FDA Regulation of Prescription Drug Promotion

Thomas W. Abrams, R.Ph., MBA

Division of Drug Marketing, Advertising, and Communications

Food and Drug Administration

November 13, 2003

Topics

- Overview
- CBER/CDER Consolidation
- Direct-to-Consumer Promotion (DTC)
- Enforcement

Goal and Objectives

- Goal
  - To protect and promote public health
- Objectives
  - Ensure that RX drug promotion is not false or misleading
  - Ensure that complete picture of drug is conveyed
  - Get more useful information about drugs and diseases to the American public

Mechanisms for Meeting Objectives

- Comprehensive surveillance and enforcement program
- Voluntary compliance
  - Guidance documents
  - Request for comments
  - Educational efforts

CBER/CDER Consolidation

- Transfer of therapeutic products from CBER to CDER
- Transfer of review of the promotional materials for these products from APLB to DDMAC
- DDMAC and APLB worked together for smooth transition

Professional (Biologic) Review Group in DDMAC

- Acting Group Leader
  - Marci Kiester
- 3 Reviewers
  - Carole Broadnax
  - Eva Barrion
  - New reviewer
- Additional Assistance
  - Cathy Miller

Submission of Materials

- From June 30, 2003, to September 15, 2003
  - To CBER document room for delivery to APLB
  - APLB sorts and routes items to DDMAC
- Effective immediately
  - Submit directly to DDMAC
    - Division of Drug Marketing, Advertising, and Communications; HFD-42, Rm. 8B-45
      5600 Fishers Lane
      Rockville, MD 20857

DTC

- Public Meeting on DTC Research
- Future guidance on “Brief Summary”

DTC Public Meeting

- Public Meeting on DTC Research
  - Sept 22-23
  - Federal Register Notice dated August 12, 2003
- Purpose is to gather data from DTC research
  - Comment docket open until December 1
  - Impact of DTC on public health evaluation

Brief Summary

- Brief summary
  - important information
  - current brief summary not optimal for best communicating this information
- Developing guidance on brief summary
  - Part of the FDA Strategic Plan
  - Plan is to publish by end of 2003

Enforcement

- Warning Letters (January - September)
  - OxyContin
  - Xeloda
  - Viread
  - Pravachol

Xanodyne Warning Letter

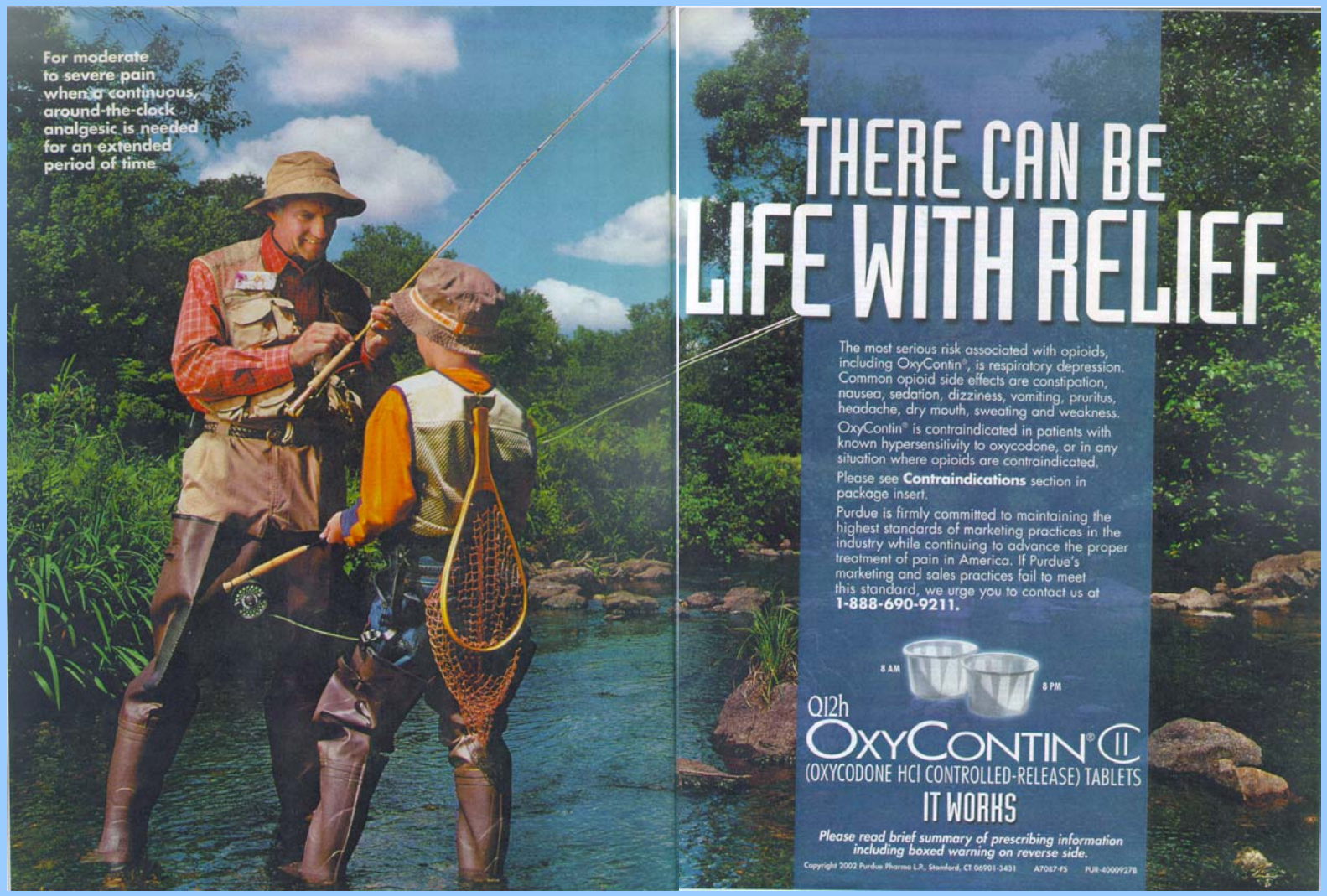
- Methotrexate, Leucovorin, and Amicar
- Promotional Brochure
- No risk information
- Omission of limitations on indications

Methotrexate

- Boxed warning about serious toxic reactions (potentially fatal)
- Monitoring necessary for bone marrow, liver, lung, and kidney toxicities
- Reported fetal deaths and congenital anomalies
- Severe, occasionally fatal, skin reactions

OxyContin Warning Letter

- Journal advertisements
- Lack of important risk information
- Overbroadening of the indication
- Omission from body of ad
  - crucial facts related to potentially fatal risk
  - potential for abuse
  - limitations on appropriate indicated use


For moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time
THERE CAN BE
LIFE WITH RELIEF
The most serious risk associated with opioids, including OxyContin®, is respiratory depression. Common opioid side effects are constipation, nausea, sedation, dizziness, vomiting, pruritus, headache, dry mouth, sweating and weakness.
OxyContin® is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated.
Please see Contraindications section in package insert.
Purdue is firmly committed to maintaining the highest standards of marketing practices in the industry while continuing to advance the proper treatment of pain in America. If Purdue's marketing and sales practices fail to meet this standard, we urge you to contact us at 1-888-690-9211.
8 AM
8 PM
Q12h
OXYCONTIN® CII
(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS
IT WORKS
Please read brief summary of prescribing information including boxed warning on reverse side.
Copyright 2002 Purdue Pharma L.P., Stamford, CT 06901-3431 A7087-FS PUR-4000927B

OxyContin® CII

(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

10 mg 20 mg 40 mg 80 mg* 160 mg*

*80 mg and 160 mg for use in opioid-tolerant patients only

WARNING:

OxyContin is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

OxyContin Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

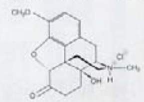
OxyContin Tablets are NOT intended for use as a prn analgesic.

OxyContin 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

OxyContin TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.

DESCRIPTION

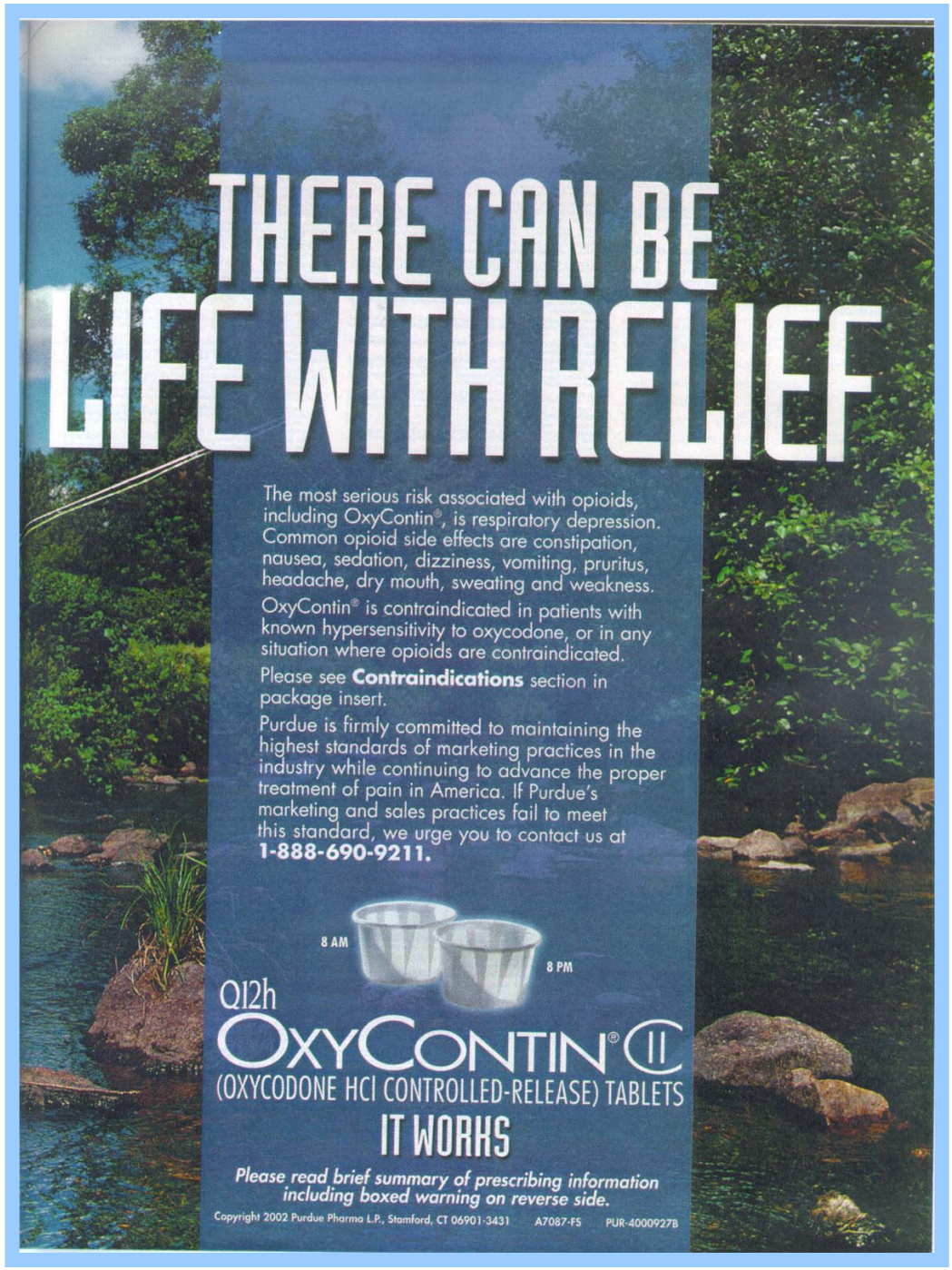
OxyContin® (oxycodone hydrochloride controlled-release) Tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, 80 mg, and 160 mg tablet strengths for oral administration.



	OxyContin (n=227) (%)	Immediate-Release (n=225) (%)	Placebo (n=45) (%)
Constipation	(23)	(26)	(7)
Nausea	(23)	(27)	(11)
Somnolence	(23)	(24)	(4)
Dizziness	(13)	(16)	(9)
Pruritus	(13)	(12)	(2)
Vomiting	(12)	(14)	(7)
Headache	(7)	(8)	(7)
Dry Mouth	(6)	(7)	(2)
Asthenia	(6)	(7)	—
Sweating	(5)	(6)	(2)

PURDUE


For moderate
to severe pain
when a continuous,
around-the-clock
analgesic is needed
for an extended
period of time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IMPORTANT CORRECTION

PURDUE

Purdue Pharma L.P.
One Stamford Forum
Stamford, CT 06901-3431
(203) 588 8000
Fax (203) 588 8850
www.purduepharma.com

January 2003

Dear Healthcare Practitioner,

Earlier publications of this journal contained advertisements for OxyContin® (oxycodone HCl controlled-release) Tablets that were the subject of a Warning Letter from the U.S. Food and Drug Administration in January 2003, stating that the advertisements violated provisions of the drug advertising and promotion regulations.

The Warning Letter stated that information concerning important risks associated with OxyContin® Tablets that appears in the boxed warning of the OxyContin® Prescribing Information was not presented in the main body of the advertisements. This information concerns potentially fatal risks associated with the use of OxyContin® and the abuse liability of OxyContin®. In addition, the Warning Letter stated that the body of the advertisements did not present important information regarding limitations on the indicated use of OxyContin®.

Consequently, we direct you to the information on safety, risks, and indications for OxyContin® Tablets, including the boxed warning, located on the adjacent page.

Sincerely,

Robert F. Reder, MD
Vice President,
Medical Affairs and Worldwide Drug Safety

OF DRUG INFORMATION

OxyContin®

(oxycodone HCl controlled-release) Tablets CII

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Indications and Usage

- OxyContin® Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.
- OxyContin® is **NOT** intended for use as a prn analgesic.
- Physicians should individualize treatment in every case, initiating therapy at the appropriate point along a progression from non-opioid analgesics, such as non-steroidal anti-inflammatory drugs and acetaminophen, to opioids in a plan of pain management such as outlined by the World Health Organization, the Agency for Healthcare Research and Quality (formerly known as the Agency for Health Care Policy and Research), the Federation of State Medical Boards Model Guidelines, or the American Pain Society.
- OxyContin® is not indicated for pain in the immediate postoperative period (the first 12 to 24 hours following surgery), or if the pain is mild, or not expected to persist for an extended period of time.
- OxyContin® is only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate (see American Pain Society guidelines).

Please read brief summary of prescribing information on reverse side.

A7216 PUR-4001135

Xeloda Warning Letter

- Sales aid
  - disseminated in promotional exhibit area
- Patient-directed video

Xeloda: Violations

- Minimization of risk information
- Misleading comparative safety claims
- Misleading efficacy claims
- Promotion of unapproved uses

Xeloda: Risk information

- Sales aid
  - failed to provide any risk information
- Video
  - Claims that Xeloda, unlike other chemo drugs, does not make you feel too tired or too sick to do your daily activities
  - Claims that Xeloda is safer and has fewer toxicities than IV chemo drugs
  - Minimize serious adverse events including severe diarrhea

Xeloda: Misleading Claims

- It gives me more freedom, I feel stronger, I mean I go to the gym now - work out
- I can do anything I want to do ….
- I can do all the daily things that sometimes ….

Viread Warning Letter

- Sales representative promotion
- Promotion at HIV/AIDS conference
- Minimization of risk information
- Promotion of unapproved uses

Viread: Risk Information

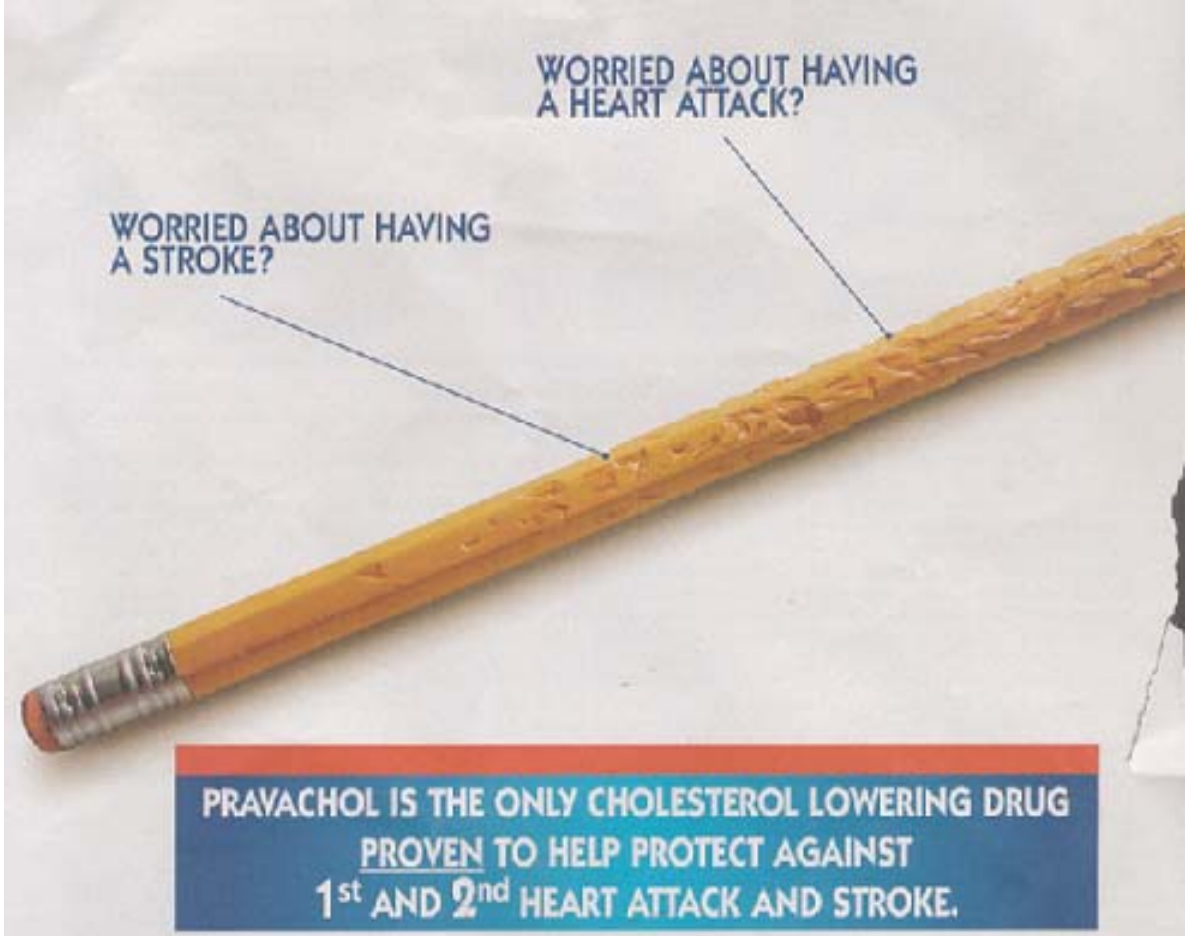
- Untitled letter on March 14, 2002
- No risk information about boxed warning about lactic acidosis
- Claims about Viread is a nucleotide, not a nucleoside
  - boxed warning is a class effect and did apply to Viread
  - more potent
  - fewer side effects, safer

Pravachol Warning Letter

- DTC ads and labeling pieces
- Healthcare professional directed labeling pieces
- Promotion of unapproved uses

Pravachol: Promotion of Unapproved Uses

- Not indicated to reduce risk of strokes in patients who do not have clinically evident CHD
- Claims
  - WORRIED ABOUT HAVING A HEART ATTACK? WORRIED ABOUT HAVING A STROKE?
  - PRAVACHOL IS THE ONLY CHOLESTEROL LOWERING DRUG PROVEN TO HELP PROTECT 1ST AND 2ND HEART ATTACKS AND STROKE



PRAVACHOL IS THE ONLY CHOLESTEROL LOWERING DRUG PROVEN TO HELP PROTECT AGAINST 1st AND 2nd HEART ATTACK AND STROKE.

IMPORTANT CONSIDERATIONS:

Pravachol® (pravastatin sodium), a prescription drug, is not for everyone, including women who are pregnant or nursing or may become pregnant, or people with liver problems. And because serious side effects can result, tell your doctor about any unexplained muscle pain or weakness you experience while on Pravachol, and about any other medications you are taking. Your doctor may do blood tests to check for liver problems. Some mild side effects, such as slight rash or stomach upset, occur in 2-4% of patients.

Ask your doctor if Pravachol is right for you.

Please see product information following this advertisement.

1-877-PRAVA-CALL

Bristol-Myers Squibb Company

www.pravachol.com

Summary

- CBER/CDER Consolidation
- DTC
- Enforcement