FDA Drug Topics: FDA's Bad Ad Program

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Objectives

- Discuss FDA's role in regulating prescription drug promotion and advertising
- Describe the role that healthcare professionals (HCPs) can play in protecting the public health by recognizing prescription drug promotion and advertising that is potentially false or misleading
- Explain how HCPs can effectively report potentially false or misleading prescription drug promotion to the FDA through the Bad Ad Program

FDA's Mission

- The FDA is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

- FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

FDA's Mission

- The FDA is also responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health.

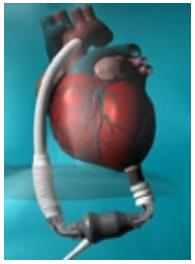
FDA Organization

Office of the Commissioner

Center for **F**ood **S**afety & **A**pplied **N**utrition

Center for **D**rug **E**valuation & **R**esearch

Center for **B**iologics **E**valuation & **R**esearch



Center for **D**evices & **R**adiological **H**ealth

Center for **V**eterinary **M**edicine

National **C**enter for **T**oxicological **R**esearch

Center for **T**obacco **P**roducts

Office of **R**egulatory **A**ffairs

Mission of the Office of Prescription Drug Promotion (OPDP)

- To protect the public health by helping to ensure that prescription drug information is truthful, balanced, and accurately communicated.

- This is accomplished through comprehensive surveillance, compliance, and education programs, and by fostering better communication of labeling and promotional information to both healthcare professionals and consumers.

Myths and Misconceptions

- FDA “legalized” DTC advertising in the late 1990’s
- Industry spends most of its advertising budget on DTC advertising
- FDA has the authority to ban DTC advertising
- FDA approves ads
- FDA regulates “good taste”

What does OPDP regulate?

- Prescription drug promotional materials made by or on behalf of the drug's manufacturer, packer, or distributor, including:
  - TV and radio commercials
  - Sales aids, journal ads, and patient brochures
  - Drug websites, e-details, webinars, and email alerts

Regulatory Authority: FD&C Act

- Prescription drug promotion **must**...
  - Not be false or misleading
  - Have balance between efficacy and risk information
  - Reveal material facts about the product being promoted, including facts about consequences that may result from the use of the drug

Regulatory Authority

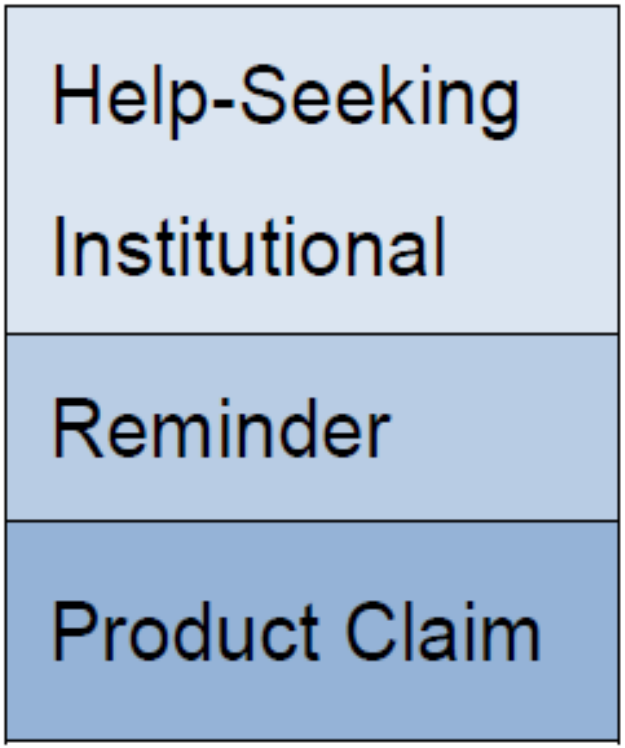
- Post-Approval Regulations located in 21 CFR 314.81(b)(3):
  - Require the submission of all promotional materials at the time of initial dissemination or publication
  - Must include Form FDA-2253 and current prescribing information (PI)

- OPDP does NOT “approve” promotional materials

Categories of Promotional Materials

- **Labeling**
  - Brochures, booklets, mailing pieces, exhibits, slide decks
  - Supplied or disseminated by the manufacturer, distributor, packer, or on their behalf
  - Accompanied by the approved product labeling
- **Advertising**
  - Advertisements in published journals, magazines, newspapers, and other periodicals
  - Broadcast (e.g., TV, radio, telephone communication systems)
  - Contains a “Brief Summary” of the drug’s side effects, contraindications, and effectiveness

Categories of Promotional Materials



Do not make any representations about a specific product

Help-Seeking or Disease Awareness

Institutional

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 Black Box Warning

Reminder

Product Claim Materials

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

Product Claim

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
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MAY 2002

Actonel
(risedronate sodium tablets)

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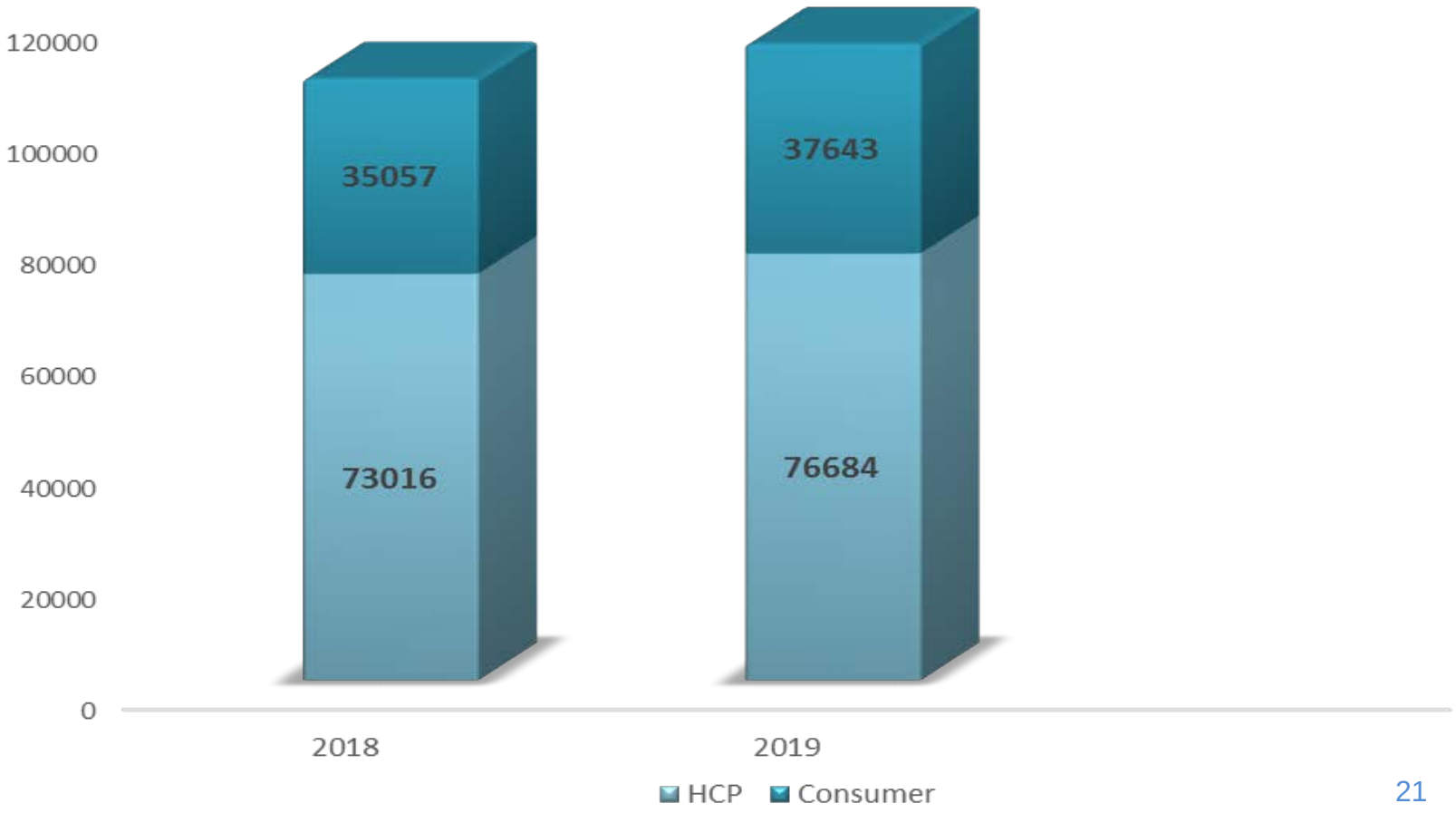
Broadcast Advertising

- "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

Total # of Promotional Pieces



What does OPDP do?

- Advice to industry
- Advice within FDA
- Guidance and policy development
- Research
- Surveillance and compliance

Common Violations

- Make claims that are not appropriately supported
- Misrepresent data from studies
- Overstate the drug's benefits
- Omit or downplay risk information

Common Violations

- Omit material facts about the drug
- Fail to present a “fair balance” of risk and benefit information
- Misbrand an investigational drug

FDA

Warning Letter Example:

Zolpimist (zolpidem tartrate) oral spray (C-IV)

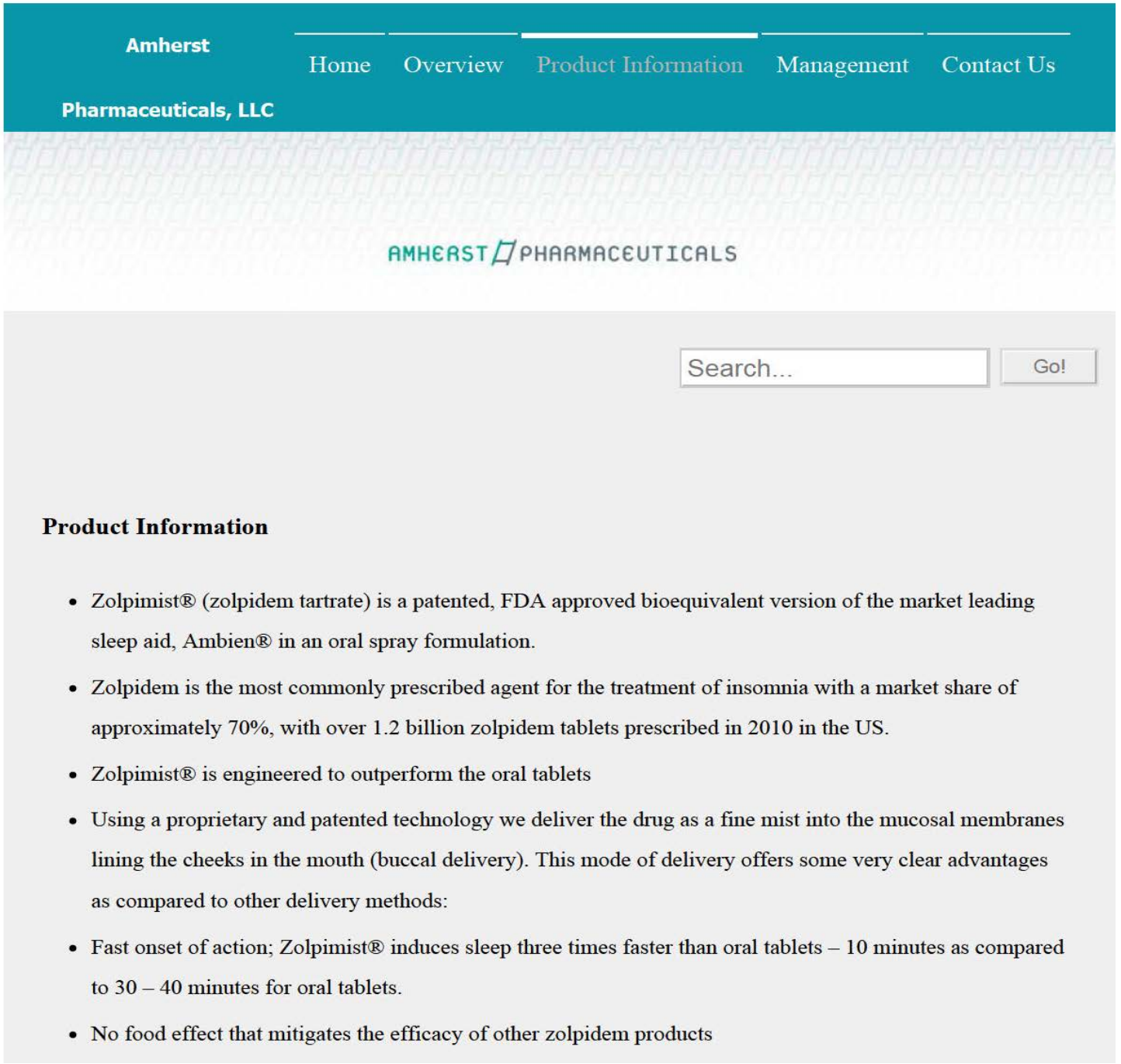
Example: Zolpimist

Indication: Indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. Zolpidem tartrate has been shown to decrease sleep latency for up to 35 days in controlled clinical studies…. The clinical trials performed in support of efficacy were 4-5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

Example: Zolpimist

- Warning and Precautions: CNS depressant effects and next day impairment, need to evaluate for co-morbid diagnoses, severe anaphylactic and anaphylactoid reactions, abnormal thinking and behavioral changes, use in patients with depression, respiratory depression, and withdrawal effects

- The most common adverse reactions reported with Zolpimist were drowsiness, dizziness, diarrhea, and “drugged feelings”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Product Information
• Zolpimist® (zolpidem tartrate) is a patented, FDA approved bioequivalent version of the market leading sleep aid, Ambien® in an oral spray formulation.
• Zolpidem is the most commonly prescribed agent for the treatment of insomnia with a market share of approximately 70%, with over 1.2 billion zolpidem tablets prescribed in 2010 in the US.
• Zolpimist® is engineered to outperform the oral tablets
• Using a proprietary and patented technology we deliver the drug as a fine mist into the mucosal membranes lining the cheeks in the mouth (buccal delivery). This mode of delivery offers some very clear advantages as compared to other delivery methods:
• Fast onset of action; Zolpimist® induces sleep three times faster than oral tablets – 10 minutes as compared to 30 – 40 minutes for oral tablets.
• No food effect that mitigates the efficacy of other zolpidem products

FDA

Warning Letter Example:

Diclegis (doxylamine succinate and pyridoxine hydrochloride)

Example: Diclegis

- Indication: Treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.

- Limitations of Use: Has not been studied in women with hyperemesis gravidarum.

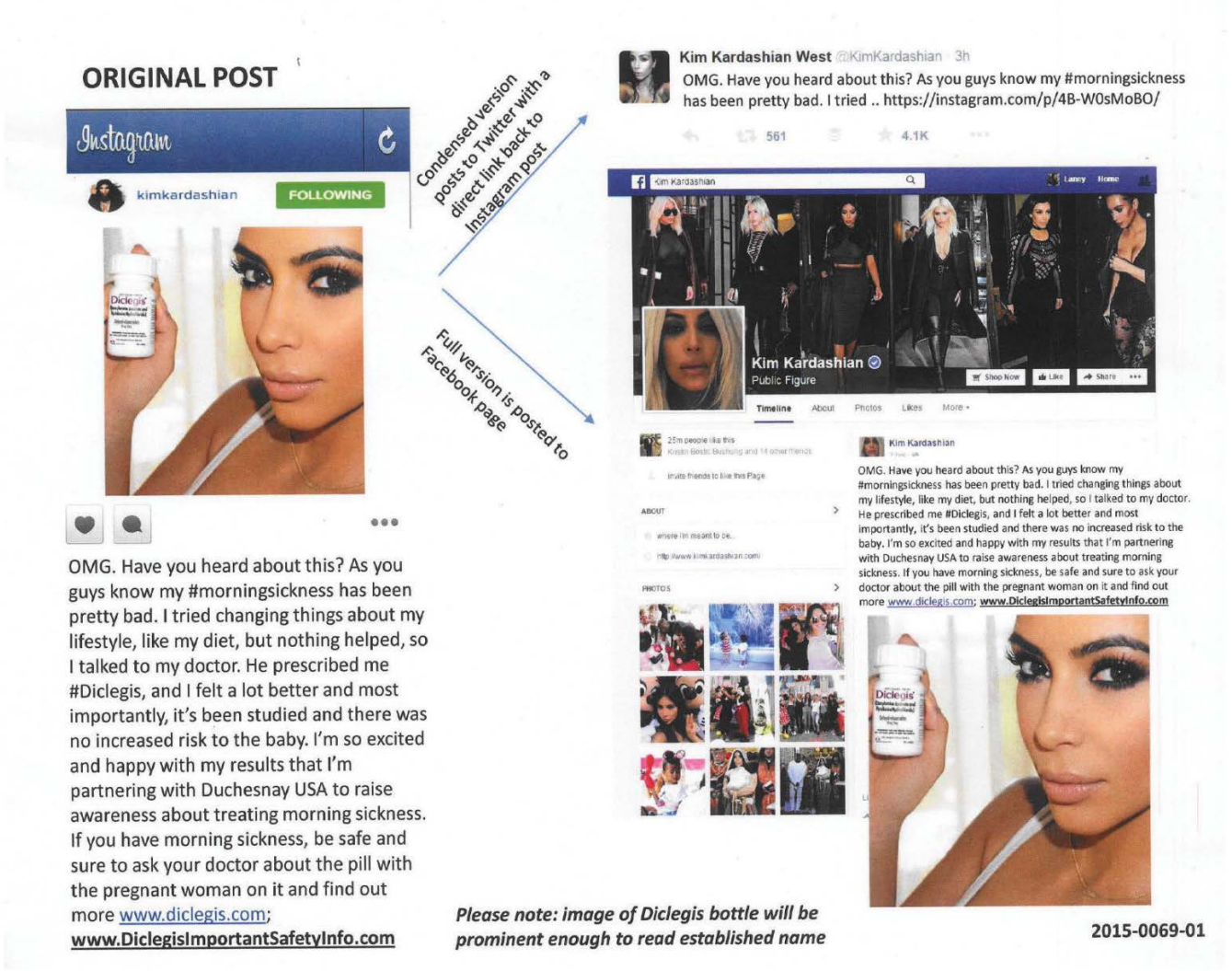
- Contraindications: Diclegis is contraindicated in women with known hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines, pyridoxine hydrochloride or any inactive ingredient in the formulation, as well as in women who are taking monoamine oxidase inhibitors (MAOIs).

Example:Diclegis

- Warning and Precautions regarding activities requiring mental alertness and concomitant medical conditions.

- The most common adverse reaction reported with Diclegis was somnolence.

Diclegis – Social Media Post



Surveillance

- OPDP's normal surveillance activities include:
  - Monitoring drug promotional materials sent to us by industry
  - Monitoring medical convention exhibit halls
  - Monitoring drug promotion on the internet and social media
  - Reviewing complaints submitted by industry competitors

Limitations to Surveillance

- However, these surveillance activities do not allow us to monitor certain types of drug promotion, such as what occurs in places such as HCPs' offices and industry-sponsored dinner and lunch programs.

- That's one of the reasons why we developed the **Bad Ad Program**

FDA

- An FDA-sponsored outreach program designed to educate HCPs about the role they can play in helping FDA ensure that prescription drug advertising and promotion is truthful and not misleading

- Bad Ad's dual mission:
  1. Education and outreach
  2. Hotline (email and telephone) for HCPs to report potential violations

FDA

- Bad Ad Education and Outreach
  - Pharmaceutical companies spend billions of dollars each year to promote drugs, yet many HCPs are not trained to identify false or misleading promotion
  - Main educational outreach includes:
    - Educational online course
    - Case studies for educational settings
    - Media campaigns and conference outreach

Educational Online Program

- 1-hour, self-paced training

- Training modules include:
  - Video presentations by OPDP reviewers
  - Video presentation on “the psychology of influence” by an expert psychologist consultant
  - Simulated interactive scenarios to test knowledge including a pharmacy scenario

- Over 1,000 course completions to date and excellent overall feedback

Bad Ad Case Studies

- Case studies based on real OPDP Untitled and Warning Letters
- Designed to be used as part of an educational curriculum or training
- Includes the violative promotional material, the resulting Untitled or Warning letter, the FDA-approved PI, and a facilitator guide

Reporting Potential Drug Promotion Issues

- Bad Ad Hotline
  - Any HCP can report potentially misleading promotion to OPDP by:
    - sending an e-mail to **BadAd@fda.gov** or
    - calling **855-RX-BADAD** (855-792-2323)
  - Can be submitted anonymously. However, FDA encourages you to include contact information in case follow-up is necessary for more information

What will OPDP do with your complaint?

- Once a Bad Ad complaint is received, OPDP will evaluate it to determine if it meets the criteria needed to take a compliance action.

- If OPDP finds the promotion to be false or misleading, we will move forward with a risk-based compliance strategy to put a stop to the promotion ourselves, or refer it for further criminal investigation.

- If the report does not meet the required criteria at the time, it will serve as valuable information in focusing our ongoing surveillance activities.

- Phone: **855-RX-BADAD**
  (855-792-2323)

- E-Mail: **BadAd@fda.gov**

- More Info: **www.fda.gov/BadAd**