

Recommendations
for
Bupropion SR

Presented by Cooney/Waters

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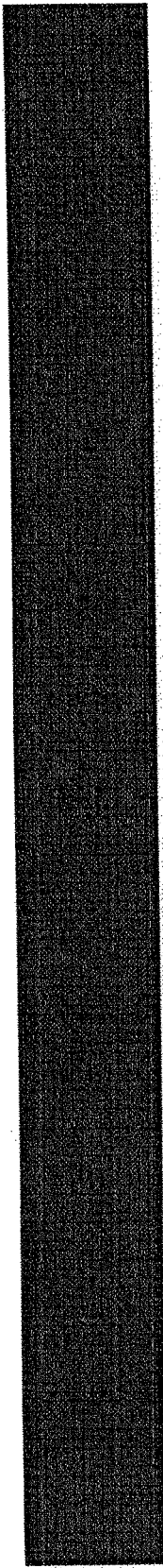
CWR 9235

GTP123-2900

Situation

- 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

CWG 9236



“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)

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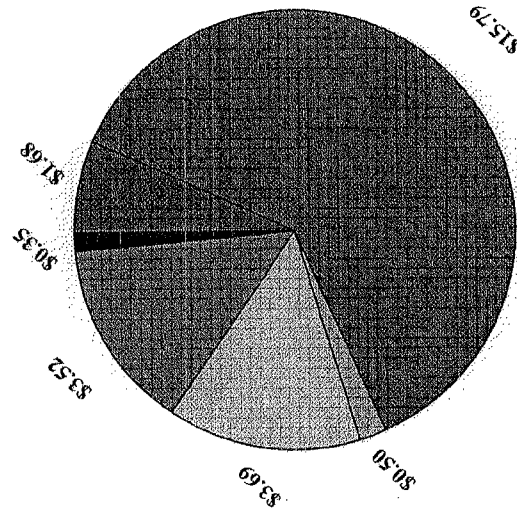
How do People Lose Weight?

- 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

CWR 9238

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

CWQ 9239

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

CWR 9240
1-11-02

Rx Products

- 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

CW4 9241

Rx Products

- 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

CWR 9242

Rx Products

- 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?

cu 9243

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

CWR

9244

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

CWR 9245

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

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Communications Objective

- Create buzz about Bupropion SR as potential weight loss therapy

CWQ 9247

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

CWR 9248

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

CWR 9249

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

CWR 9250

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

RWB 9 25/

Bupropion SR Communications Needs

- 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

CW 9252

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

CWG 9253

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

CWR 9254

Media

- 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

CWR 9255

Treaters

- Multidisciplinary:
 - Endocrinologists
 - Behavior Modification Specialists
 - Psychiatrists
 - Exercise Physiologists
 - Nutrition Specialists
 - Cardiologists
 - Bariatricians
 - Primary Care
- Supportive: dietitians, nutritionists, nurses

CWG 9256

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)

CWP 9257

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

CWQ 9258

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

CWR 9259

Influential Organizations

- Tier 1:
 - NAASO
 - Endocrine Society
- Tier 2:
 - American Association of Clinical Endocrinology
 - American Obesity Association
 - American Diabetes Association

CWG 9260

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

PWQ 9261

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

PWR 9262

Communication Options

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

CW 9263

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

PCR 9264

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

CWA 9265

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

CWR 9266

Communication Options

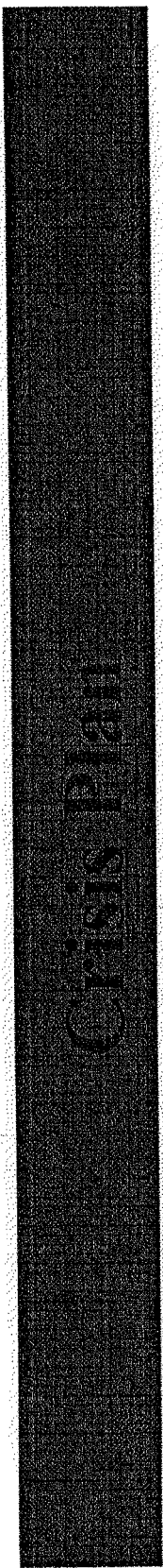
- Desk-side briefings
 - Key reporters: USA Today, CNN, New York Times, Washington Post, AP
 - Health magazines
 - Women's magazines
 - Weight loss newsletters

CWQ 9267

Communication Options

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

CWR 9268



Crisis Plan

- Prepare for adverse events
 - Immediate response
 - Know messages
 - Identify Allies
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CW4 9269