FDA Charge to the Committee: FDA Opioid Action Plan and Incorporating the Broader Public Health Impact into the Formal Risk-Benefit Assessment for Opioids

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The Challenge of Treating Pain

• Chronic pain affects scores of Americans with 20-50% of patients in the primary care setting reporting it and is a disabling condition that can have far-reaching effects on patients’ health, well-being, and function.
  – The economic cost of chronic pain is estimated at $560-$635 billion annually – *2011 IOM report Relieving Pain in America*

• Treatment options for pain generally include the following approaches: pharmacologic, physical medicine, behavioral medicine, neuromodulation, interventional, and surgical.

• Optimal patient outcomes often result from a comprehensive multidisciplinary approach where pharmacologic treatment is not the sole focus.

HOWEVER...
The Challenge of Treating Pain

• Patients experience ongoing barriers to adequate pain management
  – “many related to non-existent or insufficient insurance coverage and reimbursement for evidence- and consensus-based therapies”
    -American Academy of Pain Medicine, 2014

• As a result, treatments have often focused on prescription drugs, mainly opioids, and procedures, at least, in part, because of the reimbursement structure of our healthcare system

THEREFORE...
The Challenge of Treating Pain

• The treatment of pain in the US, particularly chronic pain, is not satisfactory, and the over-reliance on prescription opioids has contributed to widespread unintended consequences

• US experiencing a devastating epidemic of prescription opioid misuse and abuse, including a large number of overdose deaths
Prescriptions for Opioid Analgesics Dispensed by US Retail Pharmacies

The Challenge of Prescription Opioids and Overdose Deaths

Opioid overdoses driving increase in drug overdoses overall

Drug overdose deaths involving opioids, by type of opioid, United States, 2000-2014

Deaths involving any opioid
Natural & semi-synthetic opioids (e.g., oxycodone, hydrocodone)
Heroin
Other synthetic opioids (e.g., fentanyl, tramadol)
Methadone

SOURCE:
www.cdc.gov/drugoverdose
FDA’s Role in the Response to the Opioid Crisis

• FDA serves to:
  – Protect the public health by assuring the safety, efficacy and security of human drugs
  – Advance the public health by helping to speed innovations that make medicines more effective, safer, and more affordable
  – Help the public get the accurate, science-based information they need to use medicines to maintain and improve their health
FDA’s Role in the Response to the Opioid Crisis (con’t.)

• In this capacity, FDA aims to
  – Provide patients in pain access to effective relief
  – Reduce the misuse and abuse of prescription opioids through:
    • Preventing prescription drug abuse
    • Treating opioid addiction
    • Saving lives from opioid overdose
FDA Is Accomplishing These Goals Through the Use of All of Our Available Tools

- Improving the use of opioids through careful and appropriate regulatory activities
- Improving the use of opioids through careful and appropriate policy development
- Improving the treatment of pain through improved science
- Improving the safe use of opioids through communication, partnership and public discussion
Recent FDA Actions in Response to Opioid Crisis

• **Background:**
  – MSContin (morphine ER), the first extended-release/long-acting (ER/LA) opioid, approved in 1987
  – OxyContin (oxycodone ER) approved in 1995

• **2001:** OxyContin labeling changed to add and strengthen warnings for misuse and abuse

• **2003:** Warning letter issued for misleading ads for OxyContin
Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2010
  – Reformulated OxyContin approved
  – Advisory Committee (AC) meeting to discuss proposal for class-wide ER/LA opioid REMS
  – Announced plan to establish the ACTTION public private partnership to improve clinical studies of pain medicines to advance the development of novel, less abusable, safer, and more effective therapies for pain

www.fda.gov
Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2012
  – Scientific workshop to discuss making naloxone available in the community
  – Scientific workshop, in conjunction with NIH, to review the available data on the effectiveness of pain medications to treat chronic non-cancer pain
  – Approval of the Extended-release, Long-acting Opioids REMS (ER/LA REMS) to provide education to prescribers to improve opioid use
Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2013
  – FDA Advisory Committee meeting to discuss the public health benefits and risks of drugs containing hydrocodone
  – Public hearing on the use of opioids in chronic pain
  – OxyContin Actions
    • Approved abuse-deterrent (AD) language for reformulated OxyContin
    • Determined that “old” OxyContin was withdrawn for reasons of safety or effectiveness
Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2013 (cont)
  – Required additional changes to the ER/LA opioid label to change the indications for use and to enhance warnings about risks of abuse
  – Required the conduct of postmarketing studies for ER/LA opioids to improve our understanding of their safety
  – Recommended that the DEA impose new restrictions on the prescription of hydrocodone (‘upscheduling’)

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Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2014
  – Approved Evzio autoinjector, designed to deliver a dose of naloxone outside of a healthcare setting

• 2015
  – Issued final guidance on the development of abuse-deterrent forms of opioids
  – Scientific workshop to initiate a public discussion about issues surrounding the uptake of naloxone
  – Approved Narcan nasal spray, the first FDA-approved nasal spray version of naloxone hydrochloride
Recent FDA Actions in Response to Opioid Crisis (con’t.)

• 2016
  – Issued draft guidance on the development of generic abuse-deterrent opioids
  – Expanded the warnings and safety information for immediate-release opioid labeling
  – FDA Science Board meeting to discuss Agency response to opioid crisis
  – FDA Advisory Committee to discuss the Risk Evaluation and Mitigation Strategy (REMS) Program for ER-LA Opioids and to consider potential changes to improve prescriber education
Summary of Recent Drug Approvals Aimed at Addressing the Opioid Crisis

- FDA has approved 6 opioids with features likely to reduce their abuse
  - Numerous INDs for ADFs under development
- FDA has approved Probuphine, the first buprenorphine implant for the maintenance treatment of opioid dependence
- FDA has approved 2 naloxone products to expand the availability and use of naloxone to prevent overdose deaths
  - Evzio – autoinjector
  - Narcan nasal spray – first approved intranasal naloxone product
Recent FDA Action in Response to Opioid Crisis: FDA Action Plan (February 4, 2016)

• “In response to the opioid abuse epidemic, today Dr. Robert Califf, the FDA’s Deputy Commissioner for Medical Products and Tobacco, along with other FDA leaders, called for a far-reaching action plan to reassess the agency’s approach to opioid medications. The plan will focus on policies aimed at reversing the epidemic, while still providing patients in pain access to effective relief.”

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm484765.htm
FDA Opioids Action Plan

• Expand use of advisory committees and outside engagement
• Develop warnings and safety information for IR opioid labeling
• Strengthen postmarket requirements to get needed real-world data
• Consider updates to the Risk Evaluation and Mitigation Strategy (REMS) Program for ER-LA Opioids
• Expand access to abuse-deterrent formulations (ADFs) to discourage abuse
• Support better treatment for opioid substance use disorder and to prevent opioid overdose deaths
• Reassess the risk-benefit approval framework for opioid use to reflect the public health impact of opioids
Charge to the Committee

• The science and data needed to inform best practices to address pain while preventing opioid misuse and abuse are often lacking

• Because of the ongoing opioid overdose epidemic and the issues surrounding inadequate pain management in America and in light of the numerous regulatory activities FDA is already undertaking to address the opioid overdose epidemic, FDA is commissioning NASEM to conduct a study
  – To update the state of the science regarding prescription opioid abuse and misuse
  – To provide an update from the 2011 IOM report *Relieving Pain in America*, including the further evolving role of opioids
  – To make recommendations on the options available to FDA to address the prescription opioid overdose epidemic, from both the individual and public health perspectives
Charge to the Committee

• Of these tasks, it will be critical to understand the additional actions FDA can take to address the opioid epidemic in America

• Among the areas of focus, FDA is, in particular, seeking input on
  – How to formally incorporate the broader public health impact of opioid abuse in future FDA approval decisions regarding opioids
  – The public health consequences of any actions we take or could take with regard to opioid misuse, abuse, overdose, and death
Summary

• FDA is using all available tools to address prescription opioid abuse while assuring availability of appropriate treatments for pain:
  – Enormous level of activity across FDA
  – We are focusing on regulatory actions, policy development, improved science, and stronger communication and collaboration

• FDA is one of many groups with important roles to play.

• The NASEM study is one critical part of our commitment to seeking outside input on the best actions for us to consider.
Conclusion

• FDA will act within its authorities in support of our public health mission to help defeat the epidemic of opioid abuse through a science-based and continuously evolving approach. Our aim is to make a difference in the lives of the many people who are struggling under the weight of this terrible crisis.
Thank you
Statement of Task

• Provide an update on the state of the science of pain research, care, and education since the 2011 IOM report and characterize the evolving role of opioid analgesics in pain management.

• Review the available evidence on best practices with regard to safe and effective pain management, including practices to reduce opioid abuse and misuse, including an assessment of possible barriers to implementation of those best practices by prescribers and patients.
Statement of Task

• Characterize the epidemiology of prescription opioid abuse and misuse, to include an assessment with regard to patient characteristics (such as indication, acute versus chronic pain; formulation, immediate-release versus extended-release; duration of use; and dose) and approaches to address the problem (such as approval of abuse-deterrent opioids, FDA communication strategies, prescription drug monitoring programs, and state or local policies) and review the available evidence on differences in pain experiences and treatment effectiveness across subpopulations.
Statement of Task

• Given the state of the available data, the Committee should identify additional actions FDA and others should consider now, with a particular focus on those actions the FDA can undertake, to balance the needs of pain patients and the need to address opioid misuse and abuse.

• FDA actions to be taken as a part of development, review and approval, and safe use of pain medicines, could include:
Statement of Task

- Development of a formal method to incorporate the broader public health impact of opioid abuse in future FDA approval decisions regarding opioid;
- The development of non-opioid pain medicines to treat severe pain;
- The development of abuse-deterrent opioids;
- The incorporation of prevention strategies into safe opioid prescribing, including modification of the standard opioid indication statements;
- The development of medicines for medication assisted treatment for patients with opioid use disorder;
- The development of medicines to treat opioid overdose;
- The education of prescribers and patients about safe use of pain medications;
- The education of prescribers and patients about appropriate medication storage and disposal;
- Actions by prescribers, professional societies, and government agencies (local, state, and federal)