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Zyprexa US and Global Marketing

Subject: Diabetes Update

To: Policy Committee

cc:

From: Alan Breier, Zyprexa Product Team, Jack Jordan, US Marketing, Denice Torres, Global Marketing, Mike Bandick, Zyprexa Marketplace Management

Date: July 7, 2003

The purpose of this document is to provide additional information on topics associated with Zyprexa and perceptions surrounding weight gain and diabetes. Specifically, the following topics will be covered:

- New Zyprexa "Focus" Team
- Corporate Response Letter
- Third-Party Support
- Taking a More Assertive Stance
- Summary

Underlying all our efforts is, of course, to do what is right for patients and customers. We want to avoid confusion and, as such, an important goal is to keep our message factual and consistent over time.

New Zyprexa "Focus" Team

As discussed during the recent Policy Committee meeting, there are already multiple initiatives underway. In order to intensify our efforts, we have organized a Focus team whose charge is to deliver, by July 28, a more assertive, fully integrated and customer-tested approach to changing the way key stakeholders view and address this issue. Focus team membership includes an external psychiatrist / endocrinologist, a Lilly endocrinologist, one sales director, six members of U.S. and global marketing management and representatives from Lilly Market Research, our advertising agency and a newly-retained specialty PR firm.

Our goal is to influence key stakeholders (clinicians, Lilly sales representatives, patients, Wall Street, the media, Lilly senior management, caregivers and thought leaders) with the facts about diabetes relative to the seriously mentally ill, Zyprexa and other atypical agents. Our message:

1. The seriously mentally ill are at an increased risk of diabetes relative to the population as a whole
2. Diabetes IS an increasingly important issue in this patient population
3. Noise on this issue can lead to confusion, which in turn can result in discontinuation and sub optimal treatment decisions
4. Data do NOT support a causal link between Zyprexa and diabetes; while the scientific literature is mixed there does not appear to be consistent differences among atypicals

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5. The best predictor of who will develop diabetes is the presence of ADA risk factors, independent of drug treatment
6. The diagnosis of diabetes does not rule out treatment with Zyprexa; physicians should choose the best treatment for the core psychiatric illness
7. Lilly remains committed to researching this further; Zyprexa is a dependable and life-saving medication experienced by more than 12 million patients worldwide

The Focus team will further market research test the framework and verbatims from July 9-15. As part of the July 28 deliverables, the team will identify specific plans for speaker programs, lunch-n-learns and key medical conference symposia; in addition, we will provide a more robust media / communications plan with specific metrics.

We will modify these messages only when it is necessary (based on results of market research in July and/or in the advent of substantial new scientific data).

Corporate Response Letter

On July 11, customers will begin to receive the Corporate Response Letter (Attachment 1), a letter targeted to clinicians, delivered by their Lilly sales representative. The letter is written on behalf of Lilly and signed by Dr. Alan Breier. Market research on the letter was conducted July 2-3 and was very positive:

- 95% of customers consider the document “informative”
- 75% say it addresses their concerns about the issue
- 83% feel better equipped to treat their patients in the context of the issue
- 98% say it’s appropriate for Lilly to communicate with them in this manner

We intend to disseminate this broadly, and will measure number of exposures per key customer during the next 90 days. Concurrently, sales representatives will have an approved verbatim regarding indemnification (Attachment 2). In addition, in July we will be testing proposed Q & A content designed to address the most frequent questions posed by customers so that sales representatives can deliver factual, credible, consistent answers with confidence. Those results will be available the week of July 21.

Last month, U.S. sales representatives began sharing information from a new diabetes sell sheet (Attachment 3) and a newly published reprint from the Advanced PCS database. While limited to published data, these provide a clear review of the data and are consistent with our message points. Feedback on these pieces has been positive, but we do not expect a sell sheet and a reprint (“business as usual”) to be a panacea. We need a clear, compelling message and strong, objective messengers to help our customers better understand the facts.

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Third Party Support

Third-party support is critical to achieving our goals of credibility and objectivity.

Recently, there have been a number of positive messages with third-party validation. These include: Column by the Hudson Institute's Michael Fumento (Attachment 4), Koller's risperidone-associated diabetes mellitus review in *Pharmacotherapy*, upcoming Citrome article in the *Journal of Clinical Psychiatry*, Bellnier's University of Buffalo study. While these are important communications, they unfortunately pale in comparison to the collective noise of our competitors and unflattering press. The sheer volume of negative messages around Zyprexa is fueling confusion and misperception, which has the potential to harm patients.

We have an ongoing dialogue with the American Diabetes Association, and expect the ADA to issue consensus guidelines on this issue in September or October, with a publication in *Diabetes Care* (possibly by year-end). We also expect the Canadian Diabetes Association to publish guidelines in November. In the nearer term, Dr. Paul Keck is leading a small but influential group to publish a white paper on diabetes later this summer. Separately, during Brand Council II Zyprexa Global Marketing initiated and allocated funding (up to \$100,000 per non-US Brand Council affiliate) to insure the development of consensus guidelines. Each of the affiliates, led by the regional marketing leaders, is well on their way toward implementation. Taken collectively, these actions should help speed an emerging standard of care to screen and assess all patients, not just those on a specific drug.

On the regulatory front, we continue to anticipate action from both FDA and Health Canada. We cannot predict the timing or substance of FDA action, but note that "class labeling" is frequently mentioned in investment analyst reports. Still, even a best-case label would not immediately and fully address customer perceptions of differential risk. Therefore, education is key.

Working with colleagues in U.S. *Diabetes Care*, we will soon have 25-35 endocrinologist consultants who will become intimate with the psychiatric literature and Zyprexa data in particular, deepening our bench strength of suitable advisors, spokespersons and customer program speakers. Many of these consultants will be introduced to our data while attending a Lilly program in Toronto July 25-26.

Last month, approximately 300 Zyprexa speakers were convened to sharpen their knowledge of Zyprexa Zydis. At this time, we also shared safety data on metabolic issues, which should result in more consistent and confident peer-to-peer interactions. Internally, we are re-training our neuroscience medical liaisons, Zyprexa clinical research physicians, and other key personnel to enable them to also confidently and consistently share this important information. This is part of *Operation Restore Confidence*, sponsored by Alan Breier, which during Q3 will result in hundreds of face-to-face medical or medical liaison responses to customer inquiries. These efforts highlight the commitment of medical organization to address the issue at the customer level, and

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underscores that we are all – individually and collectively -- accountable for doing what is right for our patients and customers.

Despite these initiatives, we have a long way to go before being satisfied that we have a fully developed capability of disseminated good, objective data. We need to find new ways to mobilize our allies. Hence, we must also focus on taking a more assertive stance.

Taking a More Assertive Stance

We must embrace the fact that many physicians are curtailing their use of Zyprexa (particularly in the moderately-ill patient and in the maintenance phase), solely on the basis of personal fear (of being sued). In order to address these concerns, we are evaluating several options, including:

1. **Indemnification.** We have asked our legal colleagues to revisit this controversial topic. The AMA has published its view (Ethical Opinion 802.6, June 2002) that indemnification represents an “inappropriate incentive” to physicians. We are evaluating avenues to explore this indemnification with the Office of the Inspector General. Indemnification represents the most meaningful demonstration of confidence in Zyprexa – both with our customers and with our employees. Our experience with Prozac confirms the impact and goodwill of such an initiative. We are investigating the viability of this action, and are preparing a business case analysis for senior management’s consideration – ASAP.
2. **NAMI National Screening Month.** By providing NAMI a multimillion dollar grant to stage a national screening, we help educate physicians and patients on the inherent risks of diabetes – regardless of the antipsychotic
3. **Market Research** designed to document and quantify inappropriate competitive behavior that violates legal standards (misrepresentation). This information could lead to an injunction against one or more of those companies, and ultimately, collection of damages (which we would potentially donate to mental health causes).

Summary

In summary, managing the diabetes issues is extremely complex. Our goal is to (1) do what is in the best interest of patients and our customers, (2) provide insight into diabetes and the seriously mentally ill, (3) provide meaningful answers to questions regarding Zyprexa and diabetes, (4) reinforce that at the end of the day, EFFICACY MATTERS. We are all in the business of helping those afflicted with serious mental illness... help move their lives forward. We will continue to keep you updated.

Attachments:

- 1) Corporate Response Letter
- 2) Approved verbatim: “Will Lilly Indemnify...?”
- 3) Diabetes Sell Sheet: “Diabetes and Patients with Mental Illness”
- 4) Fumento column: “Lawyers Exploiting the Mentally Ill”

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