

Zyprexa - Weight Change

Scientific Facts

- All antipsychotics and mood stabilizers cause weight gain
 - Zyprexa 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 thiorazine
- 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 \Rightarrow 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