Regulatory Approaches for Prescription to OTC Switch

Theresa M. Michele, M.D.
Director, Division of Nonprescription Drug Products
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (FDA)
July 2, 2015
Disclaimer

- In these presentations I am relaying personal views and opinion. These presentations are not intended to convey official US FDA policy, and no official support or endorsement by the US FDA is provided or should be inferred.

- The materials presented are available in the public domain.

- I do not have any financial interest or conflict of interest with any pharmaceutical company.
Outline

• Differences between prescription and OTC drugs
• Development program for Rx to OTC switch products
• Nonprescription Safe Use Regulatory Expansion (NSURE)
When is a Drug Considered a Prescription Drug Product?

- **FD&C Act**: A drug is regulated as a prescription drug product if it is not safe for use except under supervision of a practitioner licensed to administer the drug because of
  - Toxicity or other potentially harmful effects
  - Method of use
  - Collateral measures necessary for use
OTC Drug Products

OTC drug products generally have these characteristics:

• Can be adequately labeled such that
  – The consumer can self-diagnose, self-treat, and self-manage the condition being treated
  – No health practitioner is needed for the safe and effective use of the product

• Drug has low potential for misuse and abuse

• Safety margin is such that the benefits of OTC availability outweigh the risks
Development Program for Rx to OTC Switch

- Often relies on safety and efficacy established for the prescription product
- New studies may be required if proposing a new indication or a new patient population
- Need to “translate” key elements of the prescription label into consumer-friendly terms
- Consumer studies needed to evaluate the “OTC-ness” of product
- Issues to be addressed identified from prescription label and clinical use of product
Issues from Rx Naloxone Label

- **Diagnosis** of opioid overdose
- **Use** by caretaker or family member
- **Seek emergency medical care** immediately after use ➔ **duration** of naloxone effect shorter than duration of opioid effect
- **Additional doses** may be necessary
Issues from Rx Naloxone Label (cont.)

- Correct dosing, use of device
- Precipitation of severe opioid withdrawal
- Need to monitor for cardiovascular effects
- Limited efficacy with partial or mixed agonists
- Contraindicated if naloxone allergy
OTC Consumer Studies

**Label Comprehension Study**
- Understanding the key label message

**Self-Selection Study**
- Choosing the right product

**Actual Use Study**
- Using according to labeled directions

**Human Factors Study**
- Interacting with the product
# Issues Addressed by Consumer Studies

<table>
<thead>
<tr>
<th>Issue(s)</th>
<th>Label Comprehension</th>
<th>Self Selection</th>
<th>Actual Use</th>
<th>Human Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=300-600</td>
<td>N=400-800</td>
<td>N=500-1300</td>
<td>N=50-200</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Correct Use</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Seek Emergency care/ Duration</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>More than 1 dose</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Correct Dose/ Device Use</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor CV effect</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy limits</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Note: X indicates the issue was addressed in the respective category.*
Regulatory Pathway for Rx to OTC Switch

• New Drug Application (NDA or sNDA)
• Sponsors strongly encouraged to request milestone meetings with FDA during OTC development
  – Pre-IND
  – End of Phase 2
  – Pre-NDA
• Review timelines: Standard 10 months
Who Can Request an OTC switch?

• The holder of an approved prescription NDA
  – Must provide full data to support the switch

• Other parties
  – can request an OTC switch through a citizen petition (under 21 CFR section 10.30)
  – must provide full data to support the switch
  – cannot just submit a CP requesting the switch action, without any data to support the switch

• FDA does not conduct studies to support Rx to OTC switches
What Dosage Forms are Suitable for OTC Switch?

- Any approved dosage form is a possible switch candidate
- Sponsor must provide adequate data to support that consumers can correctly administer the drug by following the directions
- If there are unique attributes for administration of the drug, the sponsor must develop and test a user-friendly format for the labeling/packaging
Duration of Rx Marketing Before OTC Switch?

- Product typically marketed for several years before a switch is considered.
- Prescription use provides data on
  - Intrinsic factors: drug specific adverse events
  - Extrinsic factors: understanding of self-selection, directions for use, and self-administration
- Naloxone marketed for many years → good understanding of adverse event profile.
- A strong consumer program could aid with extrinsic factors for a specific dosage form.
Current Challenges for OTC Switch

- Consumers must base purchasing decision on information in Drug Facts label (DFL)
- Under current regulations, it is difficult for FDA to consider other means of improving safe and effective use

Image found at http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143551.htm
Nonprescription Safe Use Regulatory Expansion (NSURE)

Objectives:

• Alleviate the undertreatment of common conditions or diseases by using innovative technologies or other conditions of safe use to expand which drug products can be considered nonprescription

• Explore regulatory approaches that allow for the expansion of the nonprescription drug market

FDA, with public and stakeholder input, is working on a practical regulatory framework for the NSURE concept.
Could NSURE Apply to OTC Naloxone?

- New prepurchase technologies to increase likelihood of correct self-selection
- New prepurchase technologies to educate purchasers on when and how to use naloxone
- Other new methods of pre- or post- purchase education
- New self-administration technologies to increase likelihood of correct use
- Other innovative approaches outside label
- DNDP is open to discussions with sponsors
Summary

• Prescription to OTC switch pathways available
• OTC products must demonstrate that a consumer can correctly self-diagnose, self-treat, and self-manage the condition without the intervention of a health care professional
• NSURE initiative could expand potential for novel switch products
• DNDP encourages sponsors to discuss potential naloxone switch programs with the division
• Cooperative effort with industry and other stakeholders needed
Contact Information

• For questions regarding OTC drugs
  Division of Nonprescription Drug Products
  Food and Drug Administration
  10903 New Hampshire Ave.
  Building 22, Room 5491
  Silver Spring, MD 20993-0002
  240-402-4246
  Division Phone: 301-796-2080

• Please e-mail any questions concerning NSURE to the Office of Medical Policy at:
  CDER-OMP-DMPP@fda.hhs.gov
Additional Information

• **Label Comprehension Study Guidance**
  

• **Self-Selection Study Guidance**
  