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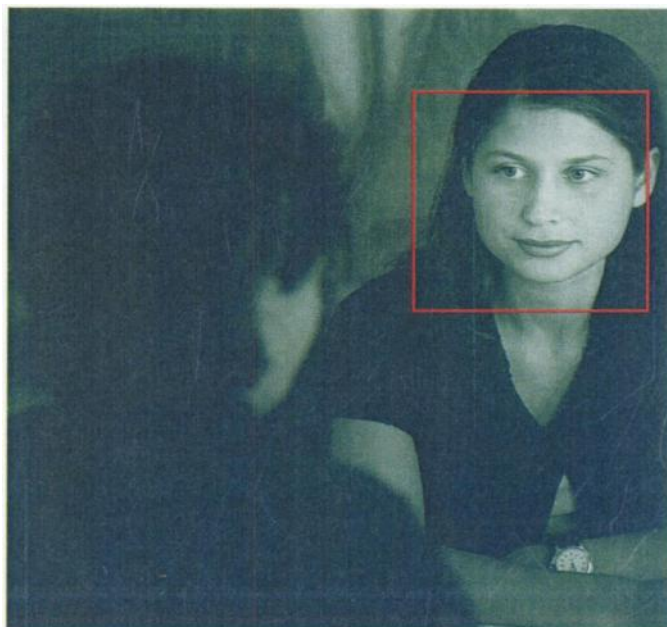
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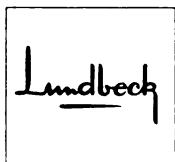
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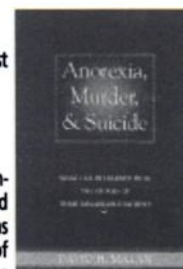
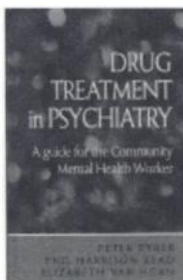
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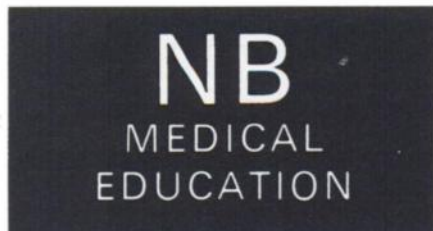
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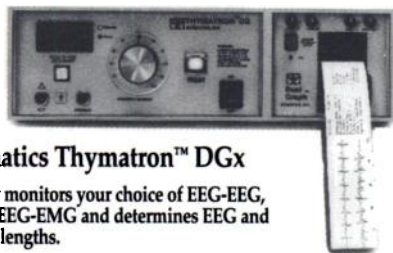
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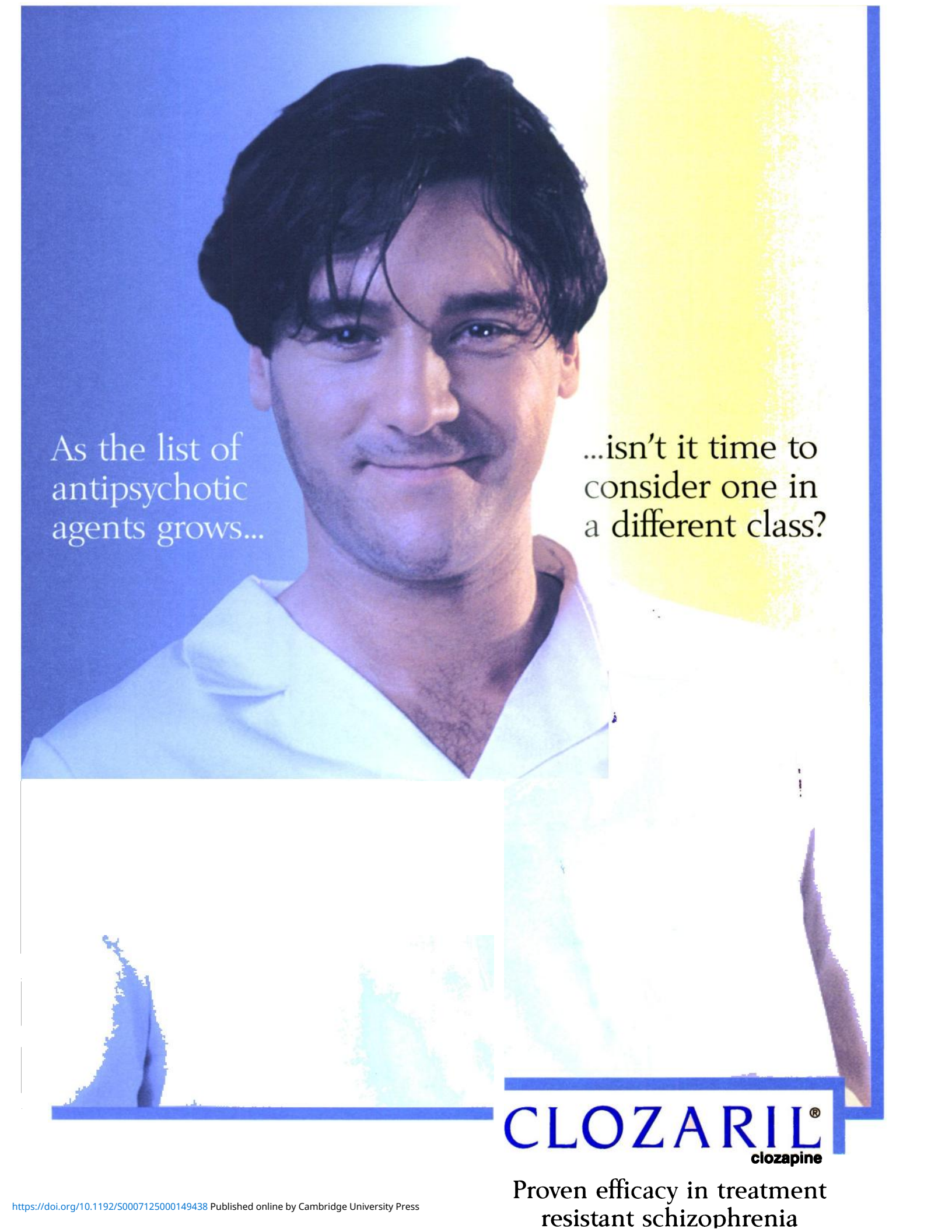
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operate machinery, administer with caution to patients who participate in activities requiring complete mental alertness. Monitor hepatic function regularly in liver disease. Investigate any signs of liver disease immediately with a view to drug discontinuation. 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 possess 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 Ic 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. 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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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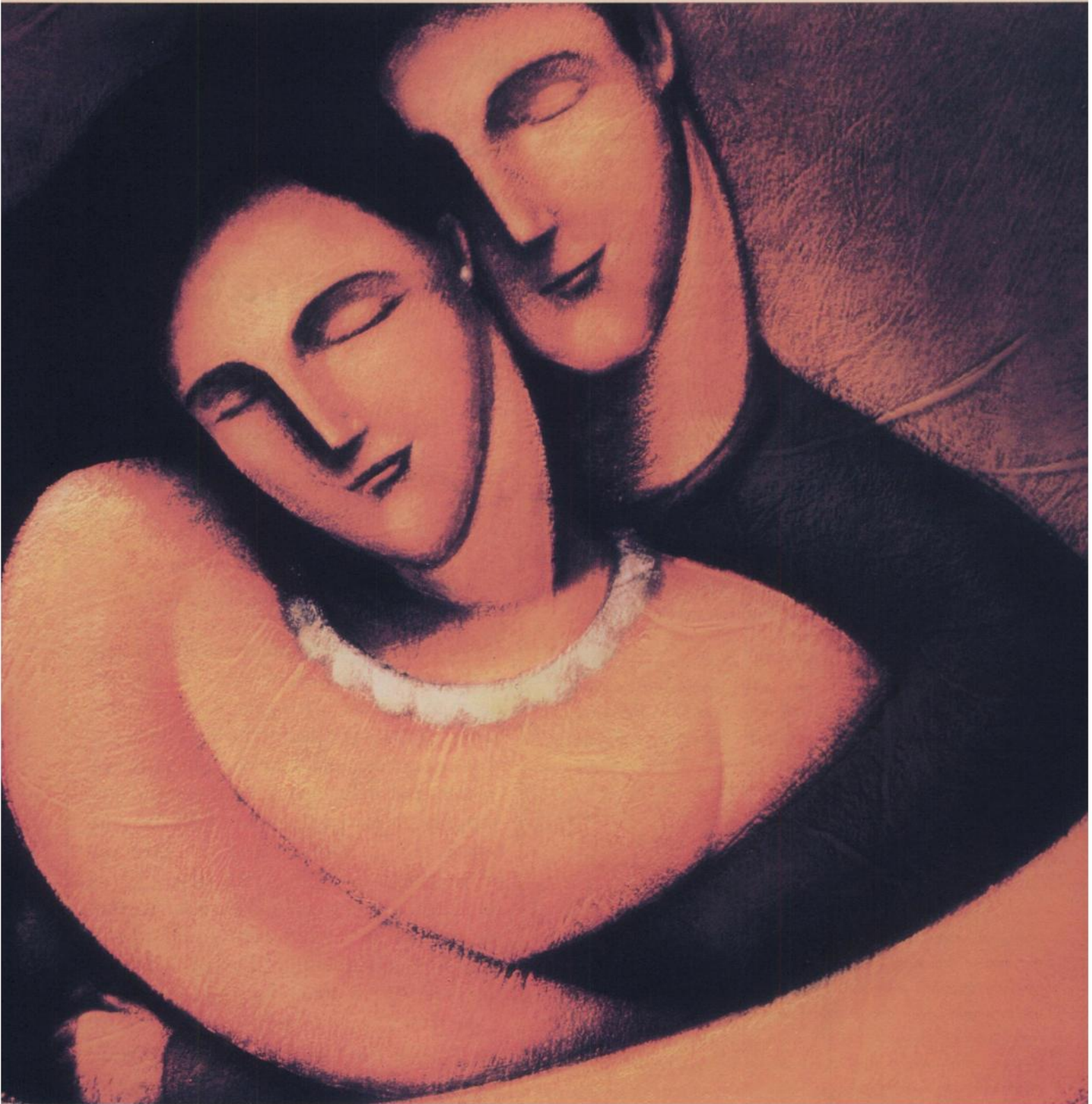


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200 mg tablet: 12619/0114

Basic NHS cost:

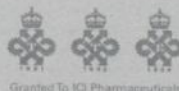
Starter pack: £6.59; 60 x 25 mg tablets: £28.20;
60 x 100 mg tablets: £113.10; 90 x 100 mg tablets: £169.65;
60 x 200 mg tablets: £113.10; 90 x 200 mg tablets: £169.65

Further information is available from:

ZENECA Pharma on 0800 200 123 please ask for Medical Information, or write to King's Court, Water Lane, Wilmslow, Cheshire SK9 5AZ.

References

1. Fabre LF, Arvanitis L, Pultz J *et al.* Clin Ther 1995; **17** (No.3): 366-378.
2. Arvanitis LA *et al.* Biol Psychiatry 1997; **42**: 233-246.
3. Small JG, Hirsch SR, Arvanitis LA *et al.* Arch Gen Psychiatry 1997; **54**: 549-557.
4. Borison RL, Arvanitis LA, Miller MS *et al.* J Clin Psychopharmacol 1996; **16** (2):158-169.
5. Data on File, Zeneca Pharmaceuticals.
6. Data on File, Zeneca Pharmaceuticals.
7. 'Seroquel' Summary of Product Characteristics.



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There's a depressed patient sitting in front of you. Ask them if it's good to talk.

Communicating confidently, whether it's at work or with friends and family, is just one sign of how well a depressed patient is re-adapting socially. And social interaction is an extremely valuable measure of successful treatment.

Edronax is a new selective NorAdrenaline Re-uptake Inhibitor (NARI). It not only lifts depressed mood,¹ but also significantly improves social interaction.²

These improvements in social functioning have been trial-proven by using the innovative SASS questionnaire (Social Adaptation Self-evaluation Scale).³

Edronax improves mood one week earlier than fluoxetine.¹ Additionally, when compared to fluoxetine, Edronax shows a significantly better outcome in terms of social functioning.²

Edronax helps restore patients' appreciation of friends, family, work and hobbies, and improves their self-perception.

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For free copies of the SASS questionnaire, please telephone 01908 603083.


Edronax[®]
REBOXETINE

**A NEW SELECTIVE NARI. LIFTS DEPRESSION.
HELPS RESTORE SOCIAL INTERACTION.**

**EDRONAX[®]
ABBREVIATED PRESCRIBING INFORMATION**

Presentation: Tablets containing 4mg reboxetine. **Indications:** Use in the acute treatment of depressive illness, and maintenance of clinical benefit in patients responsive to treatment. **Posology and method of administration:** Adults 4 mg b.i.d. (8 mg/day) administered orally. After 3-4 weeks, can increase to 10 mg/day. **Elderly and children:** Elderly patients have been studied in comparative clinical trials at doses of 2 mg b.i.d., although not in placebo controlled conditions. There is no experience in children and therefore reboxetine cannot be recommended in either of these groups. **Renal/Hepatic insufficiency:** 2 mg b.i.d. which can be increased based on

Special warnings and precautions for use: Close supervision is required for subjects with a history of convulsive disorders and must be discontinued if the patient develops seizures. Avoid concomitant use with MAO inhibitors. Close supervision of bipolar patients is recommended. Close supervision should be applied in patients with current evidence of urinary retention, glaucoma, prostatic hypertrophy and cardiac disease. At doses higher than the maximum recommended, orthostatic hypotension has been observed with greater frequency. Particular attention should be paid when administering reboxetine with other drugs known to lower blood pressure. **Interactions with other medicaments and other forms of interaction:** Reboxetine should not be

that have a narrow therapeutic margin and are metabolised by CYP3A4 or CYP2D6 e.g. anti-arrhythmics (flecainide), anti-psychotic drugs and tricyclic anti-depressants. No pharmacokinetic interaction with lorazepam. Reboxetine does not appear to potentiate the effect of alcohol. **Pregnancy and lactation:** Reboxetine is contraindicated in pregnancy and lactation. **Effects on ability to drive and use machines:** Reboxetine is not sedative per se. However, as with all psychoactive drugs, caution patients about operating machinery and driving. **Undesirable effects:** Adverse events occurring more frequently than placebo are: dry mouth, constipation, insomnia, paraesthesia, increased sweating, tachycardia, vertigo, urinary hesitancy/retention, impotence.

required. **Package and NHS Price:** Pack of 60 tablets in blisters £19.80. **Legal Category:** POM **Marketing Authorisation Holder:** Pharmacia & Upjohn Limited, Davy Avenue, Milton Keynes, MK5 8PH, UK. **Marketing Authorisation Number:** PL 0032/0216. **Date of Preparation:** October 1997. **References:** 1. Montgomery SA. *Journal of Psychopharmacology* 1997 (in press). 2. Dubini A. et al. *European Neuropsychopharmacol.* 1997; 7 (Suppl 1): S57-S70. 3. Bosc M. et al. *European Neuropsychopharmacol.* 1997; 7 (Suppl 1): S57-S70. Further information is available from Pharmacia & Upjohn Limited, Davy Avenue, Knowlhill, Milton Keynes, MK5 8PH, UK.





Because
community
re-integration
is not that
simple.

ABBREVIATED PRESCRIBING INFORMATION:

Presentation: Coated tablets containing 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. **Hepatic and/or renal impairment:** A lower starting dose (5mg) may be considered. 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 for 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. Although, in clinical trials, there were no reported cases of NMS in patients receiving olanzapine, if such an event occurs, or if there is unexplained high fever, 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. Caution when taken in combination with other centrally acting drugs and alcohol. Olanzapine may antagonise the effects of direct and

Antipsychotic Efficacy for First-line Use

ZYPREXA
Olanzapine



Making Community Re-integration the Goal

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 foetus. 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.

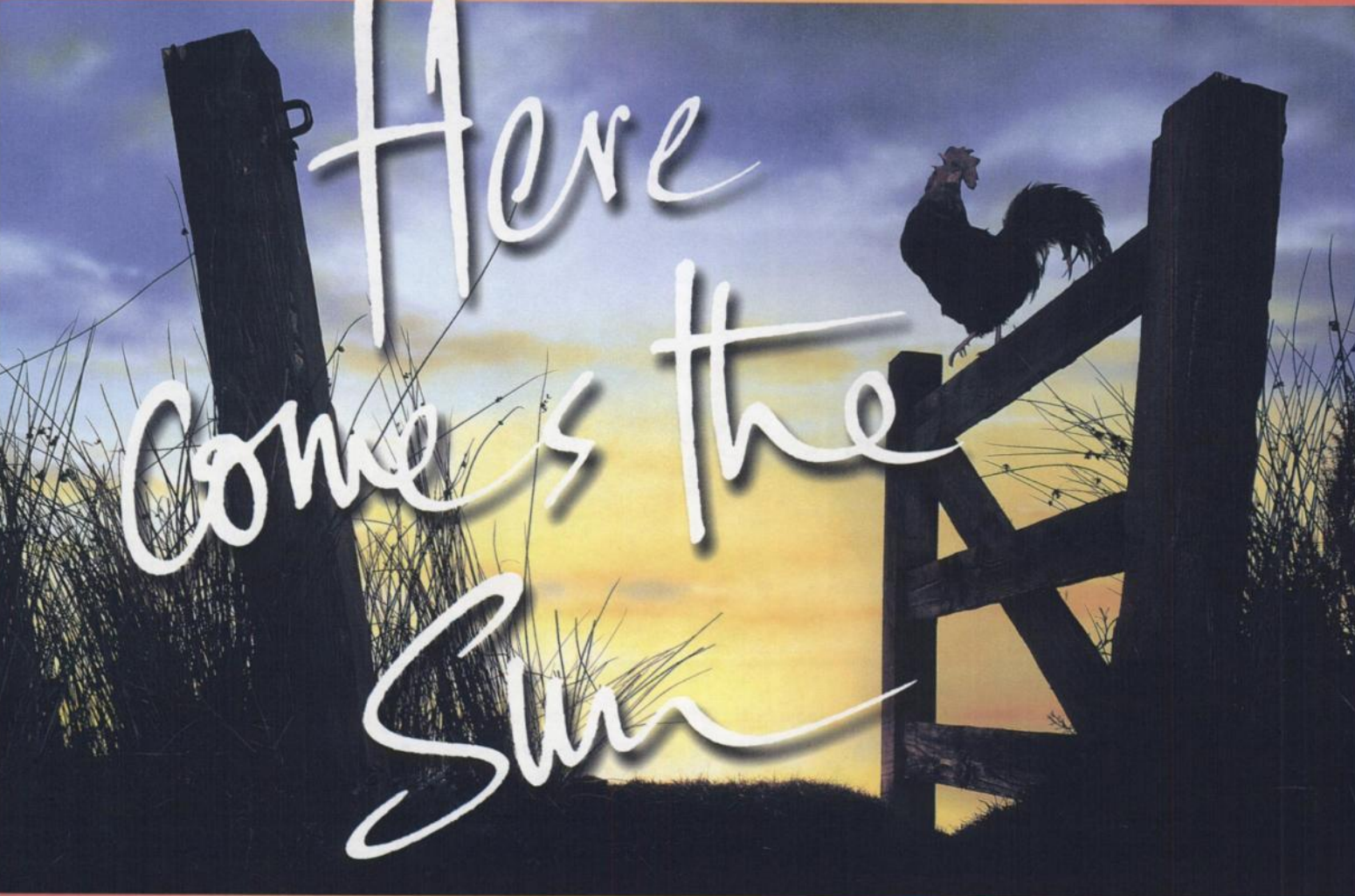
Driving, etc: Because olanzapine may cause somnolence, patients should be cautioned about operating hazardous machinery, including motor vehicles. **Undesirable Effects:** The only frequent (>10%) undesirable effects associated with the use of olanzapine in clinical trials were somnolence and weight 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 or high creatinine phosphokinase were reported rarely. Plasma prolactin levels were sometimes elevated, but associated clinical manifestations were rare. Asymptomatic haematological variations were occasionally seen in trials. For further information see summary of product characteristics. **Legal Category:** POM. **Marketing Authorisation Numbers:** EU/1/96/022/004 EU/1/96/022/006 EU/1/96/022/008 EU/1/96/022/009 EU/1/96/022/010. **Basic NHS Cost:** £52.73 per pack of 28 x 5mg tablets. £105.47 per pack of 28 x 10mg tablets. £158.20 per pack of 56 x 7.5mg tablets. £210.93 per pack of 56 x 10mg tablets. **Date of Preparation or Last Review:** April 1997. **Full Prescribing Information is Available From:** Eli Lilly and Company Limited, Dextra Court, Chapel Hill, Basingstoke, Hampshire RG21 5SY. Telephone: Basingstoke (01256) 315000.



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

dreams, vasodilatation, hypertension, rash, agitation, 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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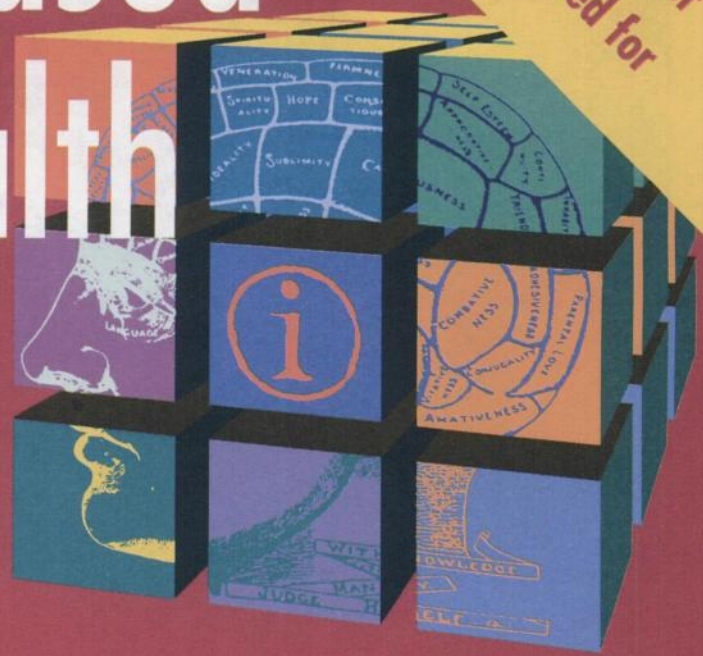
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