ZYPREXA® VELOTAB™

Orodispersible Tablets, Olanzapine

ZYPREXA® Olanzapine

HELPING MOVE LIVES FORWARD

Zyprexa is the number 1 prescribed antipsychotic with mood-stabilising properties in Ireland[1]

There are reasons why:

- ✓ Rapid symptom control* in mania[2,3,4,5]
- ✓ Lower hospitalisation rates compared to lithium[6]
- ✓ Prevention of relapse into mania or depression[7]

*Symptom control can be defined as a decrease of 50% or more from baseline YMRS total score.[2] Zyprexa is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to Zyprexa treatment, Zyprexa is indicated for the prevention of recurrence in patients with bipolar disorder.[8] In a 12-month recurrence prevention study in manic episode, patients who achieved remission on olanzapine and were then randomised to olanzapine or placebo, olanzapine demonstrated statistically significant superiority over placebo on the primary endpoint of bipolar recurrence. Olanzapine also showed a statistically significant advantage over placebo in terms of preventing either recurrence into mania or recurrence into depression.[8]

ZYPREXA* TABLETS (OLANZAPINE) REPUBLIC OF IRELAND ABBREVIATED PRESCRIBING INFORMATION ZYPREXA VELOTABS ZYPREXA INTRAMUSCULAR INJECTION. Presentations Tablets 2.5mg, 5mg, 7.5mg, 10mg, 15mg, or 20mg of olanzapine. Also contain lactose. Velotab* 5mg, 10mg, 15mg, or 20mg orodispersible tablets. Also contain gelatin, aspartame, mannitol, and parahydroxybenzoates. Powder for solution for injection, containing 10mg olanzapine. **Uses** *Tablets and Velotabs:* Schizophrenia, both as initial therapy and for maintenance. Moderate to severe manic episode; prevention of recurrence in bipolar disorder in patients whose manic episode has responded to olanzapine treatment. *Injection:* Rapid control of agitation and disturbed behaviours in patients with schizophrenia or manic episode, when oral therapy is not appropriate. **Dosage and Administration** *Tablets and Velotabs: Schizophrenia:* 10mg/day orally. *Manic episode:* 15mg/day in monotherapy; 10mg/day in combination therapy. *Preventing recurrence in bipolar disorder:* 10mg/day, or for patients who have been receiving olanzapine for treatment of manic episode, continue therapy for preventing recurrence at the same dose. May subsequently be adjusted to 5-20mg daily. *Injection:* Intramuscular use only for a maximum of three consecutive days. Initial dose 10mg. A second injection, 5-10mg, may be administered 2 hours after. Maximum daily dose is 20mg, with not more than 3 injections in any 24-hour period. Treatment with Zyprexa Intramuscular Injection should be discontinued, and oral Zyprexa initiated, as soon as clinically appropriate. Do not administer intravenously or subcutaneously. *Children:* Not recommended (under 18 years). *Elderly patients:* Oral therapy - a lower starting dose (5mg/day) is not routinely indicated but should be considered when clinical factors warrant. Injection - recommended starting dose is 2.5-5mg. *Renal and/or hepatic impairment:* 5mg starting dose in moderate hepatic insufficiency. When more than one factor which might cause slower metabolism, consider a decreased starting dose. Gradual dose reduction should be considered when discontinuing olanzapine. **Contra-indications** Known hypersensitivity to any ingredient. Known risk of narrow-angle glaucoma. **Warnings and Special Precautions** Olanzapine is not approved for the treatment of dementia-related psychosis and/or behavioural disturbances because of an increase in mortality and the risk of CVAE. Olanzapine is not indicated for use in the treatment of children and adolescents. *Injection:* Efficacy not established in patients with agitation and disturbed behaviours related to conditions other than schizophrenia or manic episode. Should not be administered to patients with unstable medical conditions (see Summary of Product Characteristics [SPC]). Safety and efficacy have not been evaluated in patients with alcohol or drug intoxication. Patients should be closely observed for hypotension, including postural hypotension, bradyarrhythmia, and/or hypoventilation (see SPC). Simultaneous injection with parenteral benzodiazepine is not recommended. Use to treat drug-induced psychosis with Parkinson's disease is not recommended. Caution in patients: • who receive other medicinal products having haemodynamic properties similar to those of Zyprexa Intramuscular Injection. • with prostatic hypertrophy, or paralytic ileus and related conditions. • with elevated ALT and/or AST, hepatic impairment, limited hepatic functional reserve, and in patients treated with hepatotoxic drugs. If hepatitis is diagnosed, discontinue Zyprexa. • with low leucocyte and/or neutrophil counts, bone marrow depression, in patients receiving medicines known to cause neutropenia, and in patients with hypereosinophilic conditions or with myeloproliferative disease. • who have a history of seizures or are subject to factors which may lower the seizure threshold. • using other centrally acting drugs and alcohol. As with other antipsychotics, caution should be exercised when olanzapine is prescribed with medicines known to increase QTc interval. As with other atypical antipsychotics, sudden cardiac death has been reported in patients taking olanzapine. Discontinue if signs and symptoms indicative of NMS, or unexplained high fever. If tardive dyskinesia appears, consider dose reduction or discontinuation. Appropriate clinical monitoring for hyperglycaemia is advisable in accordance with utilised antipsychotic guidelines. Patients treated with any antipsychotic agents, including Zyprexa, should be observed for signs and symptoms of hyperglycaemia (such as polydipsia, polyuria, polyphagia, and weakness) and patients with diabetes mellitus or with risk factors for diabetes mellitus should be monitored regularly for worsening of glucose control. Weight should be monitored regularly. Blood pressure should be measured periodically in patients over 65 years. Patients treated with any antipsychotic agents, including Zyprexa, should be monitored regularly for lipids in accordance with utilised antipsychotic guidelines. May antagonise effects of dopamine agonists. *Phenylalanine:* Velotabs contain aspartame - a source of phenylalanine. *Sodium methyl parahydroxybenzoate and sodium propyl parahydroxybenzoate:* Contained in Velotabs; known to cause urticaria, contact dermatitis, and, rarely, immediate reactions with bronchospasm. **Interactions** Metabolism may be affected by substances that can specifically induce (eg, concomitant smoking or carbamazepine) or inhibit (eg, fluvoxamine) the isoenzyme P450-CYP1A2 which metabolises olanzapine. Activated charcoal reduces the bioavailability of oral olanzapine. Olanzapine may antagonise the effects of direct and indirect dopamine agonists. Olanzapine showed no interaction when co-administered with lithium or biperiden. Zyprexa Intramuscular Injection 5mg, administered 1 hour before lorazepam 2mg, added to the somnolence observed with either drug alone. **Pregnancy and Lactation** Should be used in pregnancy only if the potential benefit justifies the potential risk to foetus. Patients should be advised not to breast-feed an infant if they are taking Zyprexa. **Driving, etc** May cause somnolence or dizziness. Patients should be cautioned about operating hazardous machinery, including motor vehicles. **Undesirable Effects** Those observed from spontaneous reporting and in clinical trials at a rate of ≥1%, or where the event is clinically relevant, are: *Clinical Trial Adverse Event Reporting and Investigations*, and *Post-Marketing Spontaneous Reporting with Oral Zyprexa. Very common (>10%):* Weight gain[1], somnolence[1], elevated plasma prolactin levels. *Common (1-10%):* Eosinophilia, increased appetite[1], elevated glucose levels, elevated triglyceride levels[1], elevated cholesterol levels[1], glycosuria, dizziness, akathisia, parkinsonism, dyskinesia, orthostatic hypotension, mild transient anticholinergic effects, including constipation and dry mouth[1], transient asymptomatic elevations of ALT and AST[1], asthenia, fatigue, oedema, rash. *Uncommon (0.1-1%):* Bradycardia, QTc prolongation, leucopenia, neutropenia, photosensitivity reaction, alopecia, urinary incontinence, high creatinine phosphokinase, increased total bilirubin. *Not known:* Thrombocytopenia, allergic reaction, development or exacerbation of diabetes occasionally associated with ketoacidosis or coma, including some fatal cases, hypothermia, seizures where in most cases a history of seizures or risk factors for seizures were reported, neuroleptic malignant syndrome, dystonia, tardive dyskinesia, discontinuation symptoms, ventricular tachycardia/fibrillation, sudden death, thromboembolism, pancreatitis, hepatitis, rhabdomyolysis, urinary hesitation, priapism, increased alkaline phosphatase. In clinical trials of elderly patients with dementia, olanzapine was associated with a higher incidence of death and cerebrovascular adverse events compared to placebo. Very common (>10%) undesirable effects in this patient group were abnormal gait and falls. Pneumonia, increased body temperature, lethargy, erythema, visual hallucinations, and urinary incontinence were observed commonly (1-10%). [1]Adverse events in adolescents (13-17 years) with different frequency to adults. *Additional Clinical Trial Adverse Event Reporting and Investigations with Zyprexa Intramuscular Injection. Common (1-10%):* Bradycardia, with or without hypotension or syncope, tachycardia. Injection site discomfort, somnolence, postural hypotension, hypotension. *Uncommon (0.1-1%):* Sinus pause, hypotension. *Post-Marketing Spontaneous Events with Zyprexa Intramuscular Injection.* Temporal association in cases of respiratory depression, hypotension, or bradycardia, and death reported very rarely, mostly with concomitant use of benzodiazepines and/or other antipsychotic drugs, or use of olanzapine in excess of recommended dose. *For full details of these and other side-effects, please see the Summary of Product Characteristics,* which is available at http://www.medicines.ie/. **Legal Category POM Marketing Authorisation Numbers and Holder** EU/1/96/022/002, EU/1/96/022/004, EU/1/96/022/006, EU/1/96/022/009, EU/1/96/022/010, EU/1/96/022/012, EU/1/96/022/014, EU/1/96/022/016, EU/1/99/125/001, EU/1/99/125/002, EU/1/99/125/003, EU/1/99/125/004. Eli Lilly Nederland BV, Grootslag 1-5, 3991 RA Houten, The Netherlands. **Date of Preparation or Last Review** December 2009 **Full Prescribing Information is Available From** Eli Lilly and Company Limited, Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL. Telephone: Basingstoke (01256) 315 000 or Eli Lilly and Company (Ireland) Limited, Hyde House, 65 Adelaide Road, Dublin 2, Republic of Ireland. Telephone: Dublin (01) 661 4377. *ZYPREXA (olanzapine) and VELOTAB are trademarks of Eli Lilly and Company.

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