meeting 12-14-00
Zyprexa strategy ; ↑ glucose ↑ Wt gain.
comp

Agenda (3 hours)

Review situation	15 min
Review Message/Market Research results	45 min
Non-SF plan	30 min
SF plan	90 min

- Option 1 vs Option 2
- When in the context of the detail
- Training

Market Research

There are two groups of MDs -- the 60% who do not see diabetes as a particular concern with APs and the 40% who are concerned.

- Most of the 40% are more concerned about Zyprexa specifically
- Even some of the 60% have concerns, but they only voice those concerns after some discussion on the topic

Almost all physicians do fear diabetes as a potential consequence of weight gain

- Their fear is generally based on the "logical" argument, but is also reinforced to some extent through anecdotal experience or case reports in the literature
- Psychiatrists fear diabetes because they are not that comfortable with the science around the disease and treatments, and they are fearful of "causing" a disease that can lead to permanent complications

Situation Analysis

Hyperglycemia Sell sheet (Beasley PBO analysis) in June 2000 + DTP Efforts (CME, SCC, etc.)

FDA request for complete data from all manufacturers

FDA Letter (October)

Probable future FDA action

Some Lessons learned from Weight Gain & P450

Brush fires can turn into forest fires

Be forthcoming, don't just deny, address and own the issue

Don't just fight battle, pull back to positives

Give tools to the sales force to help tell MDs what to do

Be relentlessly consistent

- across marketing mix
- SF alignment and execution

Tailor objection handling by segment

Zyprexa and Diabetes -- what we want physicians to think

Key Message:

- Diabetes may occur in patients on antipsychotics and/or MSs, including Zyprexa, at rates that are comparable to each other.

Additional Key Message Elements (as necessary)

- Diabetes is quite common in general population, and is higher in patients with psychiatric illness
  - Diabetes has been associated with APs since 1950's.
- To date, Lilly clinical and pre-clinical data have ~~not~~ established ~~any~~ direct adverse effect on glycemic control.
- There are a number of factors that influence glucose control, including intrinsic factors (family history, etc) and variable factors (including weight gain)
- Physician guidelines for individual patients

Key Action Statement

- Fear of diabetes is not a reason to avoid starting a patient on Zyprexa

Draft Hyperglycemia Story

Patients treated with Zyprexa have comparable rates of hyperglycemia as patients treated with Risperdal or Haldol.

- Percent of patients without treatment-emergent hyperglycemia over time (as defined by random glucose levels above 160 mg/dl) showed now significant differences between Zyprexa and risperidone or between Zyprexa and clozapine
- 3.1% of Patients treated with Zyprexa have treatment-emergent hyperglycemia (defined as ←160 mg/dl measured with random glucose tests) in clinical trials
- Mean blood glucose levels in patients treated with Zyprexa increased between 2.6 and 3.8 mg/dl. These changes were 11.4 mg/dl below patients treated with clozapine, 0.7 mg/dl above risperidone, and 3.9 mg/dl above haloperidol in randomized comparative clinical trials
- To date, the Lilly clinical and preclinical trials have not established a direct adverse effect of Zyprexa on glycemic control (e.g. decreased insulin release or antagonism)

Draft Hyperglycemia story (con't)

Diabetes is quite common in the general population, and is higher in patients with psychiatric illness

- Approximately 7.5% of the general population has either diagnosed or undiagnosed diabetes (5% are diagnosed, 2.5% are undiagnosed)
- Additionally, 6.9% of the general population has hyperglycemia
- Rates of type 2 diabetes among schizophrenic and bipolar patients may be as high as 2-4 times greater than the general population
- An association between psychotropic drug treatment and hyperglycemia has been reported since the 1950's. And patients treated with certain mood stabilizers may have disrupted glucose control as compared with the general population.

There are a number of factors that influence glucose control

- Some of these the patient can not change, such as family history, age, ethnicity, etc. And there are a number of other variable factors, such as weight, diet and exercise, etc. that can play a role. Clearly while some differences in blood glucose are observed, they can only be partially explained by changes in weight.

Draft hyperglycemia story (con't)

Guidelines for individual patients at risk

- If, in a particular patient, you have concerns about the possibility of hyperglycemia and/or diabetes (regardless of psychotropic agent), check the patient's fasting blood glucose levels
- If you have detected elevated blood glucose levels, check for other signs and symptoms such as polyurea, nephropathy, neuropathy, etc. Per American Diabetic Association (ADA) guidelines, you may want to perform additional fasting or glucose tolerance tests. (Abnormal results from 2 fasting or glucose tolerance tests may indicate diabetes.)
- If there are additional symptoms, or fasting levels are too high (→126 mg/dl), utilize treatments recommended by the ADA, such as modifying diet and exercise, or pharmacotherapy. Of course, you may refer as well.
- Hyperglycemia, in any individual patient, must be evaluated in the context of overall efficacy and tolerability. In instances where risks from hyperglycemia are greater than the benefits of the psychotropic therapy for that patient, discontinuation of the psychotropic may be appropriate.

Market Research on "message"

Very consistent takeaway of key message points -- comparable rates amongst relevant agents, common and complex issue where weight gain is only one factor, no demonstrated direct effect of Zyprexa

- Careful to take time to explain Kaplan-Meier curves well

This appears to be generally believable

Makes 'em think, but not all MDs change their basic premise

Critical Observations on this new information

This data is an enhancement to and consistent with our previous message

Remember, handle this objection, like weight gain, in the context of overall efficacy.

- This is all about tone. We must handle the objection in a confident and forthcoming manner, but must only answer the question to the depth required
  - Do not bypass the objection handle it when it happens.
  - Tailor the response to situation, probe, get back to joint discovery

How do we get our message out (focus on non-SF)

Medical Letter

CME

Direct mail?

MD conference call w/ Tollefson?

What are we going to do with the SF in January?

Option 1 -- keep existing piece

Positives

- Representative familiarity
- No additional error

Negatives

- FDA neuropharm (current + future)
- FDA DDMAC
- Problems with PBO data itself
- Pollyanna "just like Lilly usually does"

Option 2 -- use revised piece

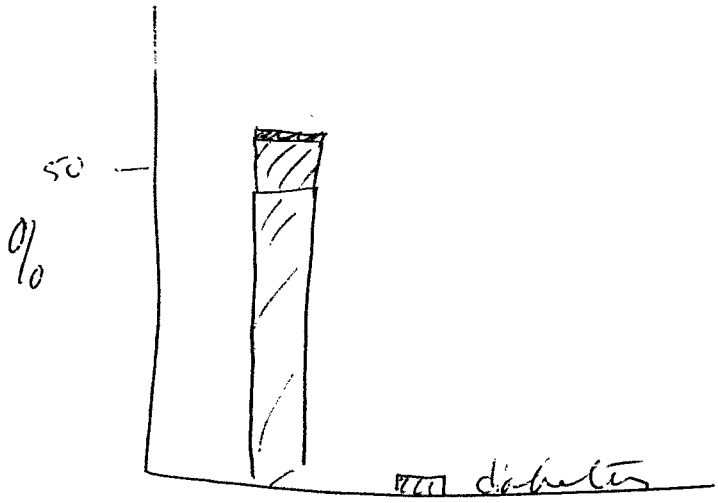
Positives

- Comparison to relevant agents
- Is more forthcoming
- Impactful with many MDs
- We believe it -- and outside experts

Negatives

- Does not (yet) clearly explain to all MDs the apparent contradiction
- It's a change and more complicated (training issue)
- May not match publication
- FDA (neuropharm + DDMAC)

In clinical trials, 60% of pt gained ≥ + weight, but only 3.1% experienced hyperglycemia def, 160



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