FILE: DIABETES

U.S. Zyprexa Issues Pre-Read
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Issues Management

Competitor-fueled intensity regarding Zyprexa and alleged links to diabetes and serious metabolic concerns has been steadily escalating over the past two years. In the past four months, we witnessed a marked increase in competitor energy and investment on this issue, culminating in the recent move into the lay press (Raleigh, NC) with an article and editorial critical of Zyprexa and advocating the FDA add a warning to the Zyprexa label. These efforts to frame the drug choice discussion around safety rather than efficacy are now impacting not only the physician prescribing choice but also our efforts to secure equal status and unrestricted access.

While according to Brand Equity data weight gain remains Zyprexa's greatest liability, market research indicates a trend that psychiatrists are more likely (vs. two years ago) to discontinue Zyprexa, or avoid it altogether, based on diabetes concerns. However, it is important to note that Zyprexa share of market has increased during that same period. It is critical to maintain a proper balance in managing these challenges.

Clinically, the data appear non-conclusive – in part because of the issue's complexity, and in part due to the motivation of those funding the research. Lilly's response on this front has been to design and conduct high quality studies that provide a basis for a rational discussion of risk and drug differential. These studies include hyperglycemic and euglycemic clamp studies, a substantial epidemiology database reviews and a review of treatment emergent diabetes. Most of these are not yet published, which has provided competition with an opportunity to make allegations that place the burden of proof on Zyprexa. The competition is utilizing spontaneous case reports to support their claims regarding relative prevalence rates, and continue to speculate to customers about the possibility of FDA action on Zyprexa (they predict a black box warning) and the resultant liability for prescribers, specifically pointing to lawyer websites soliciting Zyprexa patients.

It has long been reported that the population of patients with schizophrenia is 2-4 times more likely to develop diabetes than the general population - this was first established prior to the advent of neuroleptic medication. Further, as we've studied epidemiology and performed gold standard clamp studies, we believe that all atypical antipsychotics are associated with hyperglycemia and emergent diabetes at rates that are comparable. John Buse, M.D., Ph.D., a diabetes expert and director of the University of North Carolina Diabetes Care Center, was quoted in *Psychiatric News*: "If there is a difference between these drugs, I at this point couldn't tell you which of the drugs has the greatest diabetes risk – other than clozapine. But the difference between the one with the greatest risk and the one with the least risk is small in comparison to the absolute risk of developing diabetes that is associated simply with having a severe psychiatric illness."

On the commercial front, our message has been that "Zyprexa patients may develop diabetes but do so at rates that are comparable to patients on other agents." While we believe that the science is supportive, we have indications that this argument alone does not completely solve the clinician's problem, which is dealing with the amount of co-morbidity of diabetes and mental illness (without the training or, sometimes, inclination to do so). The Zyprexa Product Team recently updated the product position to stress the importance of offering diabetes solutions to customers, and we are updating our message verbatims to reflect this as well as to more specifically quantify both absolute and relative risk and address the role of weight gain in the risk for diabetes.

Our strategy is to elevate the discussion above "good drug, bad drug" to provide answers that matter without compromising on the role of efficacy in treating patients with schizophrenia and

bipolar disorder. To that end, we are rolling out several initiatives which build on the science of our message and more directly address clinician realities. These include:

- Sales rep resources, including a new DVD for use with customers which standardizes the message around population risk, criteria for drug choice and how manage or prevent diabetes;
- Solutions for Wellness: Personalized Program, a structured program which enhances adherence by addressing a patient's fitness and nutrition;
- A customer hotline that will address prescriber questions;
- Mobilization of trained Certified Diabetes Educators who can offer a variety of treatment strategies and wellness advice;
- Partnerships with third-party organizations, such as the ADA and the Joslin Center, to establish consensus guidelines and publications;
- Publication of an advertorial which will serve as platform for our message;
- Coordinated public relations activity designed to bring attention to the population at risk and Lilly's leadership behavior;
- Increased ability to respond to media hot spots;
- Increased DTP / CME activity, as well as an infusion of Peer-to-Peer programming;
- Strengthening of our list of thought leader support, both in psychiatry and diabetology.

In addition, we will opportunistically pursue forums with investors, thought leaders, publications and other key influencers to ensure that we are viewed as accessible, transparent and passionate about patient outcomes.

We will measure our efforts via Brand Equity (maintain low relevance on this issue; increase competitor association; increase corporate equity scores on committed, collaborative leadership), customer attitudes (decrease discontinuation and avoidance), and brand performance (achieve or exceed plan in 2002 and beyond).