Recommendations for Bupropion SR

Presented by Cooney/Waters

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- Weight loss category irrational, noisy, consumer-driven
- Lots of risk, lots of upside
- Multi-disciplinary influentials, treaters
- Legacy of Redux, Phen-Fen: Distrust
- "Pill Mills" unrestrained; mail order pharmacies
- Media will gun for anything that smacks of sensationalism
- No immediate pipeline products: Leptin four to five years out
“I’ve heard people say ‘I’d rather die thin; at least I’ll look good in my coffin’,” Dr. Susan Yanovsky, NIDDK (CNN, 1/99)

“I said ‘You could die from heart disease’ and she said ‘I want it anyway’” obesity specialist to patient wanting fen-phen after recall (New York Times, 9/97)
How do People Lose Weight?

- Exercise: health clubs, home equipment/videos, sports
- Diet Foods: frozen meals, sugar substitutes, fat-free snacks, liquid diets
- Weight loss programs
  - Medically supervised – Duke Diet and Fitness Center
  - Commercial – Weight Watchers, Jenny Craig, etc.
- Diet books, videos
- Medications: OTC, Rx
How do People Lose Weight?

Expenditures for Weight Loss 1995 = $33 Billion

- Artificial Sweeteners
- Diet Soft Drinks
- Diet Books/Videos
- Diet Foods
- Weight Loss Programs
- Medications
Public Perceptions about Weight Loss

- Will try many approaches
- Often a lifetime struggle
- Consumers frustrated by weight loss efforts
- Look for quick fix – not lifestyle change, enormous drop-out rate
- Give up upon failure to lose quickly or upon reaching goal weight
- Newly skeptical about new Rx treatments, not rushing to doctors
- Meridia (sibutramine) / Knoll Pharmaceuticals
  - "Failed Antidepressant"; Appetite suppressant (CNS active)
  - Modest weight loss with hypocaloric diet + serious consequences (increased blood pressure and pulse: co-morbidities of obesity)
  - Poor uptake; <8,000 Rx in 1st month
  - DTC advertising
  - Patient compliance program "Point of Change"
  - Pre-marketing: publicized survey on fattest cities in America through Coalition for Excessive Weight Risk Education, chaired by F. Xavier Pi-Sunyer
- Xenical (orlistat) / Hoffmann LaRoche
  - Not absorbed, works outside body
  - Perceived as safe, but with "cosmetic" GI side effects
  - 96,000 Rx in 1st month; anticipate $1 billion in sales
  - Slower than anticipated uptake due to new skepticism and perceived unpleasant side effects
  - Patient compliance program "XeniCare"
  - Xen-Phen combo started
• Redux (dexfenfluramine) / American Home Products, Interneuron
  – Pulled after 1-1/2 years due to PPH
  – ~83,000 Rx/week; 2.3 million Rx from 6/96-2/97 -- despite refill rate of 35%
  – Move to return for compassionate use?
The Rise and Fall of Redux and Fen-Phen

- Market is wide open -- no new diet drugs introduced for more than 20 years
- Interneuron promotes dexfenfluramine as the "magic bullet"
  - Stories on European experience, U.S. clinical trials appear after 1993 NDA filing
  - Company emphasizes efficacy, downplays adverse effects
- Redux rises to the top, but marketing partner AHP minimizes warnings, exaggerates efficacy
The Rise and Fall of Redux and Fen-Phen

- Campaign in fall 1996:
  - National book tour for Dr. Sheldon Levine, author of "The Redux Revolution," calling Redux "the most important weight-loss discovery of the century"
  - Market research study declaring "Primary Care Physicians Embrace Redux to Help Fight Obesity" released to media
  - Gallup Survey on diabetes and obesity generates greater awareness of Redux
The Rise and Fall of Redux and Fen-Phen

- Sales rise and so does criticism
- Growth of "pill mills"
- PPH reports downplayed by AHP; issues releases minimizing NEJM and JAMA
- Controversy rages for a year
- AHP, four days before withdrawal from market, still defending product
Communications Objective:

- Create buzz about Bupropion SR as potential weight loss therapy
Communications Strategy

- Signal Bupropion SR as a player in weight loss by being in the venues and on the agendas of the people who are arbiters in this category
Short Term Positioning:

- Bupropion SR, a licensed product, is being studied as a potential agent for weight loss
- Bupropion SR has been used in millions of people for depression and smoking cessation
Long-term Positioning

- Bupropion SR provides a one-two punch against the two most important public health problems in the world – smoking and obesity

- Bupropion SR is the first drug that comes into the obesity control arena with a wealth of safety information in a diverse population

- There’s been a huge clinical experience with Bupropion SR involving millions of people
Bupropion SR Issues

- Potential for unrestrained prescribing by "pill mills" and cosmetic use
- Perception of seizure risk
- Misuse by bulimics and anorexics
- Dosage and duration of therapy not yet known
- Negative image of weight loss products could tarnish existing indications
- Risk of formulary / reimbursement restrictions due to off-label use
- Need to properly position Bradley Bupropion SR/Phen trial
• Clarity on bulimia/anorexia seizure risk to maintain credibility with medical community

• No hype

• Credible data from credible docs/institutions

• Perception that GW is attempting to restrain inappropriate "pill mill" use
Future Development Issues

- Single-center studies have limited credibility – Need multi-center, universal protocols with name players

- Current PI is not major player, but comes from credible institution

- Need to attempt to define mechanism of action in weight loss
  - Differentiate from SSRIs among non-psychiatry obesity experts
  - Increase comfort vis a vis CNS/seizure risk among psychiatrists and PCs familiar with Bupropion SR
Future Development Issues

- Study with and without behavior modification
- Include diverse population in studies
  - Women/men
  - Patients with co-morbidities
  - Minorities, especially African-American and Hispanic
  - Morbidly obese, obese and overweight populations
- Studies to be conducted with Wellbutrin SR or Zyban?
- Role of Duke
- Will challenge any new option
- Pipeline products included in most stories, regardless of story angle (pro vs. con)
- No "wonder drug" headlines in major/national media; position meds as a tool to support diet and exercise
- Always include skeptic's perspective
- Local media hype more frequent
- Often include patient testimonials: extreme success and drop-outs/horror stories
Multidisciplinary:

- Endocrinologists
- Behavior Modification Specialists
- Psychiatrists
- Exercise Physiologists
- Supportive: dietitians, nutritionists, nurses

- Nutrition Specialists
- Cardiologists
- Bariatricians
- Primary Care
Thought Leaders

- Jules Hirsch, Rockefeller University
- Rudy Leibel, Rockefeller University (microbiologist, nutrition)
- F. Xavier Pi-Sunyer, Columbia Presbyterian/St. Lukes Roosevelt
- Ken Polansky, University of Chicago (diabetes – as comorbidity)
- James Sowers, Wayne State (endocrinology and hypertension)
- Albert Stunkard, University of Pennsylvania (behavior modification)
- George Bray, Pennington Biomedical Institute
- Robert Atkinson, University of Wisconsin
- William Dietz, CDC Division of Nutrition and Physical Activity (pediatrics, gastroenterology, nutrition)
Top Institutions

- **Tier 1:**
  - Pennington Biomedical Institute
  - Columbia University
  - Rockefeller University
  - Harvard University

- **Tier 2:**
  - University of Pennsylvania
  - University of Chicago
  - University of Michigan
  - UCLA
  - Baylor College of Medicine
  - University of Colorado HSC

- **Key Weight Loss Treatment Centers**
  - Duke University
  - Baylor College of Medicine
  - University of Colorado HSC
Key Journals

• Tier 1:
  – NEJM
  – JAMA
  – Annals of Internal Medicine
  – The Lancet
  – Science
  – Nature

• Tier 2:
  – Journal of Endocrinology and Metabolism
  – Obesity Research
  – American Journal of Clinical Nutrition
  – Proceedings of the National Academy of Sciences
Influential Organizations

- Tier 1:
  - NAASO
  - Endocrine Society

- Tier 2:
  - American Association of Clinical Endocrinology
  - American Obesity Association
  - American Diabetes Association
Influential Consumer/Government Groups

- Shape Up America! (Dr. Koop)
- NIH Task Force on Obesity
- NIH Weight Information Network
- CSPI
- Council on Size and Weight Discrimination
Communication Options

• Data Publicity
  – NAASO. AAFP? The Lancet? Zyban & Weight Loss?
  – One-on-one reporter background briefings
  – Distribution of published studies
  – B-roll with animation
  – Satellite media tour
Communication Options

- Obesity Meeting Circuit
  - With or without data presentations
  - Bupropion SR researcher networking
  - Press room staffing: backgroundering, researcher/reporter meetings
Communication Options

- Multi-Center Trial Support Program
  - National and grassroots publicity for clinical trial accrual
    - Coordinate with investigator institutions
    - Message Development/Media Training
    - Press release, fact sheet on weight loss and Gadde data
    - Local radio and print ads/PSA scripts
    - B-roll
    - Slide kits for local talks by CI: weight loss support groups, community health fair, etc.
  - Business press publicity
Communication Options

- Brief constituency groups about current study and multi-center trial plans
  - North American Association for the Study of Obesity
  - American Obesity Association
  - American Psychiatric Association
  - American Heart Association
  - American Diabetic Association
  - American Dietetic Association
  - Shape Up America!
  - Others
Communication Options

- Media briefing: "Beyond Serotonin: The Role of Neurotransmitters in Weight, Depression and Smoking"
  - Experts such as Drs. Linda Ferry, Kisshore Gadde, and James Pradko
  - Review failed use of serotonin (Prozac) in weight loss
  - Review mechanism of action of Rx treatment for smoking cessation
  - Differences between serotonin, norepinephrine and dopamine in the treatment of depression
  - Third party sponsor
Communication Options

- Desk-side briefings
  - Health magazines
  - Women’s magazines
  - Weight loss newsletters
Communication Options

- Internet
  - Health e-zine backgrounding
  - Live chats
  - Moderated forums
  - Bulletin board postings
  - News group postings
- Analyst briefing
  - Bupropion SR
Crisis Plan

- Prepare for adverse events
  - Immediate response
  - Know messages
  - Identify Allies