Regulatory Approaches for Prescription to OTC Switch

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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

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

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

Drug Facts

Active ingredient (in each tablet) — **Purpose**
Chlorpheniramine maleate 2 mg ..... Antihistamine

Uses temporarily relieves these symptoms due to hay fever or other upper respiratory allergies:
- sneezing
- runny nose
- itchy, watery eyes
- itchy throat

Warnings

Ask a doctor before use if you have
- glaucoma
- a breathing problem such as emphysema or chronic bronchitis
- trouble urinating due to an enlarged prostate gland

Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives

When using this product
- You may get drowsy
- avoid alcoholic drinks
- alcohol, sedatives, and tranquilizers may increase drowsiness
- be careful when driving a motor vehicle or operating machinery
- excitability may occur, especially in children

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years	ask a doctor

Other information store at 20-25° C (68-77° F) ■ protect from excessive moisture

Inactive ingredients D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch

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

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  Silver Spring, MD 20993-0002

  240-402-4246

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- 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**

  http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM143834.pdf

- **Self-Selection Study Guidance**

  http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM272122.pdf