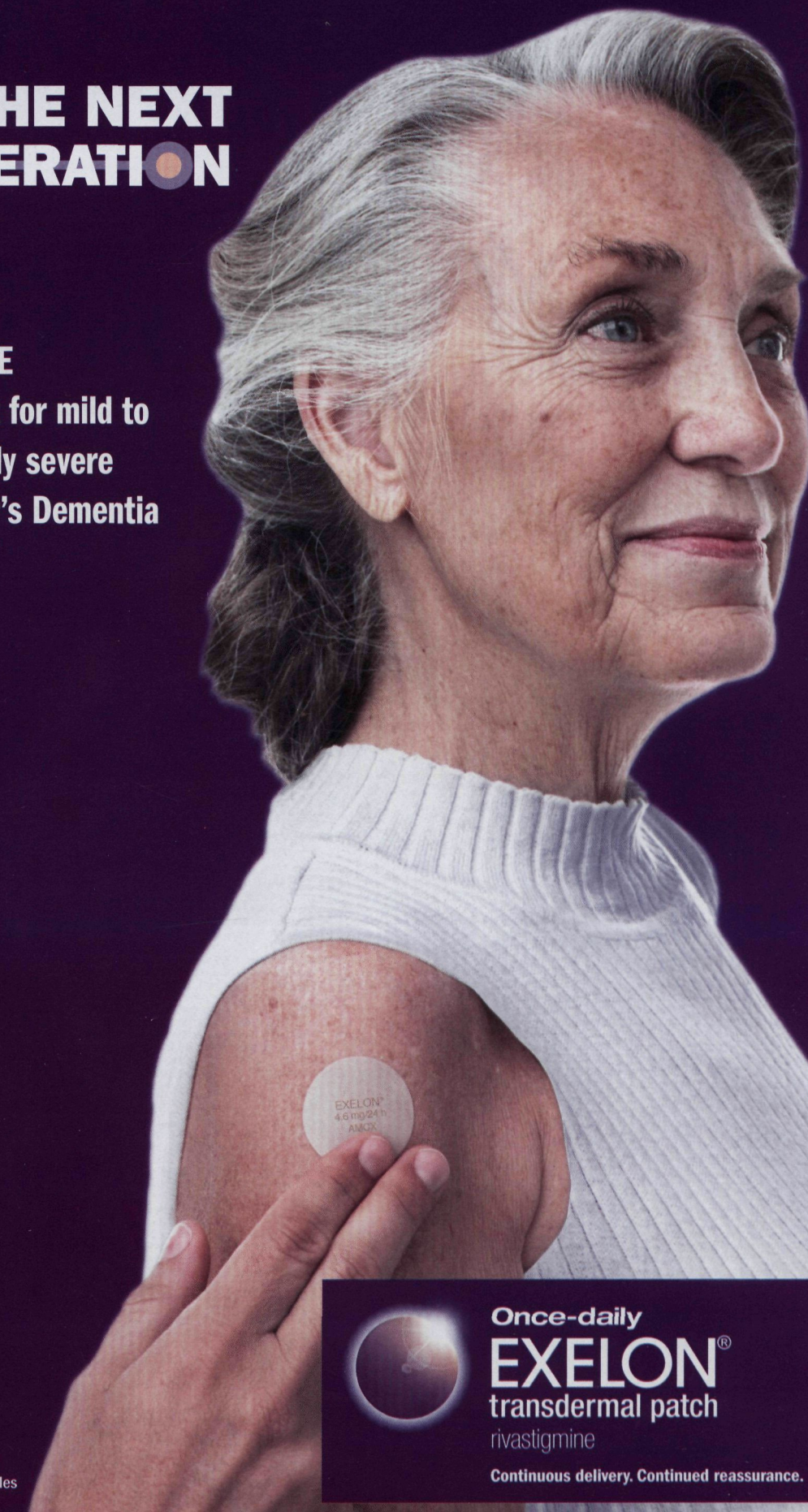
Optimal Efficacy and Tolerability with EXELON Transdermal Patch[1*]

THE NEXT GENERATION

FIRST-LINE
treatment for mild to moderately severe Alzheimer's Dementia



Once-daily
EXELON®
transdermal patch
rivastigmine
Continuous delivery. Continued reassurance.

* versus Exelon capsules

Abbreviated Prescribing Information Exelon 4.6mg/24h Transdermal patch. Exelon 9.5mg/24h Transdermal patch. Note: Before prescribing, please read full prescribing information. **Presentation:** Exelon Patch 4.6mg/24h contains 9mg rivastigmine. The release rate is 4.6mg/24h. Exelon Patch 9.5mg/24h contains 18mg rivastigmine. The release rate is 9.5mg/24h. **Indication:** Symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Dosage and Administration:** Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. A caregiver should be available to regularly administer and monitor the treatment. Initiation and re-initiation of therapy should start with one Exelon Patch 4.6mg/24h. It may be increased after a minimum of 4 weeks to one Exelon Patch 9.5mg/24h each day. Patients treated by Exelon capsules or oral suspension with a maintenance dose of 3mg/day or 6mg/day may be switched to Exelon Patch 4.6mg/24h. Patients on a dose of 9mg/day or higher may be switched to 9.5mg/24h transdermal patch. A minimum of 4 weeks of treatment and good tolerability with the previous dose should be observed before titrating up to higher doses. Transdermal patches should be applied once a day to clean, dry, hairless, intact healthy skin on the upper or lower back, upper arm or chest, in a place which will not be rubbed by tight clothing. It is not recommended to apply the transdermal patch to the thigh or to the abdomen. The transdermal patch should not be applied to skin that is red, irritated or cut. Reapplication to the exact same skin location within 14 days should be avoided. The transdermal patch should be pressed down firmly until the edges stick well. It can be used in everyday situations, including bathing and during hot weather. No dose adjustment is necessary for patients with renal impairment. **Contraindications:** Known hypersensitivity to rivastigmine, other carbamate derivatives, or other excipients used in the formulation. **Precautions/Warnings:** If treatment is interrupted for longer than several days, treatment should be re-initiated with Exelon 4.6mg/24h. Gastrointestinal adverse effects such as nausea and vomiting can occur at initiation of therapy and shortly after dose increase. Patient's weight should be monitored during therapy with Exelon Patch as they may lose weight. As with other cholinomimetics, caution is recommended in patients with sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block), with gastroduodenal ulcerative conditions or patients predisposed to these conditions, with a history of asthma or pulmonary disease, patients predisposed to urinary obstruction and seizures. Caution in patients with clinically significant hepatic impairment and in patients with body weight below 50 kg. The safety of Exelon Patch is not established in pregnant and lactating women. Not recommended in children. Contact with the eyes should be avoided after handling Exelon transdermal patches. **Interactions:** Caution in case of concomitant use with cholinomimetic drugs, anti-cholinergic medications, succinylcholine -type muscle relaxants during anaesthesia. **Adverse Reactions:** Common: vomiting, nausea, anorexia, urinary tract infection, decreased appetite, anxiety, depression, insomnia, syncope, rash, headache, diarrhoea, dyspepsia, abdominal pain, fatigue, asthenia, weight decrease, pyrexia and skin reactions (i.e. erythema, pruritus, irritation, oedema, dermatitis). Uncommon: Bradycardia, gastric ulcers, extrapyramidal symptoms. **Pack Sizes:** Cartons containing 30 sachets, each sachet contains one transdermal patch. **Legal Category:** POM. **Marketing Authorisation Numbers:** EU/1/98/066/022-026. **Date of API Preparation:** October 2007. **Full prescribing information available from:** Novartis Ireland Limited, House, Beech Hill Office Campus, Clonskeagh, Dublin 4. Tel: 01-2601255. **Reference 1.** Winblad B, Cummings J, Olsson N., et al.; Int J Geriatr Psychiatry 2007; 22 : 436-67. **Date of Preparation:** September 2008. NOO908696

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ZYPREXA
Olanzapine
HELPING MOVE LIVES FORWARD

Now I want to gain control again."

This is the story of Anna* and a lifetime of excessive buying and collecting. When she couldn't sleep, she shopped. Today, with the support of her doctor, treatment team, and family, Anna is managing her relapses in bipolar disorder with Zyprexa, and can add a university degree to her collecting.[1]

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 freq[illegible] to adults. *Post-Marketing Spontaneous Reporting With Oral Zyprexa. Rar[illegible] 0.1%):* Leucopenia, seizures, hepatitis, hyperglycaemia, and/or developm[illegible] 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.

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