

Enforcement and Policy Update from Office of Prescription Drug Promotion

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Topics

- Guidance update
- Voluntary compliance
- Enforcement update
- Operations update



Guidance Development

- Presentation of Risk Information Draft Guidance issued in May 2009
- Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements (Brief Summary)
- TV Ads – FDAAA DTC TV Pre-Review Program
- Promotion using Social Media Tools

Guidance Process for Social Media

- Information collection and analysis
 - Held a Part 15 public hearing [21 CFR 15]
 - Reviewed hearing testimony and comments submitted to the docket
 - 77 presentations at Part 15 public hearing
 - 72 submissions of comments to the docket

Guidance Process for Social Media

- Develop issue specific guidances rather than technology platform based guidances
- Research on multiple guidance topics
 - Responding to unsolicited requests for off-label information
 - Fulfilling regulatory requirements when using tools associated with space limitations
 - Fulfilling post-marketing submission requirements
 - On-line communications for which manufacturers, packers, or distributors are accountable
 - Use of links on the Internet
 - Correcting misinformation on third party websites

Guidance Process for Social Media

- Allocating resources for and commitment to develop high quality guidances
- Working closely with others in Agency including
 - Medical Product Centers (CBER, CDRH, CVM)
 - Groups within CDER
 - Office of Chief Counsel
- FDA is committed to Good Guidance Practices (GGPs) [21 CFR 10.115]
 - Prepare a draft guidance document and vet through internal clearance process
 - Issue the draft guidance
 - Review comments on the draft guidance
 - Revise the draft guidance based on comments, if appropriate
 - Issue a final guidance document

Additional Information on Social Media

- DDMAC Part 15 website
 - <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm184250.htm>
- Part 15 docket
 - www.regulations.gov
 - Search docket “FDA-2009-N-0441-0001” to view comments

Voluntary Compliance

- Objectives
 - Have compliant promotion (not false, not misleading, and balanced)
 - Have promotion be high quality and educational
- FDA benefits (public health benefits)
 - Consumers and HCPs not exposed to misleading information about prescription drugs
 - Instead consumers and HCPs obtain good and balanced information about prescription drugs
- Industry benefits
 - Provides good information to public
 - Better image
 - Avoid regulatory actions
 - No interruption in promotional campaigns

Efforts to Increase Voluntary Compliance

- FDA's Efforts
 - Guidance documents
 - Requests for comments on draft promotional materials
 - Educational and outreach efforts
 - Comprehensive surveillance and enforcement program
- Industry's Efforts



Voluntary Compliance

- Overall promotional materials appear to be improving
- Other promotional materials and activities remain concerning
- Certain promotional proposals and suggestions are also concerning
- Unproductive discussion (debate) of various issues occurring rather than focusing on issues that can benefit from discussion

Enforcement



Surveillance

- Disseminated materials submitted to FDA
 - Post-marketing reporting requirements (Form 2253)
- Conference attendance
- Complaints
- Health Care Professional Outreach Initiative
- Broad surveillance of materials used
 - Numerous, evolving and creative ways of promoting prescription drugs by industry, especially on the Internet

The Bad Ad Program

- The Bad Ad Program is 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.
- When HCPs recognize misleading drug promotion, they can help put a stop to it by reporting it to FDA:
 - Call
 - **877-RX-DDMAC (877-793-3622)**
 - Email
 - **BadAd@fda.gov**



The Bad Ad Program

- While the program is targeted at HCPs, that does not limit the type of misleading promotional materials HCPs can report to us
- HCPs and other healthcare professionals can recognize misleading DTC promotion and report it to the Bad Ad program
- Approximately 25% of the Bad Ad complaints received by OPDP (and falling under our purview) have been regarding potentially misleading DTC advertising and promotion

The Bad Ad Program

Highlights of Year 1

- Dear HCP letter sent to 33,000+ physicians and press release announcing Bad Ad Program
- Development of Bad Ad Program educational brochure, video, and reminder magnet to educate HCPs about how to recognize and report prescription drug promotion.
- Staffed exhibits at 15 medical conferences across the country, speaking with HCPs about how they can help stop misleading drug promotion
 - Began series of Bad Ad presentations at U.S. teaching hospitals
- Hosted live Bad Ad webinar for medical and pharmacy professionals



The Bad Ad Program

Year 1 Data

- Heightened sense of awareness of misleading promotion among HCPs throughout the country
 - Doctor Directory: 30% HCPs aware of Bad Ad
- 328 Bad Ad complaints; approximately triple OPDP's historical average (104)
- 5 enforcement actions



The Future of Bad Ad

- Developing Bad Ad CME to raise awareness of misleading prescription drug promotion
- Continuing presence at major medical conventions and teaching hospitals
- Targeting outreach and education to early-career HCPs (AMSA)
- Seeking to collaborate with medical, pharmacy, and nursing schools to enhance student education about misleading promotion



Risk Based Enforcement Approach

- Impact on public health
- Includes promotion of:
 - Newly approved products
 - Products with significant risks
 - Products cited for violations in the past
 - Products cited in complaints
 - Products promoted with far reaching campaigns



Most Common Violations in 2011

- Omission and minimization of risk information
- Misleading claims of efficacy
- Promotion of unapproved uses of drugs (includes broadening of the indication)
- Misleading superiority claims

Omapro Untitled Letter

- Brochure obtained from the company's exhibit at American Society of Hematology meeting
- Promotion of an investigational new drug as safe and effective
- NDA submitted in Sept 2009 for use in patients with Philadelphia chromosome-positive chronic myeloid leukemia (CML) who have failed treatment with imatinib and who have developed the Bcr-Abl T3151 mutation



Omapro Untitled Letter

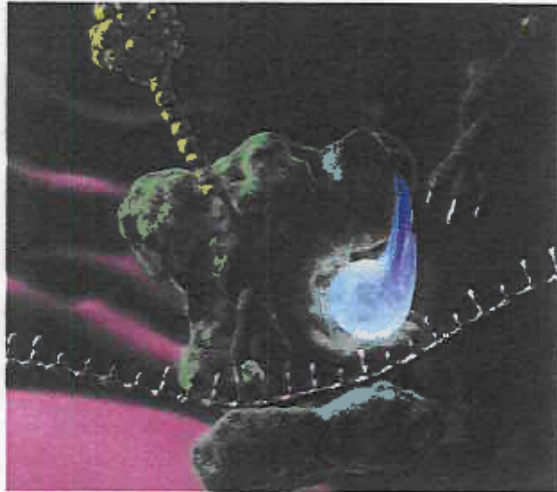
- FDA's complete response letter to company stated that the new drug application would not be approved
 - Major issues included safety concerns regarding an overfilled vial size, a single-small (66 pts) and incomplete efficacy study with 35% of ineligible patients included and low response rates

OMAPRO™ MODE OF ACTION

Protein synthesis is markedly up-regulated in malignant cells and high levels of many 'short lived proteins' (oncoproteins). These oncoproteins promote cell division, suppress apoptosis and are prevalent in many cancer types including CML.

Drugs that can interfere with the manufacture of these 'short-lived' proteins offer a new and unique way of attacking CML, particularly where TKIs have failed to have their desired effect.

OMAPRO™ works by inhibiting protein translation and is particularly active against a number of short lived proteins that are associated with CML, AML and multiple myeloma.



OMAPRO™ binds to the ribosomal A-cleft (shown above), preventing the translation and elongation of short-lived oncoproteins.



GROWING GLOBAL INTEREST IN OMAPRO™

As the positive OMAPRO™ data from clinical trials have become known, the demand for OMAPRO™ under a compassionate use/expanded access or a similar method has increased.

Meeting the needs of patients is a primary concern for ChemGenex, and the establishment of compassionate use access to OMAPRO™ has been a priority. Now established, this process is providing OMAPRO™ access to physicians and their patients around the world.

Under this program, ChemGenex has provided OMAPRO™ to patients from many regions across the globe, including: Australia, North America, South America, Europe and Africa.

"Omacetaxine is a valuable option for the treatment of patients with CML, particularly those in two categories where we do not have any available treatment options. These are patients who have failed at least two prior tyrosine kinase inhibitors and those who have a mutation T315I, since we know that with this mutation none of the available tyrosine kinase inhibitors has activity. These results correspond well with the known activity of this compound in CML."

Dr. Jorge Cortes, MD, Professor of Medicine and Deputy Chair in the Department of Leukemia at The University of Texas, MD Anderson Cancer Center. Cancer Institute

Omapro Untitled Letter

- Promotion of unapproved drug as safe and effective
- Characterization of Omapro data as “positive”
- Demand for Omapro under a compassionate/expanded access
 - No existing US expanded access programs for Omapro

Focalin XR Untitled Letter

- Professional detail aid
- Misleading superiority claims
- Indication
 - For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pts aged 6 years and older....
 - Indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for pts with this syndrome. Drug treatment may not be indicated for all children with this syndrome....
 - Effectiveness for long-term use, i.e., for more than 7 weeks, has not been systemically evaluated....

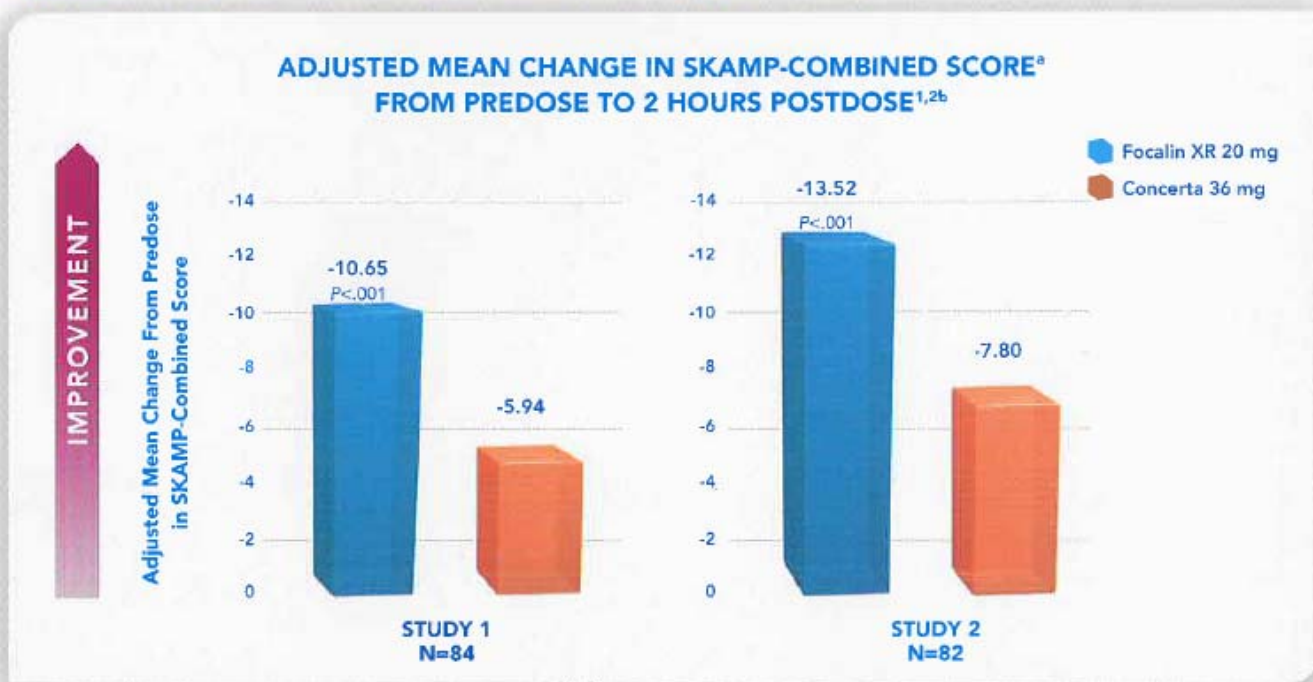
Primary End Point (for both studies)

SKAMP-Combined Score:

- Change from predose in SKAMP-combined score of Focalin XR 20 mg vs Concerta 36 mg at 2 hours postdose in a 12-hour laboratory classroom setting^{1,2}

Primary Efficacy Results

Results from 2 placebo-controlled studies of children aged 6 to 12 years



^aFor patients currently using MPH, the recommended starting dose of Focalin XR is half the total daily dose of racemic MPH. Patients currently using d-MPH immediate-release tablets may be switched to the same daily dose of Focalin XR.⁵

- Focalin XR demonstrated statistically significant superior efficacy versus Concerta 2 hours postdose^{1,2}

Conclusion

- Two well-controlled studies confirmed the superior efficacy of Focalin XR 20 mg versus Concerta 36 mg at 2 hours postdose^{1,2}



Focalin XR Untitled Letter

- Studies do not constitute substantial evidence for these superiority claims
 - Treatment of ADHD consists of symptom relief over an extended period of time (e.g., entire treatment course)
 - Studies only focused on ONE specific time point (2 hours post-dose) as the primary efficacy measure of comparative trials
 - Studies did not account for the products different pharmacokinetic profiles and subsequent efficacy profiles

Focalin XR Untitled Letters

- PK profile of Focalin XR
 - Formulated for biphasic release of drug that produces two distinct concentration peaks
- PK profile of Concerta
 - Formulated to deliver an initial amount of drug by immediate release, followed by gradually ascending concentration of drug over the next 5 to 9 hours
 - May actually provide greater symptom relief from hour nine and beyond

Office of Prescription Drug Promotion

- Office of Prescription Drug Promotion (OPDP) alignment based on functional areas
 - Review functions
 - Policy and support functions
- Office Director (Thomas Abrams)
- Associate Office Director-Review Functions (Mark Askine)
 - Division of Professional Promotion
 - Division of DTC Promotion
- Associate Office Director-Policy and Support Functions (Marci Kiester)
 - Regulatory Counsel Team and Team Leader
 - Social Science Research Team
 - Project Management Team



Office of Prescription Drug Promotion

- Immediate Office
- Division of Professional Promotion
 - Division Director (Catherine Gray)
 - 4 Review Teams and Team Leaders
- Division of DTC Promotion
 - Division Director (Robert Dean)
 - 4 Review Teams and Team Leaders

Web Addresses

- OPDP webpage
 - www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm
- OPDP organization listing
 - www.fda.gov/AboutFDA/CentersOffices/CDER/ucm154886.htm
- Warning and untitled letters
 - www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/default.htm
- Guidances
 - www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064956.htm

OPDP Contact Information

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