PCP Discussion Guide
In our discussion this evening, we will discuss:

- Patients who exhibit complicated mood symptoms associated with bipolar mania including *irritability, anxiety, disrupted sleep, and mood swings*.
- Current treatment plans and results thus far. Are you frustrated about these patients? What symptoms are you trying to alleviate?
- Using ZYPREXA® (olanzapine) for patients with complicated mood symptoms.
Profile: Ashley

- Ashley is a 42-year-old female with no previous history of depression
- She is artistically gifted, the mother of two children (17-yr-old daughter, 5-yr-old son)
- Major depression began without obvious trigger about 2 years ago and her gynecologist prescribed an SSRI
- Family history: bipolar illness in paternal grandfather
Profile: Ashley (cont’d)

- She presents to you suffering from insomnia, irritability, distractibility, and racing thoughts. She has a tendency to be over-talkative. On probing, you find that these symptoms began before she started on the antidepressant.

- Needs mood stabilization
  - ZYPREXA® (olanzapine) 5 mg qhs is started
  - She shows marked improvement in 5 days
  - ZYPREXA is eventually increased to 10 mg qhs with a good response
Profile: Andrea

- Andrea is a 21-yr-old Ivy league student
- During summer vacation, there is a marked change in her behavior
  - Ordinarily quite extroverted, she becomes withdrawn and sullen
  - Friends notify parents who bring her home
  - At home, she is hypoverbal, blunted, isolative, and hypersomnic
Profile: Andrea (cont’d)

- Her parents suggest visiting family physician and Andrea agrees
- Upon visit to PCP, she is clearly depressed and anhedonic
- No significant medical or psychiatric history
- Family psychiatric history: a maternal aunt committed suicide, and maternal grandmother suffered repeated “nervous breakdowns”
- What is your diagnosis?
Profile: Andrea (cont’d)

- She is diagnosed with major depression and started on an antidepressant
  - After 2 days on medication, she appears dramatically improved, more like her old self
  - After 10 days of treatment, she becomes increasingly irritable, restless, anxious, hypervocal, and experiences great difficulty sleeping

- What is happening here?
Profile: Andrea (cont’d)

- Diagnostic clues of bipolar disorder that went undetected:
  - Dramatic onset of depression
  - Early age of onset of illness
  - Family history of manic-depressive illness
  - About 2 years ago, she had an episode lasting one week, during which she spent $3000 on items she didn’t need, slept only 1-2 hours some nights and not at all others, was distractible, and felt agitated and irritable. That episode resolved on its own and she did not seek treatment.

- Her rapid response to an antidepressant was also suggestive of bipolar illness

- After she experienced antidepressant-mobilized mania, accurate diagnosis was made
Profile: Andrea (cont’d)

• New treatment plan:
  – Discontinued the antidepressant
  – Patient started on ZYPREXA® (olanzapine) 10 mg qhs

• Patient significantly improved within one week
Profile: Cindy

• Cindy is a 23-year-old law student who presents with “chronic depression” and anxiety
• Believing her problems began in her late teens, she says she can’t remember the last time she felt good
• Medical history negative, but has been prescribed several antidepressants in the past without benefit
• She reports that most of the medications did nothing at all, but two of them made her feel “jumpy, panicky and sleepless”
• Psychiatric family history: maternal grandfather was an alcoholic; her mother has been diagnosed as dysthymic and is in long-term psychotherapy with a social worker
Profile: Cindy (cont’d)

• At PCP visit, she complains of sadness, lack of sustained interest in anything, insomnia and several vague physical complaints
• She also reports being easily distracted at school, irritable, unable to sit still, and has racing thoughts
• She says she has been unable to complete class assignments and her grades are slipping
• What is your diagnosis?
Profile: Cindy (cont’d)

- Diagnosis of dysthyemic disorder is made, and she is started on an antidepressant
- Within 4 days, she becomes very anxious, agitated and hyperactive, with pressured speech and racing thoughts
- Now, diagnosis of antidepressant exacerbation of mixed symptom state to full-blown mania is made
- Patient begins taking ZYPREXA® (olanzapine) 10 mg qhs, and within one week she reports significant improvement
Group Questions

- What are your current treatment strategies for patients similar to those described today?
- Which specific symptoms do you attempt to resolve first?
- Once those symptoms are resolved, what are your goals for that patient?
- When treating these types of patients, how do you determine which medication to use? Which is more important – the efficacy profile, or the side effect profile of the medication?
- What benefits have you seen in using ZYPREXA® (olanzapine) for these patients?
• There are at least two commonly used algorithms for dosing: One says "start low and go slow" and the other declares "the starting dose is the therapeutic dose." When considering ZYPREXA® (olanzapine), which dosing algorithm makes the most sense to you?

• On what dose would you start a patient with complicated mood symptoms? At what dose would you expect to find a therapeutic effect?
The APA Guidelines and the Texas Medicaid Algorithm Project (TMAP) were published in the *American Journal of Psychiatry* and *The Journal of Clinical Psychiatry* respectively. Both algorithms recommend ZYPREXA® (olanzapine) as a first-line treatment for bipolar mania, like divalproex and lithium. This now makes ZYPREXA the only treatment recommended first line for schizophrenia AND bipolar mania by BOTH of these highly recognized panels.

Does this impact your view of ZYPREXA as a mood stabilizer for your patients suffering from bipolar mania? Why or why not?
Safety Information

• ZYPREXA® (olanzapine) is indicated for the treatment of schizophrenia and for acute mania associated with bipolar I disorder.

• In 6-week acute-phase schizophrenia trials, the most common treatment-emergent adverse event associated with ZYPREXA was somnolence. Other common events were dizziness, weight gain, personality disorder (COSTART term for nonaggressive objectionable behavior), constipation, akathisia, and postural hypotension.

ZYPREXA is a registered trademark of Eli Lilly and Company.
• In short-term, placebo-controlled trials in bipolar mania, the most common treatment-emergent events associated with ZYPREXA® (olanzapine) were somnolence, dry mouth, dizziness, asthenia, constipation, dyspepsia, increased appetite, and tremor.

• In premarketing trials, some patients taking ZYPREXA may have experienced orthostatic hypotension associated with dizziness, tachycardia, and, in some cases, syncope (15/2500, 0.6%).
• In placebo-controlled studies involving schizophrenia patients, clinically significant ALT (SGPT) elevations (≥3 times the upper limit of normal range) were observed in 2% (6/243) of patients exposed to ZYPREXA® (olanzapine) compared to none (0/115) of the placebo patients. None of these patients experienced jaundice. Periodic assessment of transaminases is recommended in patients with significant hepatic disease.

• Prescribing should be consistent with the need to minimize tardive dyskinesia, seizures, and orthostatic hypotension.

See accompanying prescribing information for ZYPREXA.
ZYPREXA® (Olanzapine) Tablets
ZYPREXA® ZYPDIS® (Olanzapine) Oral Disintegrating Tablets

ZYPREXA® (Olanzapine) Tablets

ZYPREXA® ZYPDIS® (Olanzapine) Oral Disintegrating Tablets

ZYPREXA (Olanzapine) is a selective serotonin and dopamine antagonist with antipsychotic properties. It is indicated for the treatment of schizophrenia, schizoaffective disorder, and bipolar disorder.

ZYPREXA is well absorbed and reaches peak concentrations in approximately 4 hours. It is extensively metabolized and undergoes extensive enterohepatic recycling. The metabolic pathways are primarily hydroxylation and glucuronidation.

The efficacy of ZYPREXA in the treatment of schizophrenia and schizoaffective disorder was established in a placebo-controlled trial in patients with the DSM-IV criteria for schizophrenia (N=1,081) or schizoaffective disorder (N=1,053). The primary endpoint was change from baseline to endpoint in the Positive and Negative Syndrome Scale (PANSS) total score. The mean change in PANSS total score at endpoint was significantly greater in the ZYPREXA group compared to the placebo group.

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Several instruments were used for assessing symptom severity and symptoms in these studies, including the Positive and Negative Syndrome Scale (PANSS), the Brief Psychiatric Rating Scale (BPRS), the National Institute of Mental Health (NIMH) Scale for the Assessment of Negative Symptoms (NAS), and the Global Assessment of Functioning (GAF).}

Given these considerations, olanzapine should be prescribed in a manner that is most likely to minimize the occurrence of side effects. The dose should be titrated upward with caution, and the highest effective dose should be used. In patients who are at risk for cardiovascular disease, it is recommended that a lower starting dose be used. ZYPREXA is approved for use in children and adolescents 10 to 17 years of age in the treatment of schizophrenia and the treatment of bipolar disorder.

There were no significant differences in the incidence of adverse events observed in clinical trials of ZYPREXA in children and adolescents compared to those observed in clinical trials of ZYPREXA in adults. The incidence of adverse events in children and adolescents was similar to that observed in adult patients in clinical trials of ZYPREXA.

Nonpsychiatric Side Effects—The efficacy of olanzapine in the treatment of schizophrenia was established in a placebo-controlled trial in patients with the DSM-IV criteria for schizophrenia. A single 10mg dose of ZYPREXA was given to healthy male subjects 6 to 10 weeks before surgery, and the mean change in PDA was significantly greater in the ZYPREXA group compared to the placebo group.

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