The primary measure was the International Prostate Symptom Score (IPSS), a questionnaire evaluating lower urinary tract symptoms (LUTS) occurring during the preceding month where lower scores indicate less severe LUTS. The key secondary measure was the BPH Impact Index (BII), a questionnaire evaluating the impact of urinary problems on health and functioning, with lower scores indicating less impact. Also, the International Index of Erectile Function-Erectile Function domain (IIEF EF), a questionnaire evaluating sexual function where higher scores indicate better erectile function, was measured in those men who had both ED and signs and symptoms of BPH (approximately 60% of subjects).

Cialis met the primary endpoint, significantly improving IPSS total scores through 12 weeks versus placebo (-2.1, $p = 0.001$). Tamsulosin also significantly improved IPSS total scores through 12 weeks versus placebo (-1.5; $p = 0.023$). After four weeks, BII significantly improved with Cialis versus placebo (-0.8; $p < 0.001$) and tamsulosin versus placebo (-0.9; $p < 0.001$), and it improved after 12 weeks (Cialis -0.8, $p = 0.003$; tamsulosin -0.6, $p = 0.026$). The IIEF-EF domain improved with Cialis versus placebo (4.0; $p < 0.001$) but not with tamsulosin versus placebo (-0.4; $p = 0.699$).

This was the first Cialis study to show significant improvement in signs and symptoms of BPH after one week and a significant increase in maximum urinary flow rate (Qmax) at 12 weeks. Both treatments significantly improved total IPSS as early as one week (Cialis and tamsulosin both -1.5; $p < 0.01$); Qmax increased significantly versus placebo with both Cialis (2.4 ml/s; $p = 0.009$) and tamsulosin (2.2 ml/s; $p = 0.014$).

This study did not directly compare Cialis versus tamsulosin.

The proportion of subjects reporting at least one treatment-emergent adverse event (TEAE) was: Cialis 23.4%, tamsulosin 23.8% and placebo 20.3%. The most common TEAEs were headache (Cialis: 2.9%; tamsulosin: 4.2%; placebo: 1.2%), stuffy nose (Cialis: 2.9%; tamsulosin: 1.8%; placebo: 4.7%), back pain (Cialis: 2.3%; tamsulosin: 1.2%; placebo: 0.6%) and upset stomach (Cialis: 2.3%; tamsulosin: 1.8%; placebo: 0). Two Cialis subjects, one tamsulosin and two placebo subjects discontinued study participation due to an adverse event.

About BPH

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

ED and BPH are conditions that may occur in the same patient. Several studies have shown that many men with ED also experience the symptoms of BPH.[1],[2],[3]

About Cialis

Men with ED have two different dosing options with Cialis in the United States — Cialis for daily use (2.5 mg and 5 mg) and Cialis for use as needed (5 mg, 10 mg and 20 mg).

Cialis for daily use can help men with ED be ready anytime between doses*, so they do not have to plan sexual activity around taking a pill. It can also treat the signs and symptoms of BPH. Cialis for daily use is the only medication approved to treat both ED and the signs and symptoms of BPH.

Cialis for use as needed is approved to treat erectile dysfunction (ED). Cialis for use as needed should be taken before sexual activity. It may go to work quickly (in as little as 30 minutes in some men) and can work up to 36 hours.*+

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 two days.

*Individual results may vary. Not studied for multiple attempts per dose.

+In clinical trials, Cialis for use as needed was shown to improve, up to 36 hours after dosing, the ability of men with ED to have a single successful intercourse attempt.

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.

* 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.

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[1] 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.

[2] Brookes ST, Link CL, Donovan JL, and McKinlay JB. Relationship between lower urinary tract symptoms and erectile dysfunction: results from the Boston Area community Health Survey. J Urol 2008;179:250-255.

[3] 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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