ZYPREXA Primary Care (ZYPCP)
Briefing document
July 21, 2000

Strategic intent:
Offer Zyprexa as a solution to unmet medical need in the office-based primary care environment

Key themes:
- Symptoms / Behaviors
- Peer-to-peer emphasis
- Improve functioning (Thought / Mood / Behavior)
- Preserve independence, enhance QOL

The following is speculation about patient types, Zyprexa benefits and prescriber perceptions. It is not intended advocate promotion of Zyprexa for non-approved indications, but rather, to illustrate potential symptom and behavior profiles for which Zyprexa may represent a much-needed solution. This is confidential, and not to be reproduced or distributed outside of Eli Lilly and Company.

Market research will guide our position and corresponding message, but this is how the world might look:

Targets (unvalidated)

1) Elderly patient with early signs/symptoms of mental deterioration

    Segment is often characterized by "young-old" (60-79) and "old-old" (80+). May be a patient whose behavior is increasingly erratic: yelling, paranoid about husband having an affair, memory slippage, repeats herself, doesn't enjoy activities she used to look forward to (e.g., seeing family, bingo night). This patient may have suffered a "baby stroke," and as part of the ischemia is showing signs of cognitive deterioration.

    This patient is still ambulatory, and lives independently. On a continuum of severity, he/she is less ill and less incapacitated than patients in nursing homes. The symptoms and behaviors may be similar, but to a lesser degree in the office setting. This patient, her family and her doctor all value preserving her independence, even if it's delaying the inevitable. Those extra months or years of independence are precious.

    Primary care physicians are not equipped to treat this patient. The doctor probably trained on Haldol, and would love to throw a little Haldol at the patient to address the behavioral issues, but feels guilty (and rightly so) about the drug's toxicity, and how it may impact the patient's activities of daily living. The doctor may be familiar with Risperdal, and if so, appreciates the microdoses (0.25 and

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0.5mg) that will be gentle on the young-old patient. The doctor may consider Aricept, which is not a great alternative, but may help the cognitive piece. Antidepressants are another option, especially if the patient seems detached, unmotivated or ruminative.

The doctor may be receptive to low-dose Zyprexa, especially given its safety profile and ease of use. He'll like the tolerability, the absence of drug-drug interactions, the absence of cardiac liability and its placebo-like incidence of EPS and parkinsonism. He will not likely be concerned about weight gain, as this patient could probably stand to gain a few pounds. He will be concerned about orthostatic hypotension and anticholinergic side effects (esp. constipation and cognitive dulling), even though Zyprexa's profile is clean here. He will be afraid of Zyprexa's power and its stigma as an antipsychotic, and he will probably bring up cost (since this is a Medicare patient).

From a marketing standpoint, there are clearly parallels with the nursing home patient profile. We should reference Zyprexa's effect on hostility, suspiciousness, cognition, confusion, depressive signs and symptoms, etc. We need to be very clear about safety, tolerability and ease of use. A photo of this patient would convey via facial expression the following: uncertainty, aware of illness but lacking total insight, neither physically vigorous nor overly frail.

2) Mild psychosis

This patient, in his 30s or 40s, is a real pain to treat. He's unpleasant to staff members, high maintenance, and not the kind of patient you want in your waiting room because he's unsettling to other patients. Problem is, he won't accept a psych referral. He doesn't trust "shrinks," which may stem from paranoia and mild delusions of conspiracy. He's in average to below average physical health, generally antisocial, not the best hygiene. He doesn't trust the government or the police, but over time, has come to trust his doctor.

If he has immediate family, their concern is that he's not improving, in fact, may be getting a little worse. His temper is worse, he rambles, his conspiracy theories are getting more grandiose. He's not decompensated to the point of needing hospitalization, but he may "disappear" from time to time.

Primary care physicians are not equipped to treat this patient. The doctor recognizes that there is psychosis here, and is inclined to try a sprinkle of Haldol or Risperdal (see above). Any adverse events, however, would lead to immediate non-compliance. He's concerned about the potential for movement disorders (EPS) and sexual side effects (hyperprolactinemia) on Haldol and Risperdal, as well as Haldol's sedation. This patient is most certainly on an antidepressant and an anxiolytic; a mood stabilizer is less likely.

The doctor may be receptive to 5mg of Zyprexa HS. The patient would sleep better, and it would address the behavioral issues. The doctor will appreciate the

safety (esp. in overdose), the tolerability (discontinuation = placebo) and the ease of use (QD). He may be concerned about weight gain and any linkage that may have to hyperglycemia and diabetes.

From a marketing standpoint, there are parallels to the "Jeanine" profile we share with private practice psychiatrists. We should tout Zyprexa's label change to "psychotropic" to address patient stigma associated with antipsychotics. We should highlight the components of efficacy captured in specific BPRS and PANSS measures, describing Zyprexa's broad spectrum of efficacy. Absence of EPS, elevated prolactin and excessive sedation are plusses. Cost will be less of an issue, especially given the doctor's motivation to see this patient less frequently.

3) Mood swings

Zyprexa is not indicated for bipolar II. Psychiatrists have shared that they have had success utilizing Zyprexa's efficacy in various mood symptoms to improve patients with this somatic complaint. This patient may vary in age, but tends to be employed and relatively highly functioning, but susceptible to mood swings which lead her into bouts of depression, low self-esteem and pessimism about the future, then rebounding with bursts of high energy and social engagement.

The patient's husband is frustrated. He doesn't really care what the causes are (Raging hormones? Stress? PMS?), he just wants relief from the rollercoaster. It's putting a strain on their marriage, and she feels guilty about that. Previous treatment has been aimed at symptoms: antidepressants, anxiolytics, possibly a mood stabilizer.

Primary care physicians may be equipped to treat this patient, but have a poor track record in accurately diagnosis bipolar disorder. The doctor was trained on lithium, but doesn't want to deal with the baggage. Depakote seems like overkill, and there's a lot to manage (incl. Blood monitoring). He's heard of Neurontin, but isn't ready to experiment with it.

The doctor may be receptive to low-dose Zyprexa, especially if it carries the endorsement of a prominent area psychiatrist. He'll appreciate Zyprexa's efficacy in mood, and its FDA-approved indication in bipolar disorder. The safety, side effect and ease of use profiles make it easier for him to justify initiating treatment with Zyprexa. He'll be very sensitive to weight gain as a side effect, and may avoid treatment based on that alone. Cost is not likely to be an issue, as the patient has drug coverage through her employer (although Zyprexa's formulary status may be uncertain).

From a marketing standpoint, there are some parallels to our bipolar value proposition. We should tout Zyprexa's label change to "psychotropic" to address patient stigma associated with antipsychotics and to prevent prescriber confusion ("why would I use an antipsychotic to treat mood swings?). We should emphasize Zyprexa's safety, tolerability and ease of use as an entrée to discussing

efficacy. Low-dose Zyprexa and its broad spectrum of proven efficacy may be the "glue" this patient needs to get back on an even keel. It would be worthwhile to cite the X millions of patients who've tried Zyprexa since its launch in 1996.

4) Anyone in the practice who is currently taking Mellaril
   Based on the recent addition of a black box re: Mellaril's questionable cardiac safety profile, we should move quickly to recommend adding on Zyprexa as a first step in titrating the Mellaril to zero.

This is by no means a comprehensive list, nor a validated one. We may find new profiles emerge, or make profound changes to the ones suggested above. The common denominator, though, is the recognition of unmet medical need and the potential value of Zyprexa as a solution for a number of clinical challenges faced by the primary care physician.

Zyprexa's attributes cut across multiple domains of thought disorders, mood disorders and behavior disorders. This can be a source of comfort to a physician who is unsure of a specific diagnosis but needs to recommend therapy, and seeks an option that is safe, well tolerated and offers some hope of efficacy. In many ways, Zyprexa is an ideal primary care agent. Safe. No titration. Well tolerated. Does a lot of different things really well. Millions of patient exposures.

However, it's not cheap. And there's weight gain. And rumors of it causing diabetes. And don't all antipsychotics carry some risk of tardive dyskinesia? There's no liquid, and no microdose. And I have no time to see reps or attend another slanted dinner program.

I'll give you 2 minutes. What have you got?

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