Prescription Drug and Medical Device Promotion and Scientific and Educational Activities

Seton Hall Law
Life Sciences Compliance Program
San Francisco, CA
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KING & SPALDING

Today's Topics

I. Advertising and Promotion: Overview of Regulation and Key Requirements

II. Specific Topics in Advertising and Promotion

A. Pre-Launch Activities: Risk Areas

B. Medical Congresses and Advisory Boards

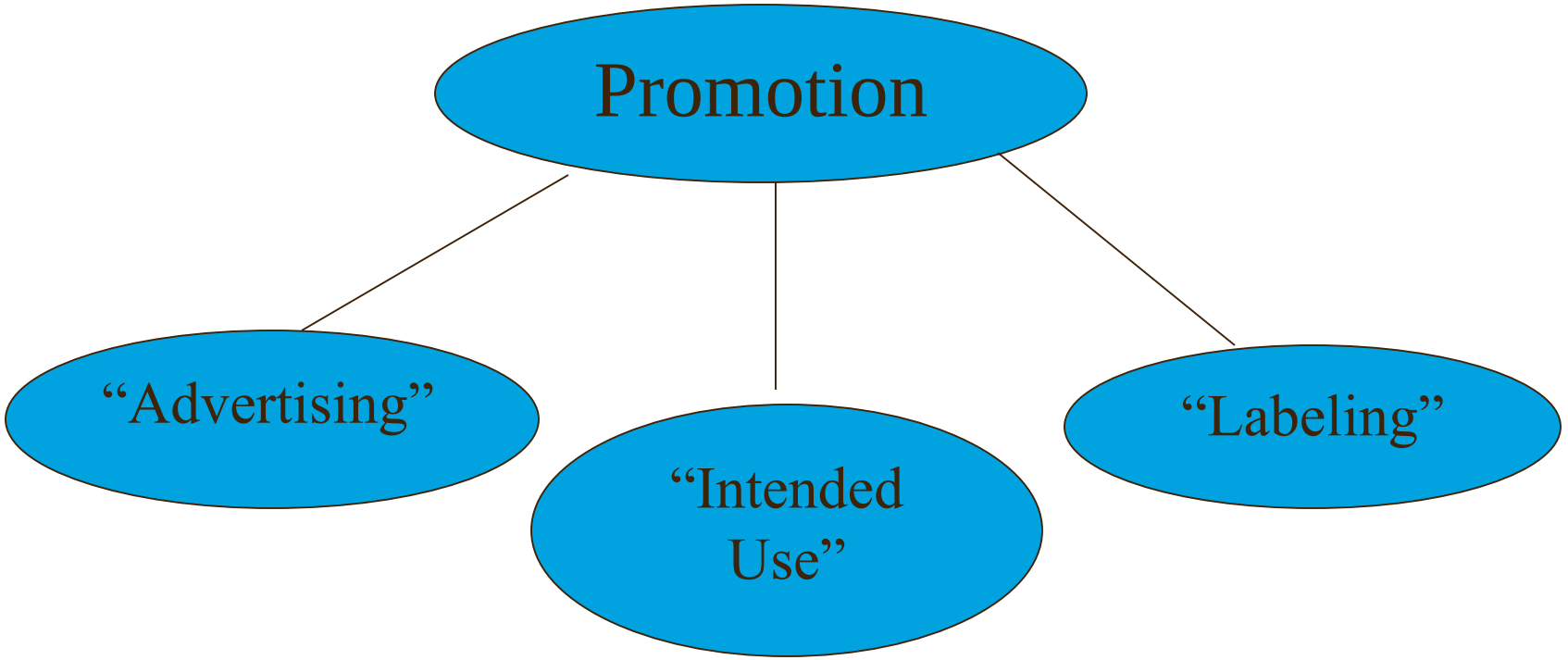
C. Social Media

III. Questions

I.A. Fundamentals: Overview of Regulation

Promotion: Broad Authority

- FDA regulates drug and device promotion via its authority over "advertising," "labeling" and "intended use"



Promotion: Broad Authority (cont'd)

- "Advertising"

  Defined in drug regulations to include:

  — print advertisements in journals, magazines, other periodicals, and newspapers, and

  — broadcast advertisements on media such as radio, television, and telephone communications systems.

  (See 21 C.F.R. 202.1(l)(1))

Promotion: Broad Authority (cont'd)

- "Labeling"
  - "All written, printed, or graphic matter upon an article or container or accompanying such article"

(FDCA § 201(m); see also 21 C.F.R. 202.1(l)(2))

  - Broadly interpreted to include any information that supplements or explains a drug or device and is disseminated by or for the manufacturer
    - Examples include videos, conference materials, reprints, formulary kits, press releases, Internet

Promotion: Broad Authority (cont'd)

- Evidence of manufacturer's "intended use"
  - Implicates approval/clearance requirements
  - Per regulation:

"…The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. …."

(21 C.F.R. 201.128; 21 C.F.R. 801.4) (but revision proposed in 2015)

Promotion: Complex Landscape

- Together with broad regulation, surveillance is active (FDA, physicians ("Bad Ad" program), competitors, whistleblowers)

- First Amendment and practice-of-medicine are important checks; boundaries evolving and rules not always clear
  - FDA has "front burner" initiative to review its policies in light of recent, adverse 1st A jurisprudence (e.g., *Amarin (2016), Pacira (2015), Vascular Solutions (2016)*): shift from "off-label" speech to "truthful and non-misleading"?

Promotion: Noncompliance is Consequential

- Stakes are high for promotional noncompliance
  - Warning Letters, untitled letters
  - Seizure, injunction, civil penalties
  - Prosecution (civil/criminal)/settlement
    - Various legal theories (FDCA, FCA, AKS, state laws)
    - Corporations and/or individuals
    - Strict liability
  - Debarment/exclusion (HHS, FDA)
  - Private litigation

FOR IMMEDIATE RELEASE Thursday, September 3, 2015

Genzyme Corporation to Pay $32.5 Million to Resolve Criminal Liability Relating to Seprafilm

Sanofi Subsidiary Admits Unlawful Conduct and Agrees to Enhance its Compliance Program

Genzyme Corporation, a wholly-owned biotechnology subsidiary of French pharmaceutical company Sanofi, agreed today to resolve criminal charges that it violated the federal Food, Drug and Cosmetic Act (FDCA) with regard to the unlawful distribution of Seprafilm, a surgical device it markets and promotes, the Justice Department announced.

The New York Times

Regulators say the ads overstated the drug's ability to improve women's moods and clear up acne, while playing down its potential health risks. Under a settlement with the states, Bayer agreed last Friday to spend at least $20 million on the campaign and for the next six years to submit all Yaz ads for federal screening before they appear.

JOHN W. SUTHERS
ATTORNEY GENERAL
COLORADO DEPARTMENT OF LAW

COLORADO ATTORNEY GENERAL REACHES $35 MILLION SETTLMENT WITH PFIZER CONCERNING RAPAMUNE®

08/06/2014
42 State Attorneys General Allege Pfizer's Off-Label Marketing Violated FDA Warning

June 12, 2014: Supreme Court Holds Lanham Act Action is Not Pre-empted by FDA Regulation

I.B. Fundamentals:
Key Requirements and Risk Areas

Fundamentals: Key Requirements

- Promotional activities for drugs and devices must:
  - Be consistent with FDA approval (not "off-label")
  - Provide fair balance (adequate risk information)
  - Not be false or misleading
  - Be adequately substantiated

- Examples of violative promotion in prescription drug advertising regulations. (See 21 C.F.R. 202.1(e)(6) and (7)).

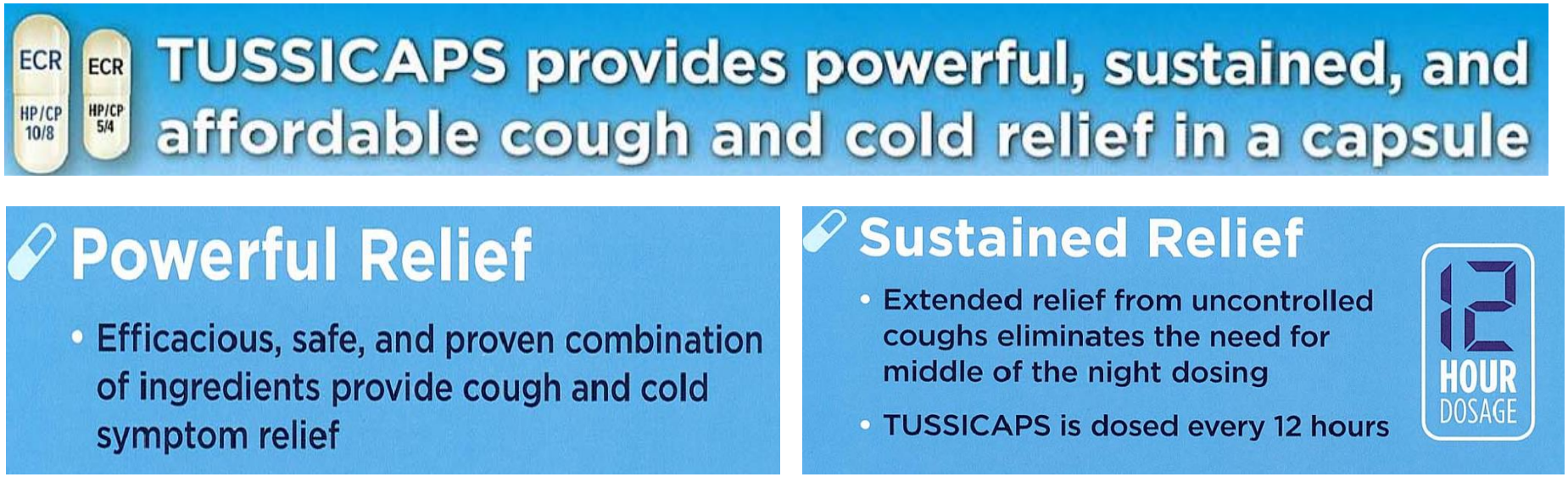
- Submission requirements for prescription drugs (Form 2253).

* *Additional general labeling requirements at 21 C.F.R. 201 (drugs) and 801 (devices); 21 U.S.C. 352(n) (DTC drug ads)*

Examples: Off-Label Promotion (Lack of Adequate Directions for Use)

- Approved product for unapproved condition or unapproved population
- Approved product beyond limitation(s) in approved indication
- Unapproved dosage or dosing regimens
- Screening vs. diagnosis
- Treatment vs. prevention
- General vs. specific use (devices)

Example: Lack of Fair Balance (2015 Warning Letter)

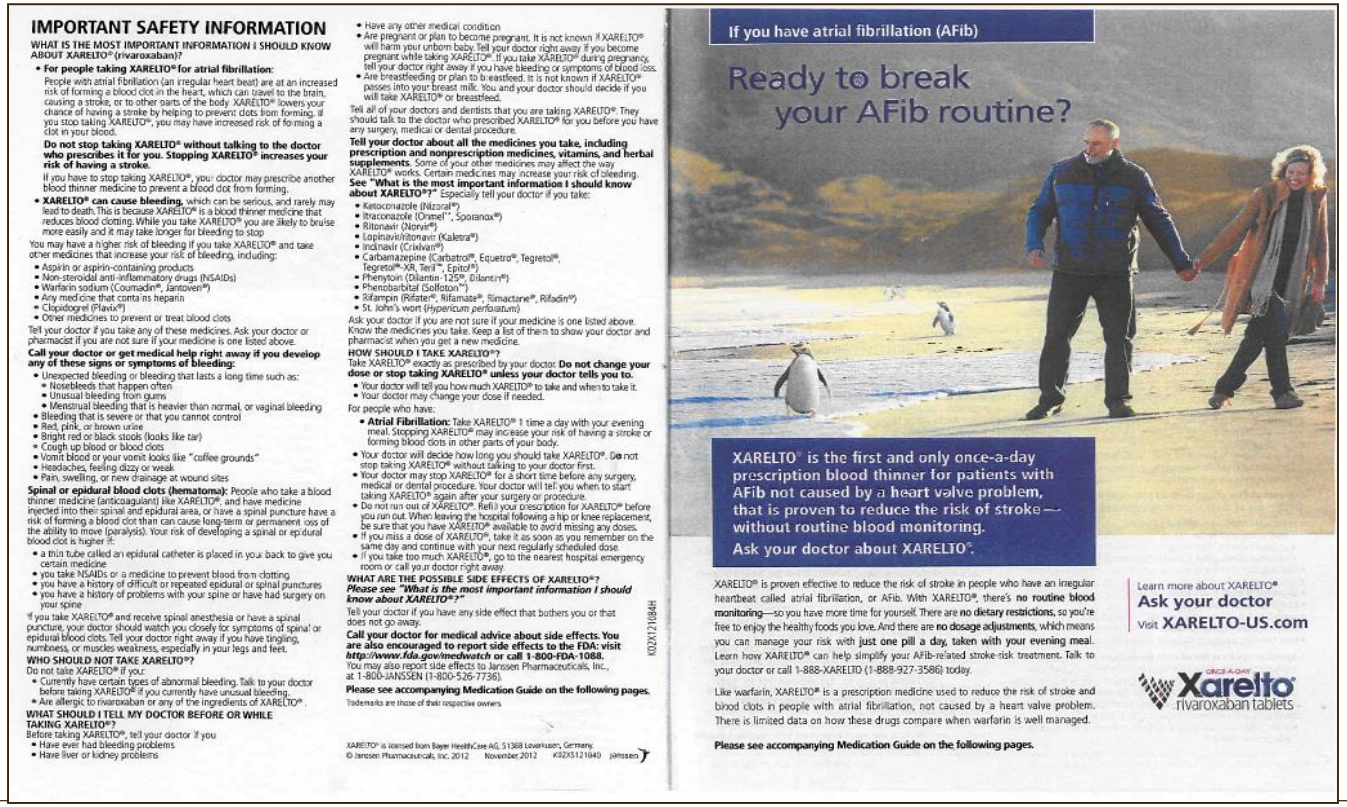


The four page sales aid is misleading because it includes numerous efficacy claims for TussiCaps, but fails to include **any** risk information about the product. We note that the

Example: Lack of Fair Balance

- Risk disclosure must be adequate in terms of content and also presented with **comparable prominence to and integrated with benefit** information.

U.S. Food an Drug Administration, "*Draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion"* (May 2009).



IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO® (rivaroxaban)?

- **For people taking XARELTO® for atrial fibrillation:**

People with atrial fibrillation (an irregular heart beat) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have increased risk of forming a clot in your blood.

Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke.

If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.

- **XARELTO® can cause bleeding,** which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner medicine that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop.

You may have a higher risk of bleeding if you take XARELTO® and take other medicines that increase your risk of bleeding, including:

- Aspirin or aspirin-containing products
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Warfarin sodium (Coumadin®, Jantoven®)
- Any medicine that contains heparin
- Clopidogrel (Plavix®)
- Other medicines to prevent or treat blood clots

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- Unexpected bleeding or bleeding that lasts a long time such as:
  - Nosebleeds that happen often
  - Unusual bleeding from gums
  - Menstrual bleeding that is heavier than normal, or vaginal bleeding
- Bleeding that is severe or that you cannot control
- Red, pink, or brown urine
- Bright red or black stools (looks like tar)
- Cough up blood or blood clots
- Vomit blood or your vomit looks like "coffee grounds"
- Headaches, feeling dizzy or weak
- Pain, swelling, or new drainage at wound sites

Spinal or epidural blood clots (hematoma): People who take a blood thinner medicine (anticoagulant) like XARELTO®, and have medicine injected into their spinal and epidural area, or have a spinal puncture have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:

- a thin tube called an epidural catheter is placed in you back to give you certain medicine
- you take NSAIDs or a medicine to prevent blood from clotting
- you have a history of difficult or repeated epidural or spinal punctures
- you have a history of problems with your spine or have had surgery on your spine

If you take XARELTO® and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have tingling, numbness, or muscles weakness, especially in your legs and feet.

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- Currently have certain types of abnormal bleeding. Talk to your doctor before taking XARELTO® if you currently have unusual bleeding.
- Are allergic to rivaroxaban or any of the ingredients of XARELTO®.

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?

Before taking XARELTO®, tell your doctor if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- Are pregnant or plan to become pregnant. It is not known if XARELTO® will harm your unborn baby. Tell your doctor right away if you become pregnant while taking XARELTO®. If you take XARELTO® during pregnancy, tell your doctor right away if you have bleeding or symptoms of blood loss.
- Are breastfeeding or plan to breastfeed. It is not known if XARELTO® passes into your breast milk. You and your doctor should decide if you will take XARELTO® or breastfeed.

Tell all of your doctors and dentists that you are taking XARELTO®. They should talk to the doctor who prescribed XARELTO® for you before you have any surgery, medical or dental procedure.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO® works. Certain medicines may increase your risk of bleeding.

See "What is the most important information I should know about XARELTO®?" Especially tell your doctor if you take:

- Ketoconazole (Nizoral®)
- Itraconazole (Onmel™, Sporanox®)
- Ritonavir (Norvir®)
- Lopinavir/ritonavir (Kaletra®)
- Indinavir (Crixivan®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril™, Epitol®)
- Phenytoin (Dilantin-125®, Dilantin®)
- Phenobarbital (Solfoton™)
- Rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- St. John's wort (*Hypericum perforatum*)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE XARELTO®?

Take XARELTO® exactly as prescribed by your doctor. **Do not change your dose or stop taking XARELTO® unless your doctor tells you to.**

- Your doctor will tell you how much XARELTO® to take and when to take it.
- Your doctor may change your dose if needed.

For people who have:

- **Atrial Fibrillation:** Take XARELTO® 1 time a day with your evening meal. Stopping XARELTO® may increase your risk of having a stroke or forming blood clots in other parts of your body.
- Your doctor will decide how long you should take XARELTO®. Do not stop taking XARELTO® without talking to your doctor first.
- Your doctor may stop XARELTO® for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO® again after your surgery or procedure.
- Do not run out of XARELTO®. Refill your prescription for XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you have XARELTO® available to avoid missing any doses.
- If you miss a dose of XARELTO®, take it as soon as you remember on the same day and continue with your next regularly scheduled dose.
- If you take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

Please see "What is the most important information I should know about XARELTO®?"

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit *http://www.fda.gov/medwatch* or call 1-800-FDA-1088.

You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please see accompanying Medication Guide on the following pages.

Trademarks are those of their respective owners.

XARELTO® is licensed from Bayer HealthCare AG, 51368 Leverkusen, Germany.
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K02X5121184H

If you have atrial fibrillation (AFib)

Ready to break your AFib routine?

XARELTO® is the first and only once-a-day prescription blood thinner for patients with AFib not caused by a heart valve problem, that is proven to reduce the risk of stroke — without routine blood monitoring.

Ask your doctor about XARELTO®.

XARELTO® is proven effective to reduce the risk of stroke in people who have an irregular heartbeat called atrial fibrillation, or AFib. With XARELTO®, there's **no routine blood monitoring**—so you have more time for yourself. There are **no dietary restrictions**, so you're free to enjoy the healthy foods you love. And there are **no dosage adjustments**, which means you can manage your risk with **just one pill a day, taken with your evening meal.** Learn how XARELTO® can help simplify your AFib-related stroke-risk treatment. Talk to your doctor or call 1-888-XARELTO (1-888-927-3586) today.

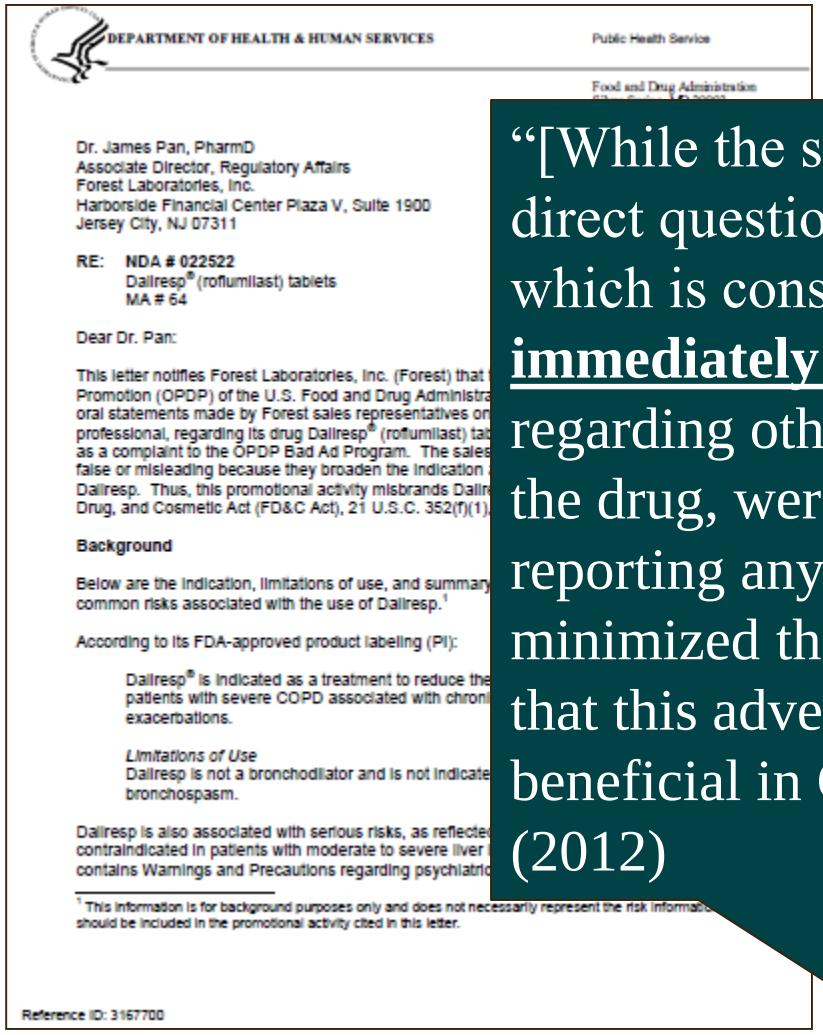
Like warfarin, XARELTO® is a prescription medicine used to reduce the risk of stroke and blood clots in people with atrial fibrillation, not caused by a heart valve problem. There is limited data on how these drugs compare when warfarin is well managed.

Please see accompanying Medication Guide on the following pages.

Learn more about XARELTO®
Ask your doctor
Visit **XARELTO-US.com**

ONCE-A-DAY Xarelto® rivaroxaban tablets

Example: Inadequate Risk Information



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration

Dr. James Pan, PharmD
Associate Director, Regulatory Affairs
Forest Laboratories, Inc.
Harborside Financial Center Plaza V, Suite 1900
Jersey City, NJ 07311

RE: NDA # 022522
Daliresp® (roflumilast) tablets
MA # 64

Dear Dr. Pan:

This letter notifies Forest Laboratories, Inc. (Forest) that
Promotion (OPDP) of the U.S. Food and Drug Administra
oral statements made by Forest sales representatives on
professional, regarding its drug Daliresp® (roflumilast) tab
as a complaint to the OPDP Bad Ad Program. The sales
false or misleading because they broaden the indication
Daliresp. Thus, this promotional activity misbrands Dalir
Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(f)(1).

Background

Below are the indication, limitations of use, and summary
common risks associated with the use of Daliresp.[1]

According to its FDA-approved product labeling (PI):

> Daliresp® is indicated as a treatment to reduce the
> patients with severe COPD associated with chroni
> exacerbations.
>
> *Limitations of Use*
> Daliresp is not a bronchodilator and is not indicate
> bronchospasm.

Daliresp is also associated with serious risks, as reflecte
contraindicated in patients with moderate to severe liver
contains Warnings and Precautions regarding psychiatric

[1] This information is for background purposes only and does not necessarily represent the risk informati
should be included in the promotional activity cited in this letter.

Reference ID: 3167700

"[While the sales representatives responded to direct questions regarding the risks…in a manner which is consistent with the…PI, **these risks were immediately downplayed** with anecdotal claims regarding other physicians who have prescribed the drug, were pleased with it, and were not reporting any adverse events. Furthermore, [they] minimized the risk of weight loss by indicating that this adverse reaction may actually be beneficial in COPD patients who are overweight." (2012)

Example: Other "False or Misleading" Representations – Implied Superiority

– Example: 2015 FDA Untitled Letter

- Misleadingly implies that Surfaxin (synthetic surfactant) is superior because it has "evolved" from more primitive, animal-derived surfactants.

Example: Other "False or Misleading" Representations - Overstatement of Efficacy

- Testimonials or patient experiences often draw objection.
  - Suggest 'better than average' results. *"Only patients with good outcomes have testimonials."* (Deborah Wolf, Center for Devices, FDA)
  - Disclaimers ("individual results may vary") not sufficient.
    (*Cf.* FTC, Guides Concerning the Use of Endorsements and Testimonials in Advertising (16 C.F.R. Part 255)
  - Also, "While these statements may be an accurate reflection of [patient's] own experience…[t]he personal experience of a…patient…does not constitute…evidence" adequate to substantiate product effectiveness. (FDA Warning Letter 2009)
  - May also overstate product benefits (e.g.., effects on not only disease but also broader quality of life).

Example: Misleading Characterization of Risk

- YouTube video for surgical sedative (Jan. 2016 FDA letter) - company cited for describing risk information as a benefit:
  - Presented side effect of "arousability" as a benefit that "makes it different than other sedatives."
- Similar activity subject of government investigations and settlements, e.g.,
  - 2009 settlement involving promotion that characterized weight gain and obesity as benefits among elderly, rather than adverse events
  - Similar approach for somnolence ("5 (mg) at 5 (pm)")

Adequate Substantiation

- Promotional claims of treatment benefit generally require support by adequate and well-controlled clinical studies (See 21 C.F.R. 202.1(e)(4)(ii)(b))
  - "Substantial evidence" standard for prescription drugs (2 studies usually required)
- Different standard for healthcare economic information (competent and reliable evidence) (See FDCA section 502(a))
  - Draft guidance anticipated

"Adequate Substantiation" as Applied

- Evidence deemed inadequate to support clinical claims is frequently cited in compliance letters:

— Open-label studies

— In vitro or preclinical data (even with disclaimer 'clinical significance unknown')

— Post-hoc subgroup analyses

— Meta-analyses

— Retrospective analysis of published study or literature review

— Comparative claims not supported by head-to-head clinical trials (e.g., cross-label comparisons)

— Results from unplanned analyses or endpoints not specified in study protocol (including specification of conditions for a positive study conclusion)

— Composite endpoints as support for effect on any individual component of the endpoint

— Reported assessments (patient-reported outcomes (PROs), clinician-reported outcomes (ClinROs), or observer-reported outcomes (ObsROs) not based on measurement instruments with design or content validity

II.A. Pre-Launch Activities: Risk Areas

Pre-Launch Activities: Overview

- General rule: pre-approval / pre-clearance promotion prohibited.
- Some exceptions for limited promotion; also, some activities permitted because not promotion.

* "Scientific Exchange"
* Responding to "unsolicited requests"
* "Disease Awareness" communications
* Investor-directed information
* Institutional advertising
* "Coming Soon" ads
* Trade Show policy (devices)
* Clinical investigations (recruitment, training)

Permitted Pre-Launch Promotion

- "Coming soon": name of product; no suggestion of safety, efficacy or intended use; not if boxed warning likely, or
- "Institutional": describes therapeutic area but does not name product
- Trade show display for devices pending 510(k) clearance (FDA Compliance Policy Guide 300.600) – display only; no orders or sale

Disease State Advertising

- Disease awareness advertising is "unbranded" (*i.e.*, not labeling or advertising for a product) and, thus, not subject to FDA requirements, if the information does not:
  - Mention a particular product or
  - Include any representation or suggestion about a particular product.

- Issue is if/when a communication is considered to identify a particular product:
  - Communication close in place or time to product piece?
  - Communication "perceptually similar" to product piece?

Communications About Investigational Products/Uses: Risk Areas

- "Promotion" vs "scientific exchange"
  - 21 C.F.R. 312.7: "This provision is not intended to restrict ***the full exchange of scientific information***…including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict ***promotional claims*** of safety or effectiveness…for a[n] [investigational use…."
- Watch out for communications about investigational products in press releases, video news releases, Internet, podcasts
  - Form 2253 identifies these as categories of promotional labeling/advertising requiring submission

Investigational Product Communications Example: 2013 Untitled Letter to CBA Research

- Issue: "Positive and definitive conclusions"
  - Contrast with *"unbiased and scientific reporting of…newly available clinical data"* (FDA. 1998 Warning Letter to Eli Lilly)

- FDA objected to website discussion with conclusions such as :
  - "…**[A]chieves the required therapeutic concentration necessary** to reverse multidrug resistance in the clinical setting."
  - "NO SIGNIFICANT OR LASTING TOXIC SIDE EFFECTS ….[CBT-1] had **a very favorable adverse event profile**."
  - "Eight Phase I and II clinical trials…**showed efficacy**...in multiple cancers."
  - Preclinical and Clinical **research has consistently demonstrated the potential for CBT-1 to be safe and effective**. The drug is safe, well tolerated…and has produced clinically objective responses…."

Investigational Products/Uses: Other Risk Areas

- Phrasing promotional in tone *("could be a game changing medication" or "breakthrough," "first in class")*
- Terms associated with approved/proven products *("treatment," "indications")*
- Comparing investigational product to approved product *("at least three times more sensitive…than commercially available biochemical markers," "hopeful that the label will allow us to demonstrate a clear advantage over the market leader")*
- Statements in lay media (versus communications strictly to investors)
  - e.g., 2015 FDA letter regarding CEO interview on Lifetime morning show
  - Caution still appropriate for investor-directed communications (2013 FDA Warning Letter regarding CEO statements on "Fast Money"))
- Failure to disclose material limitations or adverse events
- Misleading statements about clinical trial results *(e.g., presenting results from unplanned subgroup analysis when pre-specified endpoints not met)*
- Devices: training, live case presentations (see April 2014 FDA draft guidance)

"Scientific Exchange"

- Full scope unclear, but FDA evaluating how to define; intends to issue guidance.
- Areas of established guidance :
  - Sponsorship of 3rd party CME (activities independent of sponsor influence are nonpromotional). See *Guidance for Industry: Industry-Supported Scientific and Educational Activities (Nov. 1997)*
  - Responding to unsolicited requests.
  - Dissemination of "off-label" publications.

Guidance on Responding to Off-Label Inquiries (Dec. 2011)

- *Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices*

- Companies may not promote off-label uses, but may respond to *unsolicited* questions about off-label uses.

- Examples of solicited requests provided, such as:
  - Promotional presentation of off-label data by paid speakers or MSLs
  - Commercial exhibits announcing new uses for products

    (*e.g.*, "Coming Soon, a new use for Product X")
  - Encouragement of users to post testimonials or videos on off-label uses (*e.g.*, on YouTube)

Responding to Off-Label Inquiries (ct'd)

- Distinguishes between "public" and "non-public" inquiries
- Any public response should be limited to providing:
  - A statement that the question pertains to unapproved/uncleared use of the product;
  - Contact for medical or scientific department to obtain more information;
  - A disclosure of the responder's involvement with the company; and
  - A mechanism for accessing the FDA-approved labeling for the product.
- Private responses should:
  - Be tailored to the specific question, non-promotional, truthful, non-misleading, accurate, balanced, and scientific;
  - Be documented;
  - Include complete copies (reprints), FDA-required labeling, and statement that FDA has not approved the use; and
  - Include disclosure of approved indications, list of references, and all important safety information.

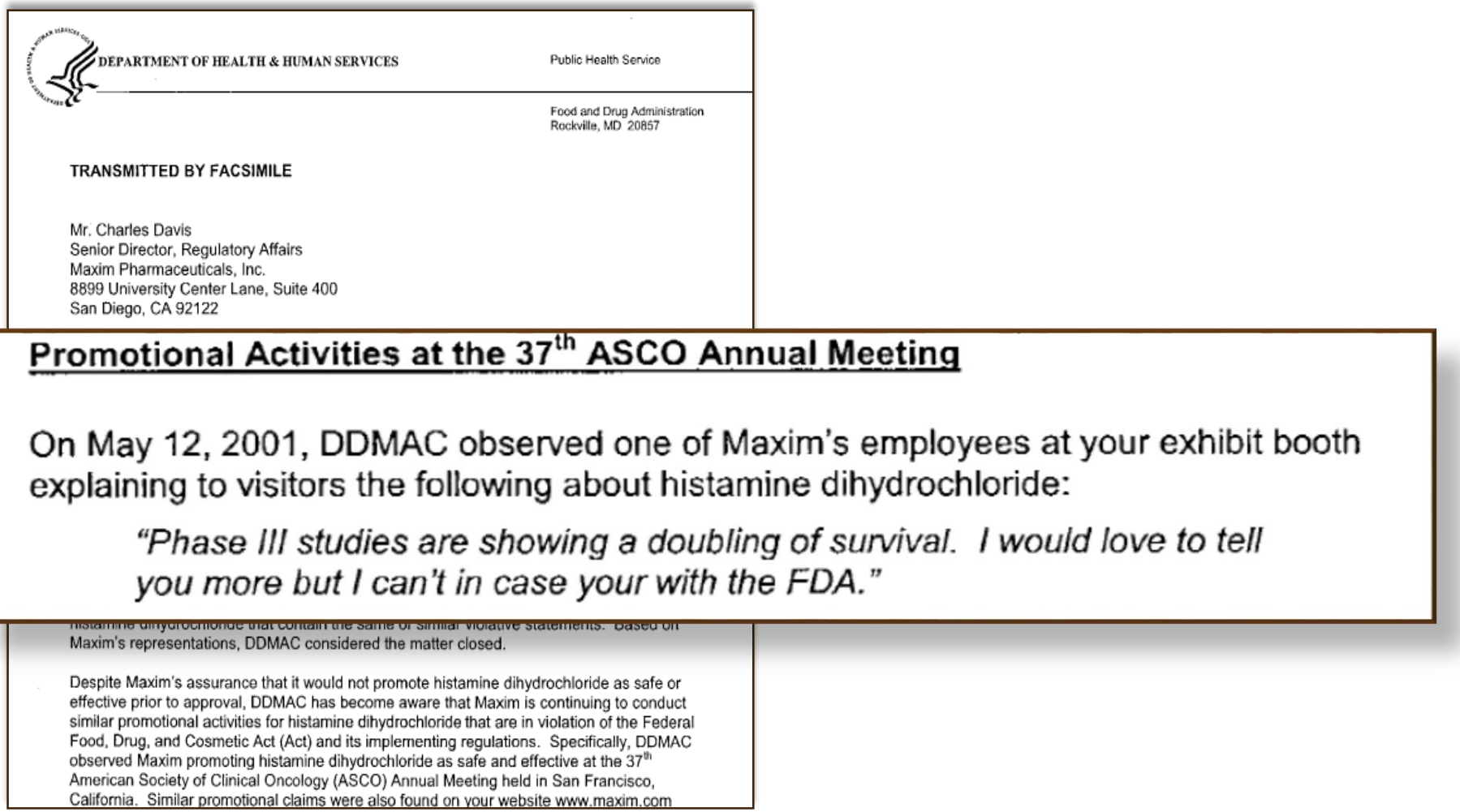
Guidance on Disseminating Off-Label Publications (Feb. 2014)

- *Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices*
- Provides "safe harbor" for affirmative distribution of certain scientific/medical journal articles, reference texts, or clinical practice guidelines (CPGs) discussing off-label use(s) to health care professionals or health care entities
  - Does not allow dissemination to patients/consumers
  - Does not address dissemination of information regarding products without any FDA approval
  - Numerous conditions for dissemination to assure quality of information and independence from manufacturer influence (e.g., disclosure of authors' financial interests and off-label nature of information, separation from promotional activity, provision of countervailing information).

II.B. Medical Congresses, Advisory Boards

Congress Considerations

- Congresses are common target of scrutiny



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Mr. Charles Davis
Senior Director, Regulatory Affairs
Maxim Pharmaceuticals, Inc.
8899 University Center Lane, Suite 400
San Diego, CA 92122

Promotional Activities at the 37th ASCO Annual Meeting

On May 12, 2001, DDMAC observed one of Maxim's employees at your exhibit booth explaining to visitors the following about histamine dihydrochloride:

"Phase III studies are showing a doubling of survival. I would love to tell you more but I can't in case your with the FDA."

Maxim's representations, DDMAC considered the matter closed.

Despite Maxim's assurance that it would not promote histamine dihydrochloride as safe or effective prior to approval, DDMAC has become aware that Maxim is continuing to conduct similar promotional activities for histamine dihydrochloride that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Specifically, DDMAC observed Maxim promoting histamine dihydrochloride as safe and effective at the 37th American Society of Clinical Oncology (ASCO) Annual Meeting held in San Francisco, California. Similar promotional claims were also found on your website www.maxim.com

Congress Considerations

- Commercial and scientific/medical information booths are closely monitored; usual requirements apply.
  - e.g., 2015 FDA letter: exhibit banner must include risk information; statement to see booth representative not sufficient
- Off-label/investigational product information permitted if:
  - In response to unsolicited requests: refer to medical affairs booth or department per FDA guidance
  - Disseminated from medical booth per FDA guidance
  - At separate booth for ex-US uses/audiences where product/use approved abroad and Congress includes global participants
- Sponsors accountable for speaker and investigator statements
  - e.g., 2015 FDA letter: study sponsor cited for promotion by study partner

Advisory Board/Consultancies

Selected key principles:

- Legitimate need for consultant pre-defined
- Number of HCPs retained is not greater than reasonably necessary
- Written contract documents nature and basis for payment
- Compensation reasonable and based on fair market value ("FMV")
- Venue and circumstances of any meeting are conducive to the services, and activities related to the services are primary focus of the meeting
- In case of speakers, training and other guardrails to ensure compliance with promotional requirements is essential.

See PhRMA and Advamed Codes, OIG Compliance Program Guidance for Pharmaceutical Manufacturers

II.C. Social Media

2014 FDA Draft Guidances on Social Media

- Regulatory Requirements / Responsibility for Social Media Content
- Correcting Misinformation
- Character Space Limitations

Backdrop: Warning and Untitled Letters have issued over the years on FDA's principle 'It's the message, not the medium.'

FDA Draft Social Media Guidance
Character Space Limitations

- FDA Draft Guidance, *Internet / Social Media Platforms with Character Space Limitations – Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices (*June 2014).

- Applies to promotional communications on an internet or social media platform *with character limitations.* E.g.,:
  - Tweets on Twitter (140 character limit)
  - Online paid search links (e.g., Google sponsored links)

Key Points

- Benefit information should be accurate, non-misleading and reveal material facts.
- If benefits are discussed, most serious risks should be too – with comparable prominence and in same tweet/communication.
- Include direct link to complete risk information.
  - URL should indicate risk information
- Communicate both proprietary (trade or brand) name and established name (i.e., generic name) within the character-limited communication.
- Depending on indication and risks, Twitter and other character-limited communications may not be a "viable promotional tool" for all products.

June 2014 Untitled Letter – Sponsored Links

- Subject: Google Sponsored Links for hepatitis drug.

> **Hepatitis B Prevention** – viread.com
> www.viread.com/TreatingHBV
> Looking for A Hep B Treatment Option? Click to Learn More?

- Omission of risk information
  - No risk information (including Boxed Warning)
  - Link to product webpage insufficient
- Failure to include established name for drug
- Failure to submit under Form FDA-2253

Other FDA Draft Social Media Guidance

- Draft Guidance, *Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media* (Jan. 2014)
  - Provides guidance on submitting Form 2253 (and 2301) for social media content over which company "exerts influence"
- Draft Guidance, *Internet / Social Media Platforms: Correcting Independent Third-Party Misinformation about Prescription Drugs and Medical Devices* (June 2014)
  - Provides guidelines for voluntary correction of misinformation disseminated by independent third parties
  - Corrections in line with guidelines will not be cited for noncompliance with advertising/labeling requirements.
- Guidance planned for 2016 on links to third-party sites

In Closing….

Takeaways

- Advertising and promotion regulation is complex and evolving
  - Application of general concepts to particular pieces and facts can be nuanced
  - Many watchdogs and interested parties.
- Procedures and training are critical.
- FDA compliance letters and facts underlying other reported enforcement provide best public source of current interpretations.
- An outside “reality check” and benchmarking can be helpful.

Questions? Thank you.