DDMAC

Division of Drug Marketing, Advertising, and Communications

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Regulatory Review Officer

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Presentation Overview

- Mission
- Organizational structure
- Regulatory authority
- Operational role
- Advertising and promotion
- Examples of enforcement actions

DDMAC's Mission

Protect the public health by assuring prescription drug information is truthful, balanced, and accurately communicated

To guard against false and misleading advertising and promotion through comprehensive surveillance, enforcement, and educational programs

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Regulatory Counsel, (Vacancy)
Regulatory Counsel, (Vacancy)
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TIA, (Vacancy)

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Cardiovascular & Renal
(Lisa Hubbard)

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Keith Olin,
Karen Rulli)

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(Andrew Haffer)

Professional Review Group III
Acting Leader
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Analgesics, Anesthetics, & Rheumatology
(Mathilda Fienkeng)

Metabolism & Endocrinology
(Samuel Skariah)

Gastroenterology, Special Pathogens & Transplant
(Kathleen Klemm)

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Anti-Infectives & Ophthalmology
(Beth Carr)

Antivirals
(Lynn Panholzer)

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(Carole Broadnax,
Jeffrey Trunzo)

Direct-To-Consumer Review Group I
Leader
Robert Dean

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(Beverly Bowers,
Stephanie Victor)

Metabolic/Endocrine, Analgesics/Anesthetics Rheumatology
(Kendra Jones,
Michael Sauers)

Derm/Dental and GI, Pulmonary/Allergy
(Shefali Doshi,
Robyn Tyler)

Research Team
(Kathryn Aikin,
Amie O'Donoghue,
Helen Sullivan)

Direct-To-Consumer Review Group II
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Cardio-renal
(Zarna Patel)

Psychiatry
(Susannah Hubert)

Neurology, Anti-Infectives, Ophthalmology, Special Pathogens, Transplant
(Sharon Watson, Twyla Thompson)

Antivirals
(Aline Moukhtara)

Reproductive, Urology, Medical Imaging, Hematology,
(Cynthia Collins,
Carrie Newcomer)

Regulatory Authority

- Federal Food, Drug and Cosmetic Act
  - Prescription drug promotion **must**...
    - Not be false or misleading
    - Have fair balance
    - Be consistent with the approved product labeling, or the package insert (PI)
    - Only include claims substantiated by adequate and well-controlled clinical studies

Regulatory Authority

- Code of Federal Regulations (CFR)
  - 202.1 - Prescription Drug Advertising
  - 312.7 - Preapproval Promotion
  - 314.550 - Subpart H, Accelerated Approval for Drugs
  - 601.40 - Subpart E, Accelerated Approval for Biologics

Regulatory Authority

- Post-Approval Regulations located in 21 CFR 314.81(b)(3):
  - Require the submission of all promotional materials at the time of initial dissemination or publication
  - Must include Form FDA 2253 and current PI
  - DDMAC receives >70K submissions per year
  - DDMAC does not generally "pre-clear" promotional materials

DDMAC's Role

- Advice to industry/within FDA
- Surveillance and enforcement
- Guidances and policy development
- Research

Advice to Industry

- Provide comments on DRAFT promotional materials (VOLUNTARY in most cases)
  - Launch materials for new drugs or new indications
  - Direct-to-consumer (DTC) broadcast ads
  - Non-launch materials

- Pre-submission required for certain drugs (e.g., Subpart H/Subpart E “accelerated approval”)

Advice within FDA

- Provide consultation on:
  - Draft labeling
  - Cartons and product labels
  - Medication Guides
  - Patient Package Inserts (PPIs)
  - Dear Healthcare Provider letters
  - Pharmacoeconomics, health-related patient-reported outcome protocols

Surveillance

- Review materials submitted to DDMAC at the time of initial dissemination (Form 2253)
- Conferences
- Complaints
  - Healthcare professionals
  - Consumers
  - Competitors

Enforcement

- Untitled letters (Notice of Violation/NOV)
- Warning letters
- Injunction/consent decree
- Seizures
- Criminal action

Categories of Promotional Materials

- Labeling
  - Audio, video, or printed matter (e.g., brochures, booklets, mailing pieces, exhibits, slides)
  - Supplied or disseminated by the manufacturer, distributor, packer, or any party acting on behalf of the sponsor
  - Accompanied by the approved product labeling
- Advertising
  - Advertisements in published journals, magazines, newspapers, and other periodicals
  - Broadcast (e.g., TV, radio, telephone communication systems)
  - Accompanied by a “Brief Summary” of the approved product label

Categories of Promotional Materials

Help-Seeking
Institutional
Reminder

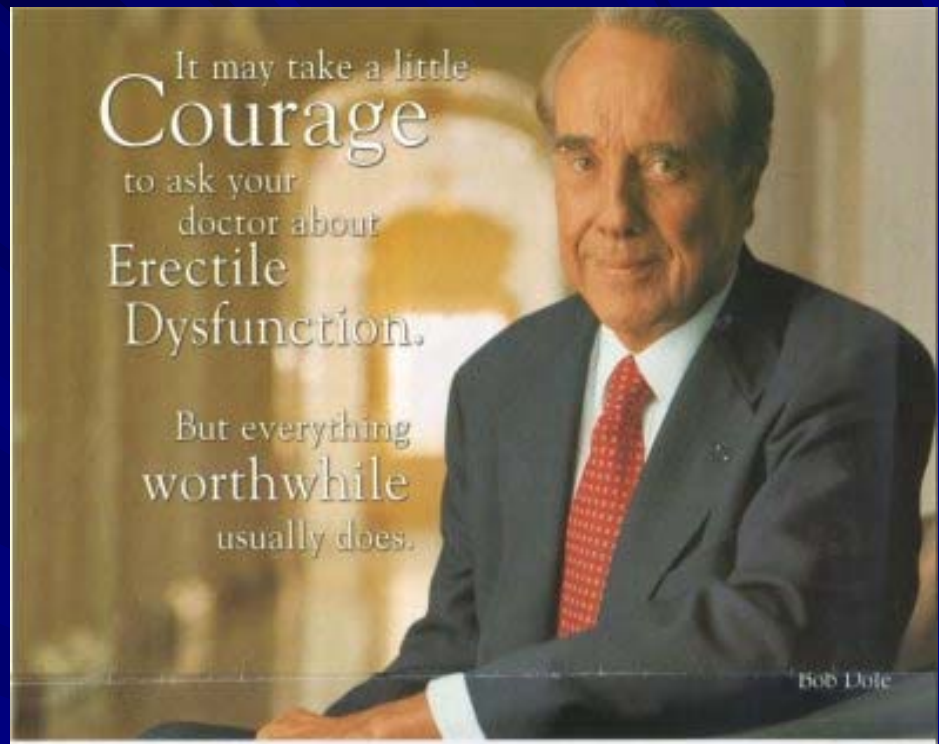
Full Product

⇦ *Cannot make any representations about a specific product - requires no balance*

Help Seeking Ad

- May discuss a medical condition or disease state
- May include a company name
- May not include drug name

Help-Seeking Ad



When I was diagnosed with prostate cancer, my first concern was ridding myself of the cancer. But I was also concerned about possible postoperative side effects, like erectile dysfunction (E.D.), often called impotence. So I asked my doctor about treatment options.

I'm speaking out now in the hope that men with E.D. will get proper treatment for a condition that affects millions of men and their partners.

Most E.D. cases are associated with physical conditions or events, like the prostate cancer surgery I underwent. The most common causes of E.D. include diabetes, high blood pressure, spinal cord injury, or surgery for the prostate or colon. E.D. can also be associated with smoking, alcohol abuse, or psychological conditions such as anxiety or stress.

The good news is that many effective treatments are available for E.D. But the important first step is to talk to your doctor. Together, you and your doctor can decide which treatment is best for you.

Now it's up to you to get the treatment you need for E.D. My advice is to get a medical checkup. It's the best way to get educated about E.D. and what can be done to treat it. It may take a little courage, but I've found that everything worthwhile usually does.

For more information about erectile dysfunction, please call 1-800-433-4215.

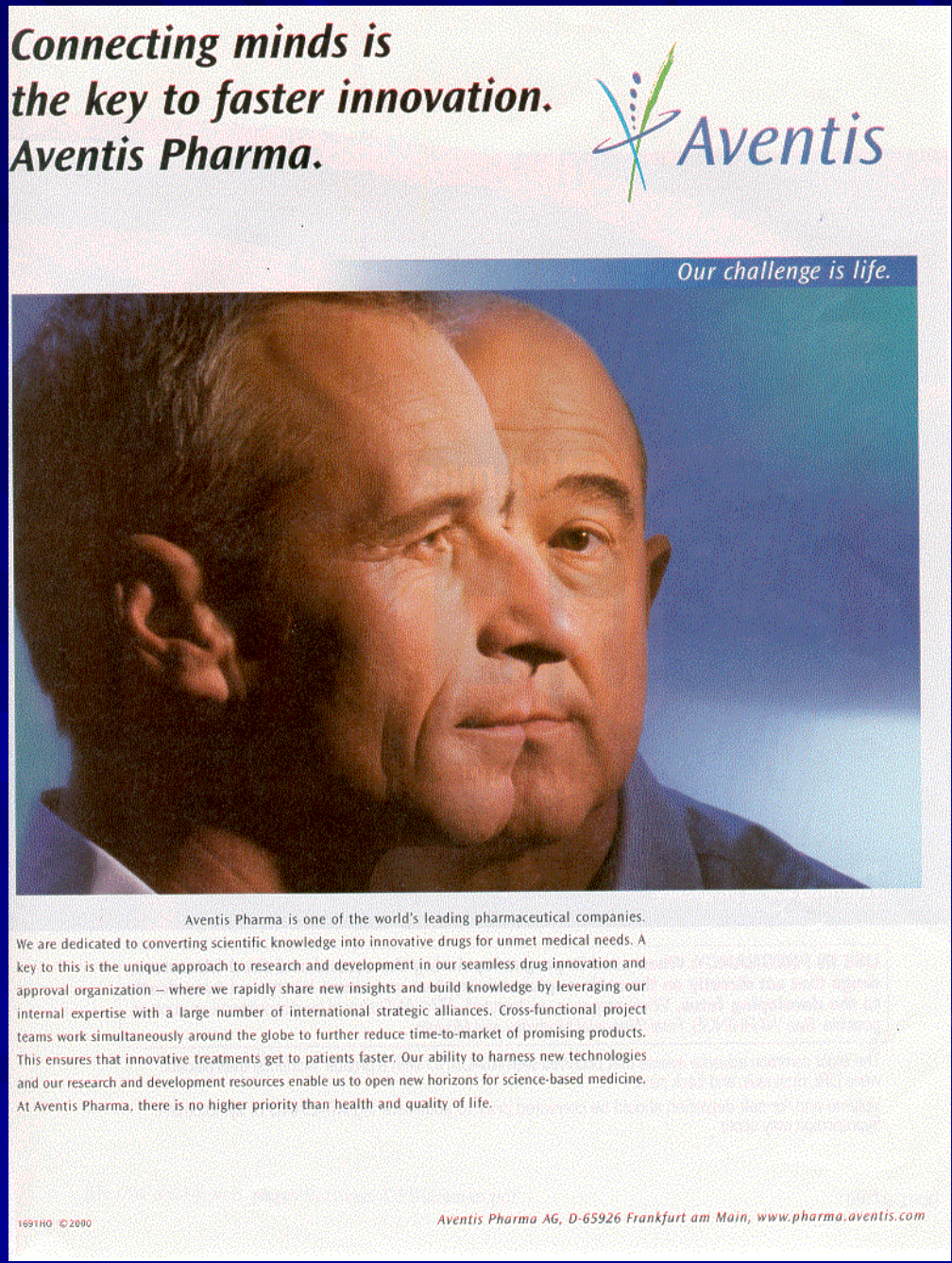
GET EDUCATED ABOUT E.D.

Pfizer

Institutional

- Company name
- Area of research
- May not mention any drug names

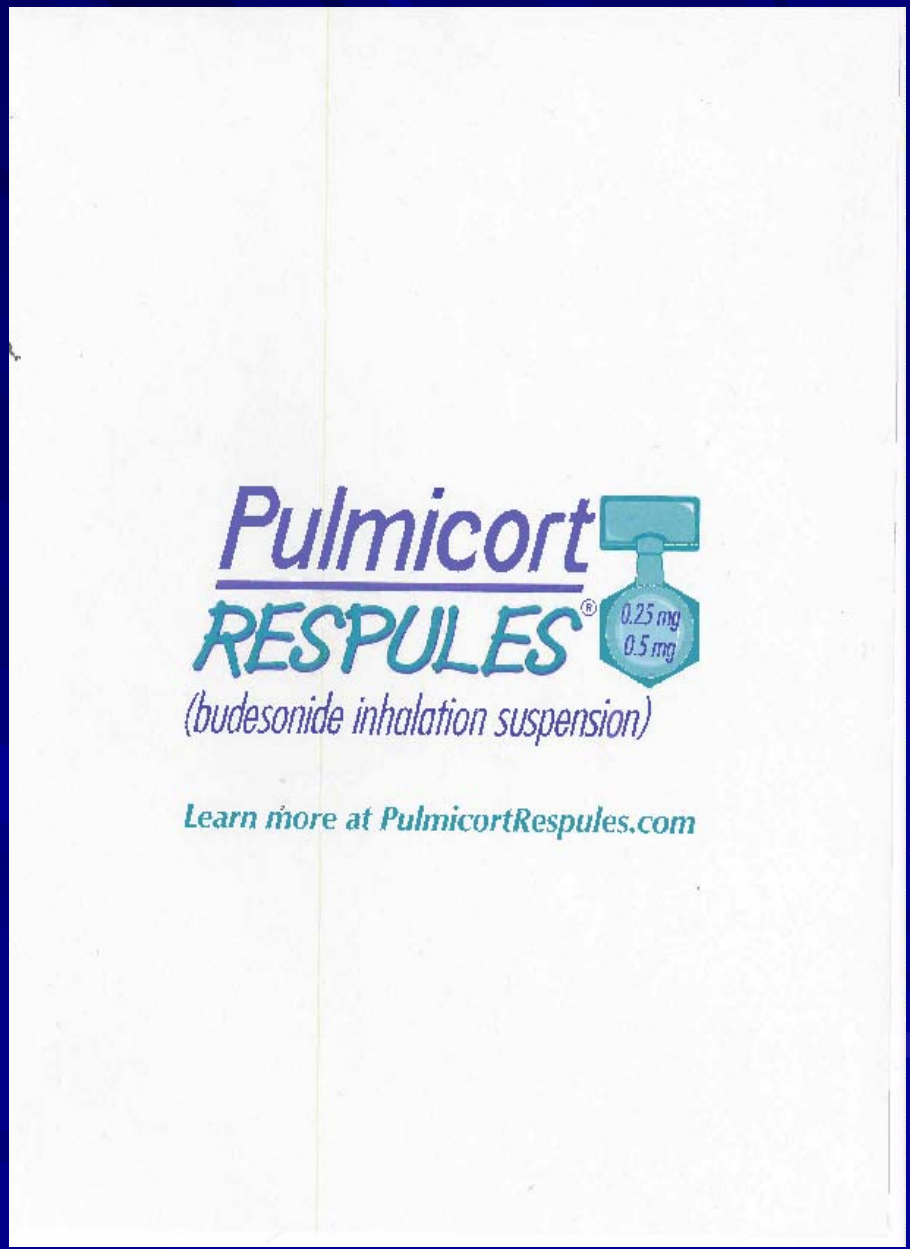
Institutional Ad



Reminder

- Must include proprietary and established name
- May call attention to drug name but may NOT contain any representation or suggestion relating to the advertised drug product
- May include dosage form, package contents, price, name of manufacturer, packer, distributor.
- Not permitted for drug with a Boxed Warning

Reminder Ad


Pulmicort
RESPULES®
0.25 mg
0.5 mg
(budesonide inhalation suspension)
Learn more at PulmicortRespules.com

Full Product Claim Ads

- Include representation or suggestion relating to the advertised drug product
- Must include a balanced risk presentation (“fair balance”)
- Must include the Brief Summary or PI

Full Product Claim DTC Ad

Product Claim
DTC Ad
Brief Summary

ACTONEL® (AK-toh-nel)
Tablets Patient Information

ACTONEL (risedronate sodium tablets) 5 mg and
ACTONEL (risedronate sodium tablets) 35 mg for Osteoporosis

Read this information carefully before you start to use your medicine. Read the information you get every time you get more medicine. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment. If you have any questions or are not sure about something, ask your healthcare provider or pharmacist.

What is the most important information I should know about ACTONEL?

ACTONEL may cause problems in your stomach and esophagus (the tube that connects the mouth and the stomach), such as trouble swallowing (dysphagia), heartburn (esophagitis), and ulcers (see "What are the possible side effects of ACTONEL?").

You must follow the instructions exactly for ACTONEL to work and to lower the chance of serious side effects (see "How should I take ACTONEL?").

What is ACTONEL?

ACTONEL is a prescription medicine used:

- to prevent and treat osteoporosis in postmenopausal women (see "What is osteoporosis?").
- to prevent and treat osteoporosis in men and women that is caused by treatment with steroid medicines such as prednisone.
- to treat Paget's disease of bone (osteitis deformans). The treatment for Paget's disease is very different than for osteoporosis and uses a different type of ACTONEL. This leaflet does not cover using ACTONEL for Paget's disease. If you have Paget's disease, ask your healthcare provider how to use ACTONEL.

ACTONEL may reverse bone loss by stopping more loss of bone and increasing bone mass in most people who take it, even though they won't be able to see or feel a difference. ACTONEL helps lower the risk of breaking bones (fractures). Your healthcare provider may measure the thickness (density) of your bones or do other tests to check your progress.

See the end of this leaflet for information about osteoporosis.

Who should not take ACTONEL?

Do not take ACTONEL if you:

- have low blood calcium (hypocalcemia).
- cannot sit or stand up for 30 minutes.
- have kidneys that work poorly.
- have an allergy to ACTONEL. The active ingredient in ACTONEL is risedronate sodium (see the end of this leaflet for a list of all the ingredients in ACTONEL).

Tell your doctor before using ACTONEL if:

- you are pregnant. We do not know if ACTONEL can harm your unborn child.
- you are breast-feeding. We do not know if ACTONEL can pass through your milk and if it can harm your baby. You will need to decide whether to stop breast-feeding or not take ACTONEL.
- you have kidney problems. ACTONEL may not be right for you.

How should I take ACTONEL?

The following instructions are for both ACTONEL 5 mg (daily) and ACTONEL 35 mg (Once-a-Week):

- Take ACTONEL first thing in the morning before you eat or drink anything except plain water.
- Take ACTONEL while you are sitting or standing up.
- Take ACTONEL with 6 to 8 ounces (about 1 cup) of plain water. Do **not** take it with any other drink besides plain water. Do not take it with coffee, tea, juice, or milk or other dairy drinks.
- Swallow ACTONEL whole. Do not chew the tablet or keep it in your mouth to melt or dissolve.
- After taking ACTONEL you must wait at least 30 minutes **BEFORE**:
  - lying down. You may sit, stand, or do normal activities like read the newspaper or take a walk.
  - eating or drinking anything except plain water.
  - you take vitamins, calcium, or antacids. Take vitamins, calcium, and antacids at a different time of the day from when you take ACTONEL.
- Keep taking ACTONEL for as long as your healthcare provider tells you.
- For ACTONEL to treat your osteoporosis or keep you from getting osteoporosis, you have to take it as often and in the way it is prescribed.
- Your healthcare provider may tell you to take calcium and vitamin D supplements and to exercise.

What is my ACTONEL schedule?

If your doctor has prescribed **ACTONEL 5 mg daily (a yellow tablet):**

- Take 1 ACTONEL 5-mg tablet every day in the morning.
- If you forget to take your ACTONEL 5 mg in the morning, do **not** take it later in the day. Take only 1 ACTONEL 5-mg tablet the next morning and continue your usual schedule of 1 tablet a day. Do **not** take 2 tablets on the same day.

If your doctor has prescribed **ACTONEL 35 mg Once-a-Week (an orange tablet):**

- Choose 1 day of the week that you will remember and that best fits your schedule to take your ACTONEL 35 mg. Every week, take 1 ACTONEL 35-mg tablet in the morning on your chosen day.
- If you forget to take your ACTONEL 35 mg in the morning, do **not** take it later in the day. Take only 1 ACTONEL 35-mg tablet the next morning and continue your usual schedule of 1 tablet on your chosen day of the week. Do **not** take 2 tablets on the same day.

What should I avoid while taking ACTONEL?

- Do not eat or drink anything except water before you take ACTONEL and for at least 30 minutes after you take it.
- Do not lie down for at least 30 minutes after you take ACTONEL.
- Foods and some vitamin supplements and medicines can stop your body from absorbing (using) ACTONEL. Therefore, do not take the following products at or near the time you take ACTONEL: food, milk, calcium supplements, or calcium-, aluminum-, or magnesium-containing medicines, such as antacids (see "How should I take ACTONEL?").

What are the possible side effects of ACTONEL?

Stop taking ACTONEL and tell your healthcare provider right away if:

- **swallowing is difficult or painful.**
- **you have chest pain.**
- **you have very bad heartburn and it doesn't get better.**

ACTONEL may cause:

- pain or trouble swallowing (dysphagia).
- heartburn (esophagitis).
- ulcers in your stomach and esophagus (the tube that connects the mouth and the stomach).

For patients with osteoporosis, the overall occurrence of side effects with ACTONEL was similar to placebo (sugar pill) and most were either mild or moderate. The most common side effects with ACTONEL include back pain, joint pain, upset stomach, abdominal (stomach area) pain, constipation, diarrhea, gas, and headache. Tell your healthcare provider if you have pain or discomfort in your stomach or esophagus.

These are not all the possible side effects of ACTONEL. You can ask your healthcare provider or pharmacist about other side effects.

What is osteoporosis?

Osteoporosis is a disease that causes bones to become thinner. Thin bones can break easily. Most people think of their bones as being solid like a rock. Actually, bone is living tissue, just like other parts of the body—your heart, brain, or skin, for example. Bone just happens to be a harder type of tissue. Bone is always changing. Your body keeps your bones strong and healthy by replacing old bone with new bone.

Osteoporosis causes the body to remove more bone than it replaces. This means that bones get weaker. Weak bones are more likely to break. Osteoporosis is a bone disease that is quite common, especially in older women. However, young people and men can develop osteoporosis, too. Osteoporosis can be prevented, and with proper therapy it can be treated.

How can osteoporosis affect me?

- You may not have any pain or other symptoms when osteoporosis begins.
- You are more likely to break (fracture) a bone especially if you fall because osteoporosis makes your bones weaker. You are most likely to break a bone in your back (spine), wrist, or hip.
- You may "shrink" (get shorter).
- You may get a "hump" (curve) in your back.
- You may have bad back pain that makes you stop some activities.

Who is at risk for osteoporosis?

Many things put people at risk for osteoporosis. The following people have a higher chance of getting osteoporosis:

Women who:

- are going through or who are past menopause ("the change").
- are white (Caucasian) or Asian.

People who:

- are thin.
- have family members with osteoporosis.
- do not get enough calcium or vitamin D.
- do not exercise.
- smoke.
- drink alcohol often.
- take bone-thinning medicines (like prednisone or other corticosteroids) for a long time.

General information about ACTONEL

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use ACTONEL for a condition for which it was not prescribed. Do not give ACTONEL to other people, even if they have the same symptoms you have. It may harm them.

What if I have other questions about ACTONEL?

This leaflet summarizes the most important information about ACTONEL for osteoporosis. If you have more questions about ACTONEL, ask your healthcare provider or pharmacist. They can give you information written for healthcare professionals. For more information, call 1-877-**ACTONEL** (toll-free) or visit our Web site at www.actonel.com.

What are the ingredients of ACTONEL?

ACTONEL (active ingredient): risedronate sodium.

ACTONEL (inactive ingredients): crospovidone, ferric oxide red (35-mg tablets only), ferric oxide yellow, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, silicon dioxide, and titanium dioxide.

ACTONEL® is marketed by:
Procter & Gamble Pharmaceuticals
Cincinnati, OH 45202
and
Aventis Pharmaceuticals Inc.
Kansas City, MO 64137

MAY 2002

Actonel
(risedronate sodium tablets)

 Printed in USA ACT-JA-15924-1 0905-6507

Broadcast Advertising

- "Major Statement"
  - Information relating to the major side effects and contraindications

- "Adequate Provision"
  - Provides for dissemination of the PI

    Recognizes the inability of broadcast advertisements of reasonable length to present and communicate this information effectively

Adequate Provision

- Currently acceptable adequate provision:
  - Toll-free number
  - Simultaneously running magazine ad
  - Reference to a healthcare provider
  - Website

Flonase Detective Video Clip

Examples of Enforcement Actions

http://www.fda.gov/cder/warn/index.htm

“Reminder Ad” for Buproprion ER

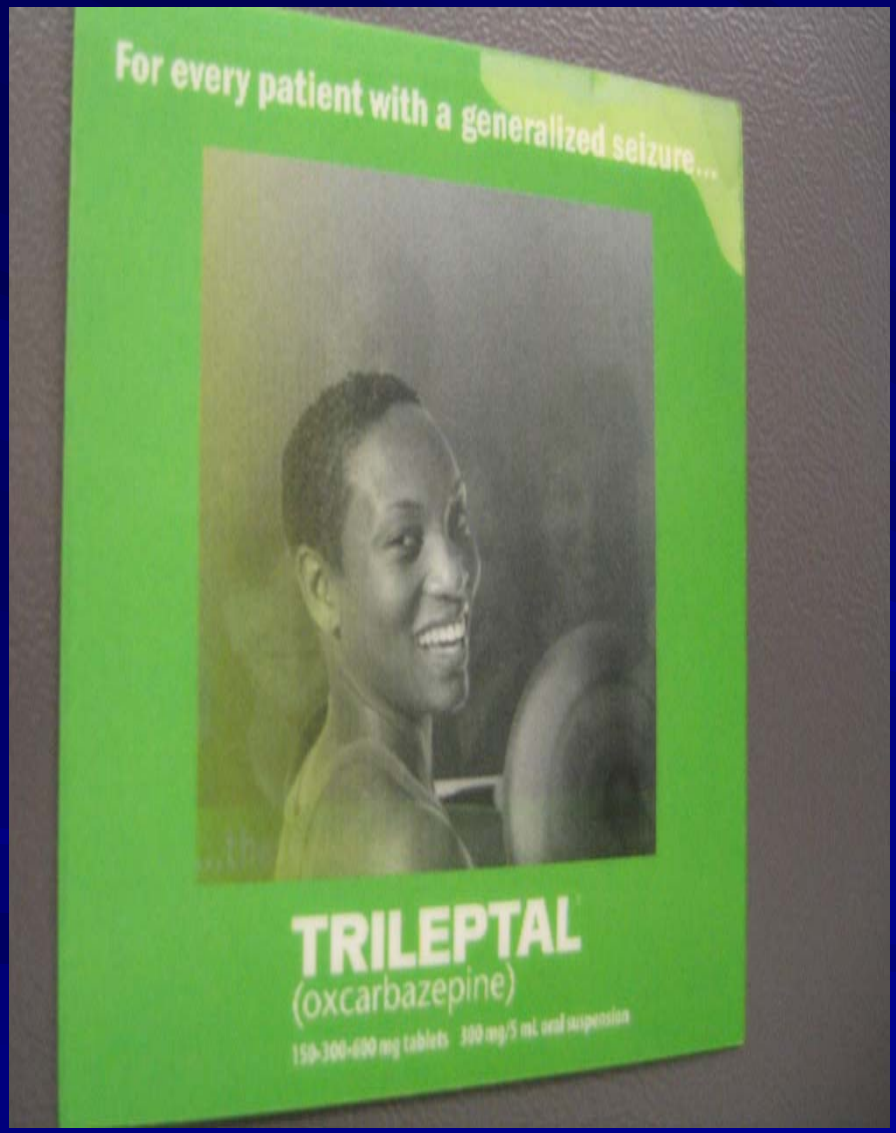
- NOV issued for this “impermissible reminder ad”
- "Reminder advertisements. . . are not permitted for a prescription drug product whose labeling contains a boxed warning relating to a serious hazard associated with the use of the drug product."
- Labeling contains a boxed warning
- Ad fails to present brief summary

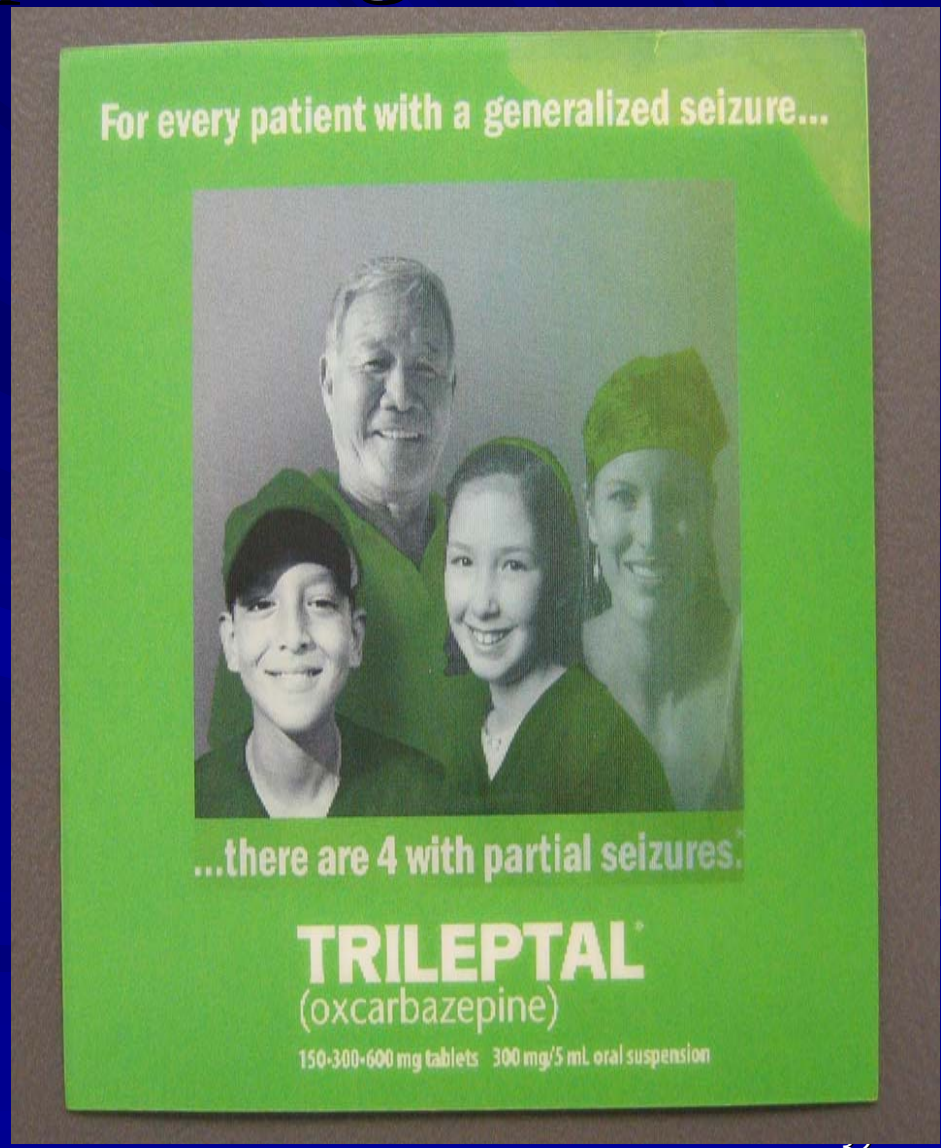
Viagra Shopping Video Clip

Viagra “Reminder” TV Ad

- Makes representations about Viagra
- Approved indication not presented
- No risk information, no adequate provision
- Overstates efficacy of product

Trileptal Magnet





Trileptal – Lenticular Magnet

- Omission of indication and risk information
  - Effectiveness claims presented, but indication and risk are not
    - (Included on back of magnet--as a practical matter, this information is not communicated)
    - Magnet is designed to adhere to magnet surfaces—once displayed, content on back is not visible
- Encourages use in circumstances other than those for which shown to be safe and effective
  - Implies drug is indicated for generalized seizures
    - Full indication is not presented on front of magnet
    - Especially problematic in the view where only generalized seizures claim is visible

Enbrel Video Clip

Enbrel Corrective Video Clip

YAZ “Balloons” TV Ad

YAZ “Not Gonna Take It” TV Ad

YAZ Corrective

Enforcement Trends

- Previous yearly average for the number of Warning Letters was generally 4-5
- 2008: 10 Warning Letters
- 2007: 9 Warning Letters
- Possible reasons
  - Prioritization of resources to have greatest impact on public health
  - “Pushing the envelope”
    - Aggressive promotion can be compliant with the regulations

Common Violations Occurring in 2005 - 2008

- Omission and minimization of risk information
- Promotion of unapproved uses of drugs
- Unsubstantiated claims of efficacy or safety
- Unsubstantiated comparative claims

DDMAC Contact Information

- **Web address:**
  - **http://www.fda.gov/cder/ddmac**
- **Phone number:**
  - **(301) 796-1200**
- **Fax number:**
  - **(301) 847-8444**

Questions?