IMPORTANT PRESCRIBING INFORMATION

This communication is to inform healthcare professionals about new and expanded safety information in the labeling for VIAGRA® (sildenafil citrate) tablets. These revisions, made in consultation with the Food and Drug Administration, reflect safety information obtained through post marketing experience as well as a reemphasis and clarification of information that was already included in the insert. Health care professionals should review the entire label, which is enclosed, to assure that they have the most current information regarding VIAGRA.

Following are some of the key revisions:

The **ADVERSE REACTIONS** Section now includes the following Postmarketing events that have been spontaneously reported.

ADVERSE REACTIONS
POST- MARKETING EXPERIENCE
Cardiovascular
Serious cardiovascular events – including myocardial infarction, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage, transient ischemic attack, and hypertension – have been reported post-marketing in temporal association with the use of VIAGRA. Most, but not all of these patients had pre-existing cardiovascular risk factors. Many of these events were reported to occur during or shortly after sexual activity, and a few were reported to occur shortly after the use of VIAGRA without sexual activity. Others were reported to have occurred hours to days after the use of VIAGRA and sexual activity. It is not possible to determine whether these events are related directly to VIAGRA, to sexual activity, to the patient's underlying cardiovascular disease, to combination of these factors, or to other factors. (see **WARNINGS** for further important cardiovascular information).
Other Events
Other events reported post marketing to have been observed in temporal association with VIAGRA and are not listed in the pre-marketing adverse reactions section above include:
Nervous System – seizure and anxiety
Urogenital – prolonged erection, priapism (see **WARNINGS**) and hematuria
Ocular – diplopia, temporary vision loss/decreased vision, ocular redness or bloodshot appearance, ocular burning, ocular swelling/pressure, increased intraocular pressure, retinal vascular disease or bleeding, vitreous detachment/traction and macular edema.

The **WARNINGS** Section discusses the cardiovascular safety of sexual activity combined with VIAGRA, the transient vasodilatory properties of sildenafil, the exclusion criteria in the clinical trials and information concerning prolonged erections/priapism.

WARNINGS SECTION
There is potential cardiac risk of sexual activity in patients with pre-existing cardiovascular disease. Therefore, treatments for erectile dysfunction, including VIAGRA, should not be generally used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status.

VIAGRA has systemic vasodilatory properties that resulted in transient decreases in supine blood pressure in healthy volunteers (mean maximum decrease of 8.4/5.5 mm Hg, see **CLINICAL PHARMACOLOGY, Pharmacodynamics**). While this normally would be expected to be of little consequence in most patients, prior to prescribing VIAGRA, physicians should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects, especially in combination with sexual activity.

There is no controlled clinical data on the safety or efficacy of VIAGRA in the following groups; if prescribed, this should be done with caution.

- Patients who have suffered a myocardial infarction, stroke, or life-threatening arrhythmia within the last 6 months
- Patients with resting hypotension (BP<90/50/) or hypertension (BP>170/100)
- Patients with cardiac failure or coronary artery disease causing unstable angina
- Patients with retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterasese).

Prolonged erection greater than 4 hours and priapism (painful erections greater than 6 hours in duration) have been reported infrequently since market approval of VIAGRA. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result.

The **CONTRAINDICATIONS** Section has been clarified and enhanced pharmacokinetic information has been added. This information is not to be interpreted as guidance from the FDA or Pfizer about the coadministration of VIAGRA and nitrates. Pfizer continues to strongly insist that VIAGRA not be coadministered to patients using nitrates at any time.

CONTRAINDICATIONS
Consistent with its known effects on the nitric oxide/cGMP pathway (see **CLINICAL PHARMACOLOGY**) VIAGRA was shown to potentiate the hypotensive effects of nitrates, and its administration to patients who are using organic nitrates, either regularly and/or intermittently, in any form is therefore contraindicated.

After patients have taken VIAGRA, it is unknown when nitrates, if necessary, can be safely administered. Based on the pharmacokinetics profile of a single 100 mg oral dose given to healthy normal volunteers, the plasma levels of sildenafil at 24 hours post-dose are approximately 2 ng/ml (compared to peak plasma levels of approximately 440 ng/ml) (see **CLINICAL PHARMACOLOGY, Pharmacokinetis and Metabolism**). In the following patients: age>65, hepatic impairment (e.g. cirrhosis), severe renal impairment (e.g. creatine clearance <30 ml/min), and concomitant use of potent cytochrome P450 3A4 hibitors (erythromycin), plasma levels of sildenafil at 24 hours post dose have been found to be 3 to 8 times higher than those seen in healthy volunteers. Although plasma levels of sildenafil at 24 hours post-dose are much lower than a peak concentration, it is unknown whether nitrates can be safely coadministered at this time point.

The **PRECAUTIONS** Section has been clarified concerning patients on multiple antihypertensive medications included in the pre-marketing clinical trials.

In addition, changes have been made to the Pharmacokinetics and Metabolism, Effects of VIAGRA on Blood Pressure, Effects of VIAGRA on Cardiac Parameters, and Clinical Studies subsections of the **CLINICAL PHARMACOLOGY** section of the package insert.

The process of reviewing the post marketing experience and updating the labeling of new products is routinely conducted. VIAGRA has been prescribed to more than 3 million patients.

Health care professionals are encouraged to report any unexpected and/or serious adverse events associated with the use of sildenafil directly to Pfizer Inc at 1-800-438-1985 or to the FDA MedWatch program by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178 or by mail (MEDWATCH, HF-2, FDA, 5600 Fisher Lane, Rockville, MD 20857).