

wilderness pt response  
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## Zyprexa Issues Message Evolution

This document has been created to serve as a resource and guidance for affiliates on the subject of metabolic issues. The focus of this document is on our core beliefs about the issues, our strategy to manage them, the key messages we will use when we discuss them and the resources available to help address the needs of our customers.

As one would expect, our beliefs and messages have not changed dramatically. What is represented here is an evolution and refinement of our messages to reflect the emergence of new data, results of global message testing, input from thought leaders and other customers and a focus on providing solutions to help our customers meet the needs of their patients.

First and foremost, the best way to meet the needs of our customers is to provide a medication that delivers the dependable control they need to manage their patient's illness, that enables a therapeutic alliance between them and their patients, and that helps their patients move their lives forward so that they may achieve their individual potential. Zyprexa meets these needs better than competitor medications. Customers have told us that an important aspect of dependable control is that a medication have a known and manageable side effect profile. It is in this context that we provide and recommend use of the information contained in this document.

The **Core Beliefs** section states our thoughts on the issue based on the scientific data, sound medical practice and how we want to be perceived by our customers (leadership role).

The **Strategy** section focuses on what we need to do, which is primarily to provide education and services as appropriate.

The **Key Messages** section list the key messages that should be driven across multiple communication channels. While there are quite a number of messages, your marketplace and your audience will be determining factors in just which messages, and with what emphasis, need to be delivered. These are the messages from which you should craft and locally test sales-force verbatims. Your local conditions and individual situations will in part determine if the various messages are delivered proactively or only in response to inquiry.

The **Tactical Resources** section is a reminder of the various tools you have available to help you to accomplish your objectives. Key among these is shared learning and best practices so that we may repeat successful tactics in additional markets where applicable.

The final section of the document relates to **Measurement**. The Brand Equity tracking tool, completed globally on a biannual basis, allows us to track, at a high level, how we compare to competitors on a number of efficacy and safety parameters, including weight gain, diabetes and lipids. Our goal is to increase the association for these issues for competitors while keeping the overall relevance to physicians low. Also on a global,

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biannual basis we will conduct additional tracking studies that look more specifically at physician perceptions and the impact of side effects on prescribing for Zyprexa and competitors. Finally, we will continue to collect global data on our key messages and evolve them as necessary. Clearly, the most immediate and impactful market research and feedback will be that which you conduct in your own markets.

For years now the competitors have been singular in their focus in their attacks on Zyprexa's safety profile. They cannot win the battle on efficacy, so we can expect more of the same. Despite the relentless attacks, Zyprexa continues to grow at a healthy rate. This is a testament to your persistence and dedication to patients with schizophrenia and bipolar disorder that truly deserve the dependable control that Zyprexa provides so that, ultimately, they may move their lives forward and achieve their individual potential.

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## **Weight Gain**

### **Issue**

Weight gain remains a significant issue for Zyprexa due to its impact on physicians' prescribing habits. The competition is exploiting the weight gain liability by inferring this issue is related to other issues (weight gain leads to issues with diabetes and/or DKA, lipids, CVD and Syndrome X). Weight gain is often undesirable and potentially unhealthy.

### **Core Beliefs**

When choosing a medication, side effects should be considered within the context of overall efficacy, tolerability and the seriousness of the illness. Significant weight gain can occur with Zyprexa, as with other psychotropic medications. Therapeutic interventions including diet and exercise have proven effective in the prevention and treatment for some patients, allowing them to receive the extraordinary benefits Zyprexa offers. Lilly is committed to patient well being and will continue to provide answers and solutions that promote physical and mental health.

### **Strategy**

- Acknowledge that weight gain, sometimes substantial, can occur with Zyprexa
- Determine how the physician is currently handling the issue with Zyprexa and other psychotropic medications
- Suggest interventions and resources as appropriate, such as affiliate sponsored fitness and nutrition programs
- Acknowledge that not all patients should remain on Zyprexa (e.g.-significant weight gain with minimal therapeutic response)
- Reinforce that the handling the issue is worth the physician's and patient's time and effort due to the extraordinary benefits Zyprexa offers

### **Key Messages**

- When choosing a medication, side effects should be considered within the context of overall efficacy, tolerability and the seriousness of the illness.
- Weight gain can occur with Zyprexa
- Therapeutic interventions including diet and exercise may prove effective in the prevention and treatment for some patients, allowing them to receive the extraordinary benefits Zyprexa offers

**Tactical Resources**

- Medical Letters (GRDs)
- Stand-by Statements
- Sales Force Training
- Sales Force Verbatim
- Slide Sets
- Issues Management Literature Review
- Shared Learning / Best Practice
- Affiliate fitness/nutrition education programs

**Measurement**

- Brand Equity – biannual reporting
- Global Market Assessment
  - Key message testing - annual
  - Global issues perception testing – biannual beginning Q4 '02
- Key message media impressions

**Resources** – See Infonet

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## **Diabetes**

### **Issue**

Diabetes is a significant issue for Zyprexa due to considerable competitive pressure, its impact on physicians' prescribing habits and treatment population risk factors. Diabetic ketoacidosis and diabetic coma, acute and serious complications of diabetes, have become the subject of increasing competitive noise and concern by clinicians.

### **Core Beliefs**

When choosing a medication, side effects should be considered within the context of overall efficacy, tolerability and the seriousness of the illness. Diabetes occurs at a higher rate in patients with schizophrenia and bipolar disorder than in the general population. A direct causal relationship between Zyprexa and the development of diabetes has not been established. While obesity is associated with higher rates of diabetes, diabetes is a chronic multifactorial disorder that is influenced by multiple risk factors. Head to head clinical trials and most epidemiological studies suggest that diabetes may occur in patients taking commonly prescribed antipsychotic medications at comparable rates. Because the differences between commonly prescribed agents – if any – appears to be relatively small, and the patient population is at higher risk, all patients should be monitored appropriately and the primary focus should be on treating the underlying schizophrenia or bipolar disorder. Lilly is committed to patient well being and will continue to provide answers and solutions that promote physical and mental health.

### **Strategy**

- Educate health care professionals with regards to:
  - the risk of diabetes in their patient population
  - the relative comparability of risk for diabetes in patients taking commonly prescribed psychotropic drug treatments
  - how to diagnose and monitor for diabetes
  - available treatment options and resources for their patients with diabetes or risk factors
- Address customer concerns and then refocus on Zyprexa efficacy and benefits

### **Key Messages**

- Diabetes occurs at a higher rate (estimates range from 2-4 times greater) in patients with schizophrenia and bipolar disorder than in the general population, therefore it is not surprising that some will first develop diabetes during the course of treatment for their psychiatric illness.

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- A number of factors affect risks for the development of diabetes such as: family history, aging, ethnicity, previous history of glucose intolerance, long term obesity, dyslipidemia, lack of exercise, hypertension and high-fat diet. Therefore, one should assess patients for risk factors and consider recommending preventative therapy when indicated.
- Several epidemiological studies indicate comparable rates of diabetes among patients treated with commonly prescribed antipsychotics and direct causality has not been established.
- The reported differences, if any, in head to head trials and epidemiological studies between antipsychotic medications is very small when compared to the absolute risk of developing diabetes that is associated with having a severe psychiatric illness
- DKA is an infrequent complication of DM. Cases of DKA have been reported in association with Zyprexa treatment, as well as with other atypicals. However, these are very rare, reported in less than 0.01% percent of the patients treated with Zyprexa and a direct causal relationship has not been established.
- The primary considerations for choosing an antipsychotic should be its overall risk/benefit profile- that is, its efficacy in treating the psychiatric illness and its overall tolerability.

#### **Tactical Resources**

- Medical Letters (GRDs)
- Studies (PCS, HGIM, SO13, TED, etc.)
- Stand-by Statements
- Sales Force Training
- Sales Force Verbatim
- Slide Sets
- Issues Management Literature Review
- Shared Learning / Best Practice

#### **Measurement**

- Brand Equity – biannual reporting
- Global Market Assessment
  - Key message testing - annual
  - Global issues perception testing – biannual beginning Q4 '02
- Key message media impressions

#### **References – See Infonet**

## **Lipids – as a Risk Factor for Coronary Heart Disease (CHD)**

### **Issue**

Competitors are attempting to link Zyprexa associated weight gain to dyslipidemia and subsequently to coronary heart disease (CHD)

### **Core Beliefs**

When choosing a medication, side effects should be considered within the context of overall efficacy, tolerability and the seriousness of the illness. Elevated cholesterol and/or triglycerides are very common in the general population and some dyslipidemias (especially elevated LDL) are major risk factors for CHD. Elevated cholesterol and triglycerides can be seen in some patients who gain weight or who are obese, however other factors such as family history, cigarette smoking and lifestyle are important risk factors for the development of CHD. Some elevation of triglyceride level may appear during treatment with Zyprexa, whereas most studies show little or no change in cholesterol levels. In recognition of these facts, and the understanding that many patients treated with psychotropic medications have risk factors for dyslipidemia regardless of treatment choice, Lilly is committed to being the dedicated leader in providing answers and solutions that matter.

### **Strategy**

- Educate health care professionals with regards to:
  - the risk of abnormal cholesterol/lipids in their patient population
  - the risk factors for CHD
  - treatment options and resources for their patients with CHD risk factors
- Address customer concerns and then refocus on Zyprexa efficacy and benefits

### **Key Messages**

- Abnormalities in cholesterol and/or triglycerides levels are very common in the general population, occurring in as high as 50 percent of the U.S. population (insert local stats)
- Elevated cholesterol and triglycerides can be seen in some patients who gain weight or who are obese, however other factors such as family history, cigarette smoking and lifestyle play are important risk factors for the development of CHD.
- Clinical trial and spontaneous adverse event reports of elevated triglycerides in patients taking Zyprexa are rare

- Some elevation of triglyceride level may appear during treatment with Zyprexa, whereas most studies show little or no change in cholesterol levels
- For many patients, increases in lipids can be managed through dietary interventions, medication and behavior modifications such as exercising and refraining from smoking
- The primary considerations for choosing an antipsychotic should be its overall risk/benefit profile – that is, its efficacy in treating the psychiatric illness and its overall tolerability

#### **Tactical Resources**

- Medical Letter (GRD)
- Stand-by Statement
- Slide Set
- Sales Force Training
- Sales Force Verbatim
- Issues Management Literature Review
- Shared Learning / Best Practice

#### **Measurement**

- Brand Equity – biannual reporting
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#### **References – See Infonet**



## Diabetes Initiatives:

Our strategy is to elevate the discussion above “good drug, bad drug,” providing answers that matter without compromising on the role of dependable control that helps physicians help their patients with schizophrenia and bipolar disorder. To that end, the US affiliate is rolling out several initiatives, which build on the science of our diabetes message while directly addressing clinician challenges in dealing with the co-morbidity of serious and persistent mental illness and diabetes. Should you have any questions about the initiatives below, please contact Matt Pike at (317 651-3990) or Tony Fiola at (317 276-9417).

Here is an example of what the US is in the process of developing:

1. Partnership with local diabetes association to establish consensus guidelines.
  - Intent: Raise awareness and educate a broad audience about the level of co-morbidity of diabetes and serious and persistent mental illness.
  - Key Players: Cross-functional team of neuroscience medical and marketing as well as a cross-functional team of endocrinology medical and marketing.
  - Action: Form team to initiate and manage project with appropriate local organizations
  - Resources: Dedicated Lilly team to manage project and relationships with various organizations – especially a dedicated endocrinologist.
  - Timing: 4-12 months depending on organizations involved
  - Redacted
  - What success looks like: Publication of positive guidelines that raises the awareness of a population at risk for diabetes and the need for routine screening.
  
2. Mobilization of trained Certified Diabetes Educators (CDE) who can offer perspective on the co-morbidity of the illness and the roll of the psychiatrist in the assessment and enabling patients to obtain appropriate care including information on a variety of treatment strategies and wellness advice.
  - Intent: Provide support (education and perspective, referral options, treatment options if desired) to customers who recognize the importance of proper assessment for all psychiatric patients at risk of developing diabetes.
  - Key Players: Project owner, endocrinology contact, established CDE’s
  - Action: Engage CDE’s to be available to provide physician support at request of Lilly sales management. CDE will need basic training on population specific issues and adequate background on Zyprexa’s safety profile to gain their buy-in.
  - Resources: Available CDE’s (1 per District Sales Manager in the US, N=84), Funding, CDE Training, sales manager/CDE coordination process, project owner
  - Timing: 8 weeks (to develop content and train)

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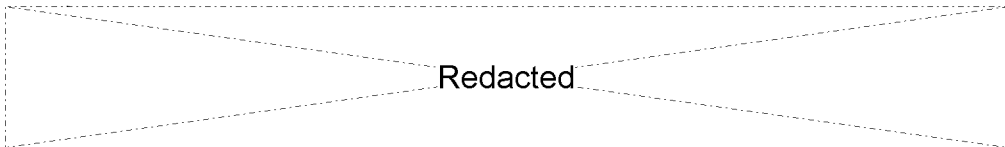
- **What success looks like:** Physicians have access to information they desire and are confident in their role and willing to deal with co-morbidity.
3. A customer hotline (1-800#) that will address questions.
- **Intent:** Provide real time answers for physicians with questions about psychiatric patients and diabetes.
  - **Key Players:** Trained medical professionals to address customer questions. (Decision point: internally staffed verses grant given to third party)
  - **Action:** Determine vendor, set-up hotline number and promote availability.
  - **Resources:** Funding, training for hotline staff, project owner
  - **Timing:** Minimum 2-4 weeks from initiation
  - **Cost:** Depends on resources already available (if internal, add funds for fulfillment / if grant = \$\$)
  - **What success looks like:** Trained professionals address specific questions about diabetes and antipsychotic use.
4. A sales representative implemented promotional DVD for use with customers, which standardizes much of the diabetes message (population risk, comparable rates, and treatment options for diabetes) through the use of thought leaders and internal physicians to answer difficult questions and deliver key messages.
- **Intent:** Increase accuracy and credibility of key message elements.
  - **Key Players:** Marketing, medical, legal & regulatory.
  - **Action:** Assess local need through local market research, localize DVD to your market place, and obtain local medical, legal, and regulatory sign-off.
  - **Resources:** Project Coordinator, external thought leaders, vendor.
  - **Timing:** November 4<sup>th</sup>/US

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- **What success looks like:** A standardized message around diabetes that can be utilized by a sales professional to address the concerns voiced by a customer.
5. Solutions for Wellness: Personalized Program; a sales representative delivered structured program that enhances Zyprexa adherence by addressing a patient's fitness and nutrition (pilots underway in both Canada and U.S.)
- **Intent:** Solutions for Wellness: Personalized Program is a program designed to change the overall wellness behavior of psychiatric patients over 24 weeks. (Note: depending on the market, this may have to be a non-product program, offering service to any patient, regardless of the agent they are taking)

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- **Key Players:** Program Sponsor (affiliate Brand Team Leader), affiliate coordinator, affiliate IT, affiliate market research, affiliate sales force, affiliate key customers (to target patients) and a third party to cover the call center and its reports.
- **Action:** There is a four part process for Solutions for Wellness: Personalized Program;
  1. Assess the Affiliate market place fit/need for the service offerings.
  2. Develop the program infrastructure and materials consistent with the affiliate regulations
  3. Training of the sales force and brand team
  4. Launch the program
- **Resources:** The affiliate needs to provide the program sponsor and coordinator. During the implementation of the infrastructure, IT and market research areas will need to provide assistance. The Sales Force will introduce the program to the market place. A third party to cover the call center and its reports.
- **Timing:** The 'needs' assessment can be completed in two weeks. The development step can take 7 weeks to 7 months depending on the culture, other participating affiliates and amount of material reused. The training preparation and execution can occur in two weeks. The launch should take two-months.



- **What success looks like:** Patients report great satisfaction with treatment; MDs are less willing to switch patients of medication due to weight change and fear of diabetes.
6. Coordinated public relations activity designed to bring attention to the population at risk and Lilly's leadership behavior.
- **Intent:** Educate broad audience through articles, case reports and interviews for a net result of fewer negatives, a less abusive media & increased attention diffusing the notion that Zyprexa causes early on-set of diabetes.
  - **Key Players:** Project Manager, 3<sup>rd</sup> party educators (endocrinologist & psychiatrist), PR agencies, all Lilly spokes people.
  - **Action:** Engage local PR firms to generate media stories related to issue and counter competitive efforts.
    1. Integrated Media Plan
      - Increase Share of Voice
      - Focus on differentiation, tone and framing, co-morbidity and the patient.
    2. Rapid Response Plan
      - Increase ability to handle competitive initiatives.

3. Public Relations – Expose Junk Science

- Increase ability to handle competitive initiatives.
- **Resources:** Project owner, Funding, Consultant
- **Timing:** Immediate
- **Redacted**
- **What success looks like:** Improved SOV, tone & message framing; position serious nature of SPMI vs. risk of diabetes; improved focus on the patient; exposing junk science; rapid, aggressive response mechanism; good competitive intelligence.

7. Increased Data Commercialization through Direct to Physician & Continuing Medical Education activities, as well as an infusion of Peer-to-Peer programming.

- **Intent:** Increase education and “noise level” on population specific issues, drug comparability and treatment options.
- **Key Players:** Marketing, medical and legal.
- **Action:** Significantly increase frequency of various Direct to Physician activities (see below)
- **Resources:** More Continuing Medical Education programs, Lilly consultant diabetes training, closed symposia / publication / enduring materials.
- **Timing:** Q4 / US
- **Redacted**
- **What success looks like:** Increase in delivering our key messages around diabetes to physicians as well as an increased association with diabetes for our competitors.

8. Deepen our list of thought leader support, both in psychiatry and endocrinology.

- **Intent:** Ability to select from a strong network of professionals to help deal with specific issues associated to Zyprexa.
- **Key Players:** Medical and Marketing mix in both Neuroscience and Endocrinology.
- **Action:** Develop thought leader coordinator at an affiliate level.
- **Resources:** Dedicated relationship team per thought leader (activity lead at product team level, thought leader coordinator at affiliate level)
- **Timing:**
  1. **ZPT:** Define thought leader objectives and develop relationship teams by April (BC 2) 2003.
  2. **Affiliates:** Identify appropriate thought leaders, define thought leader objectives and develop relationship teams by August (BC 3) 2003.

- **Redacted**
- **What success looks like:** Ability to select from a strong network of TL's to support Zyprexa on issues for initiatives of: advisory board members, consultants, presenters, publications, regulatory, advocacy, information

releases, competitive positioning, investor relations, research and competitive intelligence.

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