THE BRITISH JOURNAL OF PSYCHIATRY

NOVEMBER 1998 VOL. 173

EDITORIALS

PRiSM PSYCHOSIS STUDY

PAPERS

COLUMNS

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Their doctor knew that their symptoms were similar

Depression

Panic disorder

Depression with anxiety symptoms

From the doctor's viewpoint, overlapping symptoms can make these mood disorders appear similar. For the patients, the same effective treatment can make a real difference to their quality of life. Cipramil combines proven efficacy with an established safety and tolerability profile, which makes it a logical first choice for patients suffering from depression, depression with anxiety symptoms, and panic disorder.

For effective relief from mood disorders, prescribe Cipramil – the most selective SSRI – and make a real difference to your patients.

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Abbreviated prescribing information: '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:*** - 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. Date of preparation: August 1998. 0998/CIP/501/049/NP

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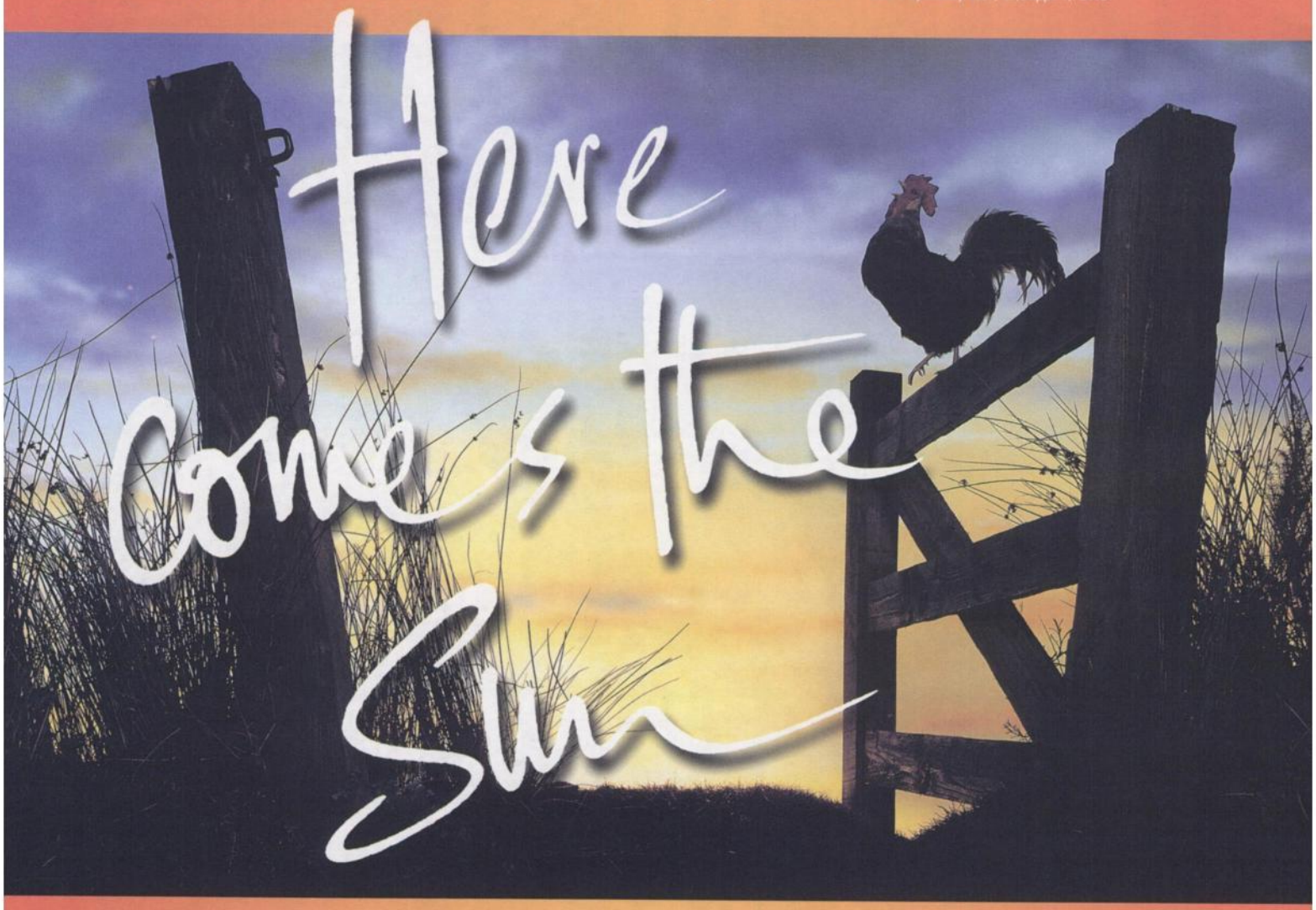
Past Editors

Eliot Slater	1961–72	John L. Crammer	1978–83
Edward H. Hare	1973–77	Hugh L. Freeman	1984–93

Founded by J. C. Bucknill in 1853 as the *Asylum Journal* and known as the *Journal of Mental Science* from 1858 to 1963.

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 avoid possibility of discontinuation effects. *Children:* Contra-indicated 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:** Use with caution in patients with myocardial infarction, unstable heart disease, renal or hepatic impairment, 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, dry mouth, somnolence, dizziness, constipation, sweating, nervousness, asthenia, abnormal ejaculation/orgasm, anorexia, abnormal vision/accommodation, impotence, vomiting, tremor, abnormal dreaming, anxiety, libido decreased, hypertonia, paraesthesia, postural hypotension, reversible increases in liver enzymes, slight increase in serum cholesterol, weight gain or loss, hyponatraemia. **Basic NHS price:** 75mg capsule (PL 00011/0223) - blister pack of 28 capsules: £23.97. 150 mg capsule (PL 00011/0224) - 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. Date of preparation: August 1997. * trade mark Code no Z777440/0897. WEFX3-UK-JA. References: 1. Muth EA *et al.* Biochem Pharmacol 1986; 35(24): 4493-4497. 2. Muth EA *et al.* Drug Development Research 1991; 23: 191-199. 3. Rudolph R *et al.* Poster presented at the New Clinical Drug Evaluation Unit (National Institute of Mental Health). Boca Raton, Florida 1997. 4. McPartlin GM *et al.* Poster at the 10th European College of Neuropsychopharmacology meeting, Vienna, September 13th-17th, 1997. 5. Salinas E. Biol Psychiatry 1997; 42(Suppl. 1): 244S.



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VIAGRA™
sildenafil citrate
ORAL TREATMENT FOR ERECTILE DYSFUNCTION

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). Small, additional reduction in blood pressure with amlodipine. 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: 3 September 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 Impotence Res, 1998, 10: 69-74.
10223d

Pfizer

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 100 mg 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, 12.5 mg once or twice on the first day, followed by one or two 25 mg tablets on the second day. Increase dose slowly, by increments to reach a therapeutic dose within the range of 200 - 450mg daily (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 300 mg daily may suffice. At daily doses not exceeding 200mg, a single administration in the evening may be appropriate. Exceptionally, doses up to 900 mg daily may be used. Patients with a history of epilepsy should be closely monitored during CLOZARIL therapy since dose-related convulsions have been reported. Patients with a history of seizures, as well as those suffering from cardiovascular, renal or hepatic disorders, together with the elderly need lower doses (12.5 mg 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. **Warning** 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 that time strict haematological monitoring of patients has been demonstrated to be effective in markedly reducing the risk of fatality. Therefore, because of this risk its 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 every two weeks thereafter for the first year of therapy. After one year's 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 complete discontinuation of CLOZARIL. Patients must be under specialist supervision and 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 as well as a drug supply audit so that CLOZARIL treatment is promptly withdrawn from any patient who develops abnormal leucocyte findings. Each time CLOZARIL is prescribed, patients should be reminded to contact the treating physician immediately if any kind of infection begins to develop, especially any flu-like symptoms. **Precautions** CLOZARIL can cause agranulocytosis. Perform pre-treatment white blood cell count and differential count to ensure only patients with normal findings receive CLOZARIL. Monitor white blood cell count weekly for the first 18 weeks and at least two-weekly for the first year of therapy. After one year's treatment, monitoring may change to four weekly intervals in patients with stable neutrophil counts. Monitoring must continue throughout treatment and for four weeks after complete discontinuation. If signs or symptoms of infection develop an immediate differential count is necessary. 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. Re-evaluate any patient developing an infection, or when a routine white blood count is 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. 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, where protective isolation and administration of GM-CSF or G-CSF and broad spectrum antibiotics may be indicated. Colony stimulating factor therapy should be discontinued 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 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 CLOZARIL 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, on rare occasions, can be profound and may lead to cardiac and/or respiratory arrest. Caution is advised with concomitant administration of therapeutic agents which are highly bound to plasma proteins. Clozapine binds to and is partially metabolised by the isoenzymes cytochrome P450 1A2 and P450 2D6. Caution is advised with drugs which posses affinity for these isoenzymes. Concomitant cimetidine and high dose CLOZARIL was 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 effectiveness of CLOZARIL. No clinically relevant interactions have been noted with antidepressants, phenothiazines and type lc antiarrhythmics, to date. Concomitant use of 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 Warning 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 eg dry mouth, disturbances of accommodation and disturbances in sweating and temperature regulation. Hypersalivation. Tachycardia and postural hypotension, with or without syncope, and less commonly hypertension may occur. In rare cases 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. Nausea, vomiting and usually mild constipation have been reported. Occasionally obstipation and paralytic ileus have occurred. Asymptomatic elevations in liver enzymes occur commonly and usually resolve. 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. Both 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 25 mg tablets: £37.54 (Basic NHS) 84 x 100 mg 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. Date of preparation, August 1997. Full prescribing information, including Product Data Sheet is available from Novartis Pharmaceuticals UK Ltd. Trading as: SANDOZ PHARMACEUTICALS, Frimley Business Park, Frimley, Camberley, Surrey, GU16 5SG.

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Topamax 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 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,

TOPAMAX®
topiramate

At the end of the day, it works.

apy for most seizure types

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. 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.
Further information is available on request from the Marketing Authorisation Holder: Janssen-Cilag Limited, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ.

Date of Preparation April 1998

JANSSEN-CILAG

ABBREVIATED PRESCRIBING INFORMATION: **Presentation:** Coated tablets containing 2.5mg, 5mg, 7.5mg or 10mg of olanzapine. The tablets also contain lactose. **Uses:** Schizophrenia, both as initial therapy and for maintenance of response. **Further Information:** In studies of patients with schizophrenia and associated depressive symptoms, mood score improved significantly more with olanzapine than with haloperidol. **Pharmacodynamics:** Olanzapine was associated with significantly greater improvements in both negative and positive schizophrenic symptoms than placebo or comparator in most studies. **Dosage and Administration:** 10mg/day orally, as a single dose without regard to meals. Dosage may subsequently be adjusted within the range of 5-20mg daily. An increase to a dose greater than the routine therapeutic dose of 10mg/day is recommended only after clinical assessment. *Children:* Not recommended under 18 years of age. *The elderly:* A lower starting dose (5mg/day) is not routinely indicated but should be considered when clinical factors warrant. *Renal and/or hepatic impairment:* A lower starting dose (5mg) should be considered. In moderate hepatic insufficiency, the starting dose should be 5mg, and only increased with caution. When more than one factor is present which might result in slower metabolism (female gender, elderly age, non-smoking status), consideration should be given to decreasing the starting dose. Dose escalation should be conservative in such patients. **Contra-indications:** Known hypersensitivity to any ingredient of the product. Known risk of narrow-angle glaucoma. **Warnings and Special Precautions:** Caution in patients with prostatic hypertrophy, or paralytic ileus and related conditions. Caution in patients with elevated ALT and/or AST, signs and symptoms of hepatic impairment, pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic drugs. As with other neuroleptic drugs, caution in patients with low leucocyte and/or neutrophil counts for any reason, a history of drug-induced bone marrow depression/toxicity, bone marrow depression caused by concomitant illness, radiation therapy or chemotherapy and in patients with hypereosinophilic conditions or with myeloproliferative disease. Thirty-two patients with clozapine-related neutropenia or agranulocytosis histories received olanzapine without decreases in baseline neutrophil counts. Rare cases reported as NMS have been received in association with olanzapine. If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fever without additional clinical manifestations of NMS, all antipsychotic drugs, including olanzapine, must be discontinued. Caution in patients who have a history of seizures or have conditions associated with seizures. If signs or symptoms of tardive dyskinesia appear a dose reduction or drug discontinuation should be considered.

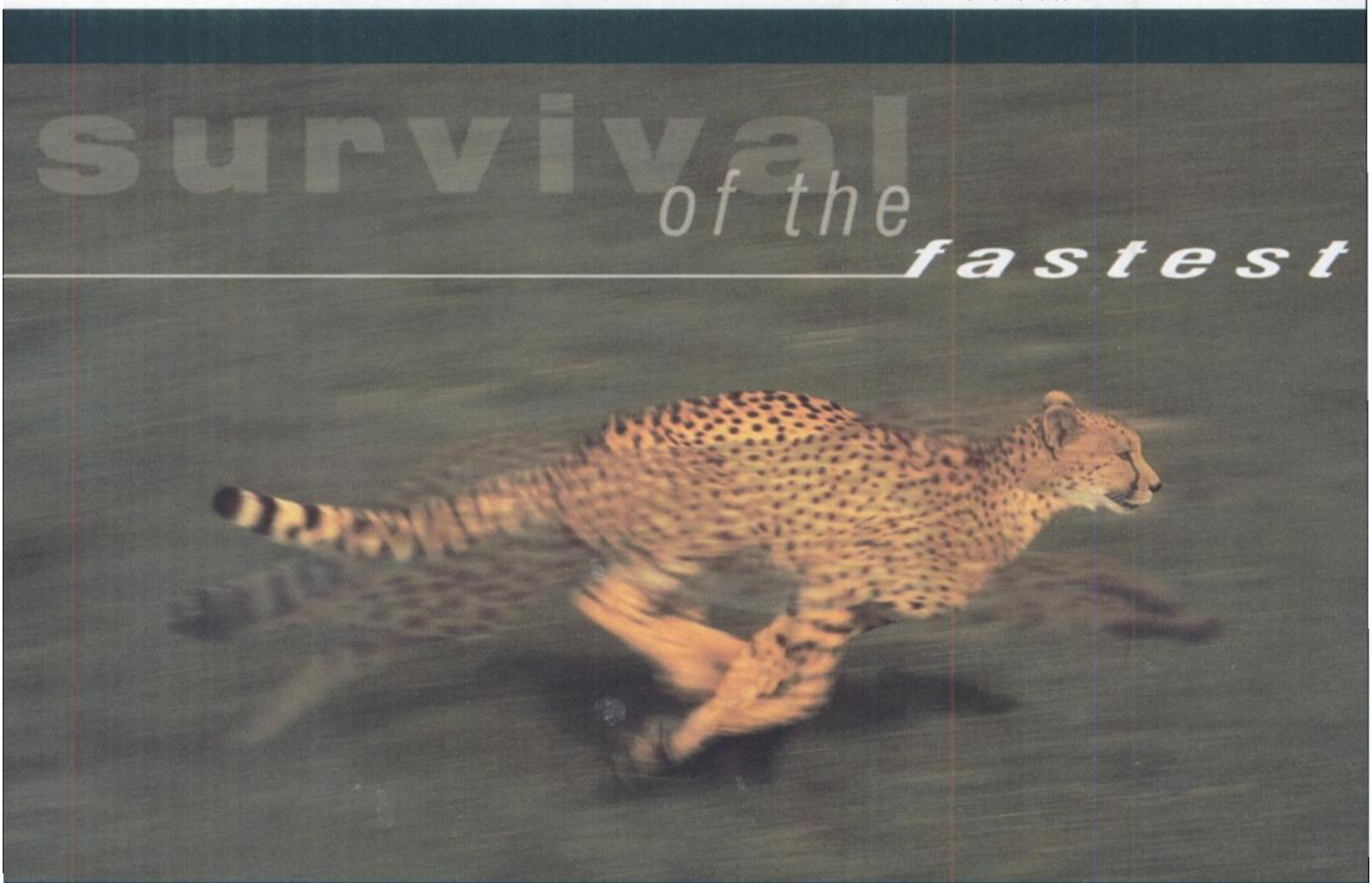
Antipsychotic Efficacy for First-line Use

ZYPREXA
Olanzapine

Making Community Re-integration the Goal

Olanzapine may antagonise the effects of direct and indirect dopamine agonists. Postural hypotension was infrequently observed in the elderly. However, blood pressure should be measured periodically in patients over 65 years, as with other antipsychotics. As with other antipsychotics, caution when prescribed with drugs known to increase QTc interval, especially in the elderly. In clinical trials, olanzapine was not associated with a persistent increase in absolute QT intervals. **Interactions:** Metabolism may be induced by concomitant smoking or carbamazepine therapy. **Pregnancy and Lactation:** Olanzapine had no teratogenic effects in animals. Because human experience is limited, olanzapine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. Olanzapine was excreted in the milk of treated rats but it is not known if it is excreted in human milk. Patients should be advised not to breast feed an infant if they are taking olanzapine. **Driving, etc:** Because olanzapine may cause somnolence, patients should be cautioned about operating hazardous machinery, including motor vehicles. **Undesirable Effects:** The only frequent (>10%) undesirable effects associated with the use of olanzapine in clinical trials were somnolence and weight gain. Occasional undesirable effects included dizziness, increased appetite, peripheral oedema, orthostatic hypotension, and mild, transient anticholinergic effects, including constipation and dry mouth. Transient, asymptomatic elevations of hepatic transaminases, ALT, AST have been seen occasionally. Olanzapine-treated patients had a lower incidence of parkinsonism, akathisia and dystonia in trials compared with titrated doses of haloperidol. Photosensitivity reaction, rash or high creatine phosphokinase were reported rarely. Rare cases reported as NMS have been received in association with olanzapine. Plasma prolactin levels were sometimes elevated, but associated clinical manifestations were rare. Haematological variations, such as leucopenia and thrombocytopenia, have been reported occasionally. *For further information see summary of product characteristics.* **Legal Category:** POM. **Marketing Authorisation Numbers:** 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. **Basic NHS Cost:** £34.27 per pack of 28 2.5mg tablets. £52.73 per pack of 28 5mg tablets. £158.20 per pack of 56 7.5mg tablets. £105.47 per pack of 28 10mg tablets. £210.93 per pack of 56 10mg tablets. **Date of Preparation or Last Review:** March 1998. **Full Prescribing Information is Available From:** Eli Lilly and Company Limited, Dextra Court, Chapel Hill, Basingstoke, Hampshire, RG21 5SY. Telephone: Basingstoke (01256) 315000. 'ZYPREXA' is an Eli Lilly and

Lilly PSYCHIATRY



IV phenytoin has evolved.

Pro-Epanutin is water soluble, with a more physiological pH than IV phenytoin

IV administration up to 3 times faster than with IV phenytoin

Significantly better tolerated than IV phenytoin

IM administration option

So when the situation calls for speed and efficiency, Pro-Epanutin represents a natural selection.

NEW **Pro-Epanutin®▼**

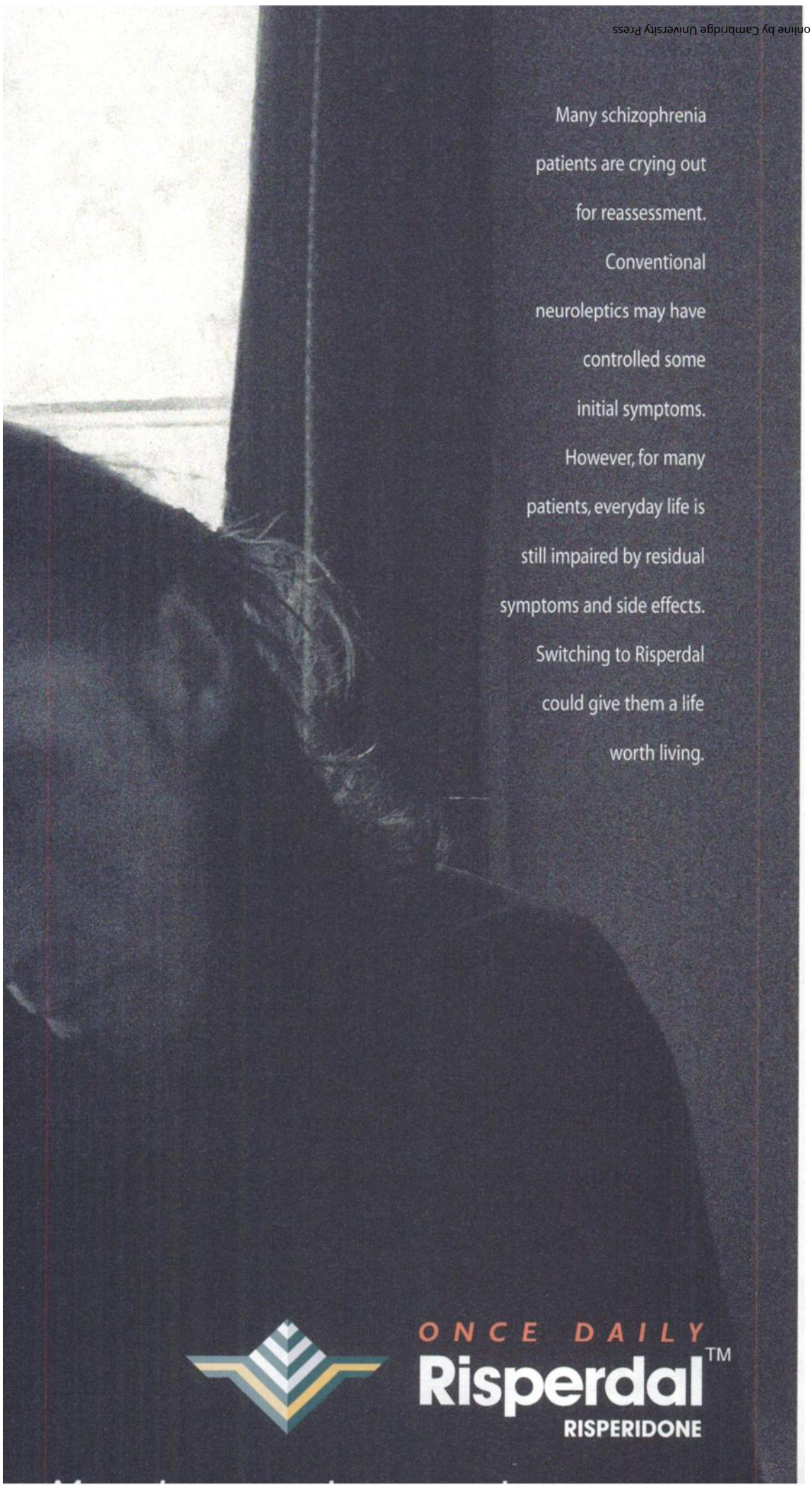
fosphenytoin sodium

Evolved for speed and convenience

ABBREVIATED PRESCRIBING INFORMATION: PRO-EPANUTIN® CONCENTRATE FOR INJECTION

Presentation: Pro-Epanutin Concentrate for Injection is supplied in 10ml vials, each containing 750mg fosphenytoin sodium (equivalent to 500mg of phenytoin sodium or 500mg PE*). One ml of Pro-Epanutin contains 50mg PE* **Indications:** Pro-Epanutin Concentrate for Injection is indicated for the control of status epilepticus; for the prevention and treatment of seizures connected with neurosurgery and/or head trauma; as a temporary substitute for oral phenytoin. **Dosage:** Pro-Epanutin should be prescribed and dispensed in PE* units. (1.5mg fosphenytoin sodium is equivalent to 1mg PE). Administration is by IV infusion or IM injection. The rate of IV infusion should not exceed 150mg PE/min (3mg PE/kg/minute for children). Pro-Epanutin should be diluted prior to administration via IV infusion. Monitor ECG, blood pressure and respiratory function during IV infusion. Cardiac resuscitative equipment should be available. N.B. IM injection should not be used for emergency administration. ***Adults:*** *Status epilepticus: Loading dose:* Following IV diazepam or lorazepam, 15mg PE/kg by IV infusion at 100 to 150mg PE/min. *Maintenance dose:* Initially 4 to 5mg PE/kg by IV infusion at 50 to 100mg PE/min or by IM injection. Use therapeutic drug monitoring to adjust dose. Transfer to oral phenytoin therapy when appropriate. *Treatment or prophylaxis of seizures: Loading dose:* 10 to 15mg PE/kg by IM Injection or IV infusion at 50 to 100mg PE/min. *Maintenance dose:* As for status epilepticus. *Temporary substitution of oral phenytoin:* Use same dose and dosing frequency as for oral phenytoin. *Children (ages 5 and above):* By IV infusion at the same mg PE/kg dose and rate as for adults. Recommended rate of IV infusion 50 to 100mg PE/min (1 to 2mg PE/kg/min) except for status epilepticus where 100 to 150mg PE/min (2 to 3mg PE/kg/min). *Elderly, renal or hepatic disease:* Doses or infusion rates may need to be reduced. (See Summary of Product Characteristics). **Contraindications:** Hypersensitivity to any of the ingredients, sinus bradycardia, sino-atrial block, second and third degree A-V block, Stokes-Adams syndrome, and acute intermittent porphyria. **Warning and precautions:** Doses are expressed as mg PE* to avoid conversion of phenytoin doses. Abrupt withdrawal may increase seizures. Discontinue therapy if skin rash, allergic or hypersensitivity reaction or syndrome or signs of hepatotoxicity or lymphadenopathy occur. Therapeutic drug monitoring should be used to assess for acute toxicity. Use with caution in patients with hypotension, severe myocardial insufficiency, renal and/or hepatic disease, pregnancy and lactation, hypoalbuminaemia or phosphate intake restriction. Reduce rate or temporarily stop IV infusion if transient itching, burning, warmth or tingling in the groin occurs. Blood glucose levels may be raised in diabetics. Alcohol intake and concomitant drug therapy can affect blood levels of phenytoin following Pro-Epanutin administration (see Summary of Product Characteristics). **Side effects:** Side effects reported for Pro-Epanutin are similar to those of phenytoin and predominantly affect the central nervous system. Cardiovascular complications, blood dyscrasias, hepatitis, liver damage, gastrointestinal disturbance, pruritus, rash, hypersensitivity syndrome have been reported. (See Summary of Product Characteristics). **Legal category:** POM. **Date of Revision:** June 1998. **Package quantities, marketing authorisation numbers and basic NHS price:** 10 vials of 10ml, £400.00, PL00019/0157. **Marketing Authorisation Holder:** Parke Davis, Lambert Court, Chestnut Avenue, Eastleigh, Hampshire SO53 3ZQ, UK. Further information is available on request from: Parke Davis, Lambert Court, Chestnut Avenue, Eastleigh, Hampshire SO53 3ZQ. Pro-Epanutin is a registered trademark. *PE = phenytoin sodium equivalents. **Date of preparation:** September 1998. **Item code:** 3410000370b

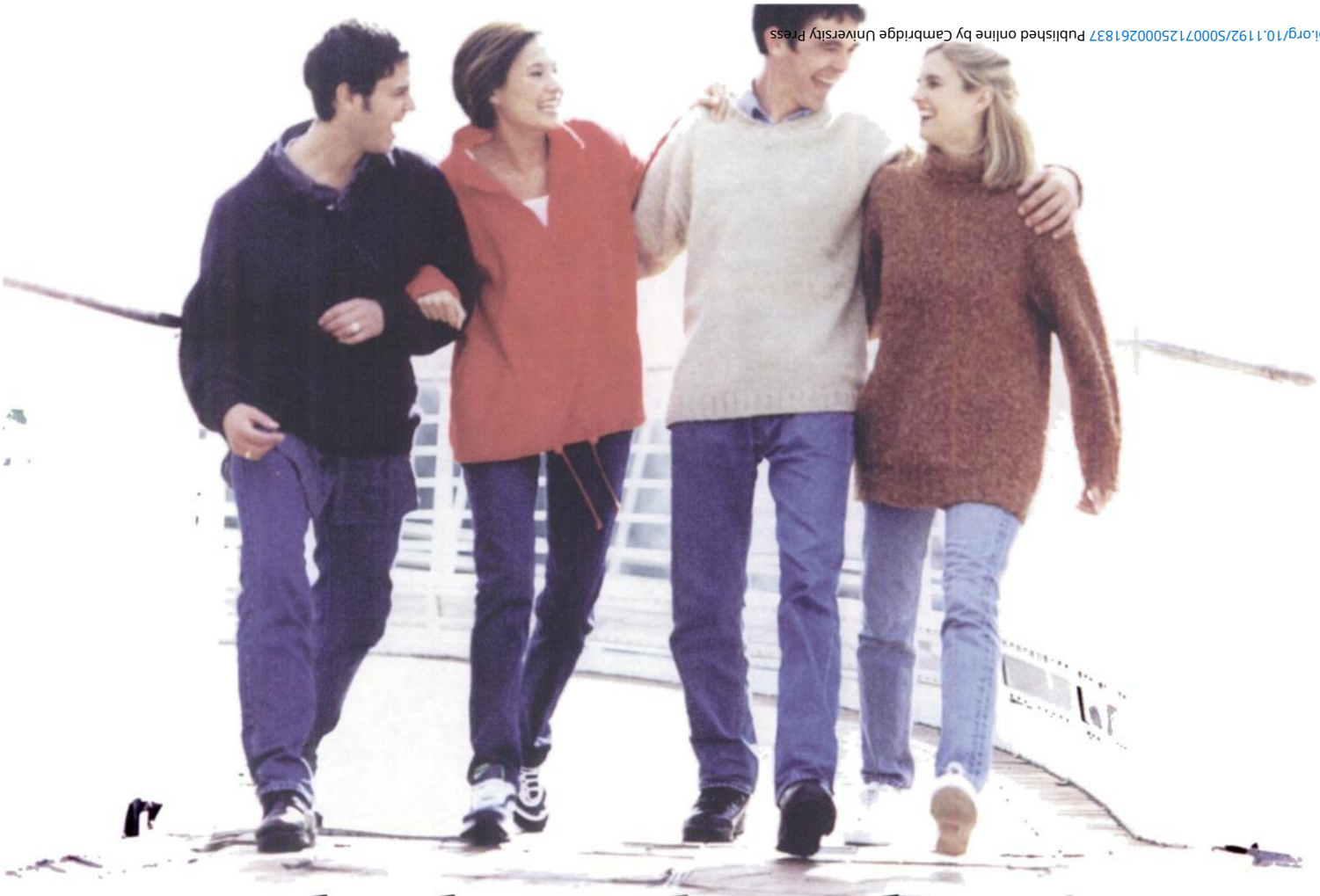
PARKE-DAVIS



Please refer to Summary of Product Characteristics before prescribing risperidal (risperidone). USES The treatment of acute and chronic schizophrenia, and other psychotic conditions, in which positive and/or negative symptoms are prominent. Risperdal also alleviates affective symptoms associated with schizophrenia. DOSAGE Where medically appropriate, gradual discontinuation of previous antipsychotic treatment while Risperdal therapy is initiated is recommended. Where medically appropriate, when switching patients from depot antipsychotics, consider initiating Risperdal therapy in place of the next scheduled injection. The need for continuing existing antiparkinson medication should be re-evaluated periodically. Adults: Risperdal may be given once or twice daily. All patients, whether acute or chronic, should start with 2 mg/day. This should be increased to 4 mg/day on the second day and 6 mg/day on the third day. However, some patients such as first-episode psychotic patients may benefit from a slower rate of titration. From then on the dosage can be maintained unchanged, or further individualised if needed. The usual effective dosage is 4 to 8 mg/day although in some patients an optimal response may be obtained at lower doses. Doses above 10 mg/day may increase the risk of extrapyramidal symptoms and should only be used if the benefit is considered to outweigh the risk. Doses above 16 mg/day should not be used. Elderly, renal and liver disease: A starting dose of 0.5 mg bd is recommended. This can be individually adjusted with 0.5 mg bd increments to 1 to 2 mg bd. Risperdal is well tolerated by the elderly. Use with caution in patients with renal and liver disease. Not recommended in children aged less than 15 years. CONTRA-INDICATIONS, WARNINGS, ETC. Contra-indications: Known hypersensitivity to Risperdal. Precautions: Orthostatic hypotension can occur (alpha-blocking effect). Use with caution in patients with known cardiovascular disease. Consider dose reduction if hypotension occurs. For further sedation, give an additional drug (such as a benzodiazepine) rather than increasing the dose of Risperdal. Drugs with dopamine antagonistic properties have been associated with tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear, the discontinuation of all antipsychotic drugs should be considered. Caution should be exercised when treating patients with Parkinson's disease or epilepsy. Patients should be advised of the potential for weight gain. Risperdal may interfere with activities requiring mental alertness. Patients should be advised not to drive or operate machinery until their individual susceptibility is known. Pregnancy and lactation: Use during pregnancy only if the benefits outweigh the risks. Women receiving Risperdal should not breast feed. Interactions: Use with caution in combination with other centrally acting drugs. Risperdal may antagonise the effect of levodopa and other dopamine agonists. On initiation of carbamazepine or other hepatic enzyme-inducing drugs, the dosage of Risperdal should be re-evaluated and increased if necessary. On discontinuation of such drugs, the dosage of Risperdal should be re-evaluated and decreased if necessary. Side effects: Risperdal is generally well tolerated and in many instances it has been difficult to differentiate adverse events from symptoms of the underlying disease. Common adverse events include: insomnia, agitation, anxiety, headache. Less common adverse events include: somnolence, fatigue, dizziness, impaired concentration, constipation, dyspepsia, nausea/vomiting, abdominal pain, blurred vision, priapism, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction, urinary incontinence, rhinitis, rash and other allergic reactions. The incidence and severity of extrapyramidal symptoms are significantly less than with haloperidol. However, the following may occur: tremor, rigidity, hypersalivation, bradykinesia, akathisia, acute dystonia. If acute, these symptoms are usually mild and reversible upon dose reduction and/or administration of antiparkinson medication. Rare cases of Neuroleptic Malignant Syndrome have been reported. In such an event, all antipsychotic drugs should be discontinued. Occasionally, orthostatic dizziness, hypotension (including orthostatic), tachycardia (including reflex) and hypertension have been observed. An increase in plasma prolactin concentration can occur which may be associated with galactorrhoea, gynaecomastia and disturbances of the menstrual cycle. Oedema and increased hepatic enzyme levels have been observed. A mild fall in neutrophil and/or thrombocyte count has been reported. Rare cases of water intoxication with hyponatraemia, tardive dyskinesia, body temperature dysregulation and seizures have been reported. Overdosage: Reported signs and symptoms include drowsiness and sedation, tachycardia and hypotension, and extrapyramidal symptoms. A prolonged QT interval was reported in a patient with concomitant hypokalaemia who had ingested 360mg. Establish and maintain a clear airway, and ensure adequate oxygenation and ventilation. Gastric lavage and activated charcoal plus a laxative should be considered. Commence cardiovascular monitoring immediately, including continuous electrocardiographic monitoring to detect possible arrhythmias. There is no specific antidote, so institute appropriate supportive measures. Treat hypotension and circulatory collapse with appropriate measures. In case of severe extrapyramidal symptoms, give anticholinergic medication. Continue close medical supervision and monitoring until the patient recovers. PHARMACEUTICAL PRECAUTIONS Tablets: Store below 30°C. Liquid: Store below 30°C; protect from freezing. LEGAL CATEGORY POM. PRESENTATIONS, PACK SIZES, PRODUCT LICENCE NUMBERS & BASIC NHS COSTS White, oblong tablets containing 1 mg risperidone in packs of 20. PL 0242/0186 £13.45. Pale orange, oblong tablets containing 2 mg risperidone in packs of 60. PL 0242/0187 £79.56. Yellow, oblong tablets containing 3 mg risperidone in packs of 60. PL 0242/0188 £117.00. Green, oblong tablets containing 4 mg risperidone in packs of 60. PL 0242/0189 £154.44. Yellow, circular tablets containing 6 mg risperidone in packs of 28. PL 0242/0317 £109.20. Starter packs containing 6 Risperdal 1 mg tablets are also available £4.15. Clear, colourless solution containing 1 mg risperidone per ml in bottles containing 100 ml. PL 0242/0199 £65.00. FURTHER INFORMATION IS AVAILABLE FROM THE PRODUCT LICENCE HOLDER: Janssen-Cilag Ltd, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ. APIVER140797

JANSSEN-CILAG Ltd

Date of preparation: August 1998



John has schizophrenia

Effective in negative and positive symptoms[1-4]
and mood*[5] in patients with schizophrenia

EPS no different from placebo across the full dose range
(150 - 750 mg/day)[1-4]

Plasma prolactin levels no different from placebo across
the full dose range (150 - 750 mg/day)[6]

Low level of sexual dysfunction (3 patients out of 1085)
in long term use (3-5 months)[6]

* Defined as the BPRS item score of depressive mood, anxiety, guilt feelings and tension.

Seroquel

Life beyond Alzheimer's.

With new Exelon, you can now help treat the symptoms of people with mild to moderately severe Alzheimer's disease.

While Exelon has not been shown to affect the disease process, six-month trials have established its effectiveness on key areas that Alzheimer's disease attacks - cognition, global functioning and activities of daily living.[1]

For carers and family, this could mean some relief from the demands for attention; for the sufferer, it could mean life beyond Alzheimer's.

NEW

EXELON®▼

(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 Psychopharmacology* 1998, 1: 55-65.

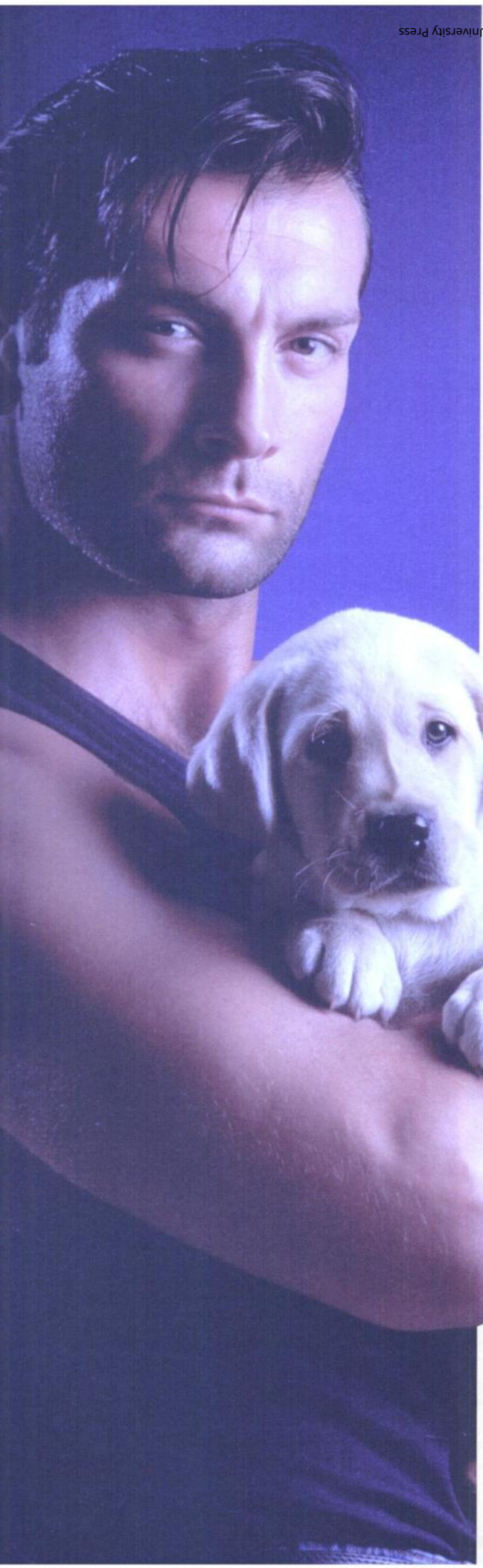
Date of preparation August 1998 Code No EXE 98/63

NOVARTIS

MIRTAZAPINE

ZISPIN® 30 mg

The NaSSA



Strong yet gentle in depression

ZISPIN 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 with: micturition disturbances like prostate hypertrophy, acute narrow-angle glaucoma and increased intra-ocular pressure and diabetes 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 reduction generally does not lead to less sedation but can jeopardize antidepressant efficacy). **Less common:** Increases in liver enzyme 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.

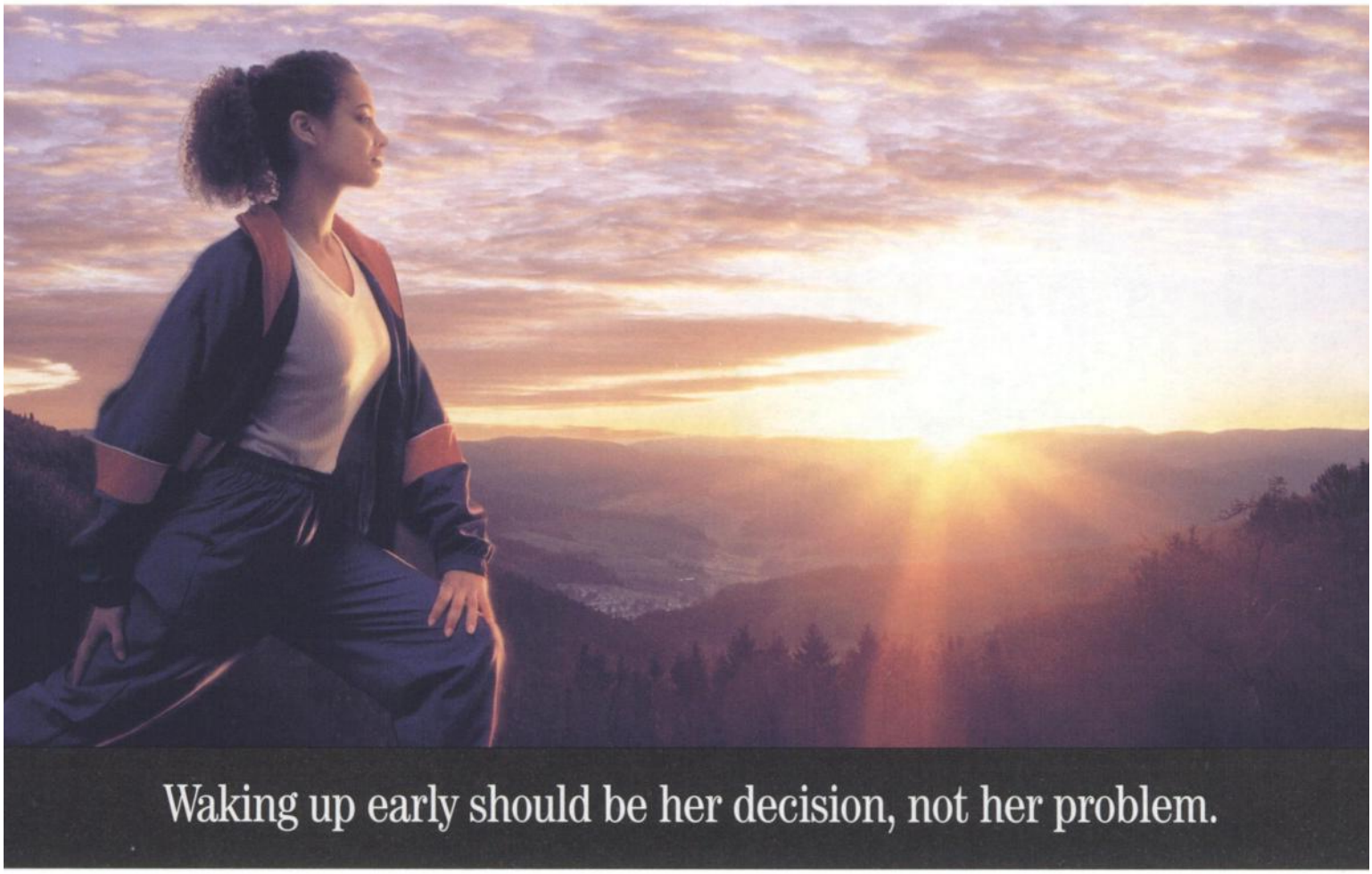
Organon

For further information, please contact:
Organon Laboratories Limited,
Cambridge Science Park, Milton Road,
Cambridge CB4 4FL.
Telephone: 01223 423445.
Fax: 01223 424368.

DUTONIN™▼ Abbreviated Prescribing Information PRESENTATION: Tablets containing 50mg, 100mg and 200mg nefazodone hydrochloride. INDICATIONS: Symptomatic treatment of all types of depressive illness, including depressive syndromes accompanied by anxiety or sleep disturbances. DOSAGE: Usual therapeutic dose 200mg twice daily. Range – 100mg - 600mg daily, see Summary of Product Characteristics. Elderly: Usual therapeutic dose 50 - 200mg twice daily. Renal and Hepatic Impairment: Lower end of dose range. Children: Not recommended below the age of 18 years. CONTRA-INDICATIONS: Hypersensitivity to nefazodone hydrochloride, tablet excipients or phenylpiperazine antidepressants. WARNINGS/ PRECAUTIONS: Hepatic or renal impairment. Patients at high risk of self harm should be kept under close supervision during initial treatment phase. Modest decrease in some psychomotor function tests but no impairment of cognitive function. Not recommended in pregnancy and lactation. Use with caution in epilepsy, history of mania/hypomania, recent M.I., unstable heart disease. No clinical studies available on concurrent use of ECT and nefazodone. DRUG INTERACTIONS: Caution is advised when combining with other CNS medication, digoxin, products metabolised by Cytochrome $P_{450}III_{A4}$; see Summary of Product Characteristics. SIDE EFFECTS: Most frequently asthenia, dry mouth, nausea, constipation, somnolence, light-headedness and dizziness; see Summary of Product Characteristics. OVERDOSAGE: There is no specific antidote for nefazodone. Gastric lavage recommended for suspected overdose. Treatment should be symptomatic and supportive in the case of hypotension or excessive sedation. PRODUCT LICENCE NUMBERS: Dutonin Tablets 50mg PL 11184/0027; Dutonin Tablets 100mg PL 11184/0028; Dutonin Tablets 200mg PL 11184/0029. PRODUCT LICENCE HOLDER: Bristol-Myers Squibb Pharmaceuticals Ltd. BASIC NHS PRICE: Treatment Initiation Pack containing 50mg tablets 14, 100mg tablets 14, 200mg tablets 28 – £16.80; 100mg tablets 56 – £16.80; 200mg tablets 56 – £16.80. LEGAL CATEGORY: POM. Further information from: Medical Information, Bristol-Myers Squibb House, 141-149 Staines Road, Hounslow, Middlesex, TW3 3JA. Telephone: 0181-754-3740. Date of preparation: July 1997.

REFERENCES: 1. Armitage R. Journal of Psychopharmacology 1996; 10(suppl1): 22-25. 2. Sharpley AL *et al.* Psychopharmacology 1996; 126: 50-54. 3. Armitage R *et al.* J Clin Psychopharmacol 1997; 17(3): 161-168. 4. Armitage R *et al.* Presented at the European College of Neuropsychopharmacology (ECNP), 30 September - 4 October 1995, Venice, Italy. 5. Fontaine R *et al.* J Clin Psychiatry 1994; 55(6): 234-241. 6. Gillin JC *et al.* J Clin Psychiatry 1997; 58: 185-192.

Bristol-Myers Squibb Pharmaceuticals Limited



It's not only depression that wakes patients up early. Sleep can also be disturbed by many SSRIs.[1-4]

Dutonin is an excellent choice. Not only does Dutonin effectively relieve depression,[5] it also normalises sleep patterns.[3,4,6]

Moreover, Dutonin lifts anxiety symptoms within the first week of treatment.[5]

Waking up early should always be your patient's choice, not their problem.

Makes the difference in depression

DUTONIN™▼

NEFAZODONE

Presentation: White to off white tablets each containing modafinil 100 mg **Indication:** Narcolepsy **Dosage:** *Adult* 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 [illegible] no clinically relevant interaction was seen in a single dose interaction study of Provigil and clomipramine [illegible] 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 [4] **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

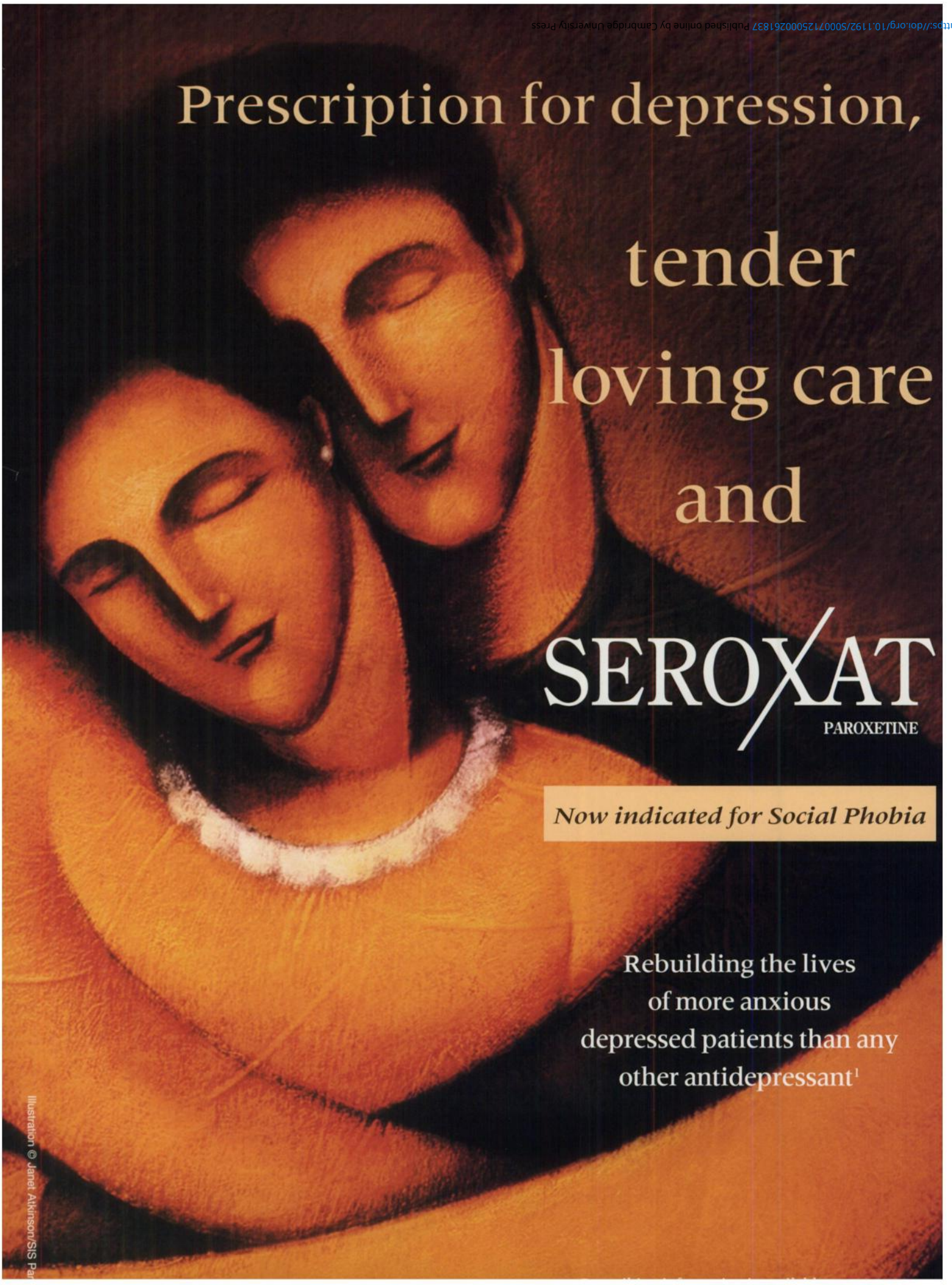
WAKE UP LITTLE SUZIE, WAKE UP

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 new 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



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

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Rebuilding the lives of anxious depressed patients