FDA Goals for the Committee on Evidence-Based Opioids Prescribing for Acute Pain

National Academies of Science, Engineering, and Medicine
February 4, 2019

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Misuse and Abuse of Rx Opioids Remains an Important Public Health Problem

• In 2017, prescription opioids were the largest category of pharmaceutical products misused and abused in US
  – 11.1 million people estimated to have past-year misuse/abuse
  – 1.7 million people estimated with DSM IV criteria for substance use disorder involving prescription opioid analgesics

• In comparison, 886,000 estimated to have past-year heroin use

Consequences: Prescription Opioids and Overdose Death in the US

Drugs Involved in U.S. Overdose Deaths, 1999 to 2017

Figure Source: National Institute on Drug Abuse  Data Source: CDC Wonder
Crisis Ongoing Despite Falling # of Prescriptions for Opioid Analgesics

*Immediate-Release formulations include oral solids, oral liquids, rectal, nasal, and transmucosal

**Extended-Release/Long-Acting formulations include oral solids and transdermal patches

Note: Include opioid analgesics only, excluding injectable formulations as well as opioid-containing cough-cold products and opioid-containing medication-assisted treatment (MAT) products
The FDA and Opioid Abuse/Misuse

"Unquestionably, our greatest immediate challenge is the problem of opioid abuse. This is a public health crisis of staggering human and economic proportion ... we have an important role to play in reducing the rate of new abuse and in giving healthcare providers the tools to reduce exposure to opioids to only clearly appropriate patients, so we can also help reduce the new cases of addiction."

- Scott Gottlieb, FDA Commissioner
  Address to FDA staff, May 15, 2017
The Opioid Crisis: FDA’s Priorities

1. Decreasing Exposure & Prevent New Addiction
2. Supporting the Treatment of Those With Opioid Use Disorder
3. Fostering the Development of Novel Pain Treatment Therapies
4. Improving Enforcement & Assessing Benefit-Risk
The Opioid Crisis: FDA’s Priorities & Strategies

1. Decreasing Exposure & Prevent New Addiction
   - Appropriate Dose/Duration Labeling
   - Appropriate Packaging, Storage, and Disposal
   - Health Care Provider Education

2. Supporting the Treatment of Those With Opioid Use Disorder
   - Naloxone
   - Medication Assisted Treatment (MAT)

3. Fostering the Development of Novel Pain Treatment Therapies
   - Partnerships & Meetings
   - Abuse Deterrent Formulations (ADFs)
   - Pain Treatment Alternatives

4. Improving Enforcement & Assessing Benefit-Risk
   - Improving Enforcement
   - Assessing Benefit-Risk
Improved Opioid Prescribing: Priorities Align with Recently Passed SUPPORT Act

- Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT)

- Many new provisions affecting FDA including tools to:
  - Reduce exposure to opioids as a way to lower the rate of new addiction
  - Require certain packaging, such as unit dose blister packs, for opioids and other drugs that pose a risk of abuse or overdose
  - Require that opioids be dispensed with a mail-back pouch or other safe disposal option
  - Stop illegal, illicit, unapproved, counterfeit and potentially dangerous drugs more efficiently from entering the U.S. through the IMFs
The Need to Improve Opioid Prescribing

• Excess numbers of opioids being prescribed for acute pain
• Potential consequences of excess opioids
Opioid Analgesic Needs Vary by Condition/Procedure--Unused Opioids Common

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mean/ (range) tablets filled</th>
<th>Mean/Median tablets used</th>
<th>~Days Used</th>
<th>~Leftover tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient Shoulder Surgery</td>
<td>60 (n.d.)*</td>
<td>37*</td>
<td>9-10</td>
<td>23</td>
</tr>
<tr>
<td>Cesarean Delivery</td>
<td>40 (5-80)*</td>
<td>20*</td>
<td>4-5</td>
<td>20</td>
</tr>
<tr>
<td>Tooth Extraction</td>
<td>28 (n.d.)</td>
<td>13</td>
<td>2-3</td>
<td>15</td>
</tr>
<tr>
<td>Upper Extremity Surgery</td>
<td>30 (n.d.)</td>
<td>14 (Bone); 9 (Soft Tissue)</td>
<td>2-3</td>
<td>15</td>
</tr>
<tr>
<td>Laparoscopic Cholecystectomy</td>
<td>30 (0-100)</td>
<td>10-12</td>
<td>2-3</td>
<td>20</td>
</tr>
<tr>
<td>Laparoscopic Appendectomy</td>
<td>30 (n.d.)*</td>
<td>12*</td>
<td>2-3</td>
<td>18</td>
</tr>
<tr>
<td>Partial Mastectomy with Node Biopsy</td>
<td>23 (0-60)</td>
<td>6</td>
<td>1-2</td>
<td>17</td>
</tr>
<tr>
<td>Laparoscopic Inguinal Hernia Repair</td>
<td>33 (15-70)</td>
<td>9</td>
<td>1-2</td>
<td>24</td>
</tr>
<tr>
<td>Open Inguinal Hernia Repair</td>
<td>30 (15-120)</td>
<td>9</td>
<td>1-2</td>
<td>21</td>
</tr>
<tr>
<td>Partial Mastectomy</td>
<td>21 (0-50)</td>
<td>3</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>Dermatologic Surgery</td>
<td>9 (3-20)</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

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6. Kumar, et al. AJSM, 2017

www.fda.gov
Leftover Opioid Analgesics Reported in Post-surgical Populations

Across many surgical procedures,
- >50% of patients reported excess supply of opioid analgesics after treatment of acute pain
- Many patients kept excess supply and stored supply in unsecured locations


*percentage of patients reporting use of 15 tablets or fewer
Opioid Analgesics in the Home Can Feed Other Problems

- Non-Secure Storage
- Lack of Disposal

Excess Supply after Treatment of Acute Pain

Available Supply → Third Party Access
Misuse and Related Outcomes → Accidental Exposure

www.fda.gov
FDA Response: Support Rational Opioid Prescribing

- Continue work to provide educational tools to prescribers through Continuing Medical Education
- Explore packaging solutions
  - Utility of a defined, short-term supply of medication packaged in a manner that limits the number of pills dispensed
  - Utility of packaging that could make it easier to track the number of doses that have been taken or reduce the risk for third-party access, such as teens ingesting pills they found in a medicine cabinet
- Support the development of objective, evidence-based guidelines for use of opioids in acute pain
Rational Prescribing for the Condition/Procedure

• “[FDA is] also taking new steps to encourage medical professional societies to develop evidence-based guidelines on appropriate prescribing of opioids for different medical indications. The FDA will be working with these important stakeholders to help advance the development of these new, evidence-based prescribing recommendations.”¹

• FDA has contracted with National Academies of Sciences, Engineering, and Medicine to develop evidence-based guidelines for opioid analgesics for acute pain specific to conditions or procedures²

¹. FDA Statement by FDA Commissioner Scott Gottlieb, M.D., on balancing access to appropriate treatment for patients with chronic and end-of-life pain with need to take steps to stem misuse and abuse of opioids. July 9, 2018. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612779.htm
². FDA Statement August 22, 2018: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm617908.htm
Tasks for the Committee

• Identify the best available evidence for prescribers and provide a framework for its evaluation

• Support more appropriate prescribing of opioids while ensuring that patients with pain are adequately treated

• Support development of new evidence where needed for clear, rigorous, evidence-based guidelines
Statement of Work: Framework Development

• Develop a framework for evaluating the evidence base underpinning clinical treatment guidelines for opioid prescribing for acute pain
  – Develop a threshold level of evidence needed to support such guidelines

• Consider standards established in the 2011 IOM Report *Clinical Practice Guidelines We Can Trust* and other established standards for clinical assessment
Statement of Work: Assess Current State of Data on Prescribing

• Inventory surgical and medical conditions associated with acute pain where opioids are used
  – Assess available information on dose and duration of opioid use by indication, including existing opioid prescribing guidelines for acute pain conditions
  – Apply evidence framework

• Identify and prioritize acute pain conditions where rigorous evidence is needed to inform prescribing guidelines
Sources of Data

Focus is on data quality and applicability not on the source
Evaluating Data Quality/Study Methods

Data Quality
• Procedures to ensure completeness, consistency, and accuracy of data collection and management;
• Frequency and type of error corrections or changes in data adjudication policies during the relevant period of data collection;
• Changes in key data elements during the study time frame and any potential effect on the study; and
• Report on missing data over time

Study Methods
• Study design, including comparator groups;
• Study population and time period of study, including:
  o Study time frame and scheduled milestones
  o Data sources used;
  o Drug exposures of interest;
  o Drug safety outcomes of interest;
  o Methods to control for sources of bias and confounding
Statement of Work: Research Agenda

• Develop a prioritized research agenda for
  – Work to develop new treatment-specific treatment guidelines
  – Work to support additional rigorous evidence to expand on existing guidelines
  – Agenda should include a minimum of 5 conditions for indications that are abuse-prone and/or commonly prescribed
Summary

• FDA goal is to improve the state of the science supporting clinical practice guidelines for acute pain
  – Creating a framework for evidence generation and assessment
  – Inventorying existing treatment of acute pain and available evidence on opioid use
  – Creating a research agenda for prioritizing future work
• This framework can then be used to improve the prescribing of opioids while ensuring that patients with acute pain are adequately treated
FDA is Seeking NASEM Help to Support Rational Opioid Prescribing for Acute Pain

Be evidence-driven

If the evidence doesn’t exist, work to get it
Thank You