



**TRANSMITTED VIA FACSIMILE**

Gregory G. Enas, Ph.D.  
Director, U.S. Regulatory Affairs  
Eli Lilly and Company  
Lilly Corporate Center  
Indianapolis, IN 46285

SEP 14 2000

RE: NDA# 20-815  
Evista (raloxifene HCl) Tablets  
MACMIS ID# 9307

Dear Dr. Enas:

This letter refers to Eli Lilly and Company's (Lilly) August 21, 2000, submission to the Division of Drug Marketing, Advertising, and Communications (DDMAC) under cover of Form FDA 2253 of a direct-to-consumer broadcast advertisement (item number RA 18086 10154789) for Evista tablets. DDMAC has reviewed this disseminated advertisement and has determined that it is in violation of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Specifically, we object for the following reasons:

**Overstatement of Benefit**

The advertisement is misleading because it mischaracterizes the nature of osteoporosis, resulting in an overstatement of Evista's benefits.

For example, claims such as "A disease of thin, weak bones that can fracture and take away your independence" and "Don't let osteoporosis stop you" misleadingly imply that having osteoporosis is, in itself, debilitating. However, while osteoporosis increases the risk of fracture, not every osteoporotic patient will suffer a fracture. In addition, those who do will not necessarily suffer any loss of independence because many osteoporotic fractures are asymptomatic. Furthermore, while Evista may reduce the risk of fracture, it does not eliminate it altogether. Therefore, these claims misleadingly imply outcomes and guarantees of efficacy for Evista that have not been demonstrated by substantial evidence.

Similarly, the claim "Up to 1/2 of women over 50 will break a bone due to osteoporosis" is misleading because it lacks context that distinguishes between symptomatic fractures of the hip or wrist and asymptomatic vertebral fractures. Vertebral fractures are the most common type of osteoporotic fractures in postmenopausal women. Yet, most vertebral fractures are not symptomatic and do not interfere with a patient's independence. The approved product labeling (PI) for Evista only cites evidence of Evista's effect on vertebral fractures. It does not include any evidence that Evista decreases the incidence of hip or wrist fractures. Therefore, this presentation misleadingly suggests that Evista provides greater efficacy than demonstrated by substantial evidence.

### **Broadening of the Patient Population**

The advertisement is misleading because it implies that Evista is useful for a broader population than that for which it is indicated. For example, the claim "If you're past menopause you should know about Evista" creates a misleading impression that all postmenopausal women will develop osteoporosis. However, menopause alone does not cause osteoporosis and only those with risk factors are candidates for Evista therapy. Thus, the claim misleadingly overstates the population appropriate for Evista therapy by implying that all women will develop osteoporosis at menopause.

Although you provide risk factors for the development of osteoporosis as supers in frames six and seven of the storyboard, your presentation lacks sufficient prominence to be readable. Thus, the supers do not adequately correct the misleading characterization of the nature of osteoporosis and do not adequately communicate the appropriate patient population for which Evista is indicated.

### **Lack of Prominence for Complete Indication and Contextual Information**

The presentation of the indication is misleading because the necessary context does not adequately accompany the indication. The approved indication for Evista includes the statement "For either osteoporosis treatment or prevention, supplemental calcium and/or vitamin D should be added to the diet if daily intake is inadequate." The advertisement presents this information by a super in small type with poor contrast in frames eighteen and nineteen. The super does not adequately qualify the indication information presented earlier in frames nine and ten. Furthermore, it lacks sufficient prominence to be readable and its presentation is further minimized by the two accompanying supers of adequate provision information appearing in these frames.

### **Inadequate Risk Disclosure**

The PI contains a precaution that the concomitant use of Evista with systemic estrogens is not recommended. Because a significant number of postmenopausal women use estrogen replacement therapy, failure to disclose this precaution in this broadcast advertisement misleadingly implies that Evista is safer than has been demonstrated.

In addition, the presentation of adverse event information is misleading because the phrase "most women did not experience these" minimizes the incidence of the side effects associated with Evista therapy. For example, hot flashes occurred in 24.6% of the women who received Evista during the prevention trials. The presentation of this phrase without accompanying contextual information is misleading because it minimizes the importance of this adverse event that occurs in a significant percentage of patients.

### **Requested Actions**

DDMAC requests that Lilly immediately discontinue the broadcast of this violative advertisement and all other promotional materials that contain the same or similar violative claims or representations. DDMAC requests that Lilly submit a written response to this letter no later than September 28, 2000, including your plan to comply with DDMAC's request. Your written response should include a list of all materials that you have discontinued and the date that they were discontinued.

If you have any questions or comments, please contact me by facsimile at (301) 594-6771 or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

DDMAC reminds you that only written communications are considered official. In all future correspondence regarding this particular matter, please refer to MACMIS ID #9307 in addition to the NDA number.

Sincerely,

*/s/*

Margaret M. Kober, R.Ph.  
Regulatory Review Officer  
Division of Drug Marketing,  
Advertising, and Communications

CAMERA MOVES THROUGH FIGURINES (ON TOP OF WEDDING CAKE), TO LINE DANCERS ESTABLISHING SHOT OF WEDDING RECEPTION.



SFX: LAUGHTER

MUSIC:

CAMERA PANS THROUGH LINE DANCERS & MOVES TOWARD CENTER STAGE.



SFX: LAUGHTER

MUSIC:

M.C HOLDING MICROPHONE TO GUEST WHO IS ENCOURAGED TO SING.



WOMAN (VO):

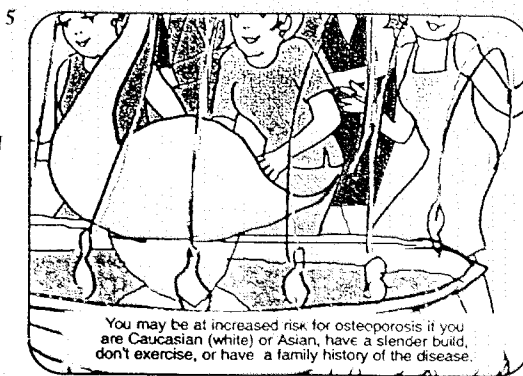
Imagine not being able to do...

LINE DANCING. WOMAN SITTING AND WATCHING WISTFULLY. WOMAN DANCING IN FRONT MOTIONS FOR HER TO JOIN THEM BUT WOMAN SEATED WAVES HER OFF MOTIONING NO.



...the things you love.

**DOLLY OUT PAST ICE SCULPTURE AND FOUNTAIN WHILE DANCING CONTINUES. ON THE WORDS "TAKE AWAY" EVERYTHING FREEZES. LOWER SCREEN DISPLAYS RISK SECTION OF FAIR BALANCE (FIRST PART) APPEARS FOR THE FIRST TIME.**



**Stopped by osteoporosis. A disease of thin, weak bones that can fracture and take away your independence.**

**FROZEN MOMENT: TWO WOMEN POSING AS SEEN BY PHOTOGRAPHER'S VIEWFINDER. ONE SIDE OF SPLIT IMAGE GOES DARK. LOWER SCREEN DISPLAYS RISK SECTION OF FAIR BALANCE (FIRST PART) STAYS ON SCREEN FROM PREVIOUS SCREEN.**



**Up to 1/2 of women over 50...**

**FROZEN MOMENT: SHE COMES TO LIFE AND WALKS TOWARD US. AS SHE TALKS, WE REALIZE THAT SHE WAS THE VOICE OVER. LOWER SCREEN DISPLAYS RISK SECTION OF FAIR BALANCE (FIRST PART) STAYS ON SCREEN FROM PREVIOUS SCREEN.**



**...will break a bone due to osteoporosis.**

**WOMAN UNFREEZES (OC): But it doesn't have to be that way.**

**FROZEN MOMENT: TWO WOMEN PASS EACH OTHER. THEY NOTICE THAT THEY'RE BOTH WEARING THE SAME DRESS. SPOKESWOMAN WALKS BETWEEN THEM AND TOWARD US.**



**If you're past menopause you should know about Evista.**

Super: Evista® (raloxifene HCl)

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**FROZEN MOMENT:**  
GUEST HOLDING TWO  
PLATES, ONE WITH FOOD  
AND ONE WITH CUP OF  
COFFEE, BACKS UP TO AVOID  
LITTLE GIRL RUNNING PAST  
HER. COFFEE CUP IS TIPPED  
AND CONTENTS ARE FROZEN  
IN MID AIR. WOMAN  
SPOKESPERSON HELPS  
OUT BY LIFTING CUP TO  
GATHER SPILT COFFEE.

Super: Evista® (raloxifene HCl)



Not only can Evista  
prevent osteoporosis...

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**FROZEN MOMENT:**  
OLDER WOMAN SWINGS  
CHILD WHILE DANCING.

Super: Evista® (raloxifene HCl)



Evista can treat it if  
you've been diagnosed.

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**FROZEN MOMENT:**  
LINE DANCE.  
CAMERA DOLLIES DOWN  
ROW OF DANCERS.



WOMAN (VO): Evista  
is not for everyone.  
You cannot take it if  
you could be pregnant  
or are nursing, have  
severe liver problems,

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**FROZEN MOMENT:**  
CAMERA DOLLIES ACROSS  
OTHER PEOPLE IN GROUP.



or have been treated for  
blood clots.

FROZEN MOMENT:  
CAMERA TURNS AS IT  
DOLLIES DOWN ROW OF  
LINE DANCERS.



An infrequent but serious side effect is blood clots in the veins--prolonged immobility may add to the risk.

FROZEN MOMENT:  
CAMERA DOLLIES BACK FROM DANCERS TO SHOW TABLE WITH PEOPLE REACTING TO CHAMPAIGN POPPING.



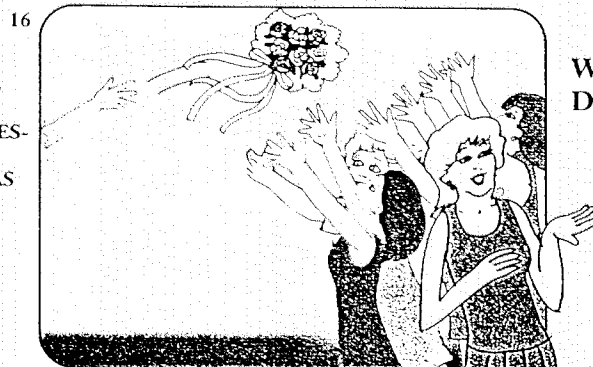
The most commonly reported side effects...

FROZEN MOMENT:  
CAMERA MOVES FROM TABLE TO GROUP OF WOMEN ADMIRING PHOTOGRAPHS.



...were hot flashes and leg cramps; most women did not experience these.

DISSOLVE TO OUTSIDE  
FROZEN MOMENT BRIDAL BOUQUET THROWN IS FROZEN IN MID AIR. SPOKESWOMAN IS FACING THE OTHER WAY GESTURING AS SHE SPEAKS.



WOMAN (OC):  
Don't let osteoporosis...

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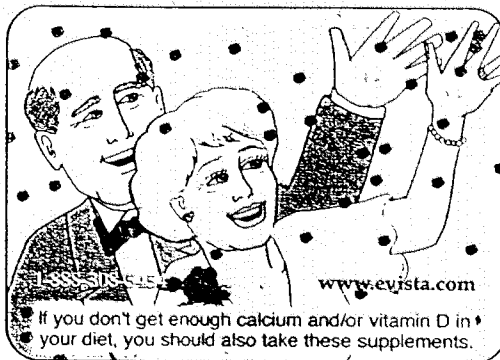
WHEN SHE SAYS "STOP"  
THE SCENE COMES TO LIFE  
AND THE BOUQUET GOES  
OVER THE HEADS OF THE  
OTHER WOMEN AND  
SUPRISINGLY FALLS INTO  
HER GESTURING HANDS.



...stop you.

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CUT TO REVEAL BOUQUET  
THROWN BY A WOMAN IN  
HER EARLY 60s. MARRIED  
COUPLE WALK AWAY  
WAVING GOODBYE AS  
EVERYONE THROWS ROSE  
PETALS.  
LOWER SCREEN DISPLAYS  
RISK SECTION OF FAIR  
BALANCE (REMAINING  
SECTION) APPEARS FOR  
THE FIRST TIME.



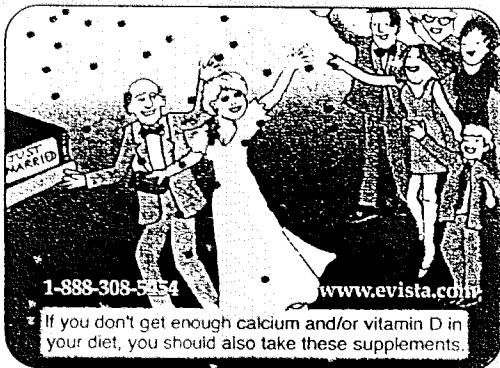
WOMAN (VO):  
The choices you  
make today,

Super: 1-888-308-5454  
www.evista.com

If you don't get enough calcium and/or vitamin D in your diet, you should also take these supplements.

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SCREEN SPLITS TO SHOW  
COUPLE RUNNING TO  
THEIR CAR AS GUESTS  
THROW ROSE PETALS.  
LOWER SCREEN DISPLAYS  
RISK SECTION OF FAIR  
BALANCE (REMAINING  
SECTION) STAYS ON SCREEN  
FROM PREVIOUS SCREEN.



can affect the life you live  
tomorrow.

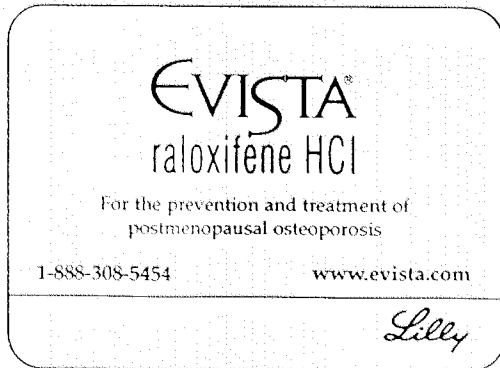
Super: 1-888-308-5454  
www.evista.com

If you don't get enough calcium and/or vitamin D in your diet, you should also take these supplements.

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END TITLE WITH EVISTA  
LOGO AND LILLY LOGO.

Super: 1-888-308-5454  
www.evista.com



MUSIC UP

Talk to your doctor about  
Evista.