

Opioid Risk Management: Current Regulatory Perspectives

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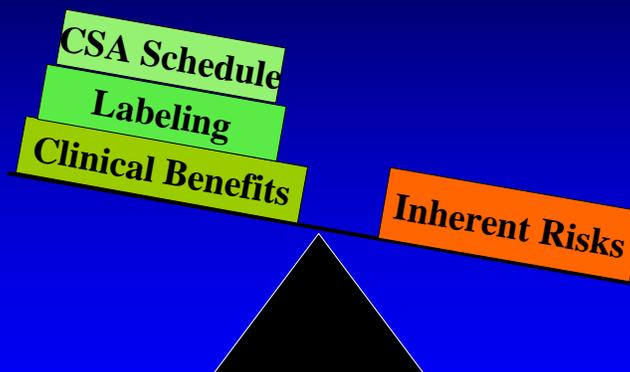
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FDA Mandate

- Public Health Mission
- Safe and Effective Drugs- (safety not absolute)
- Risk-Benefit Calculus
- Risks to Manage
- What are the risks
- Who is at risk



When is Risk Minimization/ Management Considered?



Approaches to Managing Risks Associated with Opioid Products

- Labeling
- Controls imposed under the CSA
- Risk Management Plans (RISK MAPS)

Risk Management for Drug Products

- Components
- Risk Assessment
- Need for specificity

Assessment and specific risks inform the RiskMAP (Risk Minimization Action Plan)

Goals of Opioid Risk Management

- Proper patient selection
- Prevention of accidental overdose, unintended exposure
- Prevention of misuse and abuse by patients
- Prevention of abuse, overdose, diversion



Guidances-Use of Risk Minimization Action Plans

- Three Risk Management Guidances- March 2005
- “RiskMAP” -strategic safety program designed to meet specific goals
- Goals and Tools
- Variety of systems- targeted education, performance-linked access

FDA Guidance Documents

- **Development and Use of Risk Minimization Action Plans**
 - <http://www.fda.gov/cder/guidance/6358fnl.htm>
- **Premarketing Risk Assessment**
 - <http://www.fda.gov/cder/guidance/6357fnl.htm>
- **Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment**
 - <http://www.fda.gov/cder/guidance/6359OCC.htm>

Drug Products with Restricted Distribution/Use Programs

- Isotretinoin (Accutane) - cystic acne
- Clozapine (Clozaril) - schizophrenia
- Trovafloxacin (Trovan) - serious infections
- Fentanyl (Actiq) - breakthrough cancer pain (H)
- Thalidomide (Thalomid)-e. nodosum leprosum (H)
- Dofetilide (Tikosyn) - atrial fibrillation
- Mifepristone (Mifeprex) - term. of pregnancy (H)
- Bosentan (Tracleer) - pulmonary artery HTN (H)

Non-Opioid RMPs

- Case of Clozapine
 - Risk Neutropenia/Pancytopenia
 - Registry- pharmacists, physicians, labs
 - CBC for Rx
- Accutane
 - Risk- teratogen; Objective- avoid pregnancy

Questions and Challenges

- Since March 2005 Tufts Symposium- What has changed?
- Critical questions- Experience since 2001, Outcome measures- RMPS
- Medical Model- Prevention Before Intervention!

Drug Risks and Safety

- Drug safety in general under a “microscope”
- Daily media, Congressional attention
- Dynamic context – IOM report
- Monitoring of controlled drugs, opioids in particular, by other agencies

Emergency Room Visits Climb for Misuse of Prescription and Over-the-Counter Drugs SAMHSA Press Release

March 13, 2007

- Emergency room visits related to the nonmedical use of pharmaceuticals, including prescription and over-the-counter drugs, increased 21 percent from 2004 to 2005, according to the latest estimates from the *Drug Abuse Warning Network, 2005*

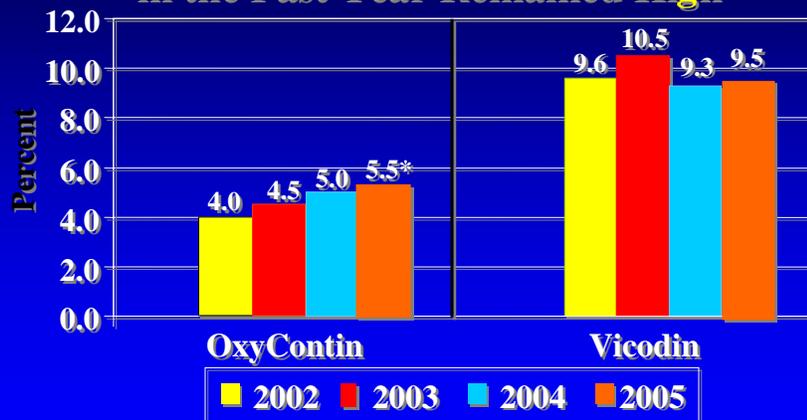
Prescription Drug Abuse, Addiction, Overdose, Death

- Public Health Problem persists and increasing; linear relationship to prescriptions, availability
- National Data- DAWN, NSDUH, TEDS, College Surveys
- Regional Data -Florida, Southwest Virginia (Prescription Monitoring Program-PMP-implemented in 2002)...

2004 Report Virginia Dept of Health- "Accidental deaths due to prescription drug abuse or misuse continues to be a significant public health concern in VA, especially in southwest."

Issues of Concern

Percent of 12th Graders Reporting Nonmedical Use of OxyContin and Vicodin in the Past Year Remained High



No year-to-year differences are statistically significant.

Source: University of Michigan, 2005 Monitoring the Future Study

* Between 2002 and 2005 the abuse of OxyContin by 12th graders increased significantly.

Appalachia- Southwest VA

Dr. Art Van Zee

- 2001

- 2007 reports OxyContin/ Oxycodone problem unchanged – “disastrous”

personal communication- March 23, 2007

High School/ College Informants

“Too many teens get opiates– or at least too many tablets-- for their sports injuries or from their family medicine cabinets....

They know the drugs, have seen the charts in health class or on line, know what they want and where to get it...”

Shifting Landscape



WASHINGTON: The White House Office of National Drug Control Policy (ONDCP)

Mar 15 2007

-has launched a wide-reaching outreach effort to educate Americans on proper disposal techniques for prescription drugs while simultaneously warning of the dangers of abusing "It's the first time we've been able to develop an inter-agency set of guidelines that take into account the challenge of prescription drug abuse and the potential environmental impact of drug disposal," said Jennifer de Vallance, ONDCP press secretary.
- ONDCP has been working with the Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA) on the push. In addition to media outreach, the effort also involves work with organizations the American Pharmacists Association, as well as health insurance providers and hospices, to spread information through their newsletters or membership channels.....
- Later this month, ONDCP will place an open letter in the top 25 newspapers across the country to educate people about the dangers of prescription drug abuse.
- "Our research shows young people as well as adults think abusing prescription drugs is safer than abusing illegal drugs," de Vallance said. "They have a false sense of safety."

ONDCP Guidelines - Proper Disposal of Prescription Drugs

- Federal Guidelines:
- Take unused, unneeded, or expired prescription drugs out of their original containers and throw them in the trash.
- Mixing prescription drugs with an undesirable substance, such as used coffee grounds or kitty litter, and putting them in impermeable, non-descript containers, such as empty cans or sealable bags, will further ensure the drugs are not diverted.
- Flush prescription drugs down the toilet *only* if the label or accompanying patient information specifically instructs doing so.
- Take advantage of community pharmaceutical take-back programs that allow the public to bring unused drugs to a central location for proper disposal. Some communities have pharmaceutical take-back programs or community solid-waste programs that allow the public to bring unused drugs to a central location for proper disposal. Where these exist, they are a good way to dispose of unused pharmaceuticals.
- The FDA advises that the following drugs be flushed down the toilet instead of thrown in the trash:
 - Actiq (fentanyl citrate)
 - Daytrana Transdermal Patch (methylphenidate)
 - Duragesic Transdermal System (fentanyl)
 - OxyContin Tablets (oxycodone)
 - Avinza Capsules (morphine sulfate)
 - Baraclude Tablets (entecavir)
 - Reyataz Capsules (atazanavir sulfate)
 - Tequin Tablets (gatifloxacin)
 - Zerit for Oral Solution (stavudine)
 - Meperidine HCl Tablets
 - Percocet (Oxycodone and Acetaminophen)
 - Xyrem (Sodium Oxybate)
 - Fentora (fentanyl buccal tablet)
- *Note: Patients should always refer to printed material accompanying their medication for specific instructions.*

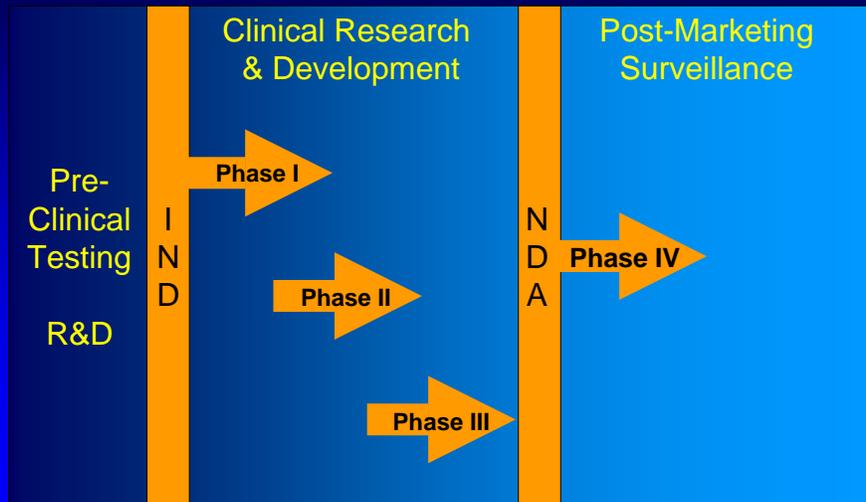
Workshop- Responding to Signals

- Challenges for consideration..
- Medical Model
 - Prevention first (easier!)
 - Diagnosis prior to treatment! (Example- impaired health care provider distinct problem from outdated skills/ overprescribing... distinct from criminal diversion)
- RiskMAP principles– specific goals, tools, outcome metrics



Discussion- Supplemental

Risk Assessment



Surveillance and Evaluation Plan

- Surveillance for overdose, misuse, unintended exposure, addiction
 - AEs monitoring for abuse, misuse, addiction and overdose
 - Surveys
 - Tracking national databases - DAWN, Toxic Exposure Surveillance System (TESS), Rocky Mountain Poison Control Centers
 - Monitoring prescription use and prescribing patterns
- Analyses of goals/objectives/tools

Targeted Education and Outreach Tools

- Health care practitioner (HCP) letters
- Training programs for HCP and patients
- Professional or public notifications
- Continuing education for HCP
- Focused or limited product promotion
- Patient-oriented labeling
 - Medication Guides (Required dispensing with each prescription)
 - Patient Package Insert (PPI)

Opioid RiskMAPs: Tools

- Targeted Education and Outreach
 - To inform
- Reminder Systems
 - To alert, remind, reinforce
- Performance-Linked Access Systems
 - To avoid unsafe use

Performance-Linked Systems

- Also known as Restricted Access System Tools
 - Dispensing limited to pharmacies or practitioners specially certified
 - Patient, physician and/or pharmacy registries
 - Product dispensed to patients with evidence of safe use conditions

Opioid Products with RMPs

- Actiq
- OxyContin and generics
- Avinza
- Subutex/Suboxone
- Ionsys
- Fentora