

Zyprexa APA Executive Summary

Core messages & tone

*** From Mike Bandick **

What we expect at the APA

Lilly's focus at the APA, unlike our competitors, will be on efficacy. Given Zyprexa's leadership position, competitors will continue to try and commoditize efficacy and create concerns about Zyprexa (issues associated with weight gain, diabetes, etc.). The companies for all of the atypical anti-psychotics and several anti-epilepsy drugs will try to expand into bipolar. BMS and Janssen will use the APA to condition the market for aripiprazole and risperidone depot. Lilly will present robust efficacy data about Zyprexa, including outstanding results in bipolar depression.

Answers to unsolicited questions about Zyprexa and safety issues

When you are asked an unsolicited question about Zyprexa and safety issues, first clarify the question, respond with appropriate verbatim and check for impact/agreement. If customer is seeking additional information, ask if a written follow up (medical letter) or representative follow up is desired. If customer still seeks additional information, escort them to our medical booth while delivering a proactive efficacy message (see attached algorithm).

What can you tell me about the Zyprexa label change in Japan?

- The Package Insert (PI) in Japan has been modified with regard to patients with diabetes.
- Lilly strongly disagrees with the conclusion of the Japanese regulatory agency because the overwhelming scientific evidence supports comparable rates among psychotropics. The Japanese decision was based on 9 case reports representing less than 0.01% of patients treated with Zyprexa in Japan.
- We support the ADA guidelines; that for patients with diabetes, or significant risk factors, good clinical practice includes assessment and follow-up regardless of what agent a patient is receiving.

I heard you recently had a change to your label in Europe. What can you tell me about that?

- Recently, the UK regulatory agency reported in its quarterly newsletter a language change with respect to appropriate clinical monitoring of patients with diabetes in the ZYPREXA European label which took place more than a year ago.
- We support the ADA guidelines; that for patients with diabetes, or significant risk factors, good clinical practice includes assessment and follow-up regardless of what agent a patient is receiving.

Is it true that Zyprexa will have a label change regarding diabetes in the US?

- I have no knowledge of any proposed label changes at this time.
- The FDA has requested safety information from *all of the manufacturers* of atypical antipsychotics so that they can conduct a thorough review of this issue.
- Lilly has looked at this issue in many different ways, including our clinical trial databases, epidemiological studies, and competitor-sponsored studies and have found comparable rates of diabetes regardless of agent studied.

Does Zyprexa cause diabetes?

- Diabetes is common in the general public and even more common in the mentally ill. Not surprisingly, if you look for it in your psychiatric patients, you'll find it, regardless of treatment agent.
- Lilly has looked at this issue in many different ways, including our clinical trial databases, epidemiological studies, and competitor-sponsored studies and have found comparable rates of diabetes regardless of agent studied.

Strictly Confidential
Property of Eli Lilly and Company

5/9/2002

ZY 8116 1540

- In other words, yes, Zyprexa patients develop diabetes at rates comparable to patients on other psychotropic agents. With this in mind, doesn't it make sense to select the agent that best treats the patient's *psychiatric* symptoms?

I've heard that Zyprexa can lead to ketoacidosis. Is this true?

- Cases of DKA have been reported in association with Zyprexa treatment, as well as other atypicals. However, these reports are very rare, reported in less than 0.01 percent of patients treated with Zyprexa and a direct causal relationship has not been established.
- Fortunately, DKA is potentially preventable if diabetes is identified and properly controlled. Therefore, it is essential that physicians counsel and refer patients with diabetes, regardless of what agent they may be taking.
- DKA should not be a factor in choosing one agent over another, as patients appear to experience diabetes at comparable rates across various treatments.

What can you tell me about Zyprexa causing increased lipid levels?

- I am aware of activity around this topic that has been generated by our competitors.
- Would a medical letter on the subject address your needs?

or

Spontaneous adverse event reports of elevated triglycerides with Zyprexa are very rare, reported at a frequency of less than 0.01 percent.

- For most patients who are compliant, 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.

What can you tell me about the tampering issues with Zyprexa?

- On May 3, Eli Lilly and Company initiated a notification of potential tampering with ZYPREXA to all health care professionals.
- We have been made aware, either by direct report to Lilly or by reports to wholesalers, of a limited number of pharmacists in the United States finding white pills marked "aspirin," instead of ZYPREXA tablets, in ZYPREXA bottles. These reports have been limited to 60 count bottles of 10 mg. and 15 mg. ZYPREXA only.
- Note that this was not a recall. We have communicated to pharmacists the need to remind anyone taking any prescription medication to carefully examine their medication before taking it, including ZYPREXA. We have given instructions to pharmacies to inspect their inventory of ZYPREXA before dispensing and have shared information on how to identify legitimate ZYPREXA tablets.

Answers to unsolicited questions about competitors

When you are asked an unsolicited question about a competitive product, first clarify the question and then acknowledge the complexity of the disease and the importance of having options.

What can you tell me about the efficacy data on aripiprazole?

- With the claims BMS is making, it seems odd that they are not sharing robust efficacy data.
- We learned from recent product launches that with unpredictable efficacy, a product will struggle to find a niche.
- Physicians count on Zyprexa because of its dependable efficacy...

What can you tell me about risperidone depot (Risperdal Consta/Long Acting)?

- It is good for customers to have another option for severely ill patients who can't be stabilized on anything other than a typical depot
- However, risperidone depot may not be an option for many patients given the dose ceiling (4 mg max.) and limitations of this formulation (3 weeks of oral supplementation, injections every 2 weeks instead of Haldol depot's 4 weeks, etc.)
- Zyprexa oral offers superior relapse prevention (show Tran data).

Strictly Confidential
Property of Eli Lilly and Company

5/9/2002

ZY 8116 1541

What can you tell me about quetiapine (Seroquel)?

- One of the benefits of Seroquel is its sedation.
- However, for dependable control of positive and negative symptoms, physicians count on Zyprexa
- You can depend on Zyprexa because....

What can you tell me about ziprasidone (Geodon)?

- Lilly's focus, unlike our competitors, will remain on Zyprexa's efficacy
- We expect that Pfizer will continue to try to minimize Geodon's unpredictable efficacy and side effects
- Zyprexa has demonstrated dependable control in over 8 million patients....

What can you tell me about divalproex (Depakote)?

- Traditionally, Depakote and Lithium were the only mood stabilizer options
- Depakote and Lithium have been around for a while, but aren't the only mood stabilizer options anymore
- *** yesterday's science, substantial limitations, advances *****
- Here is some exciting data reinforcing why you can depend on Zyprexa as a foundational mood stabilizer

What can you tell me about divalproex (Depakote)?

Lamictal

- Bipolar depression is a devastating illness but only one part of bipolar disorder
- Lamictal has been around for a while but its difficult titration and severe side effects limit its use
- Zyprexa, unlike Lamictal has the indication for bipolar mania
- Here is some exciting data reinforcing why you can depend on Zyprexa as a foundational mood stabilizer

Competitive Intelligence Questions

Your focus at the APA should be on differentiating Zyprexa. However, if you identify the strengths and weaknesses of aripiprazole and/or risperidone depot, please send a voice mail to Jerry Hoffmann

Protecting Critical Information about Lilly/Zyprexa

Strictly Confidential
Property of Eli Lilly and Company

5/9/2002

ZY 8116 1542