

# Public Citizen

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Joan Claybrook, President

October 20, 2005

Andrew Von Eschenbach, M.D., Acting Commissioner  
U.S. Food and Drug Administration  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Dear Dr. Von Eschenbach:

Public Citizen, representing more than 135,000 consumers nationwide, hereby petitions the Food and Drug Administration (FDA) pursuant to the Federal Food, Drug and Cosmetic Act 21 U.S.C. Section 355(e)(3), and 21 C.F.R. 10.30, to immediately add a black box warning regarding the risks of drug-induced blindness for the three phosphodiesterase 5 (PDE5) inhibitors that are prescribed for the treatment of erectile dysfunction [Viagra (sildenafil; Pfizer), Cialis (tadalafil; Lilly), and Levitra (vardenafil; Bayer)]. The label for Revatio, a version of sildenafil indicated for pulmonary arterial hypertension, should also be included in the changes recommended in this petition.

Public Citizen's concern is based, in part, on our findings that 1) Viagra accounts for nineteen percent of the total cases of ischemic optic neuropathy (loss of vision) in the FDA's adverse event database, more than 2-fold higher than that for the next most frequently-cited drug; and that 2) the number of cases of ischemic optic neuropathy per million prescriptions is 18-fold higher for patients taking Viagra compared with patients taking Lipitor, another drug used by people with similar risk factors.

## Additional Requests

This petition also strongly urges the FDA to require that a "Dear Doctor" letter be sent to all physicians informing them about the signs and symptoms of non-arteritic ischemic optic neuropathy (NAION), an often irreversible loss of vision. Men who have had a previous attack of NAION in one eye should not take these drugs since these men are at increased risk of NAION in the other eye, especially if they have other risk factors such as diabetes and hypertension.

In order to inform patients, FDA should require the mandatory distribution by pharmacists of scientifically accurate information for consumers, written in non-technical language in the form of FDA-approved Medication Guides, with each new and

refill prescription for these drugs. The current patient information leaflets (not FDA-approved) are given to patients when a prescription is filled and several patient information leaflets that we have collected do not adequately warn about this serious adverse reaction.

Finally, in order to try and define the causes and prevalence of NAION due to these drugs, FDA should require the manufacturers to establish a registry of all patients diagnosed with NAION and to immediately inform the FDA of new cases.

### **Background**

NAION is a pathologic condition triggered by blockage of blood flow to the eye that is sudden but painless in onset and frequently leads to permanent blindness, usually in one eye. The exact causes are unknown, but it often appears upon first awakening and thus has been hypothesized to be precipitated by hypotension occurring during sleep, mainly in people over the age of 50.

NAION first came to public attention on May 27, 2005, when the FDA announced that it was in discussions with Pfizer to update its Viagra label to mention loss of vision. The FDA announcement was apparently triggered by an article published in the March 2005 issue of the Journal of Neuro-Ophthalmology that described seven new cases of NAION apparently linked to the use of Viagra.<sup>1</sup> Although this article produced the first major public focus on the relation of Viagra to this disease, there have been 19 cases in the medical literature implicating the PDE5 inhibitors beginning in 2000 (see ref. 15-24).

After media coverage of the FDA announcement, Senator Charles Grassley became concerned about the lack of any substantive action by FDA and began his own investigation.<sup>2</sup> Grassley's staff interviewed the safety evaluator from the FDA Office of Drug Safety (ODS), who had produced the original analysis of NAION in Viagra users. By monitoring adverse event reports submitted to the FDA, the safety evaluator had concluded, as early as January 2004, that NAION was an important safety issue for Viagra users. Her review had been sufficient to convince the deputy director of the Division of Anti-inflammatory, Analgesic, and Ophthalmic Drug Products that the potential for NAION should be added to the Viagra label. The NAION report was finalized in April 2004 and sent to the Office of New Drugs (OND), the final arbiter of label changes. Nevertheless, it wasn't until July 8, 2005, 13 months after the Office of New Drugs received documents from the safety evaluator, that the FDA finally published safety alerts for patients and healthcare professionals on its web site.<sup>3</sup>

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<sup>1</sup> Pomeranz HD and Bhavsar AR. Nonarteritic ischemic optic neuropathy developing soon after use of sildenafil (Viagra): a report of seven new cases. J Neuro-Ophthalmology 2005;25:9-13.

<sup>2</sup> Grassley C. Letter to FDA. June 24, 2005. Available at <http://www.fda.gov/oc/ohrt/GrassleytoCrawford62405.doc> Accessed 10/15/2005.

<sup>3</sup> FDA Alert on Viagra. July 2005. <http://www.fda.gov/cder/consumerinfo/viagra/viagra.htm> Accessed 10/15/05.

There is now mention of NAION in the Precautions and Adverse Reactions sections of the professional labels for Viagra, Cialis, and Levitra (but no mention anywhere in the label for Revatio). However, the wording is ambiguous and the location of this information is buried: under Information for Patients in the Precautions section (information that usually is not given to patients), there is one untitled paragraph. In the Adverse Reactions section under Post-marketing Experience, one of several paragraphs discusses NAION. In the case of Viagra, NAION is discussed in one of two paragraphs under Adverse Reactions subheaded "Special Senses" which gives no indication as to what is discussed (the other two drugs have paragraphs that are at least titled "Ophthalmologic").

Emphasis in the label is on the word "rarely", downplaying the importance of NAION and is coupled with the caveat that, "It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors, to the patient's underlying vascular risk factors or anatomical defects, to a combination of these factors, or to other factors". It is probably true that many factors are involved, but one factor clearly seems to be the drug (see below).

The current label has a paragraph titled "Effects of VIAGRA on Vision" which includes no reference to NAION. This needs to be amended.

### **Public Citizen's Analysis**

Public Citizen has been concerned about a number of safety issues with Viagra's use since its approval in 1998 when we asked the FDA to include stronger warnings concerning adverse effects.<sup>4</sup> Public Citizen had, at that time, only looked at the FDA reviews since no postmarketing adverse event data were available. Our concerns relating to the eye were limited to color aberrations, increased sensitivity to light, and blurred vision. However, after the publicity in May 2005 about NAION, we began reading the literature reports and decided to undertake our own analysis using the FDA Adverse Event Reports (AERS) database.

We used the search term "ischemic optic neuropathy" (ION) as recommended by a neuro-ophthalmologist (the term NAION is not present in the AERS database). We searched the entire FDA database from 1/1/98 to 12/31/04 for all reports of ION that showed up for any drug (combining brand and generic names). We found 258 reports in which a drug was listed as the primary suspect for this adverse event.

The three drugs with the highest percentage of reports of ION in the FDA's AERS database were Viagra, interferon, and amiodarone (Table 1). These three drugs (of thousands in the data set) accounted for 42% of all reported ION cases. Viagra had the highest percentage by a factor of more than 2-fold in spite of the fact that during this

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<sup>4</sup> Letter to FDA from Public Citizen. August 20, 1998. Available at <http://www.citizen.org/publications/release.cfm?ID=6649> Accessed 10/15/05.  
Petition to FDA from Public Citizen. July 1, 1998. Available at <http://www.citizen.org/publications/release.cfm?ID=6644> Accessed 10/15/05.

time period there was no mention of NAION in the label, whereas the labels for both interferon and amiodarone had prominent Warnings and amiodarone had a statement in the Precautions section as well.<sup>5</sup> The fact that Viagra's large numbers of adverse reaction reports occurred without any warnings to the medical profession strongly suggests that Viagra is an important factor in causing ION (*all of these cases accrued before the Viagra-NAION association first came to public attention in May 2005*). All reports are for Viagra, since Revatio had not been approved during the time period we searched.

**Table 1. Ischemic optic neuropathy cases in the AERS database\***

| <b>Drug</b> | <b>Number of reports</b> | <b>% of total ION reports</b> |
|-------------|--------------------------|-------------------------------|
| Viagra      | 48                       | 19                            |
| Interferon  | 21                       | 8                             |
| Amiodarone  | 12                       | 5                             |
| Vioxx       | 9                        | 3                             |
| Lipitor     | 10                       | 4                             |
| Zocor       | 2                        | 1                             |

\*1/1/98 to 12/31/04; total number of reports was 258.

**Reports of another well-recognized adverse event**

To put into context and further understand the relevance of the disproportionate percentage of cases of ION in which Viagra was the primary suspect drug, we studied another drug with a well-recognized but rare adverse effect: Lotronex and ischemic colitis (the label for Lotronex now begins with a prominent black box warning). As was the situation for ION, a small number of drugs accounted for a vastly disproportionate percent of reports, showing that unusual adverse events can be identified among the background noise in the AERS system (Table 2). Lotronex and Zelnorm (the first and second in the list) are both drugs approved for irritable bowel syndrome. Although the Zelnorm label lacks Lotronex's black box warning, it does have a paragraph under precautions titled "Ischemic colitis".

**Table 2. Ischemic colitis cases in the AERS database**

| <b>Drug</b> | <b>Number of reports*</b> | <b>% of ischemic colitis reports</b> |
|-------------|---------------------------|--------------------------------------|
| Lotronex    | 194                       | 23                                   |
| Zelnorm     | 55                        | 6                                    |
| Vioxx       | 24                        | 3                                    |
| Remicade    | 21                        | 2                                    |
| Celebrex    | 12                        | 1                                    |

\*1/1/98 to 12/31/04; total number of reports was 852.

**Reporting rate for ION and related terms**

<sup>5</sup> Amiodarone. *Physicians' Desk Reference*. 59th Ed. Montvale, NJ.: Thomson PDR, 2005. 3256.  
Interferon. *Physicians' Desk Reference*. 59th Ed. Montvale, NJ.: Thomson PDR, 2005. 2906.

Because reports to the FDA's AERS database may not have used the same preferred terms to describe ION, we used six search terms recommended by neuro-ophthalmologist Dr. Jonathan Trobe at the University of Michigan Medical School: ischemic optic neuropathy (ION), visual field defect, blindness, blindness unilateral, scotoma, or optic nerve infarction. We broke the results into two parts: the reporting rate for ION and that of the other five terms (non-ION). A patient could have  $\geq 1$  of these terms.

We tabulated the number of cases of ION for the three PDE5 inhibitors as well as for two statin drugs, since the statins would be given to a similar group of people, i.e., older men more likely to have heart disease and/or diabetes. By dividing the number of cases by the total number of prescriptions filled, we were able to estimate the ION reporting rate for each drug (Table 3). The rate of ION with Viagra was 18 times higher than that with Lipitor, the largest-selling statin drug; Cialis was 25 times higher, but the number of Cialis cases in the database, thus far, is small.

Even though the number of cases of ION is still very small with Cialis, the numbers of prescriptions is very low compared with Viagra (Cialis was approved in November 2003, Levitra in August 2003, and Viagra in March 1998). It is clear, however, looking at the vision-related non-ION terms, that all of these drugs clearly have an adverse effect on the eye. It could be that there were many more cases of ION not reported to the FDA as such, since the numbers of non-ION cases (corrected for the number of prescriptions) are an order of magnitude higher with all three PDE5 inhibitors compared with the two statins.

**Table 3. Ischemic optic neuropathy: Comparison of three erectile dysfunction drugs with two statins, Lipitor and Zocor**

| Drug    | ION cases | Number of prescriptions 1/98-12/04 | Cases of ION per 10 <sup>6</sup> prescriptions (X10) | non-ION cases* | non-ION cases* per 10 <sup>6</sup> prescriptions (X10) |
|---------|-----------|------------------------------------|--|----------------|--|
| Levitra | 0         | 2.5 x 10 <sup>6</sup>              | 0.0  | 6              | 24   |
| Cialis  | 2         | 2.7 x 10 <sup>6</sup>              | 7.4  | 4              | 15   |
| Viagra  | 48        | 89 x 10 <sup>6</sup>               | 5.3  | 50             | 6  |
| Lipitor | 10        | 380 x 10 <sup>6</sup>              | 0.3  | 32             | 0.8  |
| Zocor   | 2         | 174 x 10 <sup>6</sup>              | 0.1  | 8              | 0.5  |

\* visual field defect, blindness, blindness unilateral, scotoma, or optic nerve infarction

## PATIENT INFORMATION LEAFLETS

Patient information leaflets are provided by private companies, not the FDA, and so are not regulated. Some of the current patient information leaflets contain no clear warnings, lump serious and less serious adverse events together, and bury information in large amounts of other material. Readability varies greatly, with small font-sizes and single-spacing being common (see Attachments).

## NAION RISK FACTORS

Two general types of risk factors for NAION have been studied: disease/lifestyle factors and those relating to the anatomy around the optic disc. Although definitive data are lacking, certain factors appear to predispose individuals to NAION.

### Disease/lifestyle

It has been implied, both from studies and anecdotal data that pre-existing hypertension, diabetes, elevated cholesterol, and/or an arteriosclerotic risk profile put patients at risk.<sup>6,7</sup> However, people taking Lipitor and Zocor fall into a group likely to have these risk factors, yet we find a much lower percentage of cases of ION with Lipitor and Zocor (Table 1).

Diabetes emerged as a risk factor in two studies undertaken before Viagra approval. One case-control study looked at diabetes, hypertension, high cholesterol, coronary artery disease, tobacco use, and body mass index as risk factors for NAION and found that only diabetes was statistically significant.<sup>8</sup> In a larger study (n=326 cases) of people each of whom already had NAION in one eye and was being followed to determine risk factors for NAION in the unaffected eye, 15% developed NAION in the other eye over a 5 year period. Diabetes was the only factor reaching statistical significance (p=0.02)<sup>9</sup> ("Vascular condition" did not quite reach statistical significance with p=0.06.) The potential risk factors of smoking, hypertension, myocardial infarction, cerebrovascular accident, transient ischemic attack, and aspirin use were not statistically significant in this study. In a review of NAION pathogenesis, Arnold stated that, "diabetes is the most consistently identified vasculopathic risk factor".<sup>10</sup>

Nocturnal hypotension may also play an important role: in a study of 544 episodes of NAION, 73% were presented as visual loss upon first awakening.<sup>11</sup>

### Anatomy

The anatomic configuration around the optic disc appears to be of great importance in NAION. Many studies have measured the optic cup and optic disc in the unaffected eye in patients with NAION (the optic disc is measured in the non-affected eye because it is

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<sup>6</sup> Pomeranz HD, Bhavsar AR. Nonarteritic ischemic optic neuropathy developing soon after use of sildenafil (viagra): a report of seven new cases. *J Neuro-Ophthalmol* 2005;25:9-13.

<sup>7</sup> Heyreh SS, Joos KM, Podhajsky PA et al. Systemic diseases associated with nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmology* 1994;118:766-780.

<sup>8</sup> Jacobson DM, Vierkant RA, Belongia EA. Nonarteritic anterior ischemic optic neuropathy. A case-control study of potential risk factors. *Arch Ophthalmology* 1999;115:1403-7.

<sup>9</sup> Newman NJ, Scherer R, Langenberg P, et al. The fellow eye in NAION: report from the ischemic optic neuropathy decompression trial follow-up study. *Am. J Ophthalmol* 2002;134:317-328.

<sup>10</sup> Arnold AC Pathogenesis of nonarteritic anterior ischemic optic neuropathy. *J Neuro-Ophthalmol* 2003;23:157-163.

<sup>11</sup> Hayreh SS, Podhajsky PA, and Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. *American J of Ophthalmology* 1997;124:641-647.

obscured by swelling in the affected eye). The optic disc is where the optic nerve enters the back of the eye; the optic cup is where the central retinal artery and vein emerge from within the optic nerve. Measurements from the unaffected eye often showed a relatively small optic nerve head (disc) and a small to absent cup resulting in a cup-to-disc ratio of 0.1 to 0.2<sup>12</sup> (see Figure).

Beck et al. "postulate that the pathogenesis of n-AION [NAION] is multifactorial with the size of optic disc as one important factor", and Bollinger and Lee state that, "Nearly all patients with NAION have a small, crowded optic nerve head ("disk at risk") . . ." <sup>13</sup>

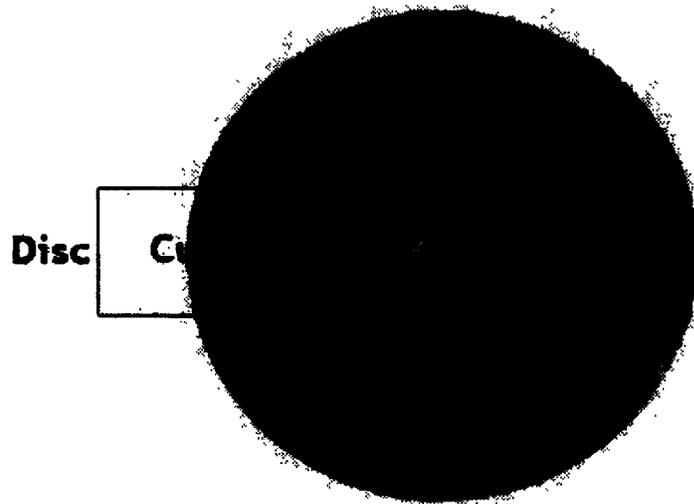


Figure. Back of eye showing optic disc and cup where arteries and veins enter the eye. The disc represents the optic nerve and the cup the region within the optic nerve where the central retinal artery and vein emerge.

#### Relation of NAION to PDE5 inhibitors

Because of so many occurrences of NAION within hours after dosing with PDE5 inhibitors, most authors find it hard not to strongly suspect a cause-and-effect relationship.<sup>14,15,16,17,18,19,20,21,22,23</sup> One case in the literature is especially compelling: a

<sup>12</sup> Beck RW, Servais GE, and Hayreh SS. Anterior ischemic optic neuropathy IX. Cup-to-disc ratio and its role in pathogenesis. *Ophthalmology* 1987;94:1503-1508.

<sup>13</sup> Bollinger K, Lee MS. Recurrent visual field defect and ischemic optic neuropathy associated with tadalafil rechallenge. *Arch Ophthalmol* 2005;123:400-401.

<sup>14</sup> Dheer S, Rekhi GS, Rekhi, Merlyn S. Sildenafil associated anterior ischaemic optic neuropathy. *JAPI* 2002;50:265.

<sup>15</sup> Egan R, Pomeranz H. Sildenafil (Viagra) associated anterior ischemic optic neuropathy. *Arch Ophthalmol* 2000;118:291-292.

<sup>16</sup> Cunningham AV and Smith KH. Anterior ischemic optic neuropathy associated with viagra. *J Neuro-Ophthalmol* 2001;21:22-25.

<sup>17</sup> Boshier A, Pambakian N., Shakir SAW. A case of nonarteritic ischemic optic neuropathy (NAION) in a male patient taking sildenafil. *Int. J Clinical Pharmacol and Therapeutics* 2002;40:422-423.

patient suffered somewhat reversible visual field defects within 2 hours of taking each of four doses of Cialis with permanent loss of vision shortly after the fifth dose.<sup>24</sup>

Although the manufacturers deny any causal effect, Cunningham and Smith state that, "The temporal relationship between the doses of sildenafil citrate [Viagra] and the onset of visual loss make it difficult to accept the notion that these were unrelated coincidental events."<sup>25</sup>

Now that sildenafil is also available under the brand name Revatio as long-term therapy for pulmonary arterial hypertension (PAH) with dosing of 20 mg three times a day<sup>26</sup> (on a par with the 25, 50, or 100 mg doses of Viagra), it is even more urgent to determine whether a link exists between these drugs and the development of NAION. Revatio (sildenafil) for PAH is used as long-term daily therapy compared to the sporadic use of Viagra (sildenafil) when indicated for erectile dysfunction. Patient populations are similar.

### Recommendations

1) FDA should immediately require a black box warning for NAION for the entire PDE5 inhibitor drug class (Viagra, Cialis, Levitra, and Revatio) since the current labeling is inadequate. Although the FDA's safety evaluator recommended NAION be added to both the Precautions and Warnings sections of the Viagra label,<sup>27</sup> at present, there are only two inconspicuous paragraphs (one in Information for Patients under *Precautions* and one in Post-marketing Experience under *Adverse Reactions*) for Viagra, Cialis, and Levitra. These sections have neither titles nor bolding to call attention to this serious adverse event; instead, everything imaginable has been done to detract from its relevance and prominence. The Revatio label has no information at all.

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<sup>18</sup> Pomeranz HD, Smith KH, Hart WM and Egan RA. Sildenafil-associated nonarteritic anterior ischemic optic neuropathy. *Ophthalmology* 2002;109:584-587.

<sup>19</sup> Pomeranz HD, Bhavsar AR. Nonarteritic ischemic optic neuropathy developing soon after use of sildenafil (viagra): a report of seven new cases. *J Neuro-Ophthalmol* 2005;25:9-13.

<sup>20</sup> Bollinger K, Lee MS. Recurrent visual field defect and ischemic optic neuropathy associated with tadalafil rechallenge. *Arch Ophthalmol* 2005;123:400-401.

<sup>21</sup> Peter NM, Singh MV, Fox PD. Tadalafil-associated anterior ischaemic optic neuropathy. *Eye* 2005;19:715-717.

<sup>22</sup> Escaravage GK, Wright JD, Givre SJ. Tadalafil associated with anterior ischemic optic neuropathy. *Arch Ophthalmol*;123:399-400.

<sup>23</sup> Gruhn N, Fiedelius HC. Unilateral optic neuropathy associated with sildenafil intake. *Acta Ophthalmologica Scand.* 2005;83:131-132.

<sup>24</sup> Egan RA, Fraunfelder FW. Viagra and anterior ischemic optic neuropathy. *Arch Ophthalmol* 2005;123:709-710.

<sup>25</sup> Cunningham AV and Smith KH. Anterior ischemic optic neuropathy associated with viagra. 2001;21:22-25.

<sup>26</sup> Revatio (sildenafil) Professional Product Labeling at [www.revatio.com/](http://www.revatio.com/) Accessed 9/22/05.

<sup>27</sup> <http://www.fda.gov/oc/ohrt/GrassleytoCrawford62405.doc>

Our model black box warning for NAION—for doctors and patients---would be:

There have been a significant number of patients taking PDE5 inhibitors (Viagra, Cialis, and Levitra) who have developed non-arteritic anterior ischemic optic neuropathy (NAION), a sudden loss of vision, usually in one eye, that can lead to permanent blindness. Patients should be told to report to their physicians any loss of vision, particularly that occurring upon waking up, not to take any more doses of drug, and to have an immediate eye exam. All physicians are encouraged to question patients appearing with NAION as to their use of these drugs and provide information on its symptoms. Patients who have experienced NAION in one eye are likely at increased risk for a second event, especially if they have other risk factors such as diabetes and hypertension and should not take these drugs.

- 2) In order to insure that patients receive the needed information, FDA needs to write a Medication Guide for consumers.
- 3) Because there is still much debate as to the causes, incidence, and risk factors for NAION, we recommend that the FDA have manufacturers establish a registry of patients taking PDE5 inhibitors who develop NAION. This will help clarify the nature of the relationship between drug use and NAION.
- 4) The manufacturers should immediately send a letter to all Health Care Professionals with all the new information. Health Care Professionals should be encouraged to report to the FDA all cases of adverse events related to the eye.

#### **ENVIRONMENTAL IMPACT STATEMENT**

Nothing requested in this petition will have an impact on the environment.

#### **CERTIFICATION**

We certify that, to the best of our knowledge and belief, this petition includes all information and views on which this petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

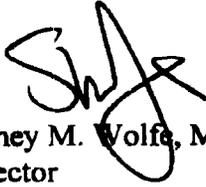
Sincerely,



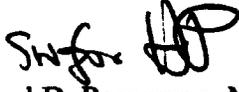
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Howard D. Pomeranz, M.D.\*

**\*Howard D. Pomeranz, MD, PhD is a neuro-ophthalmologist who recently joined the Department of Ophthalmology at North Shore Long Island Jewish Health System in Great Neck, NY. He is a Clinical Associate Professor of Ophthalmology. Prior to this, he was an Associate Professor in the Department of Ophthalmology at the University of Minnesota Medical School. He has co-authored several of the published reports about the association between sildenafil and ischemic optic neuropathy.**

# Sildenafil



## Patient Education

### Sildenafil tablets (Viagra®)

What are sildenafil tablets?

**SILDENAFIL (Viagra®)** is used to treat erection problems in men. Generic sildenafil tablets are not yet available.

What should my health care professional know before I take sildenafil?

They need to know if you have any of these conditions:

- \*anatomical deformity of the penis, Peyronie's disease, or ever had an erection that lasted more than 4 hours
- \*benign prostatic hypertrophy (BPH)
- \*bleeding disorder
- \*cancer
- \*diabetes
- \*frequent heartburn or gastroesophageal reflux disease (GERD)
- \*heart disease, angina, high or low blood pressure, a history of heart attack, or other heart problems
- \*high cholesterol
- \*kidney disease
- \*liver disease
- \*sickle cell disease
- \*stomach or intestinal ulcer
- \*stroke
- \*eye or vision problems, including a rare inherited eye disease called retinitis pigmentosa
- \*an unusual or allergic reaction to sildenafil, other medicines, foods, dyes, or preservatives
- \*pregnant or trying to get pregnant
- \*breast-feeding

How should I take this medicine?

Take sildenafil tablets by mouth. Follow the directions on the prescription label. The dose is usually taken 1 hour before sexual activity. You should not take this dose more than once per day. Swallow the tablets with a drink of water. Do not take double or extra doses.

Contact your pediatrician or health care professional regarding the use of this medicine in children. Special care may be needed.

What if I miss a dose?

This does not apply.

What drug(s) may interact with sildenafil?

*Do not take sildenafil if you are taking the following medications:*

- \*nitroglycerin-type drugs for the heart or chest pain such as amyl nitrite, isosorbide dinitrate, isosorbide

mononitrate, nitroglycerin, even if these are only taken occasionally

*Sildenafil may also interact with the following medications:*

- \*alpha blockers, used for high blood pressure or an enlarged prostate. NOTE: Do not take doses of sildenafil higher than 25 mg within 4 hours of taking alpha blockers, such as alfuzosin (UroXatral®), doxazosin (Cardura®), prazosin (Minipress®), or terazosin (Hytrin®).
- \*bosentan
- \*certain drugs used for seizures such as carbamazepine, phenytoin, and phenobarbital
- \*certain drugs used for fungal or yeast infections, such as fluconazole, ketoconazole, and voriconazole
- \*certain drugs for the treatment of HIV infection or AIDS
- \*cimetidine
- \*cisapride
- \*clarithromycin
- \*diltiazem
- \*erythromycin
- \*grapefruit juice
- \*mibefradil
- \*nitroprusside
- \*rifabutin
- \*rifampin
- \*quinidine
- \*some drugs for treating depression, anxiety or other mood problems (examples: fluoxetine, fluvoxamine, nefazodone)
- \*verapamil

Tell your prescriber or health care professional about all other medicines you are taking, including non-prescription medicines, nutritional supplements, or herbal products. Also tell your prescriber or health care professional if you are a frequent user of drinks with caffeine or alcohol, if you smoke, or if you use illegal drugs. These may affect the way your medicine works. Check with your health care professional before stopping or starting any of your medicines.

**What side effects may I notice from taking sildenafil?**

Side effects that you should report to your prescriber or health care professional as soon as possible:

- \*changes in vision such as loss of vision, blurred vision, eyes being more sensitive to light, or trouble telling the difference between blue and green objects or objects having a blue color tinge to them
- \*difficulty breathing, shortness of breath
- \*chest pain or palpitations
- \*prolonged erection (lasting longer than 4 hours)
- \*skin rash, itching

Side effects that usually do not require medical attention (report to your prescriber or health care professional if they continue or are bothersome):

- \*diarrhea
- \*dizziness
- \*flushing
- \*headache
- \*indigestion
- \*nasal congestion

**What should I watch for while taking sildenafil?**

If you notice any changes in your vision while taking this drug, notify your prescriber or health care professional as soon as possible. Stop using sildenafil right away if you have a loss of sight in one or both eyes. Contact your healthcare provider immediately.

Contact your physician immediately if the erection lasts longer than 4 hours or if it becomes painful. This may be a sign of priapism and must be treated immediately to prevent permanent damage.

If you experience symptoms of nausea, dizziness, chest pain or arm pain upon initiation of sexual activity after sildenafil use, you should refrain from further activity and should discuss the episode with your prescriber or health care professional as soon as possible.

Do not change the dose of your medication. Please call your prescriber or health care professional to determine if your dose needs to be reevaluated.

Using Viagra® (sildenafil) does not protect you or your partner against HIV infection (the virus that causes AIDS) or other sexually transmitted diseases.

**Where can I keep my medicine?**

Keep out of reach of children in a container that small children cannot open.

Store at room temperature between 15 and 30 degrees C (59 and 86 degrees F). Throw away any unused medicine after the expiration date.

[ Last Revised: 7/11/2005 9:45:00 AM ]

**NOTE: This information is not intended to cover all possible uses, precautions, interactions, or adverse effects for this drug. If you have questions about the drug(s) you are taking, check with your health care professional.**

# DRUG & ADVISOR

Pharmacy PHN(814)866-4424

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Drug: VIAGRA 50MG TAB

COMMON NAME: SILDENAFIL (sildenafil)

**COMMON USES:** This medicine is a phosphodiesterase inhibitor used to treat sexual function problems such as impotence or erectile dysfunction. In combination with sexual stimulation, this medicine works by helping the blood flow into the penis to achieve and maintain an erection. This medicine is not intended for use in women or children. This medicine will not protect against sexually transmitted diseases including HIV infection. Use "safe sex" practices such as latex condoms. Contact your doctor or pharmacist for more details.

**BEFORE USING THIS MEDICINE:** Some medicines or medical conditions may interact with this medicine. **INFORM YOUR DOCTOR OR PHARMACIST** of all prescription and over-the-counter medicines that you are taking. **DO NOT TAKE THIS MEDICINE** if you are taking any form of nitroglycerin (such as tablet, patch, or ointment dose forms) or other nitrates (such as isosorbide, nitroglycerin or any "nitric oxide donor" medicines), or recreational drugs called "poppers" containing amyl or butyl nitrate because very serious interactions may occur. If you are not sure whether a certain medicine is a nitrate, contact your doctor or pharmacist. If you are currently using any of these medicines, tell your doctor or pharmacist before using sildenafil. **ADDITIONAL MONITORING OF YOUR DOSE OR CONDITION** may be needed if you are taking other medicines for impotence, antifungals (such as fluconazole or ketoconazole), cimetidine, delavirdine, erythromycin, mifepridil, or rifampin. If you are taking an HIV protease inhibitor (such as ritonavir or zalcitabine), do not take more than a 25 mg dose of sildenafil in a 48-hour period. If you are taking more than a 25 mg dose of sildenafil and are also taking an alpha-blocker medicine (such as doxazosin, prazosin, or tamsulosin) for various conditions (such as enlarged prostate), separate the time between taking these medicines by more than 4 hours. **DO NOT START OR STOP** any medicine without doctor or pharmacist approval. Inform your doctor of any other medical conditions including penis conditions (such as angulation, fibrosis/scarring, or Peyronia's disease), history of painful/prolonged erection (priapism), sickle cell anemia, blood system cancers (such as leukemia or myeloma), vision problems (such as retina diseases like retinitis pigmentosa) or history of vision loss, kidney or liver disease, bleeding disorders, active stomach ulcers, heart problems (such as recent heart attack or irregular heartbeat within past 6 months, heart failure, coronary artery disease with unstable angina, aortic stenosis or idiopathic hypertrophic subaortic stenosis), recent stroke within past 6 months, very high or low blood pressure, or allergies. Contact your doctor or pharmacist if you have any questions or concerns about taking this medicine.

**HOW TO USE THIS MEDICINE:** Follow the directions for using this medicine provided by your doctor. **TAKE THIS MEDICINE** by mouth as needed between four hours and one-half hour before sexual activity (about 1 hour before is most effective), or take as directed by your doctor. **DO NOT TAKE THIS MEDICINE** more often than once daily as needed. A high fat meal may delay the time of onset of this medicine. Your dosage is based on your medical condition, your response to therapy, and other medicines you are taking. Consult your doctor or pharmacist for more information. **STORE THIS MEDICINE** at room temperature 77 degrees F (25 degrees C) in a tightly-closed container, away from heat, moisture, and light. Brief storage between 59 and 86 degrees F (15 and 30 degrees C) is permitted.

**CAUTIONS: DO NOT TAKE THIS MEDICINE** if you have had an allergic reaction to it in the past or to any other ingredient that is found in it. **THIS MEDICINE MAY CAUSE VISION CHANGES. DO NOT DRIVE, OPERATE MACHINERY, OR DO ANYTHING ELSE THAT COULD BE DANGEROUS** until you know how you react to this medicine. Using this medicine alone, with other medicines, or with alcohol may lessen your ability to drive or to perform other potentially dangerous tasks. **TO MINIMIZE DIZZINESS OR LIGHTEADEDNESS**, sit up or stand slowly when rising from a seated or lying position. Your dose is based on your medical condition, response to therapy, and the other medicines you are taking. **DO NOT EXCEED THE RECOMMENDED DOSE** without checking with your doctor. Rarely, this medicine may change heart rhythm, especially if taken with other medicines that can change the heart rhythm. This change in heart rhythm can result in serious, rarely fatal, irregular heartbeats. Ask your doctor for more information and if you should stop taking any of your other medicines to reduce the risk of this side effect. **BEFORE YOU BEGIN TAKING ANY NEW MEDICINE**, either prescription or over-the-counter, check with your doctor or pharmacist. **CAUTION IS ADVISED WHEN USING THIS MEDICINE IN THE ELDERLY** because they may be more sensitive to the side effects of this medicine. **THIS MEDICINE SHOULD NOT BE USED IN WOMEN OR CHILDREN.**

**POSSIBLE SIDE EFFECTS: SIDE EFFECTS** that may occur while taking this medicine include headache, flushing, stomach upset, heartburn, nasal stuffiness, diarrhea, dizziness, or lightheadedness. Vision changes such as increased sensitivity to light, blurred vision, or impaired blue/green color discrimination may also occur. If these continue or are bothersome, check with your doctor or pharmacist. **CONTACT YOUR DOCTOR IMMEDIATELY** if you experience vision loss in one or both eyes. Sexual activity may put extra strain on your heart, especially if you have heart problems. If you have heart problems and experience any serious side effects while having sex, stop having sex and tell your doctor immediately. These side effects include severe dizziness, fainting, chest pain, or nausea. In the unlikely event that you have a painful or prolonged erection (lasting more than 4 hours), stop using this medicine and seek immediate medical attention or permanent problems could occur. **AN ALLERGIC REACTION TO THIS MEDICINE** is unlikely, but seek immediate medical attention if it occurs. Symptoms of an allergic reaction include rash, itching, unusual swelling, severe dizziness, or trouble breathing. If you notice other effects not listed above, contact your doctor, nurse, or pharmacist.

**OVERDOSE:** If overdose is suspected, contact your local poison control center or emergency room immediately. Symptoms of overdose may include severe dizziness, fainting, or prolonged erection.

**ADDITIONAL INFORMATION:** If your symptoms do not improve or if they become worse, check with your doctor. **DO NOT SHARE THIS MEDICINE** with others for whom it was not prescribed, since they may have a problem that is not effectively treated with this medicine, or they may have a condition that is complicated by this medicine. **DO NOT USE THIS MEDICINE** for other health conditions. **KEEP THIS MEDICINE** out of the reach of children and pets. **IF USING THIS MEDICINE FOR AN EXTENDED PERIOD OF TIME**, obtain refills before your supply runs out.

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The information in this monograph is not intended to cover all possible uses, directions, precautions, drug interactions, or adverse