

**Department of
Veterans Affairs**

Memorandum

Date: January 12, 2006

From: Chair, VHA Medical Advisory Panel (578/119D)
Chief Consultant, Pharmacy Benefits Management-Strategic Healthcare Group (578/119D)

Subj: National Contract Award for the Phosphodiesterase Type 5 Inhibitors

To:

1. A national contract for a phosphodiesterase type 5 inhibitor (PDE5) has been awarded to vardenafil (Levitra®), for the treatment of erectile dysfunction. Sildenafil (Viagra®) and tadalafil (Cialis®) are nonformulary at the National and VISN formulary levels to facilitate this mandatory use contract. **Veterans prescribed sildenafil for the treatment of pulmonary hypertension are not to be switched to vardenafil and are to continue to receive sildenafil without interruption.**
2. *Dosing.* Vardenafil is available as 2.5, 5, 10, and 20 mg tablets. Vardenafil should be taken 1 hour before sexual activity and can be taken without regard to meals. The maximum dose of vardenafil is 20 mg per day. Concrete dose equivalents between the PDE5 inhibitors have not been determined. Based on what is known and expert opinion the following table provides guidance for dose conversion between sildenafil and vardenafil. As a safety precaution, patients currently taking a 100 mg dose of sildenafil should be converted to vardenafil 10 mg (or lower), not vardenafil 20 mg. Further dose adjustments may be needed based upon patient response.

Conditions	Sildenafil Dose	Vardenafil Dose
No restrictions	12.5 mg 25.0 mg 50.0 mg 100.0 mg	2.5 mg 5.0 mg 10.0 mg 10.0 mg
Age >65 years	Initial: 25 mg	Initial: 5 mg
Hepatic impairment	Initial: 25 mg	Initial: 5 mg
Renal impairment	CrCl<30 mL/min Initial: 25 mg	None required
CYP3A4 inhibitor	Initial: 25 mg	Drug and dose specific: <u>^CYP 3A4 inhibitors</u> Ritonavir 2.5 mg/72h Indinavir 2.5 mg/24h Ketoconazole 400 mg/day 2.5 mg/24h Itraconazole 400 mg/day 2.5 mg/24h Ketoconazole 200 mg/day 5.0 mg/24h Itraconazole 200 mg/day 5.0 mg/24h Erythromycin 5.0 mg/24h ^These recommendations are from vardenafil's labeling and dose adjustments may be appropriate for other CYP3A4 inhibitors.
Concurrent use of an alpha blocker	50 mg or 100 mg should not be taken within 4 hours of an alpha-blocker; 25 mg may be taken at any time.	Patients should be on a stable dose of alpha-blocker or vardenafil prior to the start of the other agent. Start with 2.5 or 5 mg of vardenafil and titrate based on response and tolerability

3. *Concurrent Use with Alpha-blockers.* Vardenafil's original labeling contained a contraindication for concurrent use with an alpha-blocker. In July 2005 the FDA changed this to a precaution in vardenafil's labeling. Patients must be on a stable dose of an alpha-blocker or vardenafil before the other is started. When a patient on an alpha-blocker is started on vardenafil, the initial dose is either 2.5 or 5 mg (see Table in 2 above); the two can be taken simultaneously.
4. *Drug Interactions.* Like the other PDE5 inhibitors vardenafil is contraindicated for patients taking nitrates. Vardenafil is metabolized by the cytochrome P450 3A4 isoenzyme and potent CYP3A4 inhibitors have been shown to increase vardenafil peak concentrations and area under the curve (AUC). Lower doses of vardenafil are recommended for patients taking concurrent CYP3A4 inhibitors (See #2 above). Vardenafil has not been shown to interact with other medications including glyburide, warfarin, digoxin, aluminum- and magnesium hydroxide antacids, ranitidine, or cimetidine.
5. *Adverse Effects.* Vardenafil is associated with many of the same adverse effects as the other PDE5 inhibitors including headache, flushing, rhinitis/nasal congestion, dyspepsia, dizziness, nausea, flu syndrome, sinusitis and increased creatinine kinase. The risk of non arteric ischemic optic neuropathy (NAION) may be increased with the use of PDE5 inhibitors. Men who experience visual changes or loss of vision in one or both eyes are advised to stop the medication and contact their doctor or healthcare provider immediately.
6. A drug class review of the PDE5 inhibitors, and more information on vardenafil is available at www.pbm.va.gov and <http://vaww.pbm.va.gov>.
7. We appreciate your cooperation in implementing this conversion in order to provide the best value drug therapy for our patients.

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