




Abuse Resistant Opioids

Industry Incentives... Industry Risks

Debra Travers MT (ASCP)
Marketing Director
Endo Pharmaceuticals

10/21/2005 1



Opioids are the mainstay in the treatment of moderate to severe chronic pain

- Long acting opioids used to treat 40 million patients with moderate - severe chronic pain
 - Low back pain (18MM)
 - Cancer pain (2MM)
 - OA pain (18MM)
- Market growth is still >5% in spite of decreased promotional efforts and continued media focus on abuse
- Treatment progression

● Non-opioid	→	Long acting opioids
● PCP	→	Pain Specialist / PMR
● Oncologist	→	Palliative Care
- 55K physicians prescribe almost 100% of the strong long acting opioids
- 42% of prescriptions for long acting opioids are written by PCP's

10/21/2005 2

Why opioids?

- They work
- They are predictable
 - Efficacy
 - Side effects
 - Risk of abuse

10/21/2005

3

Abuse is not a new issue



10/21/2005

4

Abuse is not a new issue...media focus on abuse is new



10/21/2005

5

Abuse Deterrent Opioid Formulations

- The "Holy Grail" for companies developing opioid medications
- The right and responsible thing to do
- More questions than answers at this point

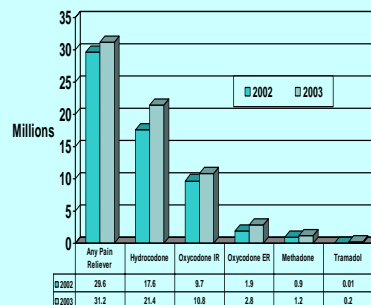
10/21/2005

6

What does industry need to know?

○ How big is the problem (opportunity)?

Self Reported Lifelong Non-Medical Users of Selected Pain Relievers Among Persons Aged 12 or Older (2002 and 2003)



Source: 2003 National Survey on Drug Abuse and Health, Substance Abuse and Mental Health Services Administration
10/21/2005

7

•80-90% of physicians identify abuse as a "big" problem and are careful when prescribing

•20-30% think it is not a problem in their practice and that they "can tell" who will abuse

•Is "fear to prescribe" resulting in under-treatment of patients with painful conditions?

What does industry need to know?

○ What kind of abuse are we trying to deter?

- Addicts with kitchen chemistry knowledge?
- Recreational users who seek an easy high?
- Diverters?
- Chemical copers?
- Pseudo-addicted?
- Physically dependent?
- Accidental misuse?

10/21/2005

8

What does industry need to know?

- **What kid of abuse are we trying to deter?**
 - Addicts with kitchen chemistry knowledge?
 - Recreational users who seek an easy high?
 - Diverters?
 - Chemical copers?
 - Pseudo-addicted?
 - Physically dependent?
 - Accidental misuse?

10/21/2005

9

What does industry need to know?

- **What kind of deterrence?**
 - Aversion?
 - Neutralization (agonist/antagonist)?
 - Mechanical integrity?
 - In-vivo conversion (pro-drug)?
- **How much deterrence is needed?**
 - Ideally, tamper proof
 - More realistically, less than 20-30% of drug released immediately after crushing or dissolution in liquid
 - No compromise in analgesia if taken as directed
- **Level of deterrence needed may differ with audience**

10/21/2005

10

What does industry need to know?

- How quickly can these drugs be developed?
 - Depends on regulatory pathway
 - ANDA vs NDA
 - New formulation vs new chemical entity (NCE)
 - ANDA quicker, but labeling is traditionally same as reference drug
 - NDA takes longer, but may allow differentiation from non-abuse deterrent formulations
 - Comparative PK?
 - Removal of "crushing and chewing" warning from Black Box?
 - "Abuse resistant"?
 - NCE may require preclinical toxicology and carcinogenicity studies


10/21/2005

11

What does industry need to know?

- Who will prescribe abuse deterrent opioids?
 - Pain specialists?
 - Primary care physicians?
- For whom will abuse deterrent opioids be prescribed?

Everyone



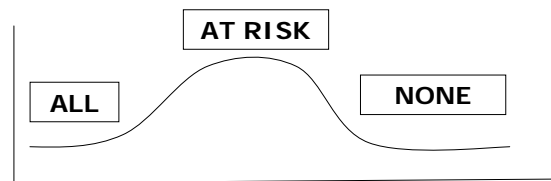
High Risk
- How is high risk determined?
 - Screening tools

10/21/2005

12

What does industry need to know?

- **Who will pay and how much?**
 - Will payors put these drugs on formulary?
 - Tier 1: \$5-10 copay
 - Tier 2: \$15-25 copay
 - Tier 3: \$35-50 copay
 - How much control will be exerted?



10/21/2005

13

What does industry need to know?

- **How will we measure success?**
 - Fewer overdoses, ER visits, deaths?
 - Less diversion and crime?
 - Lower expenditures for addiction treatment?
 - Intangibles
 - Increased productivity?
 - Less burden to society and family?
 - Less "fear to treat" = better pain management

10/21/2005

14



Conclusions

- **Industry still has a lot of unanswered questions**
- **We need to understand limitations of technologies**
- **We need to clarify expectations of patients, physicians, payors and regulators**
- **We need to manage expectations**
- **There are major educational opportunities for industry**

10/21/2005

15