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ZYPREXA* TABLETS (OLANZAPINE). ZYPREXA VELOTABS. ZYPREXA INTRAMUSCULAR INJECTION. ABBREVIATED PRESCRIBING INFORMATION REPUBLIC OF IRELAND. Presentations Tablets 2.5mg, 5mg, 7.5mg, 10mg, or 15mg of olanzapine. Also contain lactose. Velotab* 5mg, 10mg, or 15mg 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 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, 5-10 mg, 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. **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 CVA. *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. In clinical trials, clinically meaningful QTc prolongations were uncommon in patients treated with olanzapine, with no significant differences in associated cardiac events compared to placebo. As with other antipsychotics, caution should be exercised when olanzapine is prescribed with medicines known to increase QTc interval, especially in the elderly, in patients with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalaemia, or hypomagnesaemia. Discontinue if signs and symptoms indicative of NMS, or unexplained high fever. If tardive dyskinesia appears, consider dose reduction or discontinuation. Clinical monitoring advisable in diabetic patients and those with risk factors for diabetes. Blood pressure should be measured periodically in patients over 65 years. May antagonise effects of dopamine agonists. Gradual dose reduction should be considered when discontinuing olanzapine. *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** There are very rare reports of tremor, hypertonia, lethargy, and sleepiness in infants born to mothers who used olanzapine during the 3rd trimester. Should be used in pregnancy only if the potential benefit justifies the potential risk to the 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** *Clinical Trial Adverse Event Reporting and Investigations With Oral Zyprexa* In placebo-controlled clinical trials of elderly patients with dementia-related psychosis and/or disturbed behaviours, there was a 2-fold increase in mortality in olanzapine-treated patients compared to placebo (3.5% versus 1.5%, respectively). In the same clinical trials, there was a 3-fold increase in cerebrovascular adverse events (CVAE, eg, stroke, transient ischaemic attack) in patients treated with olanzapine compared to placebo (1.3% versus 0.4%, respectively). 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%). *Blood and lymphatics.* Common (1-10%): Eosinophilia. Neutropenia was seen in a valproate combination therapy trial in bipolar mania patients; a potential contributing factor could be high plasma valproate levels. *Metabolism and nutritional.* Very common (>10%): Weight gain. Common (1-10%): Increased appetite, elevated glucose levels (incidence 1.0% for Zyprexa versus 0.9% for placebo for non-fasting levels ≥11mmol/l), elevated triglyceride levels. *Nervous.* Very common (>10%): Somnolence, abnormal gait in *Alzheimer's disease patients. Worsening of Parkinsonian symptomatology and* hallucinations were reported in patients with Parkinson's disease. Common (1-10%): Dizziness, akathisia, parkinsonism, dyskinesia. (Zyprexa-treated patients had a lower incidence of parkinsonism, akathisia, and dystonia compared with titrated doses of haloperidol.) *Cardiac.* Uncommon (0.1-1%): Bradycardia, with or without hypotension or syncope. *Vascular.* Common (1-10%): Orthostatic hypotension. Very rare (<0.01%): QTc prolongation, ventricular tachycardia/ fibrillation, and sudden death. *Gastro-intestinal.* Common (1-10%): Mild, transient, anticholinergic effects, including constipation and dry mouth. *Hepatobiliary.* Common (1-10%): Transient, asymptomatic elevations of ALT, AST. *General.* Common (1-10%): Asthenia, oedema. *Investigations.* Very common (>10%): Elevated plasma prolactin levels, but associated clinical manifestations (eg, gynaecomastia, galactorrhoea, breast enlargement) were rare. *Post-Marketing Spontaneous Reporting With Oral Zyprexa. Blood and lymphatics.* Rare (0.01-0.1%): Leucopenia. Very rare (<0.01%): Thrombocytopenia, neutropenia. **Metabolism and nutritional.** Very rare (<0.01%): Hyperglycaemia and/or development or exacerbation of diabetes, occasionally associated with ketoacidosis or coma, including some fatal cases. Hypertriglyceridaemia, hypercholesterolaemia. *Additional Clinical Trial Adverse Event Reporting and Investigations With Zyprexa Intramuscular Injection. Cardiac.* Common (1-10%): Bradycardia, with or without hypotension or syncope, tachycardia. Uncommon (0.1-1%): Sinus pause. *Vascular.* Common (1-10%): Postural hypotension, hypotension. *General.* Common (1-10%): Injection site discomfort, somnolence. *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 further information see SPCs.* **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/1/96/022/016. EU/1/99/125/001. EU/1/99/125/002. EU/1/99/125/003. Eli Lilly Nederland BV, Grootslag 1-5, 3991 RA Houten, The Netherlands. **Date of Preparation or Last Review** October 2005. **Full Prescribing Information is Available From** Eli Lilly and Company Limited, Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL. Telephone: Basingstoke (01256) 315 999 *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. **References: 1.** Tran PV, Hamilton SH, Kuntz A, et al. *J Clin Psychopharmacol* 1997; 17(5):407-418. **2.** Beasley CM, Tollefson G, Tran P, et al. *Neuropsychopharmacology* 1996; 14(2):111-123. **3.** Tohen M, Zhang F, Feldman P et al. Presented at APA, May 5-10, 2001, New Orleans. **4.** Adapted from Zyprexa Summary of Product Characteristics.

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Zyprexa is manufactured in Cork.

Zyprexa is an **antipsychotic** and a **mood stabiliser**[4]

Zyprexa Olanzapine

HELPING MOVE LIVES FORWARD

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