

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-895/S-002

Trade Name: Viagra Tablets

Generic Name: sildenafil citrate

Sponsor: Pfizer Labs

Approval Date: 08/13/98

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 20-895/S-002

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Labeling	X
Medical Review(s)	X
Chemistry Review(s)	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative and Correspondence Document(s)	X

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 20-895/S-002

APPROVAL LETTER

NDA 20-895/S-002

AUG 13 1998

Pfizer Inc.
Attention: Ms. Rita A. Wittich
Director, Regulatory Affairs
235 East 42 Street
New York, NY 10017

Dear Ms. Wittich:

Please refer to your supplemental new drug application dated June 18, 1998, received June 19, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Viagra (sildenafil citrate) Tablets.

We acknowledge receipt of your submission dated July 23, 1998.

This supplemental new drug application provides for the addition of a patient package insert for this product.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (patient package insert dated July 23, 1998). Accordingly, the supplemental application is approved effective on the date of this letter.

If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

If a letter communicating important information about this drug product (i.e., a "Dear Healthcare Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

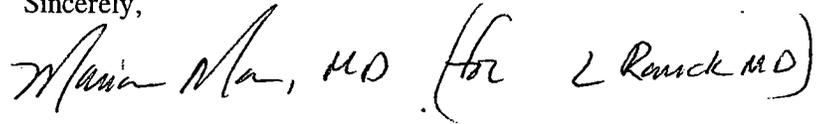
MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.



If you have any questions, contact Christina Kish, Project Manager, at (301) 827-4260.

Sincerely,



Lisa D. Rarick, M.D.

Director

Division of Reproductive and Urologic Drug Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

cc:

Archival NDA 20-895

HFD-580/Div. Files

HFD-580/TRumble/MHirsch/DShames/MMann

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-102/ADRA (with labeling)

HFD-40/DDMAC (with labeling)

HFD-613/OGD (with labeling)

HFD-95/DDMS (with labeling)

HFD-820/DNDC Division Director

DISTRICT OFFICE

HFD-580/CKish/8.12.98/n20895ap.s02

SUPPLEMENT APPROVAL (S/AP)

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 20-895/S-002

LABELING

PATIENT SUMMARY OF INFORMATION ABOUT

APPROVED

AUG 13 1998

VIAGRA™

(sildenafil citrate) tablets

This summary contains important information about VIAGRA. It is not meant to take the place of your doctor's instructions. Read this information carefully before you start taking VIAGRA. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about VIAGRA.

This medicine can help many men when it is used as prescribed by their doctors. However, VIAGRA is not for everyone. It is intended for use only by men who have a condition called erectile dysfunction. **VIAGRA must never be used by men who are taking medicines that contain nitrates of any kind. This includes nitroglycerin.**

► What Is VIAGRA?

VIAGRA is a pill used to treat erectile dysfunction (impotence) in men. It can help many men who have erectile dysfunction get and keep an erection when they become sexually excited (stimulated).

You will not get an erection just by taking this medicine. VIAGRA helps a man with erectile dysfunction get an erection only when he is sexually excited.

► How Sex Affects The Body

When a man is sexually excited, the penis rapidly fills with more blood than usual. The penis then expands and hardens. This is called an erection. After the man is done having sex, this extra blood flows out of the penis back into the body. The erection goes away. If an erection lasts for a long time (more than 6 hours), it can permanently damage your penis. You should call a doctor immediately if you ever have a prolonged erection that lasts more than four hours.

Some conditions and medicines interfere with this natural erection process. The penis cannot fill with enough blood. The man cannot have an erection. This is called erectile dysfunction if it becomes a frequent problem.

During sex, your heart works harder. Before you start any treatment for erectile dysfunction, ask your doctor if your heart is healthy enough to handle the extra stress of having sex.

► How VIAGRA Works

In many men with erectile dysfunction, VIAGRA helps the body's natural erection process. When he is sexually excited, the penis will fill with enough blood to cause an erection. After sex is over, the erection goes away.

► VIAGRA Is Not for Everyone

VIAGRA is only for patients with erectile dysfunction. VIAGRA is not for newborns, children, or women. Do not let anyone else take your VIAGRA. VIAGRA must be used only under a doctor's supervision.

As noted above (*How Sex Affects the Body*), ask your doctor if your heart is healthy enough for sexual activity.

VIAGRA must never be used by men who are taking any medicines that contain nitrates. Nitrates are found in many prescription medicines that are used to treat angina (chest pain due to heart disease) such as:

- nitroglycerin (sprays, ointments, skin patches or pastes, and tablets that are swallowed or dissolved in the mouth)
- isosorbide mononitrate and isosorbide dinitrate (tablets that are swallowed, chewed, or dissolved in the mouth)

Nitrates are also found in illicit drugs such as amyl nitrate or nitrite ("poppers"). If you are not sure if any of your medicines contain nitrates, or if you do not understand what nitrates are, ask your doctor or pharmacist. If you take VIAGRA with any nitrate medicine or illicit drug containing nitrates, your blood pressure could suddenly drop to an unsafe level. You could get dizzy, faint, or even have a heart attack or stroke.

► What VIAGRA Does Not Do

- VIAGRA does not cure erectile dysfunction. It is a treatment for erectile dysfunction.
- VIAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.
- VIAGRA is not a hormone or an aphrodisiac.

► What To Tell Your Doctor Before You Begin Viagra

Only your doctor can decide if VIAGRA is right for you. You will need to have a physical exam to diagnose your erectile dysfunction and to find out if you can take VIAGRA alone or with your other medicines.

Be sure to tell your doctor if you:

- have ever had any heart problems (angina, chest pain)
- have ever had any kidney problems
- have ever had any liver problems
- have ever had any blood problems, including sickle cell anemia or leukemia
- are allergic to sildenafil or any of the other ingredients of VIAGRA tablets
- have a deformed penis, Peyronie's disease, or ever had an erection that lasted more than 6 hours
- have stomach ulcers or any types of bleeding problems
- have a rare inherited eye disease called retinitis pigmentosa
- are taking any other medicines

► VIAGRA and Other Medicines

Some medicines can change the way VIAGRA works. Tell your doctor about any medicines you are taking. Do not start taking any new medicines before checking with your doctor or pharmacist. This includes prescription and nonprescription medicines or remedies. Remember, VIAGRA should never be used with medicines that contain nitrates (see *VIAGRA Is Not For Everyone*). VIAGRA should not be used with any other medical treatments that cause erections. These treatments include pills, medicines that are injected or inserted into the penis, implants or vacuum pumps.

► Finding the Right Dose for You

You will learn how well VIAGRA works for you through your personal experience. If you do not get the results you expect, talk with your doctor. VIAGRA comes in different doses (25 mg, 50 mg and 100 mg). You and your doctor can determine the dose that works best for you.

- Do not take more VIAGRA than your doctor prescribes.
- If you think you need a larger dose of VIAGRA, check with your doctor.
- VIAGRA should not be taken more than once a day.

If you are older than age 65, or have serious liver or kidney problems, your doctor may start you at the lowest dose (25 mg) of VIAGRA.

► How To Take VIAGRA

Take VIAGRA about one hour before you plan to have sex. Beginning in about 30 minutes and for up to 4 hours, VIAGRA can help you get an erection if you are sexually excited. If you take VIAGRA after a high-fat meal (such as a cheeseburger and french fries), the medicine may take a little longer to start working. VIAGRA can help you get an erection when you are sexually excited. You will not get an erection just by taking the pill.

► Possible Side Effects

Like all medicines, VIAGRA can cause some side effects. These effects are usually mild and do not last long. Some of these side effects are more likely to occur with higher doses. The most common side effects of VIAGRA are headache, flushing of the face, and upset stomach.

Less common side effects that may occur are temporary changes in color vision (such as trouble telling the difference between blue and green objects or having a blue color tinge to them), eyes being more sensitive to light, or blurred vision. In extremely rare instances, men may have an erection that lasts many hours. You should call a doctor immediately if you ever have an erection that lasts more than four hours (see *How Sex Affects the Body*). VIAGRA may cause other side effects besides those listed on this sheet. If you want more information or develop any side effects or symptoms you are concerned about, call your doctor.

► Accidental Overdose

In case of accidental overdose, call your doctor right away.

► Storing VIAGRA

Keep VIAGRA out of the reach of children. Keep VIAGRA in its original container. Store at room temperature (59°-86°F or 15°-30°C).

► For More Information on VIAGRA

VIAGRA is a prescription medicine used to treat erectile dysfunction. Only your doctor can decide if it is right for you. This sheet is only a summary. If you have any questions or want more information about VIAGRA, talk with your doctor or pharmacist or call 1-888-VIAGRA.



U.S. Pharmaceuticals

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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 20-895/S-002

MEDICAL REVIEW(S)

ORIGINAL

NDA #20-895

Date received: June 18, 1998
MOR complete: June 24, 1998

JUN 24 1998

Medical Officer Review of Labeling Supplement

Drug: VIAGRA™ (sildenafil citrate) Tablets
Sponsor: Pfizer Pharmaceuticals
New York, N.Y.

Background: At the Agency's request, the sponsor has submitted a proposed patient package insert (PPI) that will accompany the current PI.

Review of the PPI:

In the second paragraph of the PPI, we recommend that the last 2 sentences be changed to **bold font**. These should read, "**VIAGRA must never be used by men who are taking medicines that contain nitrates of any kind. This includes nitroglycerin.**"

In the section **VIAGRA Is Not for Everyone**, we recommend that an additional paragraph be added regarding the health risk associated with sexual activity. Such a paragraph might read,

[
[
[

]
]

We recommend that the title, [] be changed to read, **What To Tell Your Doctor Before You Begin VIAGRA.**

In the section **VIAGRA and Other Medicines**, we recommend that an additional sentence be added to describe those specific medications which are currently known to change the way VIAGRA works.

In the section **Finding the Right Dose for You**, we recommend adding an additional bullet point regarding a 25 mg starting dose in special patient populations. Such a statement might read, "If you are older than 65, []

[
[]

]
]

In the section **Possible Side Effects**, we recommend an additional statement regarding priapism. The statement regarding priapism that currently appears in the section **How Sex Affects the Body** could simply be removed from that section and placed as an additional paragraph into the section **Possible Side Effects**.

We recommend that the title, [] be changed to read, **For More Information On VIAGRA.**

In the section [] we recommend removing the first sentence of the paragraph, which currently reads "VIAGRA is a prescription medicine []
[] erectile dysfunction".

[

]

In the section we recommend changing the final sentence to include a toll-free telephone number which patients could call directly to obtain more information about VIAGRA. The last sentence might read, "If you have any questions or want more information about VIAGRA, talk with your doctor or pharmacist or call 1-800-xxx-xxxx".

Recommended regulatory action: These comments should be conveyed to the sponsor by regulatory letter.

Mark S. Hirsch MD

Mark S. Hirsch, M.D.
Medical Officer
Division of Reproductive and Urologic Drug Products
cc: Orig NDA 20-895
HFD-580/Div File
HFD-580/LRarick/MMann/DShames/TRumble

J concur
MM MD
6/24/98

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 20-895/S-002

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-895\S-002
NDA 20-895\S-003
NDA 20-895\S-004
NDA 20-895\S-005
NDA 20-895\S-006

Pfizer, Inc.
Attention: Rita Wittich
Director/Team Leader, Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Ms. Wittich:

We acknowledge receipt of your submissions dated August 21, 1998 (S-002), January 7, 1999 (S-003), January 20, 1999 (S-004), June 30, 1999 (S-006), and March 24, 2000 (S-005), containing final printed labeling in response to our approval letters approving your supplemental new drug applications for Viagra® (sildenafil citrate) Tablets.

We have reviewed the labeling that you submitted in accordance with our approval letters dated August 13, 1998 (S-002), November 24, 1998, (S-003), December 22, 1998 (S-004), June 18, 1999 (S-006), and January 21, 2000 (S-005), and we find it acceptable.

If you have any questions, call Eufrecina DeGuia, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Daniel A. Shames
12/4/01 04:26:29 PM

Division of Reproductive and Urologic Drug Products

Regulatory Project Manager Review

Application Numbers:

NDA 20-895/S-002
NDA 20-895/S-003
NDA 20-895/S-004
NDA 20-895/S-005
NDA 20-895/S-006

Name of Drug: Viagra® (sildenafil citrate) Tablets

Sponsor: Pfizer, Inc.

Material Reviewed:

FPL submitted as FA for:

NDA	Submission Date	Material Submitted
20-895/S-002	21-AUG-1998	Patient Package Insert
20-895/S-003	07-JAN-1999	Package Insert
20-895/S-004	20-JAN-1999	Patient Package Insert
20-895/S-005	24-MAR-2000	Package Insert
20-895/S-006	30-JUN-1999	Package Insert Patient Summary of Information

Review:

The FPL submitted as FA is identical to the approved draft labeling:

NDA 20-895/S-002 **Approved** 13-AUG-1998
NDA 20-895/S-003 **Approved** 24-NOV-1998
NDA 20-895/S-004 **Approved** 22-DEC-1998
NDA 20-895/S-005 **Approved** 21-JAN-2000
NDA 20-895/S-006 **Approved** 18-JUN-1999

Conclusions:

An Acknowledge and Retain Letter will be issued for the FPL submitted as FA for these Labeling Supplements.

Jeanine A. Best, M.S.N., R.N.
Senior Regulatory Associate

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Jeanine Best
12/4/01 03:05:27 PM
CSO

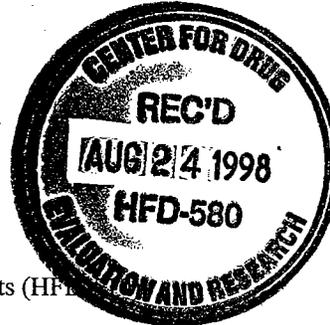
ORIGINAL



NDA SUPP AMEND

SU-000 FA

August 21, 1998



Dr. Lisa Rarick, M.D.
Division of Reproductive Health and Urologic Drug Products (HFD)
Center of Drug Evaluation and Research
Office of Drug Evaluation IV
Document Control Room 12B-30
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: Viagra® (sildenafil citrate) Tablets
NDA #20-895
Labeling Supplement – Final Printed Labeling-S-002

Dear Dr. Rarick:

Pursuant to 21 CFR 314.70(b)(3), Pfizer is hereby submitting final printed labeling for a patient package insert for Viagra (sildenafil citrate) tablets. The patient package insert was submitted to the FDA on July 23, 1998 and approved on August 13, 1998. As requested in the August 13, 1998 FDA letter and as per Lana Liem's discussion with Ms. Terri Rumble on August 19th, we are resubmitting the Viagra patient package insert as final printed labeling.

It is Pfizer's intent to include the patient package insert along with the direct to consumer promotional labeling and sample drug product in fulfillment of the adequate labeling and advertising requirements defined in 21 CFR 201.5 and 21 CFR 202.1 (1)(2). Retail drug product and professional promotional labeling will be accompanied by the full prescribing information.

Please contact me at (212) 573-2620 with any comments.

Sincerely,

Melinda Rudnicki
Melinda Rudnicki
Director, Regulatory Affairs

REVIEWS COMPLETED	
CSO ACTION:	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>OR 12/14/98</i>	
CSO INITIALS	DATE

PATIENT SUMMARY OF INFORMATION ABOUT

VIAGRA™
(sildenafil citrate) tablets



This summary contains important information about VIAGRA. It is not meant to take the place of your doctor's instructions. Read this information carefully before you start taking VIAGRA. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about VIAGRA.

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▶ What Is VIAGRA?

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You will not get an erection just by taking this medicine. VIAGRA helps a man with erectile dysfunction get an erection only when he is sexually excited.

▶ How Sex Affects The Body

When a man is sexually excited, the penis rapidly fills with more blood than usual. The penis then expands and hardens. This is called an erection. After the man is done having sex, this extra blood flows out of the penis back into the body. The erection goes away. If an erection lasts for a long time (more than 6 hours), it can permanently damage your penis. You should call a doctor immediately if you ever have a prolonged erection that lasts more than four hours.

Some conditions and medicines interfere with this natural erection process. The penis cannot fill with enough blood. The man cannot have an erection. This is called erectile dysfunction if it becomes a frequent problem.

During sex, your heart works harder. Before you start any treatment for erectile dysfunction, ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

▶ How VIAGRA Works

In many men with erectile dysfunction, VIAGRA helps the body's natural erection process. When he is sexually excited, the penis will fill with enough blood to cause an erection. After sex is over, the erection goes away.

▶ VIAGRA Is Not for Everyone

VIAGRA is only for patients with erectile dysfunction. VIAGRA is not for newborns, children, or women. Do not let anyone else take your VIAGRA. VIAGRA must be used only under a doctor's supervision.

As noted above (*How Sex Affects the Body*), ask your doctor if your heart is healthy enough for sexual activity.

VIAGRA must never be used by men who are taking any medicines that contain nitrates. Nitrates are found in many prescription medicines that are used to treat angina (chest pain due to heart disease) such as:

- nitroglycerin (sprays, ointments, skin patches or pastes, and tablets that are swallowed or dissolved in the mouth)
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Nitrates are also found in illicit drugs such as amyl nitrate or nitrite ("poppers"). If you are not sure if any of your medicines contain nitrates, or if you do not understand what nitrates are, ask your doctor or pharmacist. If you take VIAGRA with any nitrate medicine or illicit drug containing nitrates, your blood pressure could suddenly drop to an unsafe level. You could get dizzy, faint, or even have a heart attack or stroke.

▶ What VIAGRA Does Not Do

- VIAGRA does not cure erectile dysfunction. It is a treatment for erectile dysfunction.
- VIAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.
- VIAGRA is not a hormone or an aphrodisiac.

ORIGINAL

Labeling: _____

NDA No. 20-895 Rcd. 8-24-98

Reviewed by: _____

▶ What To Tell Your Doctor Before You Begin Viagra

Only your doctor can decide if VIAGRA is right for you. You will need to have a physical exam to diagnose your erectile dysfunction and to find out if you can take VIAGRA alone or with your other medicines.

Be sure to tell your doctor if you:

- have ever had any heart problems (angina, chest pain)
- have ever had any kidney problems
- have ever had any liver problems
- have ever had any blood problems, including sickle cell anemia or leukemia
- are allergic to sildenafil or any of the other ingredients of VIAGRA tablets
- have a deformed penis, Peyronie's disease, or ever had an erection that lasted more than 6 hours
- have stomach ulcers or any types of bleeding problems
- have a rare inherited eye disease called retinitis pigmentosa
- are taking any other medicines

▶ VIAGRA and Other Medicines

Some medicines can change the way VIAGRA works. Tell your doctor about **any medicines** you are taking. Do not start taking any new medicines before checking with your doctor or pharmacist. This includes prescription and nonprescription medicines or remedies. Remember, VIAGRA should never be used with medicines that contain nitrates (see *VIAGRA Is Not For Everyone*). VIAGRA should not be used with any other medical treatments that cause erections. These treatments include pills, medicines that are injected or inserted into the penis, implants or vacuum pumps.

▶ Finding the Right Dose for You

You will learn how well VIAGRA works for you through your personal experience. If you do not get the results you expect, talk with your doctor. VIAGRA comes in different doses (25 mg, 50 mg and 100 mg). You and your doctor can determine the dose that works best for you.

- Do not take more VIAGRA than your doctor prescribes.
- If you think you need a larger dose of VIAGRA, check with your doctor.
- VIAGRA should not be taken more than once a day.

If you are older than age 65, or have serious liver or kidney problems, your doctor may start you at the lowest doses (25 mg) of VIAGRA.

▶ How To Take VIAGRA

Take VIAGRA about one hour before you plan to have sex. Beginning in about 30 minutes and for up to 4 hours, VIAGRA can help you get an erection if you are sexually excited. If you take VIAGRA after a high-fat meal (such as a cheeseburger and french fries), the medicine may take a little longer to start working. VIAGRA can help you get an erection when you are sexually excited. You will not get an erection just by taking the pill.

▶ Possible Side Effects

Like all medicines, VIAGRA can cause some side effects. These effects are usually mild and do not last long. Some of these side effects are more likely to occur with higher doses. The most common side effects of VIAGRA are headache, flushing of the face, and upset stomach.

Less common side effects that may occur are temporary changes in color vision (such as trouble telling the difference between blue and green objects or having a blue color tinge to them), eyes being more sensitive to light, or blurred vision. In extremely rare instances, men may have an erection that lasts many hours. You should call a doctor immediately if you ever have an erection that lasts more than four hours (see *How Sex Affects the Body*). VIAGRA may cause other side effects besides those listed on this sheet. If you want more information or develop any side effects or symptoms you are concerned about, call your doctor.

▶ Accidental Overdose

In case of accidental overdose, call your doctor right away.

▶ Storing VIAGRA

Keep VIAGRA out of the reach of children. Keep VIAGRA in its original container. Store at room temperature (59°-86°F or 15°-30°C).

▶ For More Information on VIAGRA

VIAGRA is a prescription medicine used to treat erectile dysfunction. Only your doctor can decide if it is right for you. This sheet is only a summary. If you have any questions or want more information about VIAGRA, talk with your doctor or pharmacist or call 1-888-VIAGRA.



U.S. Pharmaceuticals

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ORIGINAL

Pfizer Pharmaceuticals Group
Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755
Tel 212 573 3833 Fax 212 573 1563



~~NDA NO. 20-895 REF. NO. 003~~
~~NDA SUPPL FOR SL~~

Pfizer Pharmaceuticals

Lana Liem
Associate Director
Drug Regulatory Affairs

NDA SUPP AMEND

SL-002 32

July 23, 1998

Dr. Lisa Rarick, M.D.
Division of Reproductive Health and Urologic Drug Products (HFD-510)
Center of Drug Evaluation and Research
Office of Drug Evaluation IV
Document Control Room 12B-30
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

REVIEWS COMPLETED
GSO ACTION:
<input checked="" type="checkbox"/> LETTER <input type="checkbox"/> N.A.X. <input type="checkbox"/> MEMO
<i>CL</i> 7/12/98
GSO INITIALS DATE

RE: **Viagra® (sildenafil citrate) Tablets**
NDA #20-895
Labeling Supplement – Expedited Review Requested

Dear Dr. Rarick:

Pursuant to 21 CFR 314.70 (b)(3), Pfizer is hereby submitting final printed labeling for a patient package insert for Viagra (sildenafil citrate) tablets. Please note that an expedited review has been requested. Please refer to the draft labeling submission on June 18, 1998, your response letter on July 7, 1998, our faxed comments on July 17, 1998, and my discussion with Ms. Terri Rumble on July 20, 1998.

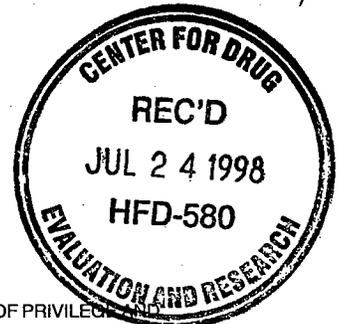
Upon approval of this supplement, it is Pfizer's intent to include the patient package insert along with the direct to consumer promotional labeling and sample drug product in fulfillment of the adequate labeling and advertising requirements defined in 21 CFR 201.5 and 21 CFR 202.1 (1)(2). Retail drug product and professional promotional labeling will be accompanied by the full prescribing information.

Please contact me at (212) 573-3833 with any comments.

Sincerely,

Lana Liem

*This supplement revises
a recent draft. The proposed patient
package insert as requested
in the medical officers
review of June 29, 1998
CL 6/29/98*



NDA 20-895/S-002

JUL 7 1998

Pfizer Pharmaceuticals
Attention: Ms. Lana Liem
Regulatory Affairs
235 42nd Street
New York, NY 10017-5755

Dear Ms. Liem:

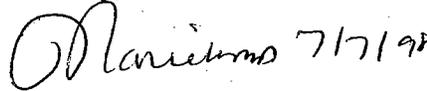
Please refer to your supplemental new drug application dated June 18, 1998, received June 19, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Viagra (sildenafil citrate) tablets.

This supplement provides for a patient package insert for Viagra.

We have completed review of the patient package insert and have several comments. These recommendations have been incorporated into the enclosed document. Comments have been noted in underline and surrounded by parentheses. Please submit your revised patient package insert as soon as possible.

If you have any questions, contact Terri F. Rumble, B.S.N., Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,



Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic
Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

NDA 20-895/S-002

Page 2

cc:

Archival NDA 20-895

HFD-580/Div. Files

HFD-580/Rarick/Mann/Shames/Hirsch/El-Hage/Jordan/Linn/Rhee/Jarugula/Dorantes/T.Rumble

HFD-715/Mele

HFD-040/Askine

HFD-95/DDMS

DISTRICT OFFICE

Drafted by: Rumble/July 2, 1998

Initialed by: Rarick,7.6.98/Mann,7.7.98/Shames7.6.98/Hirsch,7.2.98/Pauls,7.7.98/Askine7.6.98

final: Rumble,7.7.98

filename: wordfiles/nda/supplements/20895irppi.doc

INFORMATION REQUEST (IR)

NDA 20-895/S-002

The following recommendations for the patient package insert are underlined and in parentheses ():

Patient Summary of Information about VIAGRA[®] (sildenafil citrate) Tablets

This summary contains important information about VIAGRA. It is not meant to take the place of your doctor's instructions. Read this information carefully before you start taking VIAGRA. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about VIAGRA.

This medicine can help many men when it is used as prescribed by their doctors. However, VIAGRA is not for everyone. It is intended for use only by men who have a condition called erectile dysfunction. **VIAGRA must never be used by men who are taking medicines that contain nitrates of any kind. This includes nitroglycerin.**

(In the second paragraph of the PPI, we recommend that the last two sentences be bolded.)

What Is VIAGRA?

VIAGRA is a pill used to treat erectile dysfunction (impotence) in men. It can help many men who have erectile dysfunction get and keep an erection when they become sexually excited (stimulated).

You will not get an erection just by taking this medicine. VIAGRA helps a man with erectile dysfunction get an erection only when he is sexually excited.

How Sex Affects The Body

When a man is sexually excited, the penis rapidly fills with more blood than usual. The penis then expands and hardens. This is called an erection. After the man is done having sex, this extra blood flows out of the penis back into the body. The erection goes away. If an erection lasts for a long time (more than 5 hours), it can permanently damage your penis. You should call a doctor immediately if this ever happens to you.

Some conditions and medicines interfere with this natural erection process. The penis cannot fill with enough blood. The man cannot have an erection. This is called erectile dysfunction if it becomes a frequent problem.

During sex, your heart works harder. Before you start any treatment for erectile dysfunction, ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

How VIAGRA Works

In many men with erectile dysfunction, VIAGRA helps the body's natural erection process. When he is sexually excited, the penis will fill with enough blood to cause an erection. After sex is over, the erection goes away.

VIAGRA Is Not for Everyone

VIAGRA is only for patients with erectile dysfunction. VIAGRA is not for newborns, children, or women. Do not let anyone else take your VIAGRA. VIAGRA must be used only under a doctor's supervision.

(We recommend that an additional paragraph be added regarding the health risk associated with sexual activity. Such a paragraph might read, [

VIAGRA must never be used by men who are taking any medicines that contain nitrates.

Nitrates are found in many prescription medicines that are used to treat angina (chest pain due to heart disease) such as:

- nitroglycerin (sprays, ointments, skin patches or pastes, and tablets that are swallowed or dissolved in the mouth)
- isosorbide mononitrate and isosorbide dinitrate (tablets that are swallowed, chewed, or dissolved in the mouth)

Nitrates are also found in illicit drugs such as amyl nitrate or nitrite ("poppers"). If you are not sure if any of your medicines contain nitrates, or if you do not understand what nitrates are, ask your doctor or pharmacist. If you take VIAGRA with any nitrate medicine or illicit drug containing nitrates, your blood pressure could suddenly drop to an unsafe level. You could get dizzy, faint, or even have a heart attack or stroke.

What VIAGRA Does Not Do

VIAGRA does not cure erectile dysfunction. It is a treatment for erectile dysfunction.

VIAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV--the virus that causes AIDS.

VIAGRA is not a hormone or an aphrodisiac.

[] (We recommend that the title be changed to read, **What to Tell Your Doctor Before You Begin VIAGRA**)

Only your doctor can decide if VIAGRA is right for you. You will need to have a physical exam to diagnose your erectile dysfunction and to find out if you can take VIAGRA alone or with your other medicines.

Before you start taking VIAGRA, be sure to tell your doctor if you:

- have ever had any heart problems (angina, chest pain)
- have ever had any kidney problems
- have ever had any liver problems

- have ever had any blood problems, including sickle cell anemia or leukemia
- are allergic to sildenafil or any of the other ingredients of VIAGRA tablets
- have a deformed penis, Peyronie's disease, or ever had an erection that lasted more than 6 hours.
- have stomach ulcers or any types of bleeding problems
- have a rare inherited eye disease called retinitis pigmentosa
- are taking any other medicines

VIAGRA and Other Medicines

Some medicines can change the way VIAGRA works. Tell your doctor about any medicines you are taking. Do not start taking any new medicines before checking with your doctor or pharmacist. This includes prescription and nonprescription medicines or remedies.

VIAGRA should not be used with any other medical treatments that cause erections. These treatments include pills, medicines that are injected or inserted into the penis, implants or vacuum pumps.

(We recommend that an additional sentence be added to describe those specific medications that are currently known to change the way VIAGRA works.)

Finding the Right Dose for You

You will learn how well VIAGRA works for you through your personal experience. If you do not get the results you expect, talk with your doctor. VIAGRA comes in different doses. You and your doctor can determine the dose that works best for you.

Do not take more VIAGRA than your doctor prescribes.

If you think you need a larger dose of VIAGRA, check with your doctor.

VIAGRA should not be taken more than once a day.

(In the section, **Finding the Right Dose for You**, we recommend adding an additional bullet point regarding a 25 mg starting dose in special patient populations. Such a statement might read, "If you are older than 65, [

[_____]

How To Take VIAGRA

Take VIAGRA about one hour before you plan to have sex. Beginning in about 30 minutes and for up to 4 hours, VIAGRA can help you get an erection if you are sexually excited. If you take VIAGRA after a high-fat meal (such as a cheeseburger and french fries), the medicine may take a little longer to start working.

VIAGRA can help you get an erection when you are sexually excited. You will not get an erection just by taking the pill.

Possible Side Effects

Like all medicines, VIAGRA can cause some side effects. These effects are usually mild and do not last long. Some of these side effects are more likely to occur with higher doses.

The most common side effects of VIAGRA are headache, flushing of the face, and upset stomach.

Less common side effects that may occur are temporary changes in color vision (such as trouble telling the difference between blue and green or objects having a blue color tinge to them), eyes being more sensitive to light, or blurred vision. VIAGRA may cause other side effects besides those listed on this sheet. If you want more information or develop any side effects or symptoms you are concerned about, call your doctor.

(In the section **Possible Side Effects**, we recommend an additional statement regarding priapism. The statement regarding priapism that currently appears in the section **How Sex Affects the Body** could simply be removed from that section and placed as an additional paragraph into the section **Possible Side Effects**.)

Accidental Overdose

In case of accidental overdose, call your doctor right away.

Storing VIAGRA

Keep VIAGRA out of the reach of children. Keep VIAGRA in its original container. Store at room temperature (59⁰ -86⁰F or 15⁰ - 30⁰C).

[(We recommend that the title, [_____], be changed to read, **For More Information On VIAGRA**)

VIAGRA is a prescription medicine that has helped many men with a medical condition called erectile dysfunction. Only your doctor can decide if it is right for you. This sheet is only a summary. If you have any questions or want more information about VIAGRA, talk with your doctor or pharmacist.

(In the section, [_____], we recommend deleting the first sentence of the paragraph, which currently reads, "VIAGRA is a prescription medicine [_____] [_____] erectile dysfunction." Also, we recommend changing the final sentence to include a toll-free telephone number which patients could call directly to obtain more information about VIAGRA. The last sentence might read, "If you have any questions or want more information about VIAGRA, talk with your doctor or pharmacist or call 1-800-xxx-xxxx.")



Food and Drug Administration
Rockville MD 20857

NDA 20-895/S-002

JUN 30 1998

Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

Attention: Rita A. Wittich, Director
Regulatory Affairs

Dear Mrs. Wittich:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Viagra (sildenafil citrate) 25/50/100 mg tablets
NDA Number:	20-895
Supplement Number:	S-002
Date of Supplement:	June 18, 1998
Date of Receipt:	June 19, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on August 18, 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Lana L. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

NDA 20-895/S-002

Page 2

cc:

Original NDA 20-895/S-002

HFD-580/Div. Files

HFD-580/CSO/T. Rumble

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

Pfizer Pharmaceuticals Group
Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755
Tel 212 573 3833 Fax 212 573 1563



Pfizer Pharmaceuticals

June 18, 1998

NDA NO. 20-895 REF. NO. 004
NDA SUPPL FOR 3UR

Lana Liem
Associate Director
Drug Regulatory Affairs

see my review dated June 24, 1998
MLT

Noted JEL 7/7/98
noted DTC 7/6/98

Dr. Lisa Rarick, M.D.
Division of Reproductive Health and Urologic Drug Products (HFD-510)
Center of Drug Evaluation and Research
Office of Drug Evaluation IV
Document Control Room 12B-30
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



RE: Viagra™ (sildenafil citrate) Tablets
NDA #20-895
Labeling Supplement

Dear Dr. Rarick:

Pursuant to 21 CFR 314.70 (b)(3), Pfizer is hereby submitting a labeling supplement that provides for a patient package insert for Viagra tablets. Please refer to your discussion with Ms. Suzanne LoGalbo, Pfizer Inc, on May 20, 1998, and my discussion with Ms. Terri Rumble on May 21, 1998. At the Agency's request, Pfizer has prepared a patient package insert (see Attachment 1).

The enclosed proposed patient package insert is based on the full prescribing information that was approved on March 27, 1998, and is presented in a format and language that is easily understood by consumers. Our objective was to communicate the major product information that would be helpful to patients who are discussing erectile dysfunction treatment options with their physicians.

Upon approval of this supplement, it is Pfizer's intent to include the patient package insert along with the direct to consumer promotional labeling and sample drug product in fulfillment of the adequate labeling and advertising requirements defined in 21 CFR 201.5 and 21 CFR 202.1 (l)(2). Retail drug product and professional promotional labeling will be accompanied by the full prescribing information.

We would be pleased to meet with you to discuss any substantive issues. Please contact me at (212) 573-3833 with any comments.

Sincerely,

Lana Liem

REVIEWS COMPLETED
<i>IR letter sent 7/7/98</i>
CSO ACTION:
<input checked="" type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>Trumble 7/7/98</i>
CSO INITIALS DATE

CLL 6/12/98