Enhance Switch Plan — Comparison of Standards and Strategies
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Agenda

• Types of Rx to OTC Switches and development strategies
  – Types of Switches
  – Pros & Cons
  – Formulating Switch Strategy
    • Pathology, Molecule, Target population, Risk: Benefit, Unmet Need, HA partnerships

• Examine causes of recent successful and not so successful U.S. switch attempts
  – Zegerid OTC®,
  – Oxytrol® For Women
  – Singulair® Allergy
  – Nasacort® Allergy 24 hr.

• Creating a full proof dossier (clinical sections) to optimize current or future switch plans
  – Safety
  – Efficacy
  – Clinical Overview (Risk benefit Summary)

• Summary
Why Switch is exciting?

- The availability of OTC medicines provides $102 billion in value to the U.S. healthcare system annually.*
- Each dollar spent on OTC medicines saves $6-7 for the U.S. healthcare system.*
- 240 million people in the U.S. currently use OTC medicines — 60 million of them would not seek alternative (e.g., Rx) treatment if OTC medicines were not available.*

Switch creates value for:
- Patients, Payers (including Gov.), Providers, Pharma & Public Health

1: Types of Rx to OTC Switches and development strategies
Types of switches

**Category Switches**

• (E.g. US-Oxytrol for Women in 2013 for Overactive Bladder)

**Switch in existing OTC category** (New molecule or existing molecule)

• (E.g. US - Allegra for Allergic Rhinitis in 2011)
Pros & Cons: Category Switch

• Pros
  First mover advantage
  Probability of 3 year exclusivity

• Cons
  Costly filing (may include various SS, AUS and AdCom meeting)
  Lower probability of success in first attempt
## Pros & Cons: Switch in Existing category

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<tr>
<th><strong>Pros</strong></th>
<th><strong>Cons</strong></th>
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<tr>
<td>Less costly</td>
<td>No first mover advantage</td>
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<tr>
<td>Higher probability of success</td>
<td>Lesser probability of 3 year exclusivity</td>
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Formulating Switch Strategy

**Drug selection phase**
- Pathology
- Differential
- Efficacy
- Unmet need
- Safety
- Drug characteristics

**Development Phase**
- Effective label
- HA Partnership
- Safety Package
- LC, SS and AUS
- AdCom prep

**Launch phase**
- Differential characteristics
- Educational campaigns
- HCP training
- Safety experience
- LCM

In scope
Pathology / Disease Selection

• Things to consider:
  – Acute vs. Chronic Indications
    • Occasional vs. chronic constipation
  – Mild vs. Severe Indications
    • Asthma vs. allergic rhinitis
  – Symptoms
    • Self identifiable
    • Could be described in simple words to general public
      – E.g.: Asthma vs. wet/dry cough
  – Differential diagnosis
    • Possibilities of delayed diagnosis of other similar diseases and quantify harm in case of missed/delayed diagnosis
Molecule Selection

– Route of administration
  • Regulatory and consumer preferences
  • Oral, Topical
  • Efficacy and safety profile (Topical vs. Oral Oxybutynin)

– Safety profile
  • Well established safety profile
  • Ample post marketing experience (not must but preferred)

– Effects on PK and Safety in special populations
  • Pediatric
  • Pregnancy
  • Hepatic & Renal Pts…
Target population: Segmentation of patients

- **Sex:** M, F
  - Oxytrol® For Women (OTC) vs. Oxytrol (Rx)
    - Oxytrol for Women (OTC): ‘Do not use if you are male. Your symptoms may be due to a more serious condition’.*

- **Age:** Adult only, Adults + Peds…

- **Race:** Any specific effects to consider
  - Omeprazole:
    - Asian people are slow-metabolizers’ of omeprazole compared to Caucasians (15% vs. 3%) = AUC ~ 4-fold increase in Asian patients =
      - Safety assessment
      - Dose adjustment

Risk : benefit ratio

Benefits
- Reduced Healthcare costs
- Better access to effective treatment
- Fast lead time for treatment
- Treatment for less severe pathologies

Risks
- Wrong self selection
- Adverse reaction events
- Delayed diagnosis of other condition
- Possibility of harm due to No HCP
Understanding unmet need
Public health {not economic} argument

• QoL quantification
• Outcome based rationale
• Utilization of public health system
• Early treatment vs. missed opportunities
• Currently available OTC options and current unmet need in OTC arena
Partnering with Regulators (Health Authorities)
Bottom-line

- Two main types of Switches:
  - Category
  - Switch in existing category
- Switch strategy and preparation depends on type of switch
- Create dedicated resources or switch teams
  - Medical, Reg., R&D, Commercial
- Partner with HA’s early and effectively
2. Examine causes of recent successful and failed U.S. switches
ZEGERID OTC®
Switching Same molecule in existing OTC category

• Brand name:
  – ZEGERID OTC™ (omeprazole 20 mg/sodium bicarbonate 1100 mg capsules)

• Sponsor Company:
  – Schering-Plough Consumer HealthCare Products, Inc.

• Approved Indication:
  – Frequent Heartburn Relief

• Type of Switch:
  – Existing molecule within well established category of ‘Frequent Heartburn’

• Switch Characteristics
  – BE route due to existing OTC Omeprazole products but could not promote incremental value of carbonate
  – Easier navigation as FDA already believes that consumer can self manage ‘Frequent Heartburn’
  – Market launch as not a first mover to the market

Oxytrol® For Women
An example of Category switch

- Brand name:
  - OXYTROL FOR WOMEN (oxybutynin transdermal system, 3.9 mg/day)

- Sponsor Company:
  - Schering-Plough Consumer HealthCare Products, Inc.

- Approved Indication:
  - Overactive bladder in women

- Type of Switch:
  - Category Switch
  - Three years of exclusivity starting Jan 2013
  - Partial switch (Oxytrol remain Rx for OAB for Men)

- Switch Characteristics
  - Market launch as first mover to the market
  - Oxytrol For Women addresses an important unmet need for overactive bladder, or OAB, a condition that affects more than 20 million American women.
  - Other market followers could be: Detrol® (Tolterodine Tartrate), DITROPAN® (Oxybutynin chloride)

AdCom material located at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/ucm380890.htm> Accessed March 2015
Singulair Allergy®
Switching a new molecule in existing OTC category

- Proposed Brand name:
  - SINGULAIR Allergy® (montelukast sodium)

- Sponsor Company:
  - Merck Consumer Care

- Proposed Indication:
  - treatment of allergy symptoms for adults 18 years and older

- Type of Switch:
  - new molecule within well established category of ‘Allergic Rhinitis’

- Switch Characteristics
  - Different safety profile than multiple existing anti histamine allergic rhinitis OTC products
  - Multiple approved Rx indication: asthma, exercise induced bronchoconstriction (EIB), seasonal allergic rhinitis (SAR), and perennial allergic rhinitis (PAR)

AdCom material located at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/ucm380890.htm> Accessed march 2015
Nasacort® Allergy 24HR (triamcinolone acetonide) nasal spray

• AdCom: July 31, 2013

• Requested indications:
  – For the treatment of seasonal and perennial allergic rhinitis (SAR and PAR); for the temporary relief of hay fever and other respiratory allergies (nasal congestion, runny nose, sneezing, itchy nose)

• Proposed age indication:
  – 2 years and up

• AdCom Voting Question:
  – Is the risk/benefit profile of triamcinolone acetonide nasal spray supportive of OTC use for temporary relief of symptoms of hay fever or other respiratory allergies for ages 2 years and above?

• Vote results: __________________
Nasacort® Allergy 24HR (triamcinolone acetonide) nasal spray: Primary Safety Topics

Summary Primary Safety Topics

- Local effects
  - candida nasal infections
  - epistaxis
- Nasal perforation
- Ocular effects
- Systemic effects
  - Immunosuppression / worsening of infections
  - HPA axis suppression
  - Growth velocity...slowing of growth.....how to consider
Nasacort® Allergy 24HR (triamcinolone acetonide) nasal spray: Primary Safety Topics

Conclusions

- The sponsor’s postmarketing safety evaluation was adequately designed and analyzed
- No apparent delayed diagnoses of serious medical conditions (e.g., diabetes, severe infections)
- Trial and postmarketing data indicates that application site reactions (nasal) are most common, but mostly non-serious
- No new safety signals in the postmarket safety review
  - Nasal septal perforation, ocular effects and growth topic need effective labeling
- *Potential risks are manageable with proper use and labeling*
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• Vote results:
  – 10 yes, 6 no, 2 abstain, and zero not voting.

http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/ucm358284.htm
Bottom-line

- Focus on Risk Benefit ratio
- Partner with HA’s early and effectively
  - Understanding your customer
- Develop tailor-made strategies
  - Same switch in a different country is different
3. Creating a quality dossier (clinical sections) to optimize current or future switch plans
Efficacy Sections (Modules 5 and 2)

• Focused and brief approach
• Focus on areas of interest and indication pursued
  – Section 5.3.5.1: Actual Use study
  – Section 5.3.5.3: Integrated Summary of Efficacy and Consumer Behavior
    • Integrated Summary of Efficacy
    • Consumer Behavior
  – Section: 5.3.5.4: Label comprehension and Self Selection studies
• Cross reference to original NDA sections
• Form a basis for Clinical Overview section
• Develop to local Regulatory Guideline
Safety Sections (Modules 5 and 2)

- Phase 1-4
- Focus on Phase III and Phase IV
- Serious AEs
- Discontinuations

- HA discussion
- Comprehensive analysis needed
- Post marketing commitment
- Signal detection

- Internal Safety
- External Safety
- FAERS
- VigiBASE
- AAPCC
- DAWN
- Literature

- Safety experience in controlled trials
- Post marketing safety experience
- Areas of special safety interest
- AEs (on PI) not captured in DFL

- List
- Rationale
- Analysis of potential harm
Clinical Overview

• Biopharmaceutics summary
• Clinical Pharmacology
• Efficacy
• Overview of Safety
• **Summary of OTC Program: LC, SS and AUS**
• Benefits and Risks Assessment
• Conclusions
Summary

• Types of Switches and Pros & Cons of each
• Formulating switch strategy and focus areas
• Examined approach taken in four recent US switches
• Discussed creating a good quality dossier (clinical sections) for optimizing your current or future switch plans
Summary

- Types of Rx to OTC Switches and development strategies
  - Types of Switches
  - Individual Strategy
  - Each has a different value proposition

- Examine causes of recent successful and not so successful U.S. switch attempts
  - Molecule Selection: Safety & Efficacy profile of molecule
  - Target population: Segmentation of patients
  - Risk : benefit of selected molecule and selected indication/s
  - Understanding unmet need: (Public health {not economic} argument)
  - Preparation for dossiers:
  - Partnering with HAs

- Creating a full proof dossier (clinical sections) to optimize current or future switch plans
  - Safety
  - Efficacy
  - Clinical Overview (Risk benefit Summary)
Acknowledgement

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  – Schering Plough Consumer Healthcare
  – Merck Consumer Care
  – Novartis Consumer Care
Questions?