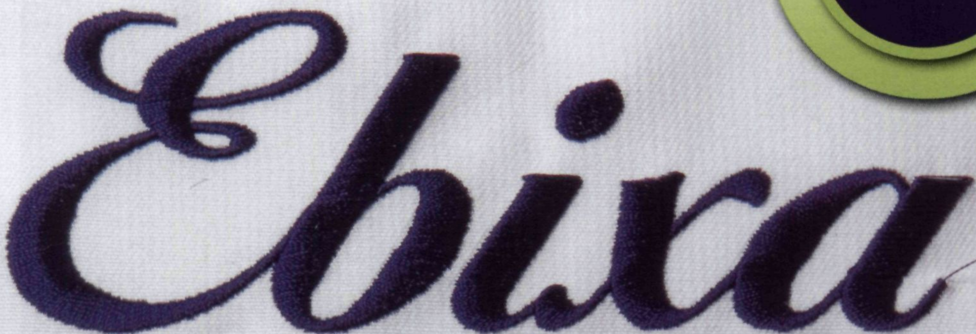
A stitch in time...

CONVENIENCE & COMPLIANCE
20mg
ONCE DAILY



Continuous treatment for Alzheimer's Disease from the moderate stage onwards[1]

- Ebixa: Now Once Daily[1]

  Easier Administration = Convenience + Compliance Benefits [2,3]

- Ebixa: Stabilises symptoms of AD*. Fewer Ebixa treated patients worsened versus placebo [4]

Lundbeck

Ebixa®
memantine

*Moderate AD onwards

Abbreviated Prescribing Information: For full prescribing information refer to the Summary of Product Characteristics. **Name:** Ebixa **Active Substance:** Memantine Hydrochloride. **Indication:** Treatment of patients with moderate to severe Alzheimer's disease. **Dosage & Administration:** Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor the intake of the medicinal product by the patient. Treatment is orally either as tablets (10 mg) or solution (10 mg/g) taken with or without food at the same time every day. Maintenance dose is 20mg/day, (two tablets or 40 drops once a day). Treatment starts with 5mg/day (half a tablet or 10 drops once a day) for the first week; the 2nd week 10mg/day (one tablet or 20 drops once a day); the 3rd week 15mg/day (one and a half tablets or 30 drops once a day) and the 4th week 20mg/day (two tablets or 40 drops once a day). Moderate renal impairment 10mg/day (one tablet or 20 drops once a day), if well tolerated after 7 days the dose can be titrated up to 20mg/day (two tablets or 40 drops once a day). Severe renal impairment- dose is 10 mg/day. Mild-moderate hepatic impairment- no dose adjustment. Severe hepatic impairment- no data available. Children & Adolescents: Not recommended. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Pregnancy and Lactation:** Pregnancy: Memantine should not be used in pregnant women unless clearly necessary. Lactation: Memantine should not be used in women who are breastfeeding. **Special Warnings and Precautions for use:** Caution is recommended in patients with epilepsy. Caution is advised in patients with raised urine pH as this may elevate plasma levels. Clinical trial data are limited on patients with myocardial infarction, uncompensated congestive heart failure and uncontrolled hypertension and patients with these conditions should be closely supervised. Avoid concomitant use of NMDA antagonists (see also interactions). Patients with sugar intolerance should not take Ebixa. Patients should be warned to take special care if driving and using machines as Ebixa has minor to moderate influence on these tasks. Interactions: Effects of L-Dopa, dopaminergic agonists and anticholinergics may be enhanced. Effects of barbiturates and neuroleptics may be reduced. Effect of concomitant treatment with antispasmodic agents e.g. dantrolene and baclofen may be modified. Plasma levels of cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine may be increased. Co-administration with hydrochlorothiazide (HCT) may lead to a reduced serum level of HCT. Concomitant use of NMDA antagonist- amantadine, ketamine, dextromethorphan or phenytoin should be avoided. Close monitoring of prothrombin time or INR is advisable for patients treated concomitantly with oral anticoagulants. **Adverse reactions:** Common (>1/100 and <1/10) headache, somnolence, hypertension, constipation and dizziness. Uncommon reactions (>1/1000 and <1/100): fatigue, fungal infections, confusion, hallucinations (mainly in severe Alzheimer's disease), venous thrombosis/thromboembolism, vomiting, gait abnormal. Very rare (<1/10,000): seizures. Not known: Isolated cases of pancreatitis and psychotic reactions have been reported post-marketing. Alzheimer's disease has been associated with depression, suicidal ideation and suicide. In post-marketing experience these events have been reported in patients treated with memantine. **Overdose:** Symptomatic treatment. **Elimination:** Mainly in unchanged form via the kidneys. **Legal Category:** POM. **Marketing Authorisation Holder:** H.Lundbeck A/S, 9 Ottiliavej, DK-2500, Valby, Denmark. **Marketing Authorisation Numbers:** EU/1/02/219/005 Ebixa 10mg/g Oral drops solution-50g bottle. EU/1/02/219/006 Ebixa 10mg/g Oral drops solution-100g bottle. EU/1/02/219/007 Ebixa Tablets 10mg, 28 pack size. EU/1/02/219/008 Ebixa Tablets 10mg, 56 pack size. Further information may be obtained from: Lundbeck (Ireland) Ltd., 7 Riverwalk, Citywest Business Campus, Citywest, Dublin 24.

References: 1. Ebixa Summary of Product Characteristics 2. Claxton et al. Clin Ther. 2001; 23:1296-1310 3. Shi et a. Exp Rev of Pharm Res. 2007;7: 187-2002 4. Wilkinson et al. Dement Geriatr Cogn Disord. 2007;24(2) 138-145

Date of Preparation: May 2008. **References:** 1. Ebixa Summary of Product Characteristics 2. Claxon et al. Clin Ther. 2001;23:1296-1310 3. hi et al. Exp Rev of Pharm Res. 2007;7:187-2002 4. Wilkinson et al. Dement Geriatr Cogn Disord. 2007; 24(2) 138-145

2/EB/05/08

But now I can let life in."

This is the story of Sinéad* and the voices she began to hear who convinced her that her neighbours wanted her dead. So she barricaded herself in her tiny apartment for three years. Today, with the support of her doctor, treatment team and family, Sinéad is managing her schizophrenia with Zyprexa.[1,2]

Knowing where you have been is one measure of how far you have come. Together you can find another way to stay on the road to improvement.

ZYPREXA TABLETS REPUBLIC OF IRELAND (OLANZAPINE) 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. 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. Undesirable alterations in lipids have been observed in olanzapine-treated patients in placebo-controlled clinical trials. Lipid alterations should be managed as clinically appropriate. 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 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** Those observed from spontaneous reporting and in placebo-controlled clinical trials at a rate of ≥1%, or where the event is clinically relevant, are: *Clinical Trial Adverse Event Reporting and Investigations With Oral Zyprexa. Very common (>10%):* Weight gain, somnolence, elevated plasma prolactin levels, elevated triglyceride levels[1], increased appetite[1], sedation[1], elevations of hepatic transaminases[1], decreased total bilirubin[1], increased GGT[1]. *Common (1-10%):* Eosinophilia, increased appetite, elevated glucose levels, elevated triglyceride levels, elevated cholesterol levels, glycosuria, dizziness, akathisia, parkinsonism, dyskinesia. Orthostatic hypotension, mild, transient anticholinergic effects, including constipation and dry mouth, transient, asymptomatic elevations of ALT, AST, asthenia, fatigue, oedema. *Uncommon (0.1-1%):* Bradycardia, with or without hypotension or syncope. 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. *Post-Marketing Spontaneous Reporting With Oral Zyprexa. Rare (0.01-0.1%):* Leucopenia, seizures, hepatitis, hyperglycaemia, and/or development or exacerbation of diabetes (occasionally associated with ketoacidosis or coma, including some fatal cases). *Very rare (<0.01%):* Thrombocytopenia, neutropenia, allergic reaction, neuroleptic malignant syndrome, parkinsonism, dystonia (including oculogyration), and tardive dyskinesia. Hypertriglyceridaemia, hypercholesterolaemia, QTc prolongation, ventricular tachycardia/fibrillation and sudden death, thromboembolism, pancreatitis, rhabdomyolysis, and priapism. *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. *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** April 2008. **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 et al. Double-blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. *J Clin Psychopharmacol* 1997;17:407-418. **2.** Kinon BJ, Hill AL, Lin L, Perahia DGS, Olanzapine orodispersible tablet in the treatment of acutely ill, non-compliant schizophrenia patients. Poster presented at American Psychiatric Association annual meeting, May 1-6 2004, New York, USA.

**Case study based on fictional characters*

Zyprexa is manufactured in Cork.

ZY/27/09/06/059

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