

Issues Management Planning

Weight Gain

The Lilly logo is written in a black, cursive script font.

Answers That Matter.

Weight Gain

• Issue

- Weight gain remains the #1 liability of Zyprexa and is leading to many of the new issues surrounding the drug (ie. diabetes, lipids, etc.)
- Zyprexa is not chosen approximately **33%** and discontinued approximately **26%** of the time due to concerns about weight gain. (HOWEVER, Consistency is the best way to describe the weight gain issue as these numbers have not changed since 1999, including through the launch of Geodon).

• Our Position

- Weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers. For most patients, this can be managed allowing them to receive the overwhelming benefits Zyprexa offers.

• Evidence for Position

- Body weight changes are associated with all antipsychotic medications as a class.
- **Clozapine:** The safety and efficacy of olanzapine were compared to clozapine in a double-blind study in treatment resistant patients. At the end of the 18 week study, there was no statistically significant difference in weight change between olanzapine-treated patients (1.8 kg increase) compared with clozapine-treated patients (2.3 kg increase)[20].
- **Risperidone:** Tran et al[10] compared the safety and efficacy of olanzapine and risperidone in 339 patients over 28 weeks. Both treatment groups experienced statistically significant weight gain from baseline to endpoint ($p < 0.001$). Comparison across treatment groups revealed a statistically significantly ($p = 0.015$) greater weight gain associated with olanzapine (4.1 kg) compared with risperidone (2.3 kg). However, the clinical significance of this difference is questionable given the relatively small (1.8 kg) absolute difference over 28 weeks.

• Rational for Position

- To minimize the liability of weight gain while at the same time increasing focus on Zyprexa's superior efficacy.

Weight Gain

- **Marketplace Feedback**

- Only 50% of MDs feel weight gain is manageable for Zyrpexa verse 87% for Risperdal and Seroquel and 92% for Geodon.
- 82% of MDs said that discussions with patients on behavioral interventions only work somewhat well or not at all well.
- "It is laughable when Lilly comes in and tries to talk about weight gain."
- "Weight gain will be a threat to psychiatrists just like TD."
- "It (Zyprexa) is an effective drug but the side effects outweigh the benefits."
- "I am more excited about the Risperdal than Zyprexa depot because of weight gain and diabetes." (group then makes fun of diet and exercise solutions provided by Lilly)

- **Customers Needs**

- MDs continue to look for solutions to the weight gain problem.
- MDs would like solutions for weight loss more so than weight prevention.

Weight Gain

- **What we Know**

- MDs associate the risk of weight gain more often with Zyprexa than any other medication.
- Overweight patients are avoided for a trial on Zyprexa.
- MDs continue to look for solutions to the problem.
- When MDs mention using less Zyprexa, it is almost always in relation to weight gain.
- Weight gain talked about as a SE of Zyprexa
- Weight gain begins to be linked to the possible cause of hyperglycemia.
- Weight gain and hyperglycemia are directly linked in MDs minds.
- Weight gain is now linked (or in the process of being linked) to hyperglycemia/diabetes, hyperlipidemia, cardiovascular disease and compliance.

- **What we Don't Know**

- Why do only 50% of MDs feel weight gain is manageable on Zyprexa verse 87% for Risperdal and Seroquel and 92% of Geodon?
- Do the solutions we provide actually change MDs writing habits?
- Knowing that weight loss programs only work approximately 5% of the time in normal volunteers, does Lilly want to provide a program where if it doesn't work, may be looked at as another "laughable attempt?" Or, should we be offering MDs the already well established guidelines from the National Institutes of Health on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults?

Weight Gain

- **Key Verbatims**

- With Zyprexa, average weight gain is 14.74 lbs (3-year data) and trends towards a plateau after approximately 9 months. Over-weight or obese patients gain the least weight 26% of patients either lose weight or gain no weight. 70% of patients gain less than 22 lbs.
- Decreasing the dose of Zyprexa does not impact weight gain (though it may negatively affect clinical response).
- Appetite increase and good clinical response are early predictors of weight gain. As the patient's level of functioning and well-being starts to improve, doctors/carers can consider advice on healthy living, diet and moderate exercise.
- Patients with low BMI to begin with tend to gain the most amount of weight.
- Weight gain as a side effect of Zyprexa is prominent given that this drug is relatively free of other side effects and should not be a common reason to deny patients the overwhelming benefits Zyprexa offers (efficacy, relapse prevention etc).
- Not all patients can be Zyprexa patients. Those that gain excessive weight and have low response to Zyprexa may do better on an alternative drug.

Weight Gain

• Desired Evolution

| Action Steps | Desired Outcome | Responsibility | Timing |
|---|--|---------------------------------|-------------------------------------|
| • Developing 'final' overall story on weight and related metabolic issues | • Ability to show how the metabolic issues with Zyprexa are linked and that they are predictable and manageable. | • Tony Fiola & Cassie Mehlman. | • Q1, 2002 |
| • More research on what benefit will be obtained from 'Lilly owned' wellness program. | • Understanding if money spent on developing and implementing program will have any ROI | • ReJana Garon & Jay Cronin. | • Q2, 2002 |
| • Shifting of focus back to Zyprexa's benefits and away from metabolic issues. | • Higher sales through focusing on benefits (improving patients lives), not features (weight gain). | • Both Product and Brand Teams. | • Q1, 2002 (if not already started) |

11/29/2001
File name/location

Issues Management Planning Company Confidential
Copyright © 2000 Eli Lilly and Company

6