Zypraxa - Weight Change
Scientific Facts

• All antipsychotics and mood stabilizers cause weight gain
  - Zypraxa causes more than other agents (except clozapine)

• Average weight gain over 3 years: 15 lbs. (risperidone average weight gain: ~ 8 lbs.)

• 70% of patients gain no more than 22 lbs. (10kg)

• Weight gain plateaus by 9 months

• Patients with low baseline weight and good response gain the most weight
Zyprexa - Hyperglycemia and Diabetes
Scientific Facts

• Schizophrenia and bipolar are associated with much greater rates of diabetes mellitus (DM) than general population

• Hyperglycemia and DM are associated with all antipsychotics - issue raised as early as 1950's with thorazine

• Obesity is major contributor to developing DM

• Since Zyprexa (and all other APD) cause weight gain, these drugs may indirectly contribute to DM

• No evidence directly links Zyprexa and DM

• In over 3.5 million exposures, 323 spontaneous case reports
Hyperglycemia Verbatim

"Lilly takes hyperglycemia that occurs while a patient is on a Lilly drug extremely seriously. The potential causal association between antipsychotic treatment and hyperglycemia has been a concern since the 1950's. In our clinical trials containing 4189 olanzapine-treated people, Zyprexa has not been directly linked to hyperglycemia. As of September 30th, 1999, with 3 years of marketing experience in 3.7 million people, 323 cases of hyperglycemia or related events have reported."
Zyprexa and Hyperglycemia
Actions

**Short Term**
- Verbatim - 2/1/00
- Updated medical letter 2/1/00
- Manuscript - submitted 2/1/00
- Scientific review - clinical trials and global spontaneous events data sets - completed
  - update label
  - customer communication
- Rapid Response Team

**Medium Term**
- Insulin clamp study
  - interim analysis Q2-00
- Other clinical trials Q2-00
  - glucose, HgA1c
Olanzapine versus Risperidone
Competitive Analysis and Product Attributes

Olanzapine superior to risperidone
• better maintenance of long-term response ⇒ long-term cost advantages
• more "dramatic" responders
• no dose-related EPS - brand dosing flexibility
• no prolactin increase (risperidone has highest of all antipsychotics)
• better for severely ill patients
• better for depressive symptoms
• better for negative symptoms
• clear anti-manic properties

Risperidone superior to olanzapine
• less weight gain

Risperidone equal to olanzapine
• positive symptoms
Efficacy - Offensive Strategy
Competitor Vulnerabilities

**Risperdal**
- TD
- EPS - dose dependent
- narrow dosing range
- prolactin (highest of all APDs)
- maintenance of response < Zyprexa
  - TOTAL costs > Zyprexa
- weight gain (> neuroleptics)
- depression/negative symptoms < Zyprexa

**Zeldox**
- QTc ? Dose dependent
- BID dosing - Take with food
- ? Efficacy - particularly in middle doses
- SAIM - injection site pain, nausea,? QTc risk