



TRANSMITTED BY FACSIMILE

P. Kaia Agarwal, M.Sc.
Senior Director, Regulatory Affairs
GlaxoSmithKline
One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101-7929

RE: NDA #20-936

**Paxil® CR (paroxetine HCl) Controlled Release Tablets
MACMIS #12439**

Dear Ms. Agarwal:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a 60-second direct-to-consumer (DTC) television broadcast advertisement (TV ad) entitled "Hello, My Name Is..." (ID _____ for Paxil CR (paroxetine HCl) submitted by GlaxoSmithKline (GSK) under cover of Form FDA 2253. The TV ad is false or misleading because it contains a representation or suggestion, not approved or permitted for use in the labeling, that Paxil CR is useful in a broader range of conditions or patients, and is safer than has been demonstrated by substantial evidence or substantial clinical experience in violation of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. 352(n)) and FDA implementing regulations (21 CFR 202.1(e)(6)(i)). This ad is concerning from a public health perspective because it broadens the use of Paxil CR beyond the narrowly-defined and more serious condition of social anxiety disorder to people experiencing more ordinary degrees of anxiety, fear or self-consciousness in social or work situations, while also minimizing the serious risks associated with the drug.

Background

Paxil CR is an orally administered psychotropic drug approved for treatment of social anxiety disorder (SAD). The Indications and Usage section of the FDA-approved labeling (PI) states (in pertinent part):

PAXIL CR is indicated for the treatment of social anxiety disorder, also known as social phobia, as defined in DSM-IV (300.23). Social anxiety disorder is characterized by a marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, anxious anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine, occupational or academic functioning,

or social activities or relationships, or there is marked distress about having the phobias. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

According to the PI, "Concomitant use in patients taking either monoamine oxidase inhibitors (MAOIs) or thioridazine is contraindicated." The Warnings section of the PI also states (in pertinent part):

In patients receiving another serotonin reuptake inhibitor drug in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma...While there are no human data showing such an interaction with paroxetine hydrochloride, limited animal data on the effects of combined use of paroxetine and MAOIs suggest that these drugs may act synergistically...Therefore it is recommended that PAXIL CR not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. At least 2 weeks should be allowed after stopping PAXIL CR before starting an MAOI.

Thioridazine administration alone produces prolongation of the QTc interval, which is associated with serious ventricular arrhythmias, such as torsade de pointes-type arrhythmias, and sudden death...An in vivo study suggests that drugs which inhibit P450IID6 such as paroxetine, will elevate plasma levels of thioridazine. Therefore, it is recommended that paroxetine not be used in combination with thioridazine.

In addition, the Precautions section of the PI states that patients should be monitored for symptoms such as dizziness, sensory disturbances, agitation, anxiety, nausea, and sweating when discontinuing treatment with Paxil CR. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. Furthermore, the Adverse Reactions section of the PI identifies nausea, asthenia, abnormal ejaculation, sweating, somnolence, impotence, insomnia, and decreased libido as side effects observed in some patients with SAD.

Misleading Communication of Indication

The TV ad broadens the indication for Paxil CR by failing to distinguish between SAD and the lesser degrees of performance anxiety or shyness that do not generally require psychopharmacological treatment. The TV ad suggests that *anyone* experiencing anxiety, fear, or self-consciousness in social or work situations is an appropriate candidate for Paxil CR.

The TV ad presents a series of brief vignettes. Actors are seen in a variety of situations (e.g., walking into a cafeteria, sitting on a couch at a party, applying lipstick in a bathroom mirror), wearing nametags indicating their emotions. Some of the emotions presented on the actors' nametags are very general

(e.g., "NERVOUS," "SELF-CONSCIOUS"). The TV ad does not convey that Paxil CR is indicated only for patients with a disorder characterized by a marked and persistent fear, in which exposure to the feared situation almost always provokes anxiety that may approach the intensity of a panic attack. Overall, the TV ad suggests that Paxil CR therapy is appropriate for patients with lesser degrees of performance anxiety or shyness, which do not generally require drug treatment. Although the TV ad refers in the audio to "overwhelming anxiety and intense fear of social situations with unfamiliar people," and to social anxiety disorder, in totality, the images in the vignettes contradict and overcome this important contextual information.

Minimization of Risk

The TV ad is misleading because it fails clearly to communicate the major risks associated with Paxil CR. Specifically, the ad fails clearly to communicate the contraindication that people taking MAOIs or thioridazine should not take Paxil CR and the precaution that patients should not abruptly stop taking Paxil CR before talking to their doctor because side effects may result from stopping the medicine. The ad also fails clearly to communicate the common side effects associated with Paxil CR, which may include nausea, sweating, sexual side effects, weakness, insomnia, and sleepiness. The compelling and attention-grabbing visuals and other competing modalities, such as background music and SUPERS, occurring simultaneously during presentation of this risk information in the TV ad distract from, and make it difficult for consumers adequately to process and comprehend the risk information.

Specifically, the risk information is stated in a fast-paced voiceover while important contextual information and other unrelated informational elements are presented in subtitled SUPERS. Moreover, the presentation of risk information is characterized by multiple scene changes and a variety of distracting visuals, including a "strobe-light" white-out effect. Additionally, the SUPERS containing important contextual information are presented in small type in white lettering on light backgrounds, rendering them extremely difficult to read under normal conditions, much less conditions in which they are presented against moving backgrounds and with overlying music. The overall effect of the distracting visual elements and the competing audio message is to undermine the communication of the important risk information, minimizing these risks and misleadingly suggesting that Paxil CR is safer than has been demonstrated by substantial evidence or substantial clinical experience.

Conclusion and Requested Action

For the reasons discussed above, the TV ad misbrands Paxil CR under section 502(n) of the Act, 21 U.S.C. 352(n), and FDA implementing regulations, 21 CFR 202.1(e)(6)(i).

DDMAC requests that GSK immediately cease the dissemination of promotional materials for Paxil CR the same as or similar to those described above. Please submit a written response to this letter on or before June 23, 2004, describing your intent to comply with this request, listing all promotional materials for Paxil CR the same as or similar to those described above, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 8B-45, 5600 Fishers Lane, Rockville, Maryland 20857, facsimile at (301) 594-6759. In all future correspondence regarding this matter, please refer to NDA #20-936 and MACMIS #12439. We remind you that only written communications are considered official.

If you choose to disseminate revised promotional materials, DDMAC is willing to assist you in assuring that your revised materials are in compliance with applicable provisions of the Act and of FDA regulations by reviewing the revisions before dissemination. There are different ways of revising your materials to address the issues identified in this letter. GSK could, for example, address the misleading communication of indication by stating via voice-over and communicating through visuals (e.g. more specific nametags reflective of the severity of SAD, such as “extremely anxious,” etc.) that Paxil CR is indicated for SAD, a disorder that has symptoms more severe than occasional feelings of shyness or self-consciousness. Additionally, a statement such as “lesser degrees of anxiety or shyness in social or work situations usually do not need medication” could be included in the TV ad to underscore that the need for drug therapy should be considered only in situations of marked and persistent symptoms of SAD. To correct the risk information issue, GSK could revise the audio and visual presentation of the TV ad by using less distracting images, music, and fewer scene changes, and by increasing the readability and prominence of the SUPERS.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Paxil CR comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Kay A. Chitale, PharmD
Consumer Promotion Analyst
Division of Drug Marketing,
Advertising, and Communications

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

/s/

Kay Chitale
6/9/04 03:53:21 PM

Director's notes:

The camera moves through different social moments (cafeteria, social gathering, etc.) throughout the day, we see what different people have filled in on their stickers. A close-up reveals it's not their name, but how they're feeling, as sufferers of Social Anxiety Disorder.



MUSIC & SFX: Social gatherings

Cut to a woman in a cafeteria with unfamiliar people. Her sticker reads: Hello my name is FEARFUL.



AFC:

PRODUCTION: [unreadable]

BY: [unreadable]

DATE: [unreadable]

Cut to a man looking nervous at a social gathering.



His sticker reads: Hello my name is NERVOUS.



Cut to another woman in a bathroom
anxiously checking herself in the mirror,
whose sticker reads: Hello my name is
SELF-CONSCIOUS.



with people...

Cut to another man at his office
cubicle, whose social anxiety is
making him avoid an office party.
His sticker reads: Hello, my name
is ANXIOUS.



AVO:

If you're one of the many who
suffer from overwhelming anxiety
and intense fear of social situations...

Cut to another woman who's visibly
uncomfortable as she waits for an
interview with other candidates.
Her sticker reads: Hello, my name
is PANICKY.



with unfamiliar people...

The PAXIL CR logo fades up over
the scene.



now there's PAXIL CR.

We see a woman whose sticker
reads: Hello, my name is AFRAID.



PAXIL CR

She peels off her sticker that says
AFRAID and...



helps relieve...

Sticks on a new sticker that simply
tells us her name. It reads: Hello,
my name is MAGGIE.



the symptoms of...

We see the woman with the sticker
that reads: Hello, my name is
MAGGIE.



social anxiety disorder all day...

Cut to the first woman's response.
We see different people in group
sessions talking stickers with
names on them.

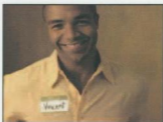
Cut to a smiling woman whose
sticker reads: Hello, my name is
KEISHA.



...and PAXIL CR is here for
so the real you...

Super reads: Help a woman out
"I agree, social anxiety affects

We see the same woman who had
cut to a man whose sticker reads:
Hello, my name is VINCENT.



...and PAXIL CR is here for
can come through.

Cut to a graphic pill sequence. We
see the special coating sweep
around clock-wise.



PAXIL CR has a special coating...

Super reads: Available by prescrip-
tion only.

Available by prescription only.

Pill graphic builds until the "CR"
glows through the coating.

Super reads: Symptom relief usual-
ly requires 2 or more weeks of
daily treatment.



Symptom relief usually requires 2 or more
weeks of daily treatment.

that allows for a controlled
release for continuous relief all
day.

PAXIL CR 02.11.04
SAD: "Hello My Name Is" :60
TV BOARD 5 of 7

PAXIL CR
PAROXETINE HCl
CONTROLLED SUBSTANCE

Cut to the fair balance sequence. We see different people in social situations wearing stickers with their names, feeling like themselves again. First we see a woman interacting with friends at a book club.

Super reads: Only a doctor can diagnose social anxiety disorder.



Only a doctor can diagnose social anxiety disorder.

Prescription PAXIL CR is not for everyone. www.paxil.com

We see the same woman and can see her sticker that says: Hello, my name is SONDRA.

Super reads: For adults 18 and over.



For adults 18 and over.

People taking MAOIs or thioridazine should not take PAXIL CR.

Cut to a group of comfortable people laughing while watching a Cut to a man feeling comfortable at a dinner party.

Super reads: www.paxil.com
1-800-441-7124



Don't drink, taking PAXIL CR, or driving while taking PAXIL CR until you know how it affects you. Read the package insert for more information. Tell your doctor... www.paxil.com

We see a close-up of the man with a sticker that says: Hello, my name is STEVEN.

Super reads: For more information talk to your doctor.



For more information talk to your doctor.

what medicines you're taking.

Cut to a woman walking her dog and meeting with friends at a park.



Side effects may include nausea, sweating, sexual side effects...

The same woman is shown sharing a laugh with her friends.



weakness, insomnia or sleepiness.

Super reads: See our ad in Marie Claire.

See our ad in US News & World Report.

Cut to a group of construction workers laughing while grabbing a cup of coffee.



Don't stop taking PAXIL CR before talking to your doctor, since side effects may result from stopping the medicine.

Supers say: www.paxilcr.com
1-888-PAXILCR.

www.paxilcr.com

1-888-PAXILCR.

The construction workers are seen together smiling. The man in the middle is wearing a sticker that says: Hello, my name is SEAN.



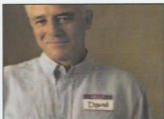
Let the world...

David's name.

The camera moves through a crowd of people, introducing ourselves, David.

*Cut to a man whose sticker reads:
Hello, my name is DAVID.*

David is smiling warmly. A crowd of people's faces are seen, but they are looking at someone or something away from David.



say hello...

*Cut to a woman. Her sticker reads:
Hello, my name is NIKKI.*

Nikki is smiling warmly.



to the real...

*Cut to another woman. Her sticker
reads: Hello, my name is TARA.*

Tara is smiling warmly.



you.

*Cut to our final woman, who was
featured in an earlier scene. Her
sticker reads: Hello, my name is
ME. The PAXIL CR logo and line
fade up as she gives us a smile.*



Ask your doctor about all day
relief with PAXIL CR.