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An Open-Label Trial of Venlafaxine in Body Dysmorphic Disorder

Psychiatric Comorbidity of Internet Addiction in College Students: An Interview Study
C-H. Ko, J-Y. Yen, C-S. Chen, C-C. Chen, and C-F. Yen

CASE REPORTS

Auditory, Visual, Tactile, Olfactory, and Bodily Hallucinations in Patients with Obsessive-Compulsive Disorder

Paradoxical Excitation on Diphenhydramine May Be Associated with Being a CYP2D6 Ultrarapid Metabolizer: Three Case Reports
J. de Leon and D.M. Nikoloff

TRENDS IN PSYCHOPHARMACOLOGY

Personalized Medicine, Pharmacogenomics, and the Practice of Psychiatry: On the Threshold of Predictive Therapeutics in Psychopharmacology?
S.M. Stahl

IN SESSION

The Development Process for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
D.A. Regier

COMMUNIQUE

Anti-suicidal and Self-harm Properties of Lithium Carbonate
Manage the diabetic peripheral neuropathic pain (DPNP) symptoms your patients talk about, and those they don’t. Many times, patients don’t mention some of their symptoms because they don’t realize they are related. That’s where Cymbalta can help. Cymbalta provides relief from the dominant symptoms of DPNP and may help relieve underlying symptoms, allowing you to treat patients more completely. To learn more about treating beyond the obvious, visit www.insidecymbalta.com

In pooled analysis and in individual studies, Cymbalta produced a significant separation (P < .05) from placebo on the weekly mean 24-hour average pain score at 12 weeks, the primary outcome of the study.

Important Safety Information

- Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children, adolescents, and young adults with major depressive disorder (MDD) and other psychiatric disorders.
- Patients of all ages started on therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior.
- Cymbalta is not approved for use in pediatric patients.

Cymbalta should not be administered to patients with any hepatic insufficiency or patients with end-stage renal disease (requiring dialysis) or severe renal impairment (CrCl < 30 mL/min).

Postmarketing, severe elevations of liver enzymes or liver injury with a hepatocellular, cholestatic, or mixed pattern have been reported.

Cymbalta should generally not be prescribed to patients with substantial alcohol use or evidence of chronic liver disease.

As observed in DPNP clinical trials, Cymbalta treatment worsens glycemic control in some patients with diabetes. In the extension phases up to 52 weeks, an increase in HbA1c in both the Cymbalta (0.5%) and routine care groups (0.2%) was noted.

Cymbalta should not be administered concomitantly with monoamine oxidase inhibitors (MAOIs) or thioridazine and not in patients with a known hypersensitivity or with uncontrolled narrow-angle glaucoma.

Clinical worsening and suicide risk: All patients being treated with an antidepressant for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially within the first few months of treatment and when changing the dose. A health professional should be immediately notified if the depression is persistently worse or there are symptoms that are severe, sudden, or were not part of the patient’s presentation. If discontinuing treatment, taper the medication.

Development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including Cymbalta treatment, particularly with concomitant use of serotonergic drugs, including triptans. Concomitant use is not recommended.

See Brief Summary of full Prescribing Information, including Boxed Warning, on adjacent page.
INDICATIONS AND USAGE: Cymbalta is indicated for the treatment of major depressive disorder (MDD); the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN; Treatment of generalized anxiety disorder (GAD)).

CONTRAINDICATIONS: Hypersensitivity—Known hypersensitivity to duloxetine or any of the inactive ingredients. Mucous Membrane Ulcers (MUs)—Concomitant use with Cymbalta is contraindicated (see WARNINGS). Drug Interactions—Duloxetine is a potent inhibitor of CYP2D6 and a moderate inhibitor of CYP3A4 (see CLINICAL PHARMACOLOGY, Drug-Drug Interactions). Duloxetine is contraindicated in patients receiving strong CYP3A4 inducers (see CLINICAL PHARMACOLOGY, Drug Interactions).

WARNINGS: Clinical Worsening and Suicidal Risk—Patients with a history of suicide attempt or thoughts of suicide who were started on antidepressant therapy should be observed closely and should be monitored for clinical worsening or suicidality, especially during the initial phases of treatment. These observations should include daily monitoring by health care providers. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant is better than placebo for the prevention of future episodes. Mortality Risk—Cymbalta should not be used in patients with a history of untreated MAO inhibitor use or hypertensive emergency. The risk of suicidality is unknown and should be closely monitored in patients with bipolar depression. Depression and Manic-Depressive Illness—Patients with bipolar depression are at an increased risk of suicide. Patients with bipolar depression should not receive Cymbalta more than 12 weeks of treatment. Cymbalta should not be used in patients with a history of bipolar disorder. Symptoms of mania or hypomania should be observed closely whenever antidepressants are started in patients with a history of a bipolar disorder. Cymbalta is not approved for use in patients with a concurrent history of bipolar disorder.

Neuroendocrine Changes—Cymbalta is a potent inhibitor of CYP3A4 and may increase the risk of hyperglycemia in patients with diabetes. 

Drug-Induced Hypertension—Cymbalta is a potent inhibitor of CYP3A4 and may increase the risk of hypertension. Monitor patients closely for hypertension.

Dyspepsia—In patients treated with Cymbalta, the incidence of dyspepsia was higher than placebo. 

Drug Interactions with MAOIs—In patients receiving a serotonin reuptake inhibitor (SSRI) in combination with an MAOI, there have been reports of serotonin syndrome (SSS) and deaths. The concomitant use of Cymbalta with serotonin precursors (such as tryptophan) is not recommended (see WARNINGS and PRECAUTIONS, Drug Interactions). Consult the package insert for complete prescribing information.

CYP3A4—In patients receiving a serotonin reuptake inhibitor (SSRI) in combination with a CYP3A4 inhibitor, there have been reports of serotonin syndrome (SSS) and deaths. The concomitant use of Cymbalta with serotonin precursors (such as tryptophan) is not recommended (see WARNINGS and PRECAUTIONS, Drug Interactions). Consult the package insert for complete prescribing information.

CYP2D6—Cymbalta is a moderate inhibitor of CYP2D6. When duloxetine is coadministered with a strong CYP2D6 inhibitor, the plasma concentration of the CYP2D6 substrate should be monitored. The concomitant use of Cymbalta with serotonin precursors (such as tryptophan) is not recommended (see WARNINGS and PRECAUTIONS, Drug Interactions). Consult the package insert for complete prescribing information.

CYP1A2—Cymbalta is a potent inhibitor of CYP1A2. The concomitant use of Cymbalta with drugs that are both inhibitors and substrates of CYP1A2 (such as theophylline, aminophylline, caffeine, theobromine) may increase the risk of theophylline toxicity.

CYP2C19—Cymbalta is a weak inhibitor of CYP2C19. The concomitant use of Cymbalta with drugs that are both inhibitors and substrates of CYP2C19 (such as acetylsalicylic acid (ASA), warfarin) may increase the risk of ASA toxicity.

CYP3A4—Cymbalta is a potent inhibitor of CYP3A4. The concomitant use of Cymbalta with drugs that are both inhibitors and substrates of CYP3A4 (such as HIV protease inhibitors, clarithromycin, azithromycin, delavirdine, saquinavir, itraconazole, delavirdine, nefazodone) may increase the risk of drug toxicity.

CYP2C9—Cymbalta is a weak inhibitor of CYP2C9. The concomitant use of Cymbalta with drugs that are both inhibitors and substrates of CYP2C9 (such as clopidogrel) may increase the risk of clopidogrel toxicity.

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Mynsaid® Tablets (lost in translation)

...necessarily caused by the therapy, and the frequencies do not reflect investigator impression (assessment) of causality. 7% of the 223 patients receiving placebo. Nausea (Cymbalta 3.5%, placebo 0.4%), dizziness (Cymbalta 1.6%, placebo 1.0%), vomiting (Cymbalta 1.2%, placebo 0.1%), constipation (Cymbalta 1.6%, placebo 1.3%), dry mouth (Cymbalta 1.3%, placebo 0.5%), glaucoma (Cymbalta 0.7%, placebo 0.3%), and agitation (Cymbalta 0.6%, placebo 0.4%) were observed in pups following exposure to duloxetine. In duloxetine clinical trials, adverse reactions were assessed by collecting adverse events, results from physical examinations, vital signs, weight, laboratory values, and symptoms. Clinical trials of Cymbalta in patients aged 65 and older did not show age-related differences in the frequency of adverse events, compared to younger patients. The most commonly observed adverse events in Cymbalta-treated PD patients (incidence 45% and at least twice the rate of placebo) were: nausea, constipation, diarrhea, constipation and increased bowel movement. Nausea, dry mouth, vomiting, delayed emptying of the stomach, weight loss, lightheadedness, and headache were observed in placebo-treated patients. In clinical trials, a total of 23,983 patients have been exposed to duloxetine. PAH is in a class of drugs known to affect urethral resistance. If symptoms of urinary retention develop, treatment with Cymbalta should be discontinued and other appropriate management instituted. A meta-analysis of all duloxetine clinical trials across depressive disorder, diabetic peripheral neuropathy, and fibromyalgia indicated that the incidence of adverse events was similar across treatments. The most commonly observed adverse events in Cymbalta-treated PD patients (incidence 45% and at least twice the rate of placebo) were: nausea, constipation, diarrhea, constipation and increased bowel movement. Nausea, dry mouth, vomiting, delayed emptying of the stomach, weight loss, lightheadedness, and headache were observed in placebo-treated patients. In clinical trials, a total of 23,983 patients have been exposed to duloxetine.
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Length Reviews and Original Research should not exceed 5,000 words (excluding References). Diagnostic and treatment algorithms should contain an introduction, flowcharts or a series of graphs, and a concise summary. At least 2 tables or figures are required. Letters should not exceed 1,500 words. Single-Case Reports should not exceed 3,750 words and may be submitted with a photograph, if applicable.

Please note: If your article is Original Research, it should be formatted as: Abstract; Introduction; Methods; Results; Discussion; Conclusion; References (numbered and comprehensive list).

Spacing and Pagination Manuscripts should be double-spaced and numbered.

Abstract Authors must provide a brief abstract of 100–200 words.

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Upon the completion of this lecture the participants will be able to:
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Needs Assessment Please provide a brief summary (35–50 words) outlining the educational needs and reasons for reading the article. It should address a deficit or gap in knowledge, skills, attitudes, and/or behavior among the expected readers about the main topic of the article. It should justify the reasons for focusing on the given topic and offering it as a CME activity. Reasons would include recurrent discussions with colleagues about the topic, new therapy or treatment techniques, new data published, “hot topic” in the field, clinical trials in progress, etc.

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□ Six multiple-choice CME questions with answers
□ 3–6 focus points that dictate the main focus of the manuscript in bulleted format
□ 3–6 learning objectives, which begin with an action verb and specify what the reader should know after reading the article
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The voices in his head are back.
I can’t bear to see him like this.

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This will ruin everything.
It could send him back to the hospital.

We’re fighting to get
things back under control.
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For resources to help you help your patients with schizophrenia, visit www.ToolsForTheFight.com
The labeling for ZYPREXA includes a boxed warning:

- Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo.
- ZYPREXA is not approved for the treatment of elderly patients with dementia-related psychosis.

ZYPREXA is approved for the treatment of schizophrenia, acute bipolar mania, and for maintenance treatment in bipolar disorder.

For Important Safety Information, including boxed warning, see adjacent page and accompanying Brief Summary of Prescribing Information.
Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. ZYPREXA is not approved for the treatment of elderly patients with dementia-related psychosis.

Cerebrovascular adverse events (CVAE), including stroke, in elderly patients with dementia—Cerebrovascular adverse events (eg, stroke, transient ischemic attack), including fatalities, were reported in patients in trials of ZYPREXA in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of CVAE in patients treated with ZYPREXA compared to patients treated with placebo. ZYPREXA is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia—Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including olanzapine. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics. Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus, or to have a greater association than some other atypical antipsychotics. Patients with risk factors for diabetes who are starting on atypical antipsychotics should undergo baseline and periodic fasting blood glucose testing. Patients who develop symptoms of hyperglycemia during treatment should undergo fasting blood glucose testing.

Hyperlipidemia—Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using olanzapine, is advised. Significant, and sometimes very high, elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Weight gain—Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight.

Neuroleptic malignant syndrome (NMS)—As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with olanzapine. If signs and symptoms appear, immediate discontinuation is recommended. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

Tardive dyskinesia (TD)—As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of TD. The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Other potentially serious adverse events include orthostatic hypotension, seizures, hyperprolactinemia, transaminase elevations, and dysphagia.

The safety and efficacy of ZYPREXA have not been established in patients under the age of 18 years.

Medication dispensing and prescribing errors have occurred between ZYPREXA® (olanzapine) and Zyrtec® (cetirizine HCl). These errors could result in unnecessary adverse events or potential relapse in patients suffering from schizophrenia or bipolar disorder. To reduce the potential for dispensing errors, please write ZYPREXA clearly.

The most common treatment-emergent adverse event associated with ZYPREXA (vs placebo) in 6-week acute-phase schizophrenia trials was somnolence (26% vs 15%). Other common events were dizziness (11% vs 4%), weight gain (6% vs 1%), personality disorder (COSTART term for nonaggressive objectionable behavior; 8% vs 4%), constipation (9% vs 3%), akathisia (5% vs 1%), and postural hypotension (5% vs 2%).

The most common treatment-emergent adverse event associated with ZYPREXA (vs placebo) in 3- and 4-week bipolar mania trials was somnolence (35% vs 13%). Other common events were dry mouth (22% vs 7%), dizziness (18% vs 6%), asthenia (15% vs 6%), constipation (11% vs 5%), dyspepsia (11% vs 5%), increased appetite (6% vs 3%), and tremor (5% vs 3%).

For complete safety profile, see the full Prescribing Information.

ZYPREXA is a registered trademark of Eli Lilly and Company. Zyrtec is a registered trademark of UCB, SA.
ZYPREXA® (Olanzapine Tablets)
ZYPREXA® Zydis® (Olanzapine Orally Disintegrating Tablets)
ZYPREXA® IntraMuscular (Olanzapine for Injection)

Brief Summary: Please consult package insert for complete prescribing information.

INDICATIONS AND USAGE: ZYPREXA® and ZYPREXA Zydis® are indicated for short- and long-term treatment of schizophrenia (ZYPREXA for oral tablets and Zydis tablets only), for short-term treatment of acute mania associated with bipolar disorder (ZYPREXA for intramuscular injection only) and for the management of symptoms associated with dementia-related psychosis. Use of ZYPREXA for extended periods should be periodically re-evaluated as to the long-term epidemiologic studies have shown an association between chronic administration of this class of drugs and carefully monitored since recurrences have been reported.

Bipolar Disorder—The use of ZYPREXA for extended periods should be periodically re-evaluated as to the long-term

Suicide—The possibility of a suicide attempt is inherent in schizophrenia and in bipolar disorder, and close supervision of patients with a history of suicide is imperative. ZYPREXA should not be prescribed for patients with a history of suicidal ideation or behavior who do not present a clear improvement in symptomatology following initial treatment with a satisfactory antidepressant drug. If the improvement is not sufficiently sustained, the patient should be monitored closely. Patients at risk for suicidal ideation or behavior may include those with a recent history of a psychiatric hospitalization or suicide attempt, patients with a current serious life-threatening diagnosis, patients taking an antidepressant with a high risk of suicidal ideation or behavior or other treatments with a high risk of suicidal ideation or behavior (e.g., anxiolytics, sedatives, hypnotics), or patients with a history of non-suicidal self-injurious behavior (e.g., impulsive, aggressive, and parasuicidal behaviors).

Suicidal ideation and behavior—Suicidal ideation and behavior are common findings associated with a variety of psychiatric disorders, including schizophrenia and bipolar disorder. Patients with schizophrenia and bipolar disorder who are treated with antidepressant drugs are at an increased risk of suicide. In addition, there is an increased risk of suicide, particularly during the early phases of treatment.

Bipolar Disorder—Bipolar disorder is a chronic, recurrent, and potentially life-threatening illness characterized by manic or hypomanic episodes, often accompanied by depressive episodes. The manic or hypomanic episodes are characterized by periods of elation, increased activity, grandiosity, and a sense of well-being, whereas the depressive episodes are characterized by periods of sadness, decreased activity, and feelings of worthlessness. The course of bipolar disorder can be quite variable, with periods of remission and exacerbation.

Bipolar Disorder—Bipolar disorder is characterized by periods of elation, increased activity, grandiosity, and a sense of well-being, known as manic or hypomanic episodes, and periods of sadness, decreased activity, and feelings of worthlessness, known as depressive episodes. The course of bipolar disorder can be quite variable, with periods of remission and exacerbation.

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Adverse Events with an incidence ≥ 1% in Intramuscular Trials—Extrapyramidal Symptoms—In an acute-phase controlled clinical trial in schizophrenia, there was no significant difference in any extrapyramidal symptoms (as measured using Simpson-Angus Scale total score) in patients receiving oral olanzapine (10±2.5, 15±2.5, or 20±2.5 mg/d) compared with placebo. The incidence of extrapyramidal symptoms was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (10±2.5, 15±2.5, or 20±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: dystonia, akathisia, and dyskinesia. In an open, randomized, double-blind study in patients with schizophrenia, schizoaffective disorder, or bipolar disorder comparing fixed doses of 5 mg/d, 10 mg/d, and 20 mg/d: statistically significant differences were seen between doses for the following: baseline to endpoint weight gain, 10 vs 40 mg/d; incidence of treatment-emergent prolactin elevations >12.2 ng/mL (female) or >18.77 ng/mL (male); 10 vs 40 mg/d; and 20 vs 40 mg/d; fatigue, 10 vs 40 mg/d and 20 vs 40 mg/d; and dizziness, 20 vs 40 mg/d.

Side Effects—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (see PRECAUTIONS).

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (see PRECAUTIONS). Asymptomatic elevation of SGOT and SGPT was reported in 0.2% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

ECG Changes—Analyses of pooled placebo-controlled trials revealed no statistically significant changes in PR, QRS, QT, or QTc intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

Other Adverse Events Observed During Clinical Trials—The following treatment-emergent events were reported with oral olanzapine at multiple doses (≥2.5 mg/d in clinical trials [8661 patients; 4165 patient-years of exposure]). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. Frequent events occurred in ≥1/100 patients; infrequent events occurred in 1/100 to 1/1000 patients; rare events occurred in <1/1000 patients.

Body as a Whole—Fatigue, accidental injury, chest pain, dizziness, face edema, abdominal pain, accidental injury, malaise, nausea, neck pain, neck rigidity, pelvis pain, photophobia, respiratory infection, suicidal attempt, chills, abdominal pain, fever.

Cardiovascular—Abdominal pain, abdominal pain, facial edema, back pain, accidental injury, chest pain, dizziness, tremor.

Digestive—Dry mouth, increased thirst, constipation, increased salivation, abdominal pain, nausea.

Metabolic and Nutritional—Weight gain, peripheral edema, edema.

Nervous System—Somnolence, dizziness, tremor.

Skin and Appendages—Sweating, acne, dry skin.

Special Senses—Aphthous ulcer, amaurosis, visual loss, dysguesia, vertigo.

Other Adverse Events—Dose-relatedness of adverse events was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (10±2.5, 15±2.5, or 20±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: astasia, back pain, accidental injury, chest pain.

ZYPREXA® Oral Disintegrating Tablets

ZYPREXA® Intramuscular (Olanzapine for Injection)

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