



PIC QUESTION OF THE WEEK: 09/12/05

Q: What are the guidelines for concomitant use of alpha-1-antagonists or nitrates in patients taking phosphodiesterase type 5 (PDE5) inhibitors for erectile dysfunction?

A: Penile erection is dependent on the release of nitric oxide (NO) which activates the enzyme guanylate cyclase. This produces an increase in the synthesis of cyclic guanosine monophosphate (cGMP). In turn, cGMP triggers smooth muscle relaxation and results in increased blood flow to the penis causing erection. PDE5 degrades cGMP in smooth muscle cells, thus its inhibition would lead to increased effects of NO. Sildenafil, vardenafil, and tadalafil are selective inhibitors of PDE5. Alpha-blockers (e.g. doxazosin, prazosin, etc.) exert an antihypertensive effect, and their combined use with PDE5 inhibitors may lead to significant and symptomatic hypotension. The probable mechanism for the interaction is currently unknown, but may be due to the additive effects of both drugs. PDE5 inhibitors potentiate the vasodilatory effect of circulating NO, resulting in a significant and potentially fatal drop in blood pressure. For this reason, concomitant use of nitrates and PDE5 inhibitors is considered contraindicated. The following chart lists the general guidelines regarding the concomitant use of alpha-blockers or nitrates with PDE5 inhibitors.

	Sildenafil (Viagra®)	Vardenafil (Levitra®)	Tadalafil (Cialis®)
Alfuzosin (Uroxatral®)	Doses of 50 or 100 mg should not be given within 4 hours of administering alpha-blockers. Doses of 25 mg sildenafil can be taken at any time.	Co-administration is contraindicated with ALL alpha-blockers.	Co-administration is contraindicated.
Doxazosin (Cardura®)			
Prazosin (Minipress®)			
Terazosin (Hytrin®)			
Tamsulosin (Flomax®)			Co-administration with 0.4 mg/day of tamsulosin is NOT contraindicated.
Nitrates	Concomitant use is contraindicated, but nitrates can be given cautiously in an emergency care setting to patients taking PDE5 inhibitors. At least 24 hours should have elapsed since the last dose of a PDE5 inhibitor.		Concomitant use is contraindicated, but nitrates can be given cautiously in an emergency care setting to patients taking PDE5 inhibitors. Allow at least 48 hours before using nitrates.

References:

1. Sublingual Viagra (Sildenafil). Pharmacist's Letter/Prescriber's Letter 2005;21(8):210811.
2. Kastrup, Erwin K., ed. Drug Facts and Comparisons. St. Louis: Wolters Kluwar Health, Inc., 2005. 582-584.

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