

Full Stories:

INTEGRATING WEIGHT GAIN INTO THE BRAND PROMISE

The ZYPREXA brand has many positive attributes. For physicians, ZYPREXA means offering proven benefits in the treatment and management of acute bipolar mania and schizophrenia. It means offering a dependable medication with rapid and robust system control, the flexibility to treat a variety of symptoms of bipolar mania and schizophrenia, and a predictable safety profile. For many patients, ZYPREXA can mean the ability to reach their full potential.

The ZYPREXA brand also carries with it a reputation for causing fear of weight gain and diabetes in the minds of our customers. Physicians' perceptions of weight gain and increased risk of diabetes are often linked.

Physicians believe weight gain is the key issue for ZYPREXA, and, they think if you can address weight gain it may reduce the risk of diabetes and other health-related consequences. They are looking for tools to address weight gain that will enable them to continue to use ZYPREXA due to its efficacy. According to Michael W. Magdycz, RPh, manager, ZYPREXA marketplace management, "it's time for a fundamental change."

Magdycz believes a major change in tone and approach is required (empathetic with conviction) to restore confidence in our ability to realistically help our physicians handle these concerns. Weight gain will no longer be handled as an objection. Instead, weight gain will be discussed up front, and integrated into the brand promise. The brand will soon begin to reflect this shift:

Where we were...

- Weight gain is manageable
- Weight gain is predictable
- Weight gain is not the only predictor of diabetes
- Comparable rates of incidence of diabetes across all products
- Diabetes is mainly a patient population issue
- Handling diabetes and weight gain as an objection

Where we are going...

- Lilly understands the challenges physicians face in treating this population
- Lilly acknowledges weight gain challenges
- Lilly is providing physicians with options to address weight gain in their patients
- Third parties provide physicians with the facts related to diabetes
- Lilly is providing help regarding how to assess, counsel, and refer patients at risk for diabetes

As the new brand direction begins to take shape, the approach will see both a significant investment and senior management commitment to actions, beginning in the third quarter of 2003 and throughout 2004. Watch for more details on the new brand direction in upcoming issues.

For more information, contact Michael Magdycz at magdycz_michael_w@lilly.com.

AFFILIATES WORLDWIDE PREPARE TO LAUNCH THE MUCH ANTICIPATED RAPID ACTING INTRAMUSCULAR FORMULATION OF ZYPREXA

As early as January of 2004, ZYPREXA sales forces in many countries worldwide will be calling on their customers to announce the arrival of the much anticipated Rapid Acting Intramuscular (RAIM) formulation of ZYPREXA. Although the launch date for the US is still to be determined, Lilly was able to contract with a third-party supplier, [Redacted] to supply the rest of the world with staggered launches throughout the first quarter of next year. Congratulations to the hard working people in manufacturing, regulatory, packaging, and multiple other functions to finally make this launch a reality.

RAIM represents an option for our customers to help bring order and stability to the lives of those who suffer from agitation associated with schizophrenia, mania or dementia and brings our brand one step closer to realizing our goal of [Redacted] With RAIM ZYPREXA, physicians can now start their patients with agitation on RAIM and continue their patients with schizophrenia or acute bipolar mania on oral ZYPREXA if clinically indicated.

Critical to the success of the RAIM will be positioning the new formulation within the context of the ZYPREXA brand, not as the launch of a new product independent of ZYPREXA. Doing so will have multiple benefits. First, the established equity of ZYPREXA will fuel uptake of the RAIM. Second, RAIM will have a positive impact on the ZYPREXA brand image. Finally, promotion of RAIM in the context of ZYPREXA will help facilitate the transition of patients from RAIM to the tablet form of ZYPREXA if clinically indicated. The Global Marketing Team has recently distributed a CD-ROM to affiliates globally to support the launch of the new formulation. This CD-ROM is the first in a chain of communications regarding the launch that will be made available to affiliates. The RAIM Launch Center is a new Web site that has been created on the ZYPREXA Infonet (RICK LUNA-PLEASE LINK TO SITE), and additional communications regarding sales training, updated slide sets, and global/regional customer program agendas will follow. Affiliate participation will be critical as we actively seek out and share launch plans and best practices in order to realize the maximum value to the brand.

FDA TO REQUIRE DIABETES WARNING ON CLASS OF SCHIZOPHRENIA DRUGS

The Wall Street Journal
18 September 2003

By Thomas M. Burton

The Food and Drug Administration plans to require a warning label about diabetes risk for the entire class of new schizophrenia drugs, including Eli Lilly & Co.'s Zyprexa and Johnson & Johnson's Risperdal.

In a letter to the leading manufacturers of schizophrenia drugs, the FDA said it isn't certain that any of the drugs actually cause diabetes, noting that there is a "possibility of an increased background risk of diabetes" in schizophrenia patients. Nevertheless, wrote Russell Katz, director of the FDA's division of neuropharmacological drugs, "increased attention to the signs and symptoms of diabetes mellitus may lead to earlier detection and appropriate treatment."

Dr. Katz said the federal agency plans to require the labeling change for "all atypical antipsychotics," as the new top-selling schizophrenia medications are known.

Some competitors have sought to portray Zyprexa as uniquely a culprit in a small number of cases of diabetes among the millions of schizophrenia sufferers. Over an eight-year period, the FDA had received reports that 288 U.S. Zyprexa patients had indeed developed diabetes, and 23 of them died, compared with 132 cases and five deaths with the No. 2 drug, Risperdal.

[Redacted]

"This action is more of a boon to Lilly because the competition has often pointed to Zyprexa as being the causal agent for hyperglycemic events" such as diabetes, said Tony Butler, medical analyst at Lehman Brothers.

A recent study of more than 19,000 schizophrenia patients among U.S. military veterans found that Zyprexa, Risperdal and Seroquel were linked to an elevated risk of diabetes, as compared with patients on older drugs such as haloperidol. Because fewer patients were on Seroquel, the Seroquel data fell slightly short of being considered statistically significant.

Several of the class of drugs, while overall causing fewer side effects than the older medicines, are known to cause weight gain, which can contribute to the development of diabetes. It is far from certain, however, that any of the atypical antipsychotics actually is causing this illness. There is considerable evidence that diabetes occurs at a high rate among schizophrenics to begin with, and diabetes is increasing in the entire U.S. population -- issues that the FDA addressed.

"Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population," the FDA's Dr. Katz wrote.

A recent study at the State University of New York at Buffalo, focusing on the schizophrenia-diabetes connection among 592 mental patients at a New York state psychiatric hospital during the 1940s, concluded, "An association between schizophrenia and bipolar disorder and metabolic disturbances seems to exist independent of antipsychotic use."

The newer study of military veterans with schizophrenia found that Risperdal, Seroquel and Zyprexa all were linked to roughly a 50% increase in the incidence of diabetes compared with patients who took older antipsychotics such as haloperidol. The companies all say there isn't any evidence that their drugs actually cause the disease. William M. Glazer, associate clinical psychiatry professor at Harvard Medical School, points out that many patients take the newer drugs because older ones didn't work for them -- and that thus the two patient groups are inherently different.

Bristol-Myers Squibb Co.'s antipsychotic called Abilify is too new to have been included in the veterans study, and a Bristol-Myers spokeswoman said of the FDA letter, "We are reviewing all our options."

Overall, wrote Dr. Katz, "epidemiological studies suggest an increased risk" with the newer drugs, but current information is "insufficient to provide reliable estimates of differences" among the drugs.

Related Information:

DVD: "MEDICAL PERSPECTIVE ON ATYPICAL ANTIPSYCHOTICS AND DIABETES"

In June of this year, Dr. Alan Breier, chief medical officer and vice president, medical, published an open letter that addressed the question whether there is an increased risk of diabetes in patients treated with ZYPREXA or other atypical antipsychotics. Since that time, two important events – the Cunningham VA study and the FDA notification of class labeling – have clarified this important subject. In an 11-minute DVD, Dr. Breier shares his thoughts regarding those events and what they mean to patients and clinicians. His take-home point is that diabetes should not be the sole reason to choose one atypical over another. To receive a copy of the DVD, contact Gu Bin, associate marketing consultant, at 317-277-6483.

WEBCAST REPLAYS AVAILABLE

Complete Wellness – The Whole Person Treatment Approach

A recent webcast panel of mental health experts highlighted the importance of paying greater attention to the physical needs of patients with severe and persistent mental illness (SPMI) to help them reduce the risk of health problems. To replay the webcast, visit:

<http://www.completewellnessapproach.com/media.html>.

Clinical Perspectives on Diabetes and Psychiatric Illness

In a second webcast, view the discussion on the prevalence of diabetes within the US – specific emphasis is given to individuals with chronic psychiatric illness. Additional discussion points include risk factors for diabetes and identifying strategies for monitoring and treating possible metabolic or glucose abnormalities in patients with SPMI. To replay this webcast, visit: <http://www.optimaed.com/index.php> (replay available from 10/15/03-4/15/03).

LILLY PRESS RELEASE...EUROPEAN COMMISSION APPROVES ZYPREXA FOR THE PREVENTION OF RECURRENCE OF BIPOLAR DISORDER

First Atypical Antipsychotic Indicated for Treatment of Bipolar Mania Now Authorized as Mood Stabilizing Medication

Indianapolis, October 29, 2003 –The European Commission has approved ZYPREXA (olanzapine) for the prevention of recurrence of bipolar disorder for patients whose manic episode has responded to ZYPREXA treatment, Eli Lilly and Company (NYSE: LLY) announced today. ZYPREXA is the first atypical antipsychotic to be authorized as an antimanic and mood stabilizing drug for preventing relapse into manic, mixed manic or depressive episodes associated with bipolar disorder.

ZYPREXA was approved by the European Union (EU) in June 2002 as a monotherapy for the short-term treatment of acute manic episodes associated with bipolar disorder. It is the first medication approved to treat acute mania and prevent recurrences of episodes of mania and depression in bipolar disorder since lithium and carbamazepine became available decades ago.

“Bipolar disorder is a difficult-to-treat condition, and even when patients reach relatively stable periods of mood, relapse of symptoms is common and almost always inevitable,” said Eduard Vieta, MD, PhD, Director, Bipolar Disorders Program at the Clinical Institute of Psychiatry and Psychology, University of Barcelona. “With ZYPREXA’s new indication to prevent recurrence and stabilize moods, patients with bipolar disorder will now have a new option for breaking the cycle of relapse into the manic or depressive phases of the disorder and thus prolong periods of stability and wellness.”

The European Commission based its approval for the new indication on a review of a comprehensive data package including six studies in more than 1550 patients evaluating the safety and efficacy profile of ZYPREXA in the prevention of recurrence in bipolar disorder. This package included data showing that ZYPREXA was significantly more effective than lithium, the current gold standard for bipolar disorder treatment, in delaying relapse into mania (14.3 percent versus 28.0 percent), reducing the need for hospitalization and limiting the number of patients who discontinued therapy. Estimated time to relapse was 380 days for patients treated with ZYPREXA compared to 212 days for patients treated with lithium. ZYPREXA was as effective as lithium in reducing rates of relapse into a depressive episode (16.1 percent for ZYPREXA versus 15.4 percent for lithium).

Additional data from a double-blind, placebo-controlled study showed time to relapse into either mania or depression was significantly longer for ZYPREXA patients than patients treated with placebo (median times: 174 days versus 22 days). ZYPREXA-treated patients had a significantly lower rate of either a mania relapse (16.4 percent) versus placebo (41.2 percent) or depression relapse (34.7 percent for ZYPREXA versus 47.8 percent for placebo).

“ZYPREXA’s new indication as a mood stabilizing medication and its wide range of effectiveness in delaying relapses can help clinicians focus on the long-term management of the disorder, rather than just treating acute symptoms,” said Mauricio Tohen, MD, DrPH, Lilly Clinical Research Fellow, Eli Lilly and Company. “Recurrences can have devastating consequences for patients, who may experience disruptions in relationships and jobs, suffer feelings of failure or become suicidal. Prolonged periods of mood stability allow patients to have control of their lives, be productive and have a greater sense of well-being.”

WHAT IS NEUROPROTECTION?

The concept of neuroprotection is not a new one, but one that can make a tremendous difference in the long-term functioning potential of patients suffering from schizophrenia and bipolar disorder. These illnesses are known to be associated with functional decline, as well as neurodegeneration. In order to protect a patient's future, a treatment plan must be one that promotes adherence, protection from relapse, and, to whatever extent possible, protects the brain from degeneration.

By preserving a patient's brain, it is possible that acute episodes of symptom exacerbation can be avoided. It is also possible that cognitive decline is prevented or that negative symptoms are more effectively alleviated. All of these benefits are meaningful to the patient in that they may allow the patient to be more actively engaged in a therapeutic alliance and begin to reach some of their treatment goals, be they as simple as learning to tie shoelaces or as monumental as returning to work.

There is data from both controlled clinical trials and naturalistic studies that suggest patients treated with ZYPREXA are better able to adhere to their treatment and are protected from relapse. There are also several lines of data that suggest ZYPREXA may be disrupting the natural, degenerative course of schizophrenia and bipolar disorders. The global marketing team, in partnership with US and regional marketing, is currently engaged in a global market research study to evaluate these concepts and data in front of customers to determine; a) the clinical relevance of these findings, b) the relationship between some of the concepts discussed above, and c) how best to communicate these findings to our customers. The qualitative research has just concluded, and we will be running two rounds of quantitative testing before the end of the year.

BIPOLAR GMC CD-ROMS NOW AVAILABLE

CD-ROMs from the 2003 Bipolar GMC, held in London March 13-15, are now available from your ZYPREXA affiliate, care of your brand manager. Please contact your affiliate manager regarding individual affiliate-approved uses of this resource, to request availability of the CD-ROM, or to obtain additional copies. For additional information, please contact Kelli Carson, educational program consultant at kelliC@Lilly.com.

INTRODUCING MAURICIO TOHEN, MD

The ZYPREXA team would like to introduce Mauricio Tohen, MD, recently promoted to ZYPREXA product team leader. Tohen has played a key role in the investigation of ZYPREXA to treat bipolar disorder, including its unprecedented US and European Union approvals to treat bipolar mania. Tohen succeeds Alan Breier, MD, who was recently promoted to chief medical officer and vice president, medical.

"In no way is our task complete in terms of offering patients even more options and value from ZYPREXA and ensuring that patients continue to have access to the benefits of this extraordinary medicine," said Tohen. "I see a very competitive field ahead of us and our team is in good shape to take on the challenge. We need to continue to deliver value by constantly putting the patient first."

"Dr. Tohen has done a tremendous job of helping us develop the bipolar side," said Bert van den Berg, president of neuroscience products. "We look forward to his leadership in support of this marvelous product in all of its dimensions – from ZYPREXA's existing indications in schizophrenia and bipolar mania, to the plethora of other indications and formulations we have pending approval under investigation," added Breier. "Mauricio brings great scientific expertise and superb leadership qualities to this position. ZYPREXA and the ZYPREXA product team will be in excellent hands."

After leading the bipolar and psychotic disorders program at McLean Hospital, Harvard Medical School, for eight years, Tohen came to Lilly in 1996 as medical advisor leading the ZYPREXA bipolar disorder research effort. He was promoted to Lilly clinical research fellow in 2000 and was later appointed to product team posts including medical director and, more recently, executive director of bipolar disorder studies.

Tohen received his medical degree from the National University of Mexico and his doctor of public health degree from Harvard University, where he still holds a faculty position as associate clinical professor of psychiatry. He trained in psychiatry at the University of Toronto and Harvard Medical School. He also holds an MBA from Indiana University's Kelley School of Business.

Tohen received a National Service Award in Psychiatric Epidemiology from the National Institute of Mental Health (NIMH) and Harvard University. He received a FIRST award from NIMH, the Pope Award from McLean Hospital, and a NARSAD Young Investigator Award. He has served on the Epidemiology and Genetics and the Clinical Centers and Special Projects Review committees at NIMH. Tohen has contributed more than 120 original publications and co-edited two books, *Psychiatric Epidemiology* (1995 first edition, 2002 second edition) and *Mood Disorders Across the Life Span* (1996). He also edited the book, *Comorbidity in Affective Disorders* (1999).

VA STUDY FINDS NO GREATER DIABETES RISK WITH ZYPREXA VS THREE OTHER ATYPICALS

Results of a much-anticipated, 12,235 schizophrenia patient, retrospective research study by the US Department of Veterans Affairs showed no significant difference in diabetes risk among three atypical antipsychotics studied.

International news coverage to date (Wall Street Journal, Reuters, Bloomberg, Forbes, United Press International) highlight the study's news for ZYPREXA.

Cunningham VA Study on Diabetes Risk

Findings from a large-scale, independent study from the US Veterans Administration, led by Francesca Cunningham of the VA's Pharmacy Benefits Management Strategic Healthcare Group, were released August 21, 2003, at the International Society of Pharmacoepidemiology meeting. Findings of the study showed that ZYPREXA was not associated with diabetes more often than other atypical antipsychotics studied.

In fact, findings showed ZYPREXA to be associated with the least risk of diabetes compared to the other three drugs evaluated:

- Hazard ratios (95% Confidence Interval) were 1.27 for olanzapine, 1.49 for risperidone, 3.34 for quetiapine, and 1.48 for clozapine.

International news media quickly reported on this much-anticipated study...including its implications for ZYPREXA:

Wall Street Journal:

The study suggests that any (US FDA) label warnings are likely to apply to the entire class of newer antipsychotic drugs, as opposed to one drug alone. This would appear to be a boon for Lilly, because ZYPREXA has been most prominently linked to this problem. P. Murali Doraiswamy, chief of biological psychiatry at Duke University in Durham, N.C., and co-author of earlier papers that analyzed diabetes with the new drugs, known as "atypical" antipsychotics, said, "This is certainly good news for Lilly. We have reported a problem with all the atypicals."

Reuters:

"Max Hermann, an industry analyst at ING, said the news could benefit Lilly's ZYPREXA, since it had the lowest number of diabetes cases. Furthermore, Lilly's product had been associated with a higher rate of diabetes for several years and the fact that this now appears to be an effect common to the entire drug class should enhance its competitive position, he added."

Bloomberg:

"Lilly may benefit from such a move (widespread US labeling of antipsychotic drugs) because its ZYPREXA had the lowest incidence Redacted

COMPLETE WELLNESS: THE WHOLE PERSON TREATMENT APPROACH

On August 14, 2003, a virtual meeting of experts came together to discuss a new approach for treating people with Severe and Persistent Mental Illness (SPMI). Complete Wellness: The Whole Person Treatment Approach addresses primary mental symptoms and the physical health of those living with mental illness—both of which contribute to overall wellness to help move lives forward.

Complete Wellness: The Whole Person Treatment Approach

The August 14, 2003, virtual meeting brought together experts on physical and mental health to discuss the need for Complete Wellness: The Whole Person Treatment Approach, which focuses on both the physical health and mental health of people living with SPMI. Addressing the physical well-being of consumers living with mental illness is as important as treating their mental health—both of which contribute to overall wellness to help move lives forward. Featured speakers included:

- Betty Vreeland, training coordinator at the University of Medicine and Dentistry of New Jersey for the Lilly-sponsored Partners for Excellence in Psychiatry program
- Jean Russell, coordinator of the Tardive Dyskinesia Clinic and Psychiatric Movement Disorders Clinic
- Dr. Ken Duckworth, Medical Director of NAMI national
- Kimberly Hensley, a consumer with schizoaffective disorder
- Christopher Kosseff, President and Chief Executive Officer for University Behavioral Health Care at the University of Medicine and Dentistry of New Jersey (UMDNJ)

Betty Vreeland opened the discussion defining Complete Wellness: The Whole Person Treatment Approach as the treatment of both the mental illness and the physical health of persons living with mental illness. Vreeland went on to explain that with rising obesity trends in the US general population and mentally ill population, physical health and mental health treatment must go hand in hand.

Tools like Lilly's Neuroscience Treatment Team Partner Program (NTTP) help bring the Complete Wellness approach to life. Vreeland and Jean Russell presented the details of the NTTP program, which is a comprehensive educational program that encourages healthy lifestyles for people with mental illness. This program is designed for use by healthcare professionals and their patients. Divided into three detailed segments (Team Solutions, Solutions for Wellness, Abnormal Involuntary Movements Scale), it provides both an excellent training tool for treatment teams and a valuable resource for patients.

Dr. Kenneth Duckworth also presented information on NAMI's resources for Complete Wellness. NAMI has developed a Consumer Guide, which includes Strategies for a Healthy Recovery. The NAMI Consumer Guide offers commonsense, economical suggestions for healthy living. Topics include smoking cessation, healthy eating habits, increased activity, knowledge of sleep apnea, and knowledge of diabetes/metabolic syndrome.

The discussion continued with a moving personal success story from Ms. Kimberly Hensley, who was diagnosed with schizoaffective disorder in 1987. Hensley has been receiving effective medication, treatment, and support from her family for several years now. Through a Lilly scholarship, Hensley was able to earn a Master's degree. She is currently the Coordinator of Consumer Affairs at Clermont Counseling Center in Cincinnati, Ohio. During this successful time in her life, Hensley was challenged because she gained nearly 100 pounds. Through participation in a weight management program (not NTTP), Hensley was able to lose nearly 70 pounds. She now uses the NTTP program to maintain her healthy weight. She also plans to incorporate the program into her role as a counselor at the Clermont Counseling Center. Hensley emphasized the need for programs like NTTP and the NAMI Consumer Guide as consumers are frustrated by the lack of resources available to address their physical health.

Vreeland and Kosseff closed the meeting stressing the importance of collaboration between academic institutions, advocacy groups, consumers, the treatment team, and pharmaceutical companies. Such partnerships make tools like NTTP and the NAMI Consumer Guide possible.