THE BRITISH JOURNAL OF PSYCHIATRY

SEPTEMBER 1999 VOL. 175

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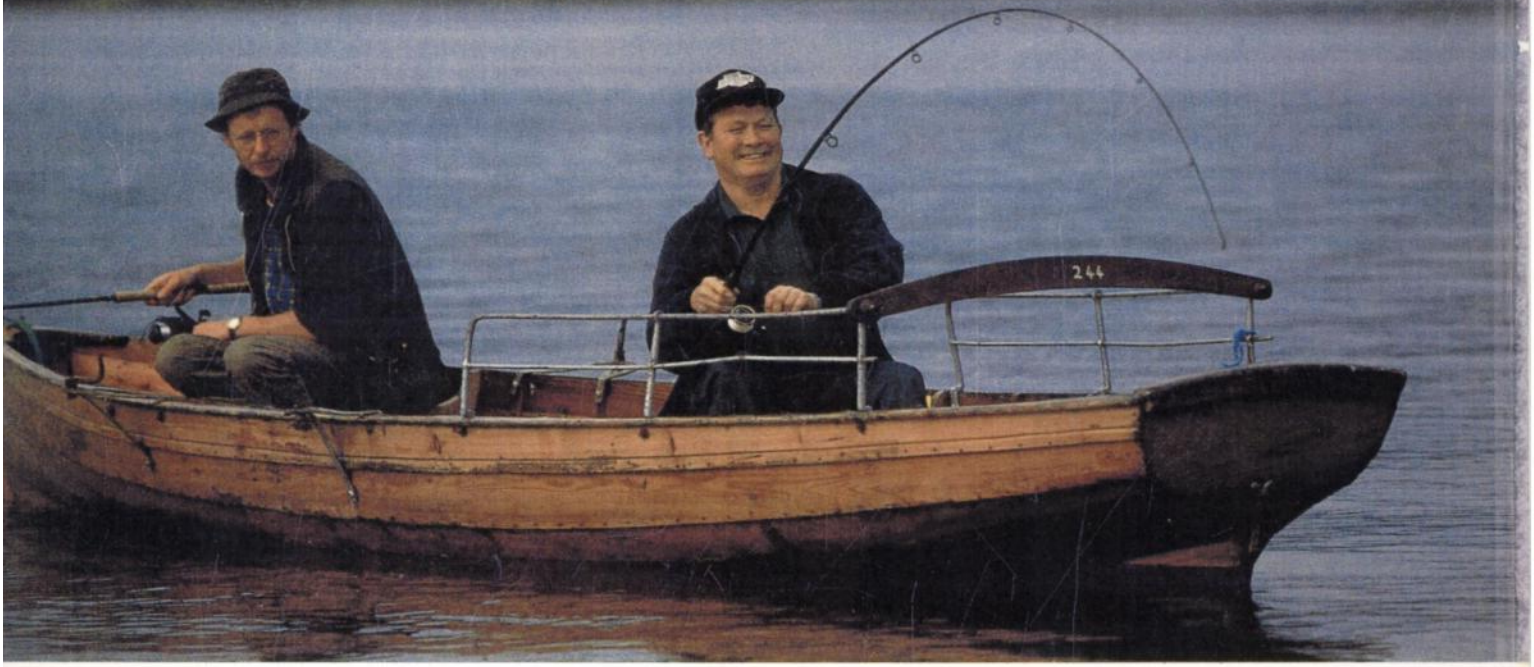
The difference is plain to see



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Abbreviated prescribing information. Presentation: 'Cipramil' tablets 10 mg: PL 0458/0057, each containing 10 mg of citalopram as the hydrobromide. 28 (OP) 10 mg tablets £10.09. 'Cipramil' tablets 20 mg: PL 0458/0058, each containing 20 mg of citalopram as the hydrobromide. 28 (OP) 20 mg tablets £16.79. 'Cipramil' tablets 40 mg: PL 0458/0059, each containing 40 mg of citalopram as the hydrobromide. 28 (OP) 40 mg tablets £28.38. **Indications:** Treatment of depressive illness in the initial phase and as maintenance against relapse/recurrence. Treatment of panic disorder, with or without agoraphobia. **Dosage:** ***Treating depression: Adults:*** 20 mg a day. Depending upon individual patient response, this may be increased in 20 mg increments to a maximum of 60 mg. Tablets should not be chewed, and should be taken as a single oral daily dose, in the morning or evening without regard for food. Treatment for at least 6 months is usually necessary to provide adequate maintenance against the potential for relapse. ***Treating panic disorder:*** 10 mg daily for the first week, increasing to 20 mg daily. Depending upon individual patient response, dosage may be further increased to a maximum of 60 mg daily. Depending upon individual patient response, it may be necessary to continue treatment for several months. ***Elderly:*** 20 mg a day increasing to a maximum of 40 mg dependent upon individual patient response. ***Children:*** Not recommended. ***Reduced hepatic/renal function:*** Restrict dosage to lower end of range in hepatic impairment. Dosage adjustment not necessary in cases of mild/moderate renal impairment. No information available in severe renal impairment (creatinine clearance <20ml/min). **Contra-indications:** Combined use of 5-HT agonists. Hypersensitivity to citalopram. ***Pregnancy and Lactation:*** Safety during human pregnancy and lactation has not been established. Use only if potential benefit outweighs possible risk. **Precautions:** Driving and operating machinery. History of mania. Caution in patients at risk of cardiac arrhythmias. Do not use with or within 14 days of MAO inhibitors: leave a seven day gap before starting MAO inhibitor treatment. Use a low starting dose for panic disorder, to reduce the likelihood of an initial anxiogenic effect (experienced by some patients) when starting pharmacotherapy. **Drug interactions:** MAO inhibitors (see Precautions). Use lithium and tryptophan with caution. Routine monitoring of lithium levels need not be adjusted. **Adverse Events:** Most commonly nausea, sweating, tremor, somnolence and dry mouth. With citalopram, adverse effects are in general mild and transient. When they occur, they are most prominent during the first two weeks of treatment and usually attenuate as the depressive state improves. Withdrawal symptoms have been reported with SSRIs. Abrupt withdrawal of citalopram should be avoided. **Overdosage:** Symptoms have included somnolence, coma, sinus tachycardia, occasional nodal rhythm, episode of grand mal convulsion, nausea, vomiting, sweating and hyperventilation. No specific antidote. Treatment is symptomatic and supportive. Early gastric lavage suggested. **Legal Category:** POM 24.1.95. Further information available upon request. Product licence holder: Lundbeck Ltd., Sunningdale House, Caldecotte Lake Business Park, Caldecotte, Milton Keynes, MK7 8LF. ® 'Cipramil' is a Registered Trade Mark. © 1999 Lundbeck Ltd. Date of preparation: May 1999. 0599/CIP/501/058

References: 1. Hyttel J. XXII Nordiske Psykiater Kongres, Reykjavik, 1988; 11-21. **2.** Eison AS et al. Psychopharmacology Bull 1990; 26 (3): 311-315. **3.** Based on 28 days' treatment, prices from MIMS, May 1999. **4.** Patris M et al. Int Clin Psychopharmacol 1996; 11: 129-138. **5.** Stahl SM. Citalopram vs sertraline vs placebo: preliminary efficacy results. Poster presented at the APA meeting, 1998. **6.** Data on file, Lundbeck Limited, to December 1998. **7.** Taylor Nelson 'Scriptcount' prescription audit data, 6 months to March 1999.

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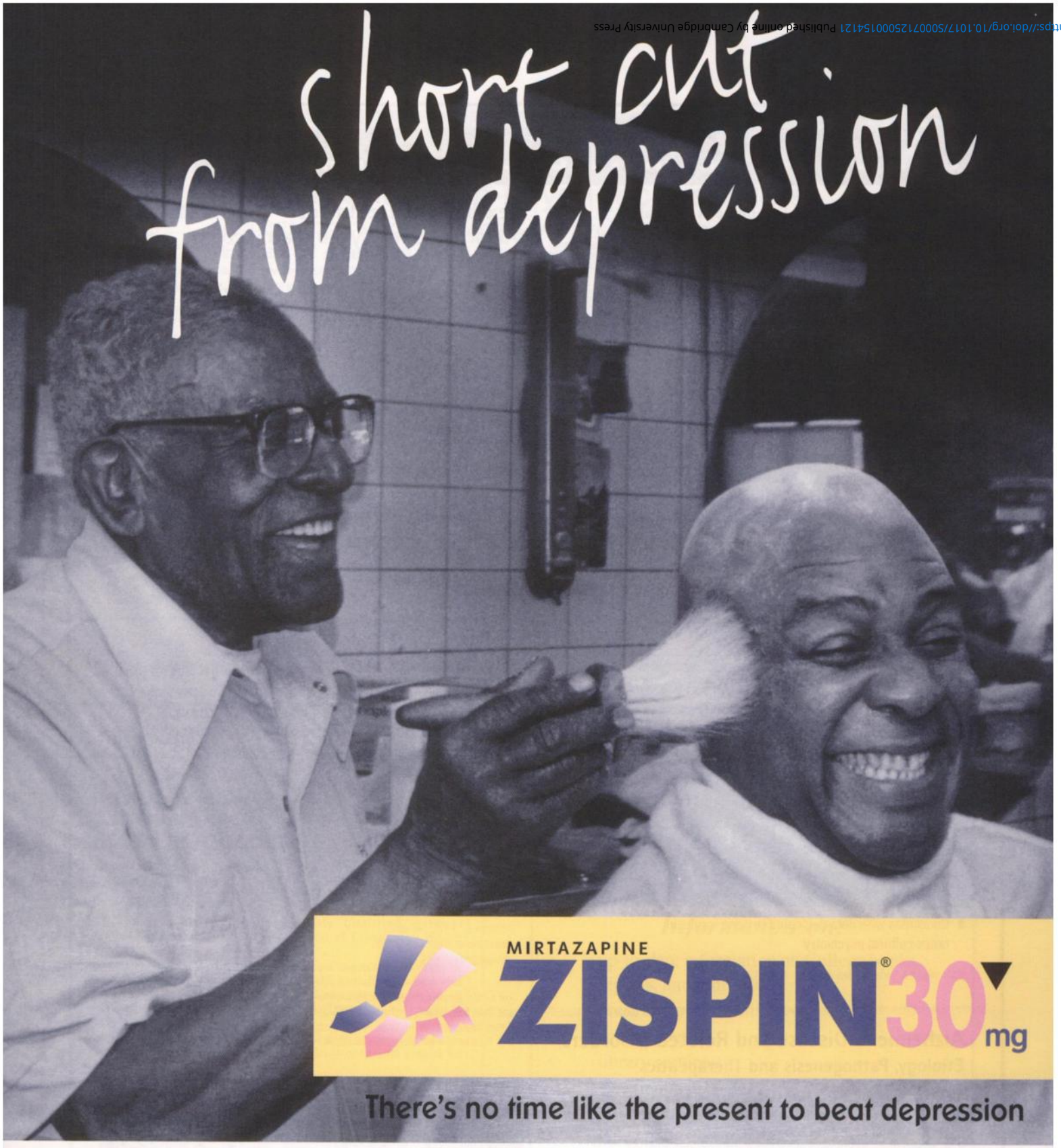

Prescribing Information

Presentation: Blister strips of 28 tablets each containing 30 mg of mirtazapine. **Uses:** Treatment of depressive illness. **Dosage and administration:** The tablets should be taken orally, if necessary with fluid, and swallowed without chewing. **Adults and elderly:** The effective daily dose is usually between 15 and 45 mg. **Children:** Not recommended. The clearance of mirtazapine may be decreased in patients with renal or hepatic insufficiency. Zispin is suitable for once-a-day administration, preferably as a single night-time dose. Treatment should be continued until the patient has been completely symptom-free for 4-6 months. **Contraindications:** Hypersensitivity to mirtazapine or any ingredients of Zispin. **Precautions and warnings:** Reversible white blood cell disorders including agranulocytosis, leukopenia and granulocytopenia have been reported with Zispin. The physician should be alert to symptoms such as fever, sore throat, stomatitis or other signs of infection; if these occur, treatment should be stopped and blood counts taken. Patients should also be advised of the importance of these symptoms. Careful dosing as well as regular and close monitoring is necessary in patients with: epilepsy and organic brain syndrome; hepatic or renal insufficiency; cardiac diseases; low blood pressure. As with other antidepressants care should be taken in patients mellitus. Treatment should be discontinued if jaundice occurs. Moreover, as with other antidepressants, the following should be taken into account: worsening of psychotic symptoms can occur when antidepressants are administered to patients with schizophrenia or other psychotic disturbances; when the depressive phase of manic-depressive psychosis is being treated, it can transform into the manic phase. Zispin has sedative properties and may impair concentration and alertness. **Interactions:** Mirtazapine may potentiate the central nervous dampening action of alcohol; patients should therefore be advised to avoid alcohol during treatment with Zispin; Zispin should not be administered concomitantly with MAO inhibitors or within two weeks of cessation of therapy with these agents; Mirtazapine may potentiate the sedative effects of benzodiazepines; In vitro data suggest that clinically significant interactions are unlikely with mirtazapine. **Pregnancy and lactation:** The safety of Zispin in human pregnancy has not been established. Use during pregnancy is not recommended. Women of child bearing potential should employ an adequate method of contraception. Use in nursing mothers is not recommended. **Adverse reactions:** The following adverse effects have been reported: **Common (>1/100):** Increase in appetite and weight gain. Drowsiness/sedation, generally occurring during the first few weeks of treatment (N.B. dose levels. **Rare (<1/1000):** Oedema and accompanying weight gain. Reversible agranulocytosis has been reported as a rare occurrence. (Orthostatic) hypotension. Exanthema. Mania, convulsions, tremor, myoclonus. **Overdosage:** Toxicity studies in animals suggest that clinically relevant cardiotoxic effects will not occur after overdosing with Zispin. Experience in clinical trials and from the market has shown that no serious adverse effects have been associated with Zispin in overdose. Symptoms of acute overdosage are confined to prolonged sedation. Cases of overdose should be treated by gastric lavage with appropriate symptomatic and supportive therapy for vital functions. **Marketing authorization number:** PL 0065/0145 **Legal category:** POM **Basic NHS cost:** £24 for 28 tablets of 30 mg.

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ABBREVIATED PRESCRIBING INFORMATION
Please refer to the SmPC before prescribing VIAGRA 25mg, 50mg or 100mg. **Presentation:** Blue film-coated, rounded diamond-shaped tablets containing sildenafil citrate equivalent to 25mg, 50mg and 100mg sildenafil. **Indications:** Erectile dysfunction. Sexual stimulation is required for efficacy. Not for use by women. **Dosage:** *Adults;* 50mg approximately one hour before sexual activity. Adjust dose based on efficacy and toleration. Maximum dose is 100mg. One single dose per day is recommended. If taken with food, the onset of activity may be delayed. *Elderly;* a first dose of 25mg should be used. *Hepatic impairment, severe renal impairment;* 25mg initial dose should be considered; adjust dose based on efficacy and toleration. *Children under 18 years;* Not indicated. **Contra-indications:** Co-administration with nitric oxide donors (such as amyl nitrite) or nitrates in any form; patients for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders); severe hepatic impairment; hypotension; recent stroke or myocardial infarction; known hereditary degenerative retinal disorders; hypersensitivity to sildenafil or to any of the excipients. **Pregnancy and lactation:** Not indicated for women. **Warnings and precautions:** A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes. Cardiovascular status, as sexual activity is associated with cardiac risk. Sildenafil has vasodilator properties resulting in mild and transient decreases in blood pressure and as such potentiates the hypotensive effect of nitrates. Patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease) or predisposed to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia). Patients with bleeding disorders or active peptic ulceration. Not recommended in combination with other treatments for erectile dysfunction. **Drug Interactions:** In combination with inhibitors of CYP3A4 eg ketoconazole, erythromycin, cimetidine, a 25mg starting dose should be considered. Potentiates the hypotensive effects of nitrates (see contra-indications). No potentiation of the increase in bleeding time caused by acetyl salicylic acid (150mg) or the hypotensive effects of alcohol. No data on non-specific phosphodiesterase inhibitors such as theophylline or dipyridamole. **Side-effects:** Clinical study experience: headache, flushing, dizziness, dyspepsia, nasal congestion, altered vision (colour tinge, increased perception of light or blurred vision). Dyspepsia and altered vision more common at 100mg. Muscle aches when sildenafil administered more frequently than recommended. Post marketing experience: priapism. Driving and operating machinery: Caution if affected by dizziness or altered vision. **Legal category:** POM. Basic NHS cost: Packs of 4, 25mg tablets [EU/1/98/077/002] £16.59; Packs of 8, 25mg tablets [EU/1/98/077/003] £33.19; Packs of 4, 50mg tablets [EU/1/98/077/006] £19.34; Packs of 8, 50mg tablets [EU/1/98/077/007] £38.67; Packs of 4, 100mg tablets [EU/1/98/077/010] £23.50; Packs of 8, 100mg tablets [EU/1/98/077/011] £46.99. **Marketing Authorisation Holder:** Pfizer Limited, Sandwich, Kent, CT13 9NJ, United Kingdom. Last revised: 21 October 1998. Further information on request: Pfizer Limited, Sandwich, Kent, CT13 9NJ. **References:** 1. Goldstein I et al. New Engl J Med, 1998, 338(20): 1397-1404. 2. Morales A et al. Int J Impot Res, 1998, 10: 69-74. 3. Holmgren E et al. Presented at AAN 50th Annual Meeting, 1998, Minneapolis. 4. Giuliano F et al. J Urol 1997; 80(2): 93 Abstr 366. 5. Young S. Br J Ob & Gyn, 1998, (Suppl): 275.

Pfizer

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CLOZARIL
clozapine

CLOZARIL ABBREVIATED PRESCRIBING INFORMATION. The use of CLOZARIL is restricted to patients registered with the CLOZARIL Patient Monitoring Service. Indication: Treatment-resistant schizophrenia (patients non-responsive to, or intolerant of, conventional neuroleptics). **Presentations:** 25mg and 100mg clozapine tablets. **Dosage and Administration:** Initiation must be in hospital in-patients and is restricted to patients with normal white blood cell and differential counts. Initially, 12.5mg once or twice on first day, followed by one or two 25mg tablets on second day. Increase dose slowly, by increments (see data sheet). The total daily dose should be divided and a larger portion of the dose may be given at night. Once control is achieved a maintenance dose of 150 to 300mg daily may suffice. At daily doses not exceeding 200mg, a single administration in the evening may be appropriate. Doses up to 900mg daily may be used. Dose-related convulsions have been reported especially during dose titration. Patients with a history of seizures, those suffering from cardiovascular, renal or hepatic disorders, and the elderly need lower doses (12.5mg given once on the first day) and more gradual titration. **Contra-Indications:** Allergy to any constituents of the formulation. History of drug-induced neutropenia/agranulocytosis, myeloproliferative disorders, uncontrolled epilepsy, alcoholic and toxic psychoses, drug intoxication, comatose conditions, circulatory collapse and/or CNS depression of any cause, severe renal or cardiac failure. Active liver disease, progressive liver disease or hepatic failure. **Warnings & Precautions:** CLOZARIL can cause agranulocytosis. A fatality rate of up to 1 in 300 has been estimated when CLOZARIL was used prior to recognition of this risk. Since then strict haematological monitoring of patients has been demonstrated to be effective in markedly reducing the risk of fatality. Because of this risk, CLOZARIL use is limited to treatment-resistant schizophrenic patients:- 1. who have normal leucocyte findings and 2. in whom regular leucocyte counts can be performed weekly during the first 18 weeks and at least two-weekly for the first year of therapy. After one years treatment, monitoring may be changed to four weekly intervals in patients with stable neutrophil counts. Monitoring must continue throughout treatment and for four weeks after discontinuation of CLOZARIL. Patients must be under specialist supervision. CLOZARIL supply is restricted to pharmacies registered with the CLOZARIL Patient Monitoring Service. Prescribing physicians must register themselves, their patients and a nominated pharmacist with the CLOZARIL Patient Monitoring Service. This service provides for the required leucocyte counts and a drug supply audit so that CLOZARIL is promptly withdrawn from any patient who develops abnormal leucocyte findings. Each time CLOZARIL is prescribed, patients should be reminded to contact their physician immediately if any kind of infection begins to develop, especially if flu-like. Immediate differential count is necessary if signs or symptoms of infection develop. Re-evaluate any patient developing an infection, or when a routine white blood count of between 3.0 and 3.5 x 10^9/L and/or a neutrophil count between 1.5 and 2.0 x 10^9/L, with a view to discontinuing CLOZARIL. If the white blood count falls below 3.0 x 10^9/L and/or the absolute neutrophil count drops below 1.5 x 10^9/L, withdraw CLOZARIL immediately and monitor the patient closely, paying particular attention to symptoms suggestive of infection. Any further fall in white blood/neutrophil count below 1.0 x 10^9/L and/or 0.5 x 10^9/L respectively, after drug withdrawal requires immediate specialised care. Protective isolation and administration of GM-CSF or G-CSF and broad spectrum antibiotics may be indicated. Discontinue colony stimulating factor when the neutrophil count returns above 1.0 x 10^9/L. CLOZARIL lowers the seizure threshold. Orthostatic hypotension can occur therefore close medical supervision is required during initial dose titration. Patients, if affected by the sedative action of CLOZARIL, should not drive or operate machinery, administer with caution to patients who participate in activities requiring complete mental alertness. Monitor hepatic function regularly in liver disease. Investigate any signs of liver disease immediately with a view to drug discontinuation. Resume only if LFTs return to normal, then closely monitor patient. Use with care in prostatic enlargement, narrow-angle glaucoma and paralytic ileus. Patients with fever should be carefully evaluated to rule out the possibility of an underlying infection or the development of agranulocytosis. Avoid immobilisation of patients due to increased risk of thromboembolism. Do not give with other drugs with a substantial potential to depress bone marrow function. CLOZARIL may enhance the effects of alcohol, MAO inhibitors, CNS depressants and drugs with anticholinergic, hypotensive or respiratory depressant effects. Caution is advised when CLOZARIL therapy is initiated in patients who are receiving (or have recently received) a benzodiazepine or any other psychotropic drug as these patients may have an increased risk of circulatory collapse, which, rarely, can be profound and may lead to cardiac and/or respiratory arrest. Caution is advised with concomitant highly protein bound drugs. Clozapine binds to and is partially metabolised by the isoenzymes cytochrome P450 1A2 and P450 2D6. Caution is advised with drugs which possess affinity for these isoenzymes. Concomitant cimetidine and high dose CLOZARIL has been associated with increased plasma clozapine levels and the occurrence of adverse effects. Concomitant fluoxetine and fluvoxamine have been associated with elevated clozapine levels. Discontinuation of concomitant carbamazepine resulted in increased clozapine levels. Phenytoin decreases clozapine levels resulting in reduced CLOZARIL effectiveness. No clinically relevant interactions have been noted with tricyclic antidepressants, phenothiazines and type lc antiarrhythmics, to date. Concomitant lithium or other CNS-active agents may increase the risk of neuroleptic malignant syndrome. The hypertensive effect of adrenaline and its derivatives may be reversed by CLOZARIL. Do not use in pregnant or nursing women. Use adequate contraceptive measures in women of child bearing potential. **Side-Effects:** Neutropenia leading to agranulocytosis (See Warnings and Precautions). Rare reports of leucocytosis including eosinophilia. Isolated cases of leukaemia and thrombocytopenia have been reported but there is no evidence to suggest a causal relationship with the drug. Most commonly fatigue, drowsiness, sedation. Dizziness or headache may also occur. CLOZARIL lowers the seizure threshold and may cause EEG changes and delirium. Myoclonic jerks or convulsions may be precipitated in individuals who have epileptogenic potential but no previous history of epilepsy. Rarely it may cause confusion, restlessness, agitation and delirium. Extrapyramidal symptoms are limited mainly to tremor, akathisia and rigidity. Tardive dyskinesia reported very rarely. Neuroleptic malignant syndrome has been reported. Transient autonomic effects e.g. dry mouth, disturbances of accommodation and sweating/temperature regulation. Hypersalivation may occur. Tachycardia and postural hypotension, with or without syncope, and less commonly hypertension may occur. Rarely, profound circulatory collapse has occurred. ECG changes, arrhythmias, pericarditis and myocarditis (with or without eosinophilia) have been reported, some of which have been fatal. Rare reports of thromboembolism. Isolated cases of respiratory depression or arrest, with or without circulatory collapse. Rarely aspiration may occur in patients presenting with dysphagia or as a consequence of acute overdosage. Rarely, parotid gland enlargement. Nausea and vomiting have been reported. Mild constipation may occur, however, it may be more severe and fatal complications including gastrointestinal obstruction and paralytic ileus have occurred. Monitor patients and prescribe laxatives, as required. Care is required in patients receiving other medicines known to cause constipation or with a history of colonic disease or lower abdominal surgery. It is important to recognise and actively treat constipation. Asymptomatic elevations in liver enzymes occur commonly and usually resolve without drug discontinuation. Rarely hepatitis and cholestatic jaundice may occur. Very rarely fulminant hepatic necrosis reported. Discontinue CLOZARIL if jaundice develops. Rare cases of acute pancreatitis have been reported. Urinary incontinence and retention and priapism have been reported. Isolated cases of interstitial nephritis have occurred. Benign hyperthermia may occur and isolated reports of skin reactions have been received. Rarely hyperglycaemia has been reported. Rarely increases in CPK values have occurred. With prolonged treatment considerable weight gain has been observed. Sudden unexplained deaths have been reported in patients receiving CLOZARIL. **Package Quantities and Price:** Community pharmacies only 28 x 25mg tablets: £12.52 (Basic NHS) 28 x 100mg tablets: £50.05 (Basic NHS) Hospital pharmacies only 84 x 25mg tablets: £37.54 (Basic NHS) 84 x 100mg tablets: £150.15 (Basic NHS) Supply of CLOZARIL is restricted to pharmacies registered with the CLOZARIL Patient Monitoring Service. **Product Licence Numbers:** 25 mg tablets: PL 0101/0228 100 mg tablets: PL 0101/0229 **Legal Category:** POM. CLOZARIL is a registered Trade Mark. Full prescribing information, including Summary of Product Characteristics is available from Novartis Pharmaceuticals UK Ltd. Trading as: SANDOZ PHARMACEUTICALS Frimley Business Park, Frimley, Camberley, Surrey, GU16 5SG.

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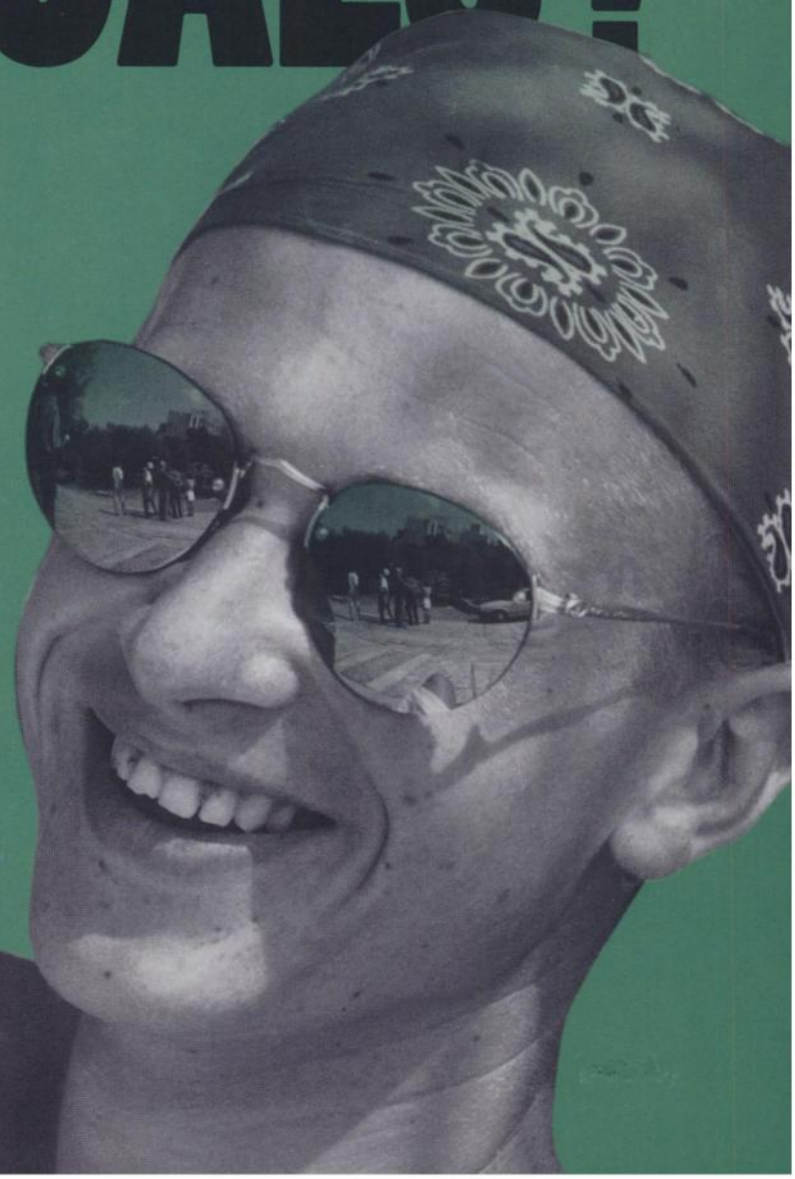

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clozapine

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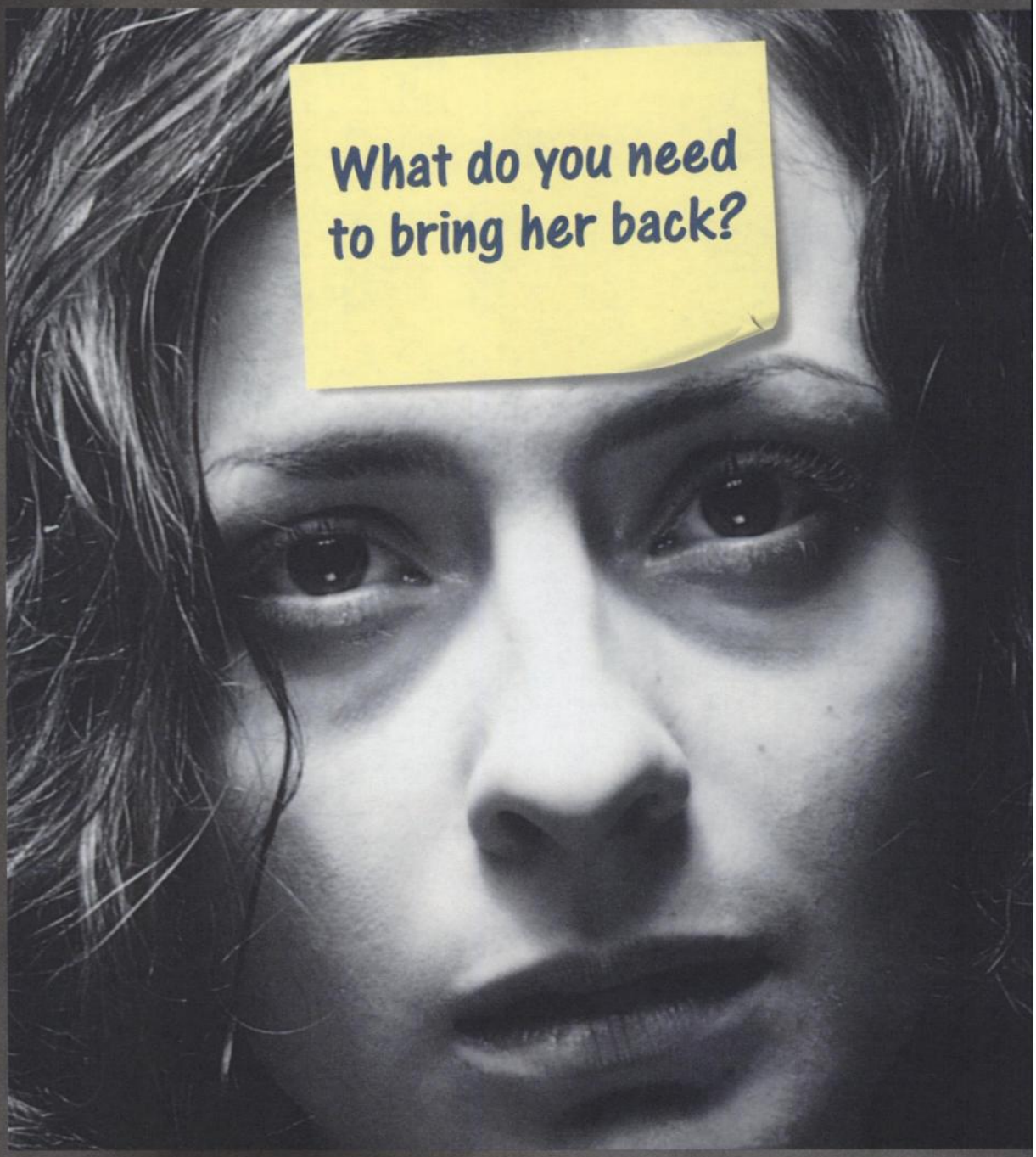

Prescribing Information - Solian 200 and Solian 50 Presentation: Solian 200 tablets contain 200mg amisulpride and Solian 50 tablets contain 50mg amisulpride. **Indication:** Acute and chronic schizophrenia including predominant negative symptoms. **Dosage:** Acute psychotic episodes: 400-800mg/day, increasing up to 1200mg/day according to individual response (dose titration not required), in divided doses. Predominantly negative symptoms: 50-300mg once daily adjusted according to individual response. Elderly: administer with caution due to the risk of hypotension or sedation. Renal insufficiency: reduce dose and consider intermittent therapy. Hepatic insufficiency: no dosage adjustment necessary. Children: contraindicated in children under 15 years (safety not established). **Contraindications:** Hypersensitivity; concomitant prolactin-dependent tumours e.g. pituitary gland prolactinaemias and breast cancer; phaeochromocytoma; children under 15 years; occur (discontinue Solian). Caution in patients with a history of epilepsy and Parkinson's disease. **Interactions:** Caution in concomitant administration of CNS depressants (including alcohol), antihypertensives and other hypotensive medications, and dopamine agonists. **Side Effects:** Insomnia, anxiety, agitation. Less commonly somnolence and GI disorders. In common with other neuroleptics Solian causes a reversible increase in plasma prolactin levels. Solian may also cause weight gain, acute dystonia, extrapyramidal symptoms, tardive dyskinesia, hypotension and bradycardia. Rarely, allergic reactions, seizures and neuroleptic malignant syndrome have been reported. **Basic NHS Cost:** Blister packs of: 200mg x 60 tablets - £60.00; 200mg x 90 tablets - £90.00; 50mg x 60 tablets - £16.45; 50mg x 90 tablets - £24.69. **Legal Category:** POM. **Product Licence Numbers:** Solian 200 - PL 15819/0002, Solian 50 - PL 15819/0001. **Product Licence Holder:** Lorex Synthélabo UK &

She's frightened, disturbed, disoriented - even disruptive. But behind her screams and tears, she's crying out to you - to bring her back from her terror of acute phase schizophrenia.

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Pharmacopsychiatry 1990; **23:** 125 - 130. **3.** Turjanski S *et al.* Presented at ECNP Congress, Paris, France, 1998, November.

Further information is available on request. Lorex Synthélabo UK & Ireland Ltd, Foundation Park, Roxborough Way, Maidenhead, Berks, SL6 3UD.

Date of preparation: April 1999

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(rivastigmine)

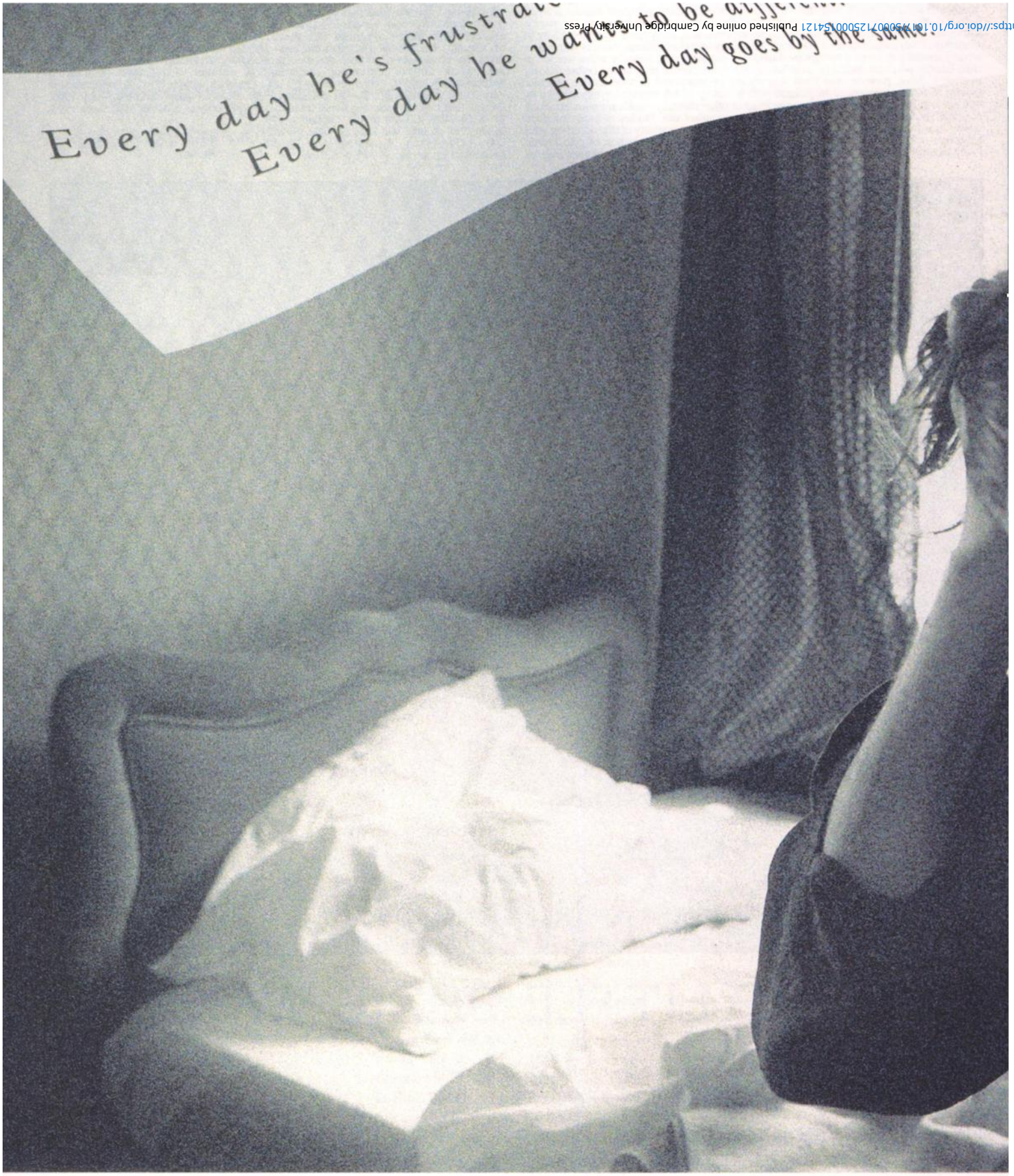
Beyond cognition: improving functional ability.

EXELON Prescribing Information. Indication: Symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Presentation**: Capsules containing 1.5, 3, 4.5 or 6mg rivastigmine. **Dosage and Administration**: Effective dose is 3 to 6mg twice a day. Maintain patients on their highest well-tolerated dose. Maximum dose 6mg twice daily. Reassess patients regularly. Initial dose 1.5mg twice daily, then build up dose, at a minimum of two week intervals, to 3mg twice daily, 4.5mg twice daily then 6mg twice daily, if tolerated well. If adverse effects or weight decrease occur, these may respond to omitting one or more doses. If persistent, daily dose should be temporarily reduced to previous well tolerated dose. **Contraindications**: Known hypersensitivity to rivastigmine or excipients or any other carbamate derivatives; severe liver impairment. **Special Warning & Precautions:** Therapy should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's disease. A caregiver should be available to monitor compliance. There is no experience of use of EXELON in other types of dementia/memory impairment. Nausea and vomiting may occur, particularly when initiating and/or increasing dose. Monitor any weight loss. Use with care in patients with Sick Sinus Syndrome, conduction defects, active gastric or duodenal ulcers, or those predisposed to ulcerative conditions, history of asthma or obstructive pulmonary disease, those predisposed to urinary obstruction and seizures. In renal and mild to moderate hepatic impairment, titrate dose individually.Safety in pregnancy not established; women should not breastfeed. Use in children not recommended. **Interactions**: May exaggerate effects of succinylcholine-type muscle relaxants during anaesthesia. Do not give with cholinomimetic drugs. May interfere with anticholinergic medications. No interactions were observed with digoxin, warfarin, diazepam, or fluoxetine (in healthy volunteers). Metabolic drug interactions unlikely, although it may inhibit butyrylcholinesterase mediated metabolism of other drugs. **Undesirable Effects**: Most commonly (≥5% and twice frequency of placebo): asthenia, anorexia, dizziness, nausea, somnolence, vomiting. Female patients more susceptible to nausea, vomiting, appetite and weight loss. Other common effects (≥5% and ≥ placebo): abdominal pain, accidental trauma, agitation, confusion, depression, diarrhoea, dyspepsia, headache, insomnia, upper respiratory tract and urinary tract infections. Increased sweating, malaise, weight loss, tremor. Rarely, angina pectoris, gastrointestinal haemorrhage and syncope. No notable abnormalities in laboratory values observed. **Package Quantities and basic NHS Price**: 1.5mg x 28, £31.50; 1.5mg x 56, £63.00; 3mg x 28, £31.50; 3mg x 56, £63.00; 4.5mg x 28, £31.50; 4.5mg x 56, £63.00; 6mg x 28, £31.50; 6mg x 56, £63.00. **Legal Classification**: POM. **Marketing Authorisation Number**: 1.5mg, EU/1/98/066/001 - 2; 3mg, EU/1/98/066/004 - 5; 4.5mg, EU/1/98/066/007 - 8; 6mg, EU/1/98/066/010 - 11. Full prescribing information including Summary of Product Characteristics is available from: Novartis Pharmaceuticals UK Ltd, Frimley Business Park, Frimley, Camberley, Surrey, GU16 5SG.

Reference: 1. Corey-Bloom J, *et al. International Journal of Geriatric Pyschopharmacology* 1998; **1**: 55-65.

Date of preparation: May 1999. Code No. EXE 99/20

NOVARTIS



Please refer to summary of product characteristics before prescribing.
Presentation: White to off-white tablets each containing modafinil 100 mg. **Indication:** Narcolepsy. **Dosage:** *Adults:* 200-400 mg daily either as two divided doses in the morning and at noon or as a single morning dose according to response. *Elderly:* Treatment should start at 100 mg daily which may be increased subsequently to the maximum adult daily dose in the absence of renal or hepatic impairment. *Severe renal or hepatic impairment:* Reduce dose by half (100-200 mg daily). *Children:* See contra-indications. **Contra-indications:** Pregnancy, lactation, use in children, moderate to severe hypertension, arrhythmia, hypersensitivity to modafinil or any excipients used in Provigil. **Warnings and precautions:** Patients with major anxiety should only receive Provigil treatment in a specialist unit. Sexually active women of child-bearing potential should be established on a contraceptive programme before starting treatment. Blood pressure and heart rate should be monitored in hypertensive patients. Provigil is not recommended in patients with a history of left ventricular hypertrophy or ischaemic ECG changes, chest pain, arrhythmia or other clinically significant manifestations of mitral valve prolapse in association with CNS stimulant use. Studies of modafinil have demonstrated a low potential for dependence although the possibility of this occurring with long-term use cannot be entirely excluded. **Drug interactions:** Induction of cytochrome P-450 isoenzymes has been observed *in vitro*. Effectiveness of oral contraceptives may be impaired. When these are used for contraception, a product containing at least 30 mcg ethinyoestradiol should be taken. Tricyclic antidepressants – no clinically relevant interaction was seen in a single dose interaction study of Provigil and clomipramine. However, patients receiving such medication should be carefully monitored. Care should be observed with co-administration of anti-convulsant drugs. **Side effects:** Nervousness, excitation, aggressive tendencies, insomnia, personality disorder, anorexia, headache, CNS stimulation, euphoria, abdominal pain, dry mouth, palpitation, tachycardia, hypertension and tremor have been reported. Nausea and gastric discomfort may occur and may improve when tablets are taken with meals. Pruritic skin rashes have been observed occasionally. Buccofacial dyskinesia has been reported very rarely. A dose related increase in alkaline phosphatase has been observed. **Basic NHS cost:** Packs of 30 blister packed 100 mg tablets: £60.00. **Marketing authorisation number:** 16260/0001. **Marketing authorisation holder:** Cephalon UK Ltd., 11/13 Frederick Sanger Road, Surrey Research Park, Guildford, GU2 5YD. **Legal category:** POM. **Date of preparation:** January 1998. Provigil and Cephalon are registered trademarks. **References: 1.** Mitler MM. Sleep 1994; **17**: S103-S106. **2.** Data on file, Cephalon [676]. **3.** Lin JS *et al. Proc Natl Acad Sci USA* 1996; **93** (24): 14128-14133. **4.** Simon P *et al.* Eur Neuropsychopharmacol 1995; **5**: 509-514.

Cephalon

PRAD/1/Feb 99

WAKE UP LITTLE SUZIE, WAKE UP

Excessive sleepiness associated with narcolepsy frequently has a disastrous effect on patients' lives, by impairing their physical, social and emotional well being. Unfortunately, treatment with amphetamines is often associated with a high incidence of unpleasant side effects, which limit their overall benefit.[1]

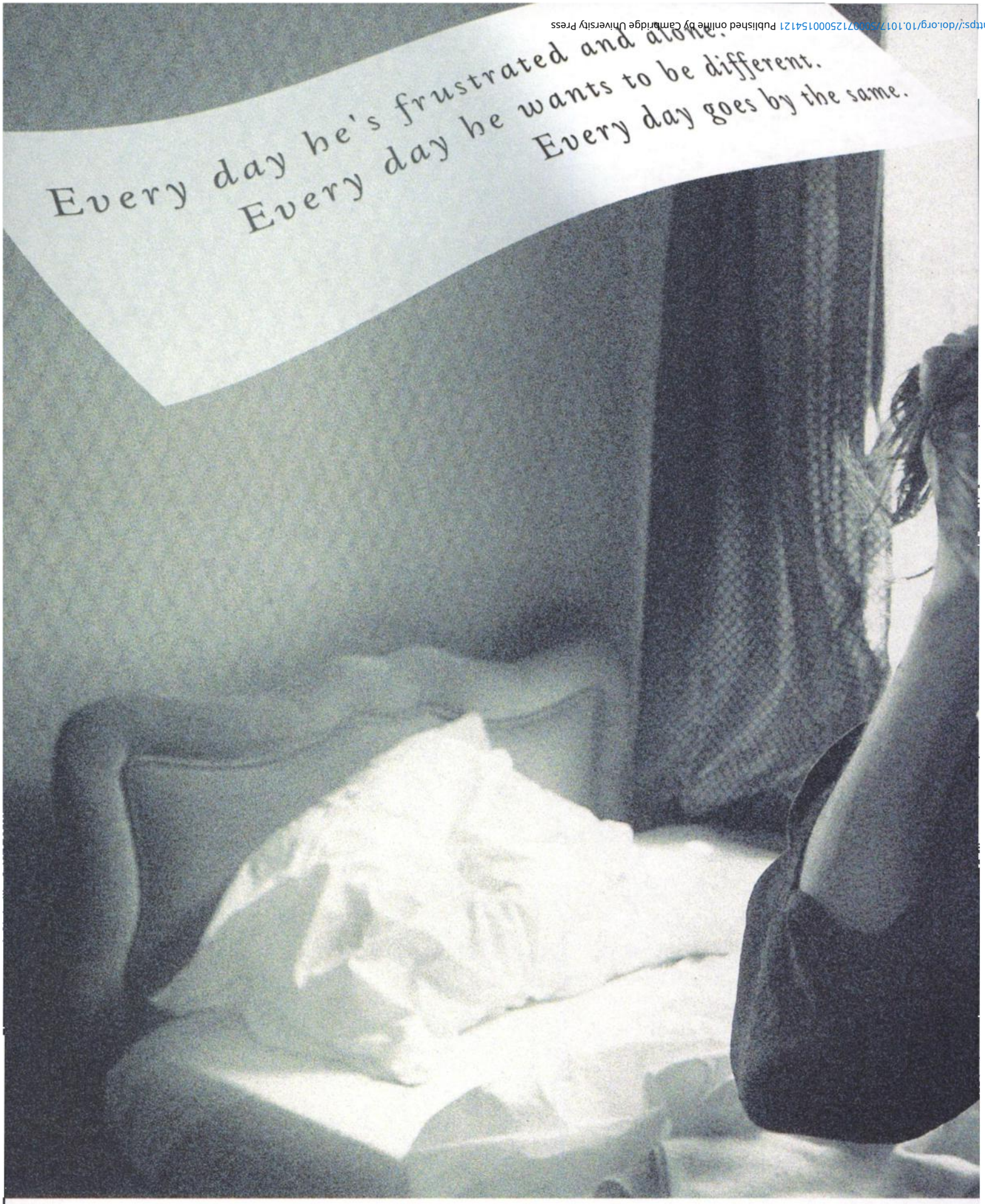
Now Provigil (modafinil) – a novel wake promoting agent – offers advantages in narcolepsy. The clinical efficacy of Provigil has been demonstrated in large controlled clinical studies. In one study,[2] one in five people with severe narcolepsy reached normal levels of daytime wakefulness while receiving Provigil.

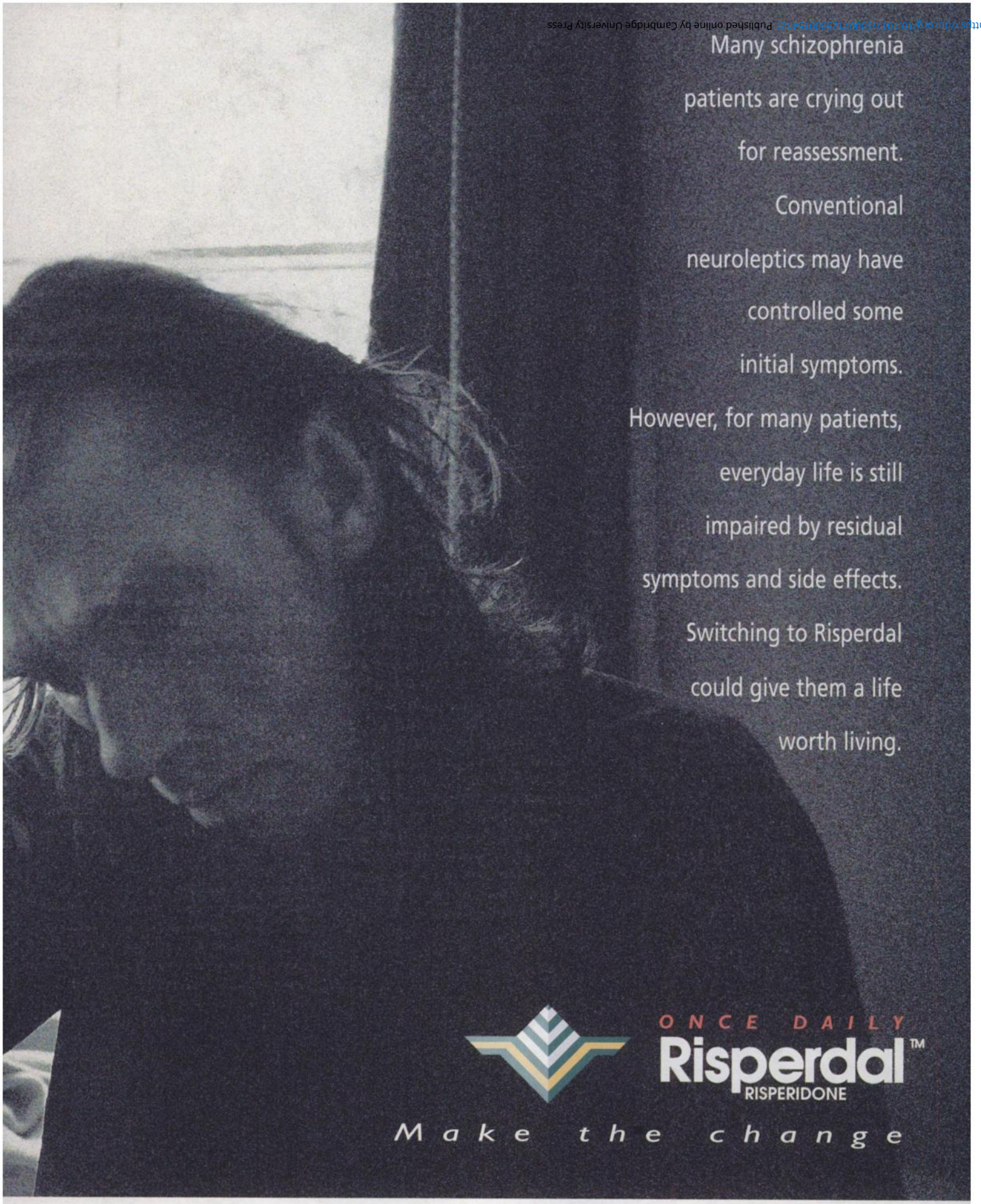
Provigil selectively activates the hypothalamus[3] and differs greatly from amphetamines in its pharmacology.[4] Consequently the incidence of amphetamine

PROVIGIL®▼
MODAFINIL

A NOVEL, NON AMPHETAMINE WAKE PROMOTING AGENT

For further information please contact our





symptoms may occur but are usually mild and reversible. Rarely Neuroleptic Malignant Syndrome. Occasionally, orthostatic dizziness, hypotension, tachycardia and hypertension observed. Plasma prolactin can increase with associated galactorrhoea, gynaecomastia and menstrual cycle disturbances. Oedema and increased hepatic enzymes. A mild fall in neutrophil and/or thrombocyte count has been reported. Rarely: water intoxication with hyponatraemia, tardive dyskinesia, body temperature dysregulation and seizures. See SmPC for full listing of side-effects. Overdosage: Drowsiness, sedation, tachycardia and hypotension, and extrapyramidal symptoms. Rare cases of

and liquid: Store below 30°C. Do not refrigerate. LEGAL CATEGORY POM. PRESENTATIONS, PACK SIZES, PRODUCT LICENCE NUMBERS & BASIC NHS COSTS 1 mg tablets (PL 0242/0186) 20: £13.45, 60: £40.35. 2 mg tablets (PL 0242/0187) 60: £79.56. 3 mg tablets (PL 0242/0188) 60: £117.00. 4 mg tablets (PL 0242/0189) 60: £154.44. 6 mg tablets (PL 0242/0317) 28: £109.20. 1 mg per ml solution: (PL 0242/0199) 100 ml: £65.00. FURTHER INFORMATION IS AVAILABLE FROM THE PRODUCT LICENCE HOLDER: Janssen-Cilag Ltd, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ. APIVER200599

Abbreviated Prescribing Information. Please read Summary of Product Characteristics before prescribing.

Presentation: Tablets containing 25 mg, 50 mg, 100 mg, or 200 mg topiramate.

Uses: Adjunctive therapy of inadequately controlled seizures: partial seizures; seizures associated with Lennox Gastaut Syndrome and primary generalised tonic-clonic seizures.

Dosage and Administration: Oral administration. *Over 16 years of age:* Usual dose: 200-400 mg/day in two divided doses. Initiate at 50 mg daily then titrate to an effective dose. A lower dose may be used. Patients with significant renal disease may require a dose modification. See SmPC for additional information. *Children age 2 to 16:* Usual dose: Approximately 5 to 9 mgs/kg/day in two divided doses. Initiate at 25 mg nightly, and increase at 1 to 2 week intervals in 1 to 3 mg/kg increments, to an effective dose.

Contraindications: Hypersensitivity to any component.

Precautions and Warnings: Withdraw all antiepileptic drugs slowly. Hydrate to reduce the risk of nephrolithiasis (especially if predisposed). Drowsiness likely. Topamax may be sedating; therefore caution if driving or operating machinery. Do not use in pregnancy unless potential benefit outweighs risk. Woman of childbearing potential should use adequate contraception. Do not use if breastfeeding.

Interactions: *Other Antiepileptic Drugs:* No clinically significant effect except in some patients on phenytoin where phenytoin plasma concentrations may increase. Phenytoin level monitoring is advised. *Effects of other antiepileptic drugs:* Phenytoin and carbamazepine decrease topiramate plasma concentration. *Digoxin:* A decrease in serum digoxin occurs. Monitor serum digoxin on addition or withdrawal of TOPAMAX®. *Oral Contraceptives:* Should contain not less than 50µg of oestrogen. Ask patients to report any change in bleeding patterns. *Others:* Avoid agents predisposing to nephrolithiasis.

Side Effects: *Adults:* In 5% or more: abdominal pain, ataxia, anorexia, asthenia, confusion, difficulty with concentration/attention, difficulty with memory, diplopia, dizziness, fatigue, language problems, nausea, nystagmus, paraesthesia, psychomotor slowing, somnolence, speech disorders/related speech problems, abnormal vision and weight decrease. May cause agitation and emotional lability (mood problems and nervousness) and depression. Less common adverse effects include, gait abnormal, aggressive reaction, apathy, cognitive problems, coordination problems, leucopenia, psychotic symptoms (such as hallucinations), and taste perversion. Venous thromboembolic events reported - causal association not established.

Children: In 5% or more: somnolence, anorexia, fatigue, insomnia, nervousness, personality disorder (behaviour problems), difficulty with concentration/attention, aggressive reaction, weight decrease, gait abnormal, mood problems, ataxia, saliva increased, nausea, difficulty with memory, hyperkinesia, dizziness, speech disorders/related speech problems and paraesthesia.

Less frequently but potentially relevant: emotional lability, agitation, apathy, cognitive problems, psychomotor slowing, confusion, hallucination, depression and leucopenia.

Topamax increases the risk of nepthrolithiasis.

Overdosage: If ingestion recent, empty stomach. Activated charcoal not recommended. Supportive treatment as appropriate. Haemodialysis is effective in removing topiramate.

Pharmaceutical Precautions: Store in a dry place at or below 25°C.

Legal Category: POM

Package Quantities and Prices: Bottles of 60 tablets. 25 mg (PL0242/0301) = £22.02, 50 mg (PL0242/0302) = £36.17; 100 mg (PL0242/0303) = £64.80; 200 mg (PL0242/0304) = £125.83.

Product licence holder: JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE HP14 4HJ ENGLAND.

APIVER200498.

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Date of preparation: May 1999

00298C

TOPAMAX® ▽

topiramate

Because life without seizures is so much better.

EFEXOR* XL venlafaxine – PRESCRIBING INFORMATION **Presentation:** Capsules containing 75mg or 150mg venlafaxine (as hydrochloride) in an extended release formulation. **Use:** Treatment of depressive illness. **Dosage:** *Adults (including the elderly):* Usually 75mg, given once daily with food, increasing to 150mg once daily if necessary. The dose can be increased further to 225mg once a day. Dose increments should be made at intervals of approximately 2 weeks or more, but not less than 4 days. Discontinue gradually to reduce the possibility of withdrawal reactions. *Children:* Contraindicated below 18 years of age. *Moderate renal or moderate hepatic impairment:* Doses should be reduced by 50%. Not recommended in severe renal or severe hepatic impairment. **Contra-indications:** Pregnancy, lactation, concomitant use with MAOIs, hypersensitivity to venlafaxine or other components, patients aged below 18 years. **Precautions:** Wyeth* Use with caution in patients with myocardial infarction, or a history of epilepsy (discontinue in event of seizure). Patients should not drive or operate machinery if their ability to do so is impaired. Possibility of postural hypotension (especially in the elderly). Women of child-bearing potential should use contraception. Prescribe smallest quantity of tablets according to good patient management. Monitor blood pressure with doses >200mg/day. Advise patients to notify their doctor should an allergy develop or if they become or intend to become pregnant. Patients with a history of drug abuse should be monitored carefully. **Interactions:** MAOIs: do not use Efexor XL in combination with MAOIs or within 14 days of stopping MAOI treatment. Allow 7 days after stopping Efexor XL before starting an MAOI. Use with caution in elderly or hepatically-impaired patients taking cimetidine, in patients taking other CNS-active drugs, and in patients taking drugs which inhibit *both* CYP2D6 and CYP3A4 hepatic enzymes. **Side-effects:** Nausea, insomnia, nervousness, asthenia, abnormal ejaculation/orgasm, anorexia, abnormal vision/accommodation, impotence, vomiting, tremor, abnormal dreams, vasodilatation, hypertension, rash, agitation, hypertonia, paraesthesia, postural hypotension, reversible increases in liver enzymes, slight increase in serum cholesterol, weight gain or loss, hyponatraemia. Symptoms reported on discontinuation of venlafaxine were mostly non-serious and self-limiting and included dizziness, insomnia, nausea and nervousness. **Basic NHS price:** 75mg capsule (PL 0011/0223) – blister pack of 28 capsules: £23.97. 150 mg capsule (PL 0011/0224) – blister pack of 28 capsules: £39.97. **Legal category:** POM. Further information is available upon request from the Product Licence holder: Wyeth Laboratories, Taplow, Maidenhead, Berkshire, SL6 0PH. References: 1. Ferrier N. Presentation at Wyeth Symposium, CINP, Glasgow, July 1998. 2. Rudolph R *et al.* Poster presented at ECNP, Vienna 1997. Date

Action in Alzheimer's

real lives - realistic expectations

Aricept▼

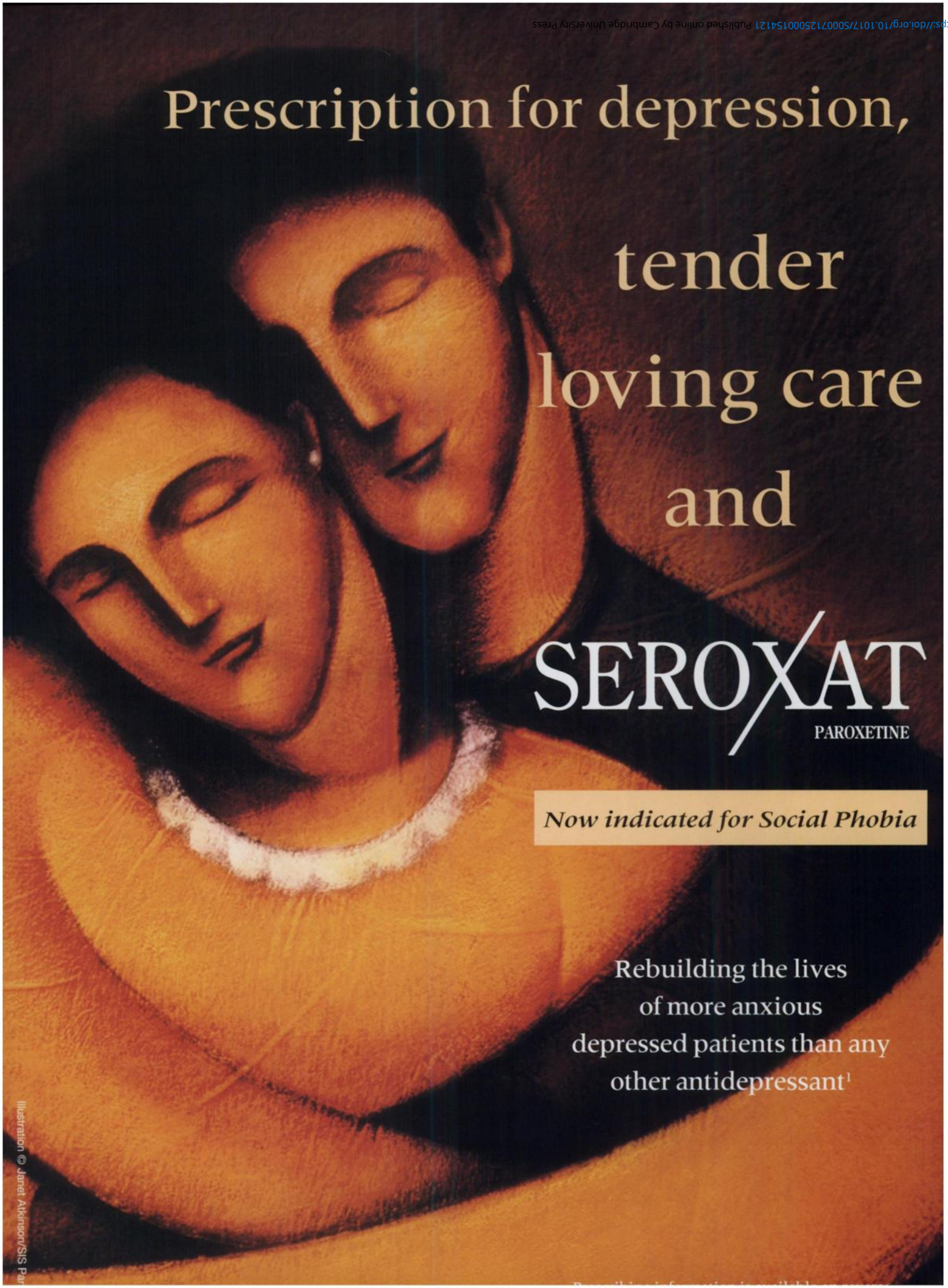
donepezil hydrochloride

Once daily in Alzheimer's

BRIEF PRESCRIBING INFORMATION
ARICEPT▼ (donepezil hydrochloride)
Please refer to the SmPC before prescribing ARICEPT 5mg or ARICEPT 10mg. **Indication:** Symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Dose and administration:** ***Adults/elderly;*** 5mg daily which may be increased to 10mg once daily after at least one month. No dose adjustment necessary for patients with renal or mild-moderate hepatic impairment. ***Children;*** Not recommended. **Contra-Indications:** Pregnancy. Hypersensitivity to donepezil, piperidine derivatives or any excipients used in ARICEPT. **Lactation:** Excretion into breast milk unknown. Women on donepezil should not breast feed. **Warnings and Precautions:** Initiation and supervision by a physician with experience of Alzheimer's dementia. A caregiver should be available to monitor compliance. Regular monitoring to ensure continued therapeutic benefit, consider discontinuation when evidence of a therapeutic effect ceases. Exaggeration of succinylcholine-type cholinergic agonists, cholinergic antagonists. Possibility of vagotonic effect on the heart which may be particularly important with "sick sinus syndrome", and supraventricular conduction conditions. Careful monitoring of patients at risk of ulcer disease including those receiving NSAIDs. Cholinomimetics may cause bladder outflow obstruction. Seizures occur in Alzheimer's disease and cholinomimetics have the potential to cause seizures. Care in patients suffering asthma and obstructive pulmonary disease. As with all Alzheimer's patients, routine evaluation of ability to drive/operate machinery. **Drug Interactions:** Experience of use with concomitant medications is limited, consider possibility of as yet unknown interactions. Interaction possible with inhibitors or inducers of Cytochrome P450; use such combinations with care. Possible synergistic activity with succinylcholine-type muscle relaxants, beta-blockers, cholinergic or anticholinergic agents. **Side effects:** Most commonly diarrhoea, muscle cramps, fatigue, nausea, vomiting, and insomnia. Other common effects in clinical trials (≥5%, disturbance and dizziness. Rare cases of syncope, bradycardia, heart block and seizures. Rare reports of liver dysfunction including hepatitis. Psychiatric disturbances, including hallucinations, agitation and aggressive behaviour have been reported; these resolved on dose reduction or discontinuation. There have been some reports of anorexia, gastric and duodenal ulcers and gastrointestinal haemorrhage. Minor increases in muscle creatine kinase. **Presentation and basic NHS cost:** Blister packed in strips of 14. ARICEPT 5mg; white, film coated tablets marked 5 and Aricept, packs of 28 £68.32. ARICEPT 10mg; yellow, film coated tablets marked 10 and Aricept, packs of 28 £95.76. **Marketing authorisation numbers:** ARICEPT 5mg; PL 10555/0006. ARICEPT 10mg; PL 10555/0007. **Marketing authorisation holder:** Eisai Ltd. **Further Information from/Marketed by:** Eisai Ltd, Hammersmith International Centre, 3 Shortlands, London, W6 8EE and Pfizer Ltd, Sandwich, Kent, CT13 9NJ. **Legal category:** POM **Date of preparation:**

Eisai Pfizer

274-30533-06-99



PRESCRIBING INFORMATION

Prescribing information

Presentation: 'Seroxat' Tablets, PL 10592/0001-2, each containing either 20 or 30 mg paroxetine as the hydrochloride. 30 (OP) 20 mg tablets, £20.77; 30 (OP) 30 mg tablets, £31.16.

'Seroxat' Liquid, PL 10592/0092, containing 20 mg paroxetine as the hydrochloride per 10 ml. 150 ml (OP), £20.77.

Indications: Treatment of symptoms of depressive illness of all types including depression accompanied by anxiety. Following satisfactory response, continuation is effective in preventing relapse. Treatment of symptoms and prevention of relapse of obsessive compulsive disorder (OCD). Treatment of symptoms and prevention of relapse of panic disorder with or without agoraphobia. Treatment of symptoms of social anxiety disorder/social phobia.

Dosage: Adults: Depression: 20 mg a day. Review response within two to three weeks and if necessary increase dose in 10 mg increments to a maximum of 50 mg according to response.

Obsessive compulsive disorder: 40 mg a day. Patients should be given 20 mg a day initially and the dose increased weekly in 10 mg increments. Some patients may benefit from a maximum dose of 60 mg a day.

Panic disorder: 40 mg a day. Patients should be given 10 mg a day initially and the dose increased weekly in 10 mg increments. Some patients may benefit from a maximum dose of 50 mg a day.

Social anxiety disorder/social phobia: 20 mg a day. Patients should start on 20 mg and if no improvement after at least two weeks they may benefit from weekly 10 mg dose increases up to a maximum of 50 mg/day according to response. 'Seroxat' has been shown to be effective in 12 week placebo-controlled trials. There is only limited evidence of efficacy after 12 weeks' treatment.

Give orally once a day in the morning with food. The tablets should not be chewed. Continue treatment for a sufficient period, which should be at least four to six months after recovery for depression and may be longer for OCD and panic disorder. As with many psychoactive medications abrupt discontinuation should be avoided – see **Adverse reactions.**

Elderly: Dosing should commence at the adult starting dose and may be increased in weekly 10 mg increments up to a maximum of 40 mg a day according to response.

Children: Not recommended.

Severe renal impairment (creatinine clearance <30 ml/min) or severe hepatic impairment: 20 mg a day. Restrict incremental dosage if required to lower end of range.

Contra-indication: Hypersensitivity to paroxetine.

Precautions: History of mania. Cardiac conditions: caution. Caution in patients with epilepsy; stop treatment if seizures develop. Driving and operating machinery.

Drug interactions: Do not use with or within two weeks after MAO inhibitors; leave a two-week gap before starting MAO inhibitor treatment. Possibility of interaction with tryptophan. Great caution with warfarin and other oral anticoagulants. Use lower doses if given with drug metabolising enzyme inhibitors; adjust dosage if necessary with drug metabolising enzyme inducers. Alcohol is not advised. Use lithium with caution and monitor lithium levels. Increased adverse effects with phenytoin; similar possibility with other anticonvulsants.

Pregnancy and lactation: Use only if potential benefit outweighs possible risk.

Adverse reactions: In controlled trials most commonly nausea, somnolence, sweating, tremor, asthenia, dry mouth, insomnia, sexual dysfunction (including impotence and ejaculation disorders), dizziness, constipation and decreased appetite.

Also spontaneous reports of dizziness, vomiting, diarrhoea, restlessness, hallucinations, hypomania, rash including urticaria with pruritus or angioedema, and symptoms suggestive of postural hypotension. Extrapyramidal reactions reported infrequently; usually reversible abnormalities of liver function tests and hyponatraemia described rarely. Symptoms including dizziness, sensory disturbance, anxiety, sleep disturbances, agitation, tremor, nausea, sweating and confusion have been reported following abrupt discontinuation of 'Seroxat'. It is recommended that when antidepressant treatment is no longer required, gradual discontinuation by dose-tapering or alternate day dosing be considered.

Overdosage: Margin of safety from available data is wide. Symptoms include nausea, vomiting, tremor, dilated pupils, dry mouth, irritability, sweating and somnolence. No specific antidote. General treatment as for overdosage with any antidepressant. Early use of activated charcoal suggested.

Legal category: POM. 10.9.98

SmithKline Beecham Pharmaceuticals

PARTNERS IN PSYCHIATRIC CARE

Welwyn Garden City, Hertfordshire AL7 1EY.

Reference: 1. Data on file.

0998/ST:AD/8/0398J

SEROXAT

Rebuilding the lives of anxious depressed patients