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## Customer Advocacy

### Medical Information

Dear Doctor,

I am writing to you both as the Medical Director for the Sexual Health Team of the U.S. Pharmaceuticals Division of Pfizer Inc. and as a former practicing and Board Certified Emergency Physician. As you may be aware, Viagra™ (sildenafil citrate), the cGMP-specific type 5 phosphodiesterase (PDE5) inhibitor discovered and developed by Pfizer, has recently received FDA approval for the treatment of male erectile dysfunction. You may also be aware, per the enclosed package insert, that the **only contraindication for taking Viagra is the concomitant administration of an organic nitrate**. We are aware that it is possible that the inadvertent combination of these agents with Viagra may occur and could involve evaluation and treatment of such patients by Emergency Physicians and/or pre-hospital emergency personnel (paramedics/EMT's). Because we would not expect Emergency Physicians to routinely be receiving information about this drug (based on its indication) and in response to several inquiries that we have received on this subject, I felt that it was important for the safety of patients taking Viagra that I write this letter to all Emergency Physicians.

In addition to the approved package insert, I have enclosed a document entitled "Nitric Oxide and Blood Pressure Control" that will provide you with additional information on this subject. Please read it carefully and share it with any of your colleagues who may not be aware of it. This explains the physiologic mechanism underlying the contraindication, which is based on data from several double-blind, placebo controlled interaction studies done with either sublingual nitroglycerine or isosorbide mononitrate in which **large and sudden drops in systemic blood pressure** occurred in the majority of patients taking Viagra. A list of commonly prescribed short- and long-acting nitrates available in the United States is also included.

It is well documented that sexual activity generally involves an increase in cardiac work and myocardial oxygen demand. Per our package insert [see PRECAUTIONS: GENERAL] for this reason, we are advising physicians to consider the cardiac status of patients for whom they are planning to prescribe Viagra and, in particular, NOT to prescribe it to patients who take organic nitrates in any form, regardless of frequency. We have thought of several possible scenarios in which Emergency Physicians need to be aware of this interaction in order to make appropriate diagnosis and treatment decisions. Those we have considered include:

1) **the man who combines a nitrate and Viagra at home, becomes severely hypotensive and is brought to an Emergency Department**. We are going to great lengths to educate every potential prescriber and patient to the nitrate contraindication. However, in spite of this, it is conceivable that a man may obtain Viagra who does use or at least may have access to such medication. For example, a patient with a history of angina could take Viagra and begin to engage in sexual activity.

If the aerobic effort involved in this were to precipitate an anginal attack and he were to take (for instance) a sublingual nitroglycerin while the Viagra was still on board, he could become acutely hypotensive. As you know, the result of a precipitous drop in blood pressure could range from no symptoms or mild symptoms of hypotension such as dizziness or light-headedness, to syncope (most likely postural), to a significant lowering of coronary perfusion and conversion of an area of myocardial ischemia to infarction, with all of its potential consequences. Such a patient could then easily end up in a paramedic ambulance or an Emergency Department and require treatment.

2) **the man with no history of angina who takes Viagra, engages in sexual activity and develops his first anginal episode.** Such a patient could be brought to an Emergency Department while still having chest pain, where a short-acting nitrate may routinely be administered to treat this. If the Emergency Physician were not aware of the potential interaction described above and did not specifically question that patient about Viagra, the same reaction described in scenario #1 above could be precipitated in the E.D., e.g. with nitroglycerin administered sublingually, transdermally or intravenously. (**NOTE:** the contraindication in our package insert also includes **sodium nitroprusside**, which acts similarly as a NO donor.) A variant of this would be the man who calls 9-1-1 upon developing chest pain and the call is responded to by a team of paramedics or EMT's. In some locales, these pre-hospital emergency personnel are permitted (either by protocol or upon voice order from a physician) to administer a short-acting nitrate on the scene or in the ambulance which could, again, result in the possible consequences described above.

3) **although we have not specifically studied this, we believe that nitrates that are inhaled for recreational use (including amyl nitrate/nitrite or "poppers" and others) will have the same effect when combined with Viagra.** As you probably know, these are often used during sexual activity and it is easily conceivable that a person would take Viagra, begin having sex and, at some point in the process, inhale one of these substances.

In addition, although Viagra is only FDA approved for the treatment of male erectile dysfunction, we are aware that women have started taking it, either on their own or via an off-label prescription from a physician. Therefore, although the scenarios described above would be more likely to occur in men, if such off-label use continues, they could also to occur in women.

I hope that the information provided here will be helpful to you with patients you encounter who may be taking Viagra. If you would like additional information about Viagra, please contact Pfizer's Medical Information Department at 1-800-438-1985 or visit our Viagra website at [www.viagra.com](http://www.viagra.com). I thank you for your attention to this important matter.

Sincerely,



Richard L. Siegel, M.D.  
Medical Director,  
Sexual Health