NATIONAL PBM BULLETIN

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VETERANS HEALTH ADMINISTRATION
PHARMACY BENEFITS MANAGEMENT STRATEGIC HEALTHCARE GROUP,
MEDICAL ADVISORY PANEL, AND
CENTER FOR MEDICATION SAFETY (VA MEDSAFE)
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Phosphodiesterase Type 5 Inhibitors and Loss of Vision

I. ISSUE - Phosphodiesterase Type 5 (PDE5) Inhibitors and Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

On July 8, 2005 the Food and Drug Administration (FDA) released a statement approving labeling changes for all three PDE5 inhibitors, sildenafil, tadalafil, and vardenafil that reflect postmarketing reports of vision loss related to NAION.

II. BACKGROUND - Reports of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)[1]

As of May 18, 2005, a total of 43 cases of ischemic optic neuropathy (ION) in temporal association with the three PDE5 inhibitors have been reported to the FDA's Adverse Event Reporting System. Since approval, 38 cases have been identified in association with sildenafil (approved Mar. 1998), 4 cases with tadalafil (approved Nov. 2003), and one case with vardenafil (approved Aug. 2003). Most of these cases (25/43) appeared to be of the NAION subtype. NAION causes sudden loss of eyesight because blood flow is blocked to the optic nerve. Thirty-six of the 43 cases reported accompanying visual loss, and 26/36 reported the visual loss as continuing or permanent. A recent published article which described seven new cases of NAION developing within 36 hours after ingestion of sildenafil demonstrated an association between the use of sildenafil and vision loss and has, thus prompted further concern in regard to the role of PDE5 inhibitors in blindness.[2] Four of these patients had been using sildenafil intermittently for weeks or years for treatment of erectile dysfunction before the occurrence of acute visual loss. Visual loss occurred most commonly on awakening the next morning. Final visual acuity in the affected eye ranged from 20/20 to light perception. As a result of these findings, the FDA-approved updated labeling for all three PDE5 inhibitors, recommending caution and close monitoring in certain patients, as well as the warning to seek immediate medical attention in the event of visual changes or sudden loss of vision.

III. DISCUSSION - REVIEW OF WARNING

It is not possible at this time to determine causality of PDE5 inhibitors and NAION. Other patient risk factors associated with NAION may be present. Among these are various underlying anatomic or vascular risk factors, including but not necessarily limited to: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking. These vascular risk factors for NAION also overlap with vascular risk factors for erectile dysfunction. In the published article, all affected individuals had pre-existing arteriosclerotic risk profiles. Given the small number of events, the large number of users of PDE5 inhibitors, and the fact that NAION occurs in a similar population to those who do not take the agents, 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 causes. A conclusion of cause and effect cannot be drawn at this time. VAMedSAFE and the FDA will continue to evaluate the issue. However, despite the inability to determine causality of PDE5 inhibitors and NAION, VAMedSAFE has issued recommendations to ensure the safe use and monitoring of patients on PDE5 inhibitors with regards to ophthalmic precautions.

IV. VA MEDSAFE RECOMMENDATIONS

1. Prior to initiation of PDE5 inhibitor therapy in all patients, practitioners must inquire about any previous history of NAION or symptoms that resemble NAION. "Have you ever experienced a sudden loss or change in your vision?" with additional probing following a positive response.
2. PDE5 inhibitors should not be prescribed in patients with a history of NAION.
3. Health care providers should discontinue all PDE-5 inhibitors in any patient who develops NAION or who presents with similar visual complaints. In addition, caution should be used with other vasodilators in these patients.
4. Health care providers should inform all patients prescribed PDE5 inhibitors of the potential for this optic neuropathy adverse event.
5. Health care providers should inform patients to stop use of all PDE5 inhibitors and seek medical attention immediately in the event of visual changes, a sudden loss of vision in one or both eyes, dizziness, flushing, or headache.
6. Ophthalmologists, optometrists and other eye care providers should ask all men with NAION about the use of PDE5 inhibitors since this information may not be readily volunteered without specific inquiry. These patients should also be advised never to take a PDE5 inhibitor.

V. USE OF PDE TYPE 5 INHIBITORS in VA

For the 3rd quarter of this year, VA dispensed PDE-5 Inhibitors (sildenafil, tadalafil and vardenafil) to 281,369 unique patients.

VI. REFERENCES

1. FDA Statement: FDA Updates Labeling for Viagra, Cialis and Levitra for Rare Post-Marketing Reports of Eye Problems. http://www.fda.gov/bbs/topics/NEWS/2005/NEW01201.html Accessed July 12, 2005.
2. Pomeranz H, Bhavsar A. Nonarteritic Ischemic Optic Neuropathy Developing Soon After Use of Sildenafil (Viagra): A Report of Seven New Cases. J Neuro-Opthalmol 2005;25:9-13.