



TRANSMITTED VIA FACSIMILE

JUL 20 2000

Donna M. Dea
Assistant Manager, Marketed Products
AstraZeneca Pharmaceuticals
1800 Concord Pike
Wilmington, DE 19850-5437

Re: **Nolvadex® (tamoxifen citrate)**
NDA 17-970
MACMIS ID# 9075

Dear Ms. Dea:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware that AstraZeneca Pharmaceuticals (Zeneca) is promoting its product, Nolvadex, in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and its implementing regulations. Reference is made to the following promotional materials:

1. Journal advertisements (ZNO9031, NL1297, NL1329)
2. Mailed consumer brochure ("Are you a helpless female?")

We have reviewed these materials and have determined that they are false or misleading for the following reasons:

Misleading Efficacy Claims

The promotional materials are misleading because they do not provide adequate context for efficacy information for Nolvadex, thereby implying greater efficacy than demonstrated by substantial evidence. For example, the following statements are presented in the mailed consumer brochure and journal advertisements, respectively:

Nolvadex is a medicine that has been used for decades to keep women who have had breast cancer from having a recurrence. But recently, a landmark study showed that it could also reduce the chance of a first occurrence of breast cancer by as much as 44% in women over 35 who were at high risk.

For the first time, there is a clinically proven way for many women at high risk of developing breast cancer to significantly reduce that risk: Nolvadex Tablets. The proof? In a landmark study of women 35 and older at high risk for breast cancer, women who took Nolvadex had 44% fewer breast cancers than women taking sugar pills.

Promoting a "44% reduction in the risk of breast cancer" without additional context is misleading because it overstates the efficacy of Nolvadex in reducing the incidence of breast cancer in women at high risk. This percentage is not further qualified with the number of cases of breast cancer annually/1000 women who took Nolvadex versus those who took placebo. Zeneca's promotional materials do not provide this, or similar, context.

In addition, the mailed consumer brochure is misleading because it does not provide adequate context for the personal risk score calculated from the Gail Model Risk Assessment. The following statements are presented in this brochure:

Your doctor calculates your personal risk, which estimates your chances of developing breast cancer over the next 5 years. If you're 35 or older and your score is 1.7 or higher, you are considered at high risk for developing breast cancer. And if you're at high risk, now there's a new option: Nolvadex Tablets.

Zeneca does not adequately communicate that women who achieve a score of 1.7 or higher will not necessarily develop breast cancer. In addition, these statements do not adequately convey that a score of 1.7 translates to a 1.7% chance of developing breast cancer in five years; rather, it implies that women with a score of ≥ 1.7 should take Nolvadex to reduce their chances of developing breast cancer. Again, Zeneca's promotional materials are misleading because they do not provide adequate context to allow evaluation of the potential benefits versus the risks of treatment with Nolvadex and they overstate the efficacy of the drug.

Lack of Fair Balance

These advertisements are also misleading because they minimize the severity of adverse effects (AE's) in high risk women who received Nolvadex for reduction in breast cancer incidence. As stated in the approved product labeling:

Hot flashes of any severity occurred in 68% of women on placebo and in 80% of women on Nolvadex. Severe hot flashes occurred in 28% of women on placebo and 45% of women on Nolvadex. Vaginal discharge occurred in 35% and 55% of women on placebo and Nolvadex, respectively, and was severe in 4.5% and 12.3%, respectively.

Zeneca undermines the significance of these AE's in these promotional materials by presenting the following statement:

Women may experience some level of hot flashes and vaginal discharge.

An 80% incidence of hot flashes and a 55% incidence of vaginal discharge is not consistent with the phrase "some level of hot flashes and vaginal discharge," especially when these severe AE's occurred at a much higher incidence in women who received Nolvadex as compared to those who received placebo.

Failure to Comply with 314.81(b)(3)(i)

The mailed consumer brochure was not submitted on Form FDA 2253 at the time of initial dissemination, in violation of the post-marketing reporting requirements of the Act.

Requested Actions

Zeneca should immediately cease dissemination of promotional materials that contain these or similar claims. Zeneca should submit in writing, on or before August 3, 2000, a description of the steps that will be taken to comply with the above request. Zeneca should also include a list of all similarly violative materials being discontinued, as well as the date of discontinuation.

Zeneca should direct its response to me by facsimile at (301) 594-6771, or by written communication at the Food and Drug Administration; Division of Drug Marketing, Advertising, and Communications, HFD-42; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Zeneca that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS ID# 9075 and NDA 17-970.

Sincerely,

/s/

Jean-Ah Choi, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

Same as

ZNO-9031

Now
predict
your chances of getting
breast cancer.

***Take the Risk Assessment Test.
It's 6 simple questions.***

For years, women have had tools like mammograms and breast self-exams that are critical to *finding* breast cancer early. *But they did not predict our chances of getting it.* Today, there's actually a way to figure out your risk of getting breast cancer.

That's why every woman should go to her doctor and take the new risk assessment test as part of her complete breast health. Six simple questions are asked regarding:

- your race
- your age
- when you got your first period
- if and when you had a first child
- family history of breast cancer
- whether you've had a breast biopsy

Answers to these questions allow your doctor to evaluate your risk. Basically, you're given a number that estimates your chances of getting breast cancer over the next five years. If you're 35 or older and your number is 1.7 or higher, you are considered at high risk for breast cancer. Please remember that *this does not mean* you will get breast cancer, only that your risk is higher than average. Most women will get scores of less than 1.7.

Why would I want to know if I'm at high risk?

It's natural to wonder if you would even *want* to know if you're at high risk or not. But today there is something you can do.

And
act on it.

Nolvadex^{TABLETS}
TAMOXIFEN CITRATE

There is something you can do

Talk to your doctor about Nolvadex.

For the first time, there is a *clinically proven* way for many women at high risk of developing breast cancer to significantly reduce that risk: Nolvadex Tablets.

The proof? In a landmark study of women 35 and older at high risk for breast cancer, women who took Nolvadex had 44% fewer breast cancers than women taking sugar pills. Nolvadex decreases but doesn't eliminate the risk of breast cancer and didn't show an increase in survival.

Nolvadex isn't for every woman at high risk. In the study, women taking Nolvadex were 2 to 3 times more likely to develop uterine cancer or blood clots in the lung and legs, although each of these occurred in less than 1% of

women. Women with a history of blood clots should not take Nolvadex. Stroke, cataracts, and cataract surgery were more common with Nolvadex. Most women experience some level of hot flashes and vaginal discharge. **Pregnant women or women planning on becoming pregnant soon should not take Nolvadex.** You and your doctor must carefully discuss whether the potential benefit of Nolvadex outweighs these potential side effects.

Call 1-800-898-2762 for a free video about Nolvadex and to learn more about the risk assessment test for your complete breast health.

www.nolvadex.com

Please see important information on adjacent page.

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N1126

Now
predict
 your chances of getting
breast cancer.

And
act
 on it.

Nolvadex^{TABLETS}
 TAMOXIFEN CITRATE

There is something you can do

***Take the Risk Assessment Test.
 It's 6 simple questions.***

Many of us sense we might be at high risk for getting breast cancer—especially if we've watched a mother or sister battle the disease. Well, now there's a way to stop wondering and actually do something about it. Because now your doctor has a way to figure out your risk of getting breast cancer. It's called the Gail Model Risk Assessment Test, and while it's important for every woman to have this test, it's even more important if you suspect you're at high risk.

Answers to six simple questions allow your doctor to evaluate your risk. Basically, you're given a number that estimates your chances of getting breast cancer over the next five years. If you're 35 or older and your number is 1.7 or higher, you're considered at high risk for breast cancer. Please remember that *this does not mean* you will get breast cancer, only that your risk is higher than average. Most women will get scores of less than 1.7.

But what can I do if I am at high risk?

***Talk to your doctor about NOLVADEX[®]
 (tamoxifen citrate) Tablets.***

For the first time, there is a *clinically proven* way for many women at high risk of developing breast cancer to significantly reduce that risk: Nolvadex Tablets.

The proof? In a landmark study of women 35 and older at high risk for breast cancer, women who took Nolvadex had 44% fewer breast cancers than women taking sugar pills. Nolvadex decreases but doesn't eliminate the risk of breast cancer and didn't show an increase in survival.

Nolvadex isn't for every woman at high risk. In the study, women taking Nolvadex were 2 to 3 times more likely to develop uterine (endometrial) cancer or blood clots in the lung and legs, although each of these occurred in less than 1% of women. Women with a history of blood clots should not take Nolvadex. Stroke, cataracts, and cataract surgery were more common with Nolvadex. In addition, women may experience some level of hot flashes and vaginal discharge. **Pregnant women or women planning on becoming pregnant soon should not take Nolvadex.** You and your doctor must carefully discuss whether the potential benefit of Nolvadex outweighs these potential side effects.

See your doctor today for your risk assessment test.

For more information: 1 800 996.3994 or www.nolvadex.com

Please see important information on adjacent page.

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NL1329 300



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ASTRAZENECA
P.O. BOX 29169
SHAWNEE, KS 66201

**ARE YOU A
HELPLESS
FEMALE?**

NOT IF THE PAST DECADE
TELLS US ANYTHING.

IN THAT TIME, IF YOU WERE A WOMAN,
YOU LED A BILLION-DOLLAR COMPANY,
COMMANDED A SPACE MISSION,
WON THE WORLD CUP IN SOCCER.

IF YOU WERE A WOMAN, YOU RAISED A KID,
GOT YOUR PHD, BUILT A BUSINESS.

IF THERE WAS SOMETHING TO BE DONE,
YOU DID IT.

So now, will you simply sit back and
ignore a way to possibly reduce your
chances of getting breast cancer?

We think not.

After all, you already do what you can to protect
yourself. Exercise, a healthy diet, the recommended
schedule of breast self-exams and mammograms.
So you'll be the first to cheer this news.

Now there's something else you
can do: Risk Assessment.

Now there's a quick and painless way for your doctor
to assess your own personal risk for developing breast
cancer. It's a set of questions regarding your own and
your family's medical history. The questions cover:

- Your age
- When you got your first period
- If and when you had a miscarriage
- Family history of breast cancer
- Whether you've had a breast biopsy
- Your race

Your doctor calculates your personal risk, which
estimates your chances of developing breast cancer
over the next 5 years. If you're 35 or older and your
score is 1.7 or higher, you are considered at high
risk for developing breast cancer.

And if you're at high risk, now
there's a new option.

NOLVADEX® (tamoxifen citrate) Tablets.

Nolvadex is a medicine that has been used for
decades to keep women who have had breast cancer
from having a recurrence. But recently, a landmark

study showed that it could also reduce the chance of a
first occurrence of breast cancer by as much as 44% in
women over 35 who were at high risk.

In this study, Nolvadex decreased but didn't eliminate
the risk of breast cancer and didn't show an increase
in survival.

**Of course, this medicine is not for
every woman at high risk.**

In the study, women taking Nolvadex were 2 to 3
times more likely to develop uterine cancer or
blood clots in the lung and legs, although each of
these occurred in less than 1% of women. Women
with a history of blood clots should not take
Nolvadex. Stroke, cataracts, and cataract surgery
were more common with Nolvadex. Most women
experience some level of hot flashes. Some women
experience discharge. Pregnant women should not take
Nolvadex. If you're pregnant or planning to become
pregnant, you should not take Nolvadex. You should
discuss whether the potential benefit of Nolvadex
outweighs the potential side effects.

So add to all the things you have
done, one more thing you will do.

Call your doctor today and ask for a risk
assessment. It may not be the easiest thing
you've ever done. But then, you've never been
one to take the easy way out, have you?

www.nolvadex.com

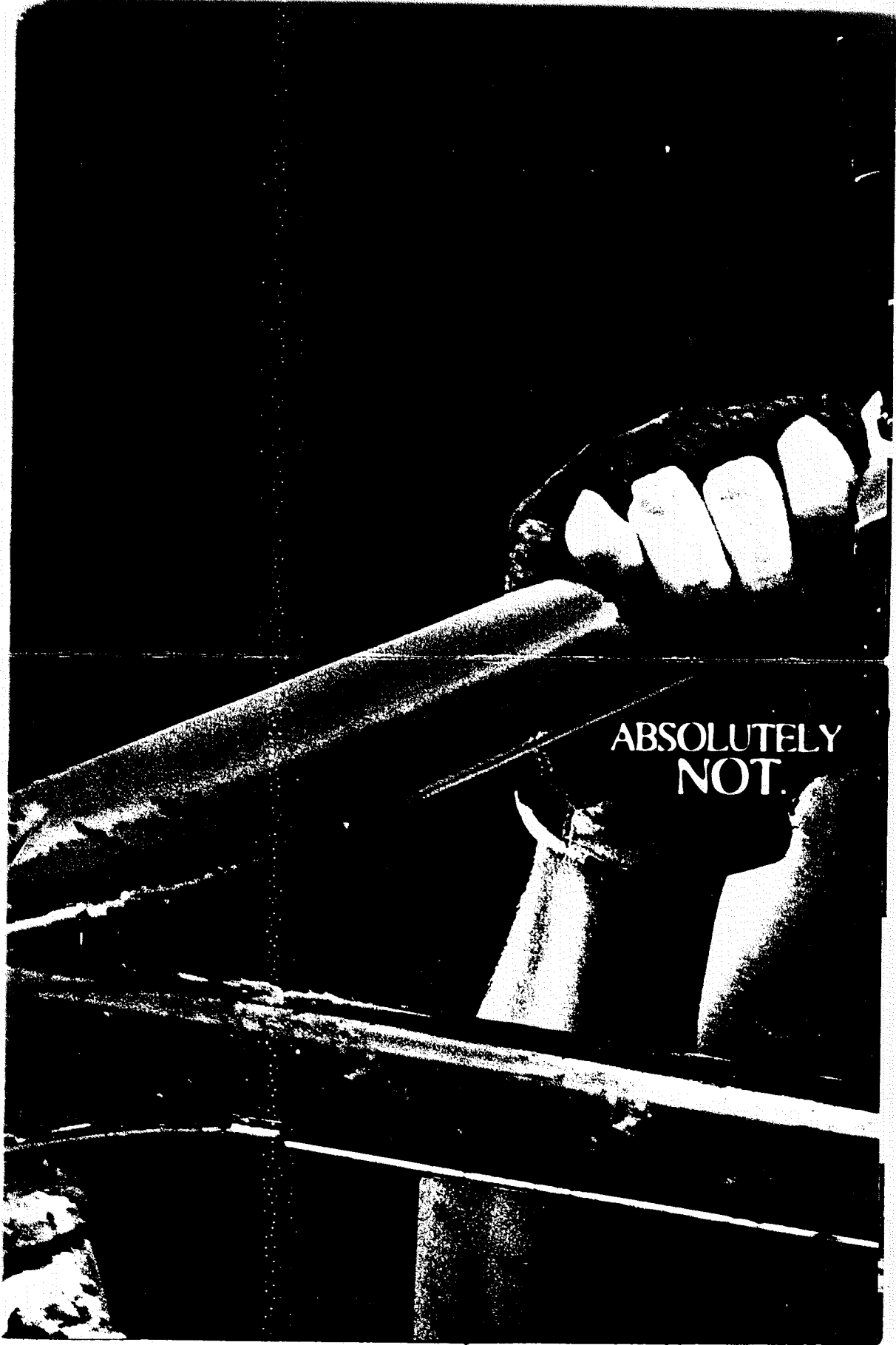
Please see additional important information enclosed.

AstraZeneca
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Roche Pharmaceuticals

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Nolvadex TABLETS®
TAMOXIFEN CITRATE
There is something you can do



ABSOLUTELY
NOT.

