THE BRITISH JOURNAL OF PSYCHIATRY

DECEMBER 1997 VOL. 171

EDITORIALS

REVIEW ARTICLES

PAPERS

COLUMNS

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Debbie doesn't know that Cipramil is now indicated for panic disorder

... she just knows her doctor made a logical choice

As a patient with Panic Disorder, Debbie is beginning to appreciate the value of the Cipramil treatment that her doctor has newly prescribed.

Of course, Debbie would no more talk of the recently extended indication for Cipramil than its high selectivity[1,2], good tolerability[3], and low risk of drug interactions[4,5,6]. She just recognises the difference that Cipramil makes to the stability and quality of her life.

Lundbeck

Cipramil
citalopram
now indicated for panic disorder

Presentation: 'Cipramil' tablets 10 mg: PL 0458/0057, each containing 10 mg of citalopram as the hydrobromide. 28 (OP) 10 mg tablets £12.77. 'Cipramil' tablets 20 mg: PL 0458/0058, each containing 20 mg of citalopram as the hydrobromide. 28 (OP) 20 mg tablets £21.28. **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. 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. **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. © 1997 Lundbeck Ltd. Date

THE BRITISH JOURNAL OF PSYCHIATRY

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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.

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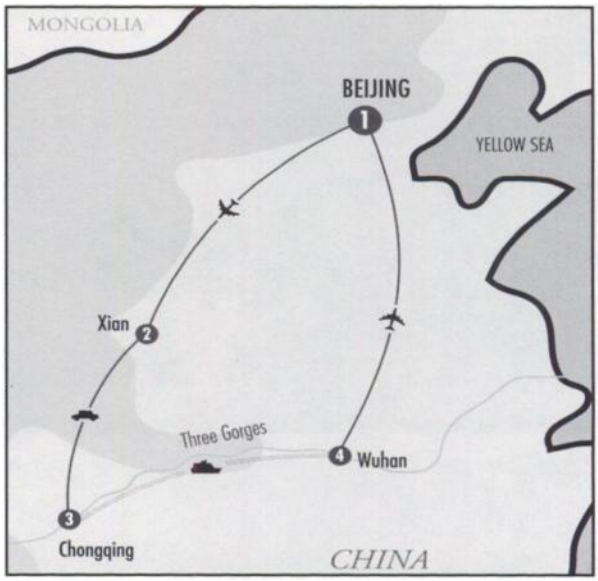
MENTAL HEALTH IN CHINA

6 - 21 JUNE 1998

This study tour represents a rare opportunity to observe Chinese psychiatric services. This is the first time a tour of this nature has been permitted to visit a range of mental health institutions in China. Mental Health in China allows participants to visit a range of psychiatric services in Beijing, Xian and Chongqing.



This unique opportunity is combined with the chance to experience the ancient culture of this country from the Great Wall to the Forbidden City, Summer Palace, Tiananmen Square and the Terracotta Warriors. The tour culminates in a four day cruise down the Yangtze river and through the huge Three Gorges , one of the wonders of the world

This may be the last opportunity to see the Three Gorges . When the new dam under construction is finished, the water level will rise flooding the Three Gorges .

Mental Health in China will be of interest to psychiatrists, psychologists and psychiatric nurses. Partners or non-medical participants are welcome.

The group will be escorted throughout the tour by Harry Field who has a wide understanding of both British and Chinese psychiatric services, together with an interpreter and local guides. This is an opportunity that should be taken before China changes forever. The fully inclusive price is £2,695.

For full details on the tour telephone Master Travel on 0181 671 7521, fax 0181 671 7327, Harry Field on 0181 940 2493 or fill in the form below and send to Master Travel, FREEPOST(SE7045), London SE24 9BR Email master.travel@MarkAllenGroup.com

Web site at http://wwwMarkAllenGroup.com/Mtravel.htm

MENTAL HEALTH STUDY TOUR TO CHINA 1998

NAME: .....

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TOPAMAX®
topiramate

At the end of the day, it works.

Adjunctive treatment for partial seizures with or without secondary generalisation

TOPAMAX Abbreviated Prescribing Information
Please read the data sheet before prescribing
Presentation: Tablets each imprinted "TOP" on one side and strength on the other containing 25mg (white), 50mg (light yellow), 100mg (yellow), and 200mg (salmon) topiramate. **Uses:** Adjunctive therapy of partial seizures, with or without secondarily generalised seizures, in patients inadequately controlled on conventional first line antiepileptic drugs. **Dosage and Administration:** Adults and Elderly: Oral administration. Usual dose: 200mg - 400mg/day in two divided doses. Maximum recommended dose: 800mg/day. Initiate therapy at 50mg bd then titrate to an effective dose. See data sheet for titration. Do not break tablets. It is not necessary to monitor topiramate plasma concentrations. Patients with renal disease/haemodialysis may require a modified titration schedule. (See data sheet). Children: Not recommended **Contra-indications:** Hypersensitivity to any component of the product. **Precautions and Warnings:** Withdraw all antiepileptic drugs gradually. Maintain adequate hydration to reduce risk of nephrolithiasis (especially increased in those with a predisposition). Drowsiness likely. TOPAMAX may be more sedating than other antiepileptic drugs therefore caution in patients driving or operating machinery, particularly until patients' experience with the drug is established. Do not use in pregnancy unless potential benefit outweighs risk to foetus. Women of child bearing potential should use adequate contraception. Do not use if breastfeeding. **Interactions:** Other Antiepileptic Drugs: No clinically significant effects except in some patients on phenytoin where plasma concentrations may increase. Phenytoin level monitoring is advised. Effects of other antiepileptic drugs: Phenytoin plasma concentrations on sodium valproate addition or withdrawal. 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:** In 5% or more: ataxia, impaired concentration, confusion, dizziness, fatigue, paraesthesia, somnolence and abnormal thinking. May cause agitation and emotional lability (which may manifest as abnormal behaviour) and depression. Less commonly: amnesia, anorexia, aphasia, diplopia, nausea, nystagmus, speech disorder, taste perversion, abnormal vision and weight decrease. Increased risk of nephrolithiasis. Venous thromboembolic events reported - causal association not established. **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. 25mg (PL0242/0301) = £22.02; 50mg (PL0242/0302) = £36.17; 100mg (PL0242/0303) = £64.80; 200mg (PL0242/0304) = £125.83.
Product Licence Holder: JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE HP14 4HJ. API VER 210397.
Further information is available on request from the Marketing Authorisation Holder: Janssen-Cilag Limited, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ.
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Date of Preparation March 1997

JANSSEN-CILAG

Add life to living with schizophrenia

Solian is a new benzamide antipsychotic, with the ability to treat both the positive[1] and negative[2] symptoms of schizophrenia.

Solian offers a lower incidence of EPS than standard neuroleptics such as haloperidol,[3] as well as avoiding some of the drawbacks of certain atypicals: it does not require routine cardiovascular[4,5] or haematological[4,6] monitoring and patients gain significantly less weight than those treated with risperidone.[2]

So when patients need the ability to cope with their condition, Solian has the power to treat their positive[1] *and* their negative[2] symptoms whilst still allowing them to do the everyday things that the rest of us take for granted.

Solian®
AMISULPRIDE

Efficacy that patients can live with

Prescribing Information - Solian 200 and Solian 50 ▼ Presentation: Solian 200mg tablets contain 200mg amisulpride and Solian 50mg tablets contain 50mg amisulpride. **Indication:** Acute and chronic schizophrenia in which positive and/or negative symptoms are prominent. **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; pregnancy; lactation; women of child-bearing potential unless using adequate contraception. **Warning and Precautions:** As with all neuroleptics, neuroleptic malignant syndrome may occur (discontinue Solian). Caution in patients with a history of epilepsy and Parkinson's disease. **Interactions:** Caution in concomitant administration with [illegible] hypotensive 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 and Ireland Ltd, Foundation Park, Roxborough Way, Maidenhead, Berks, SL6 3UD. **References:** 1. Freeman HL. Int Clin Psychopharmacol 1997;12(Suppl 2):S11-S17. 2. Möller HJ. 6th World Congress of Biological Psychiatry, Nice, France, June 22-27 1997. 3. Coukell AJ, Spencer CM, Benfield P. CNS Drugs (Adis) 1996 Sep 6 (3):237-256. 4. Solian SPC. Lorex Synthélabo. 5. Sertindole SPC. Lundbeck Ltd. 6. Clozapine SPC. Novartis. Date of preparation: October 1997. SOL. 7b

SYNTHÉLABO
CNS DIVISION

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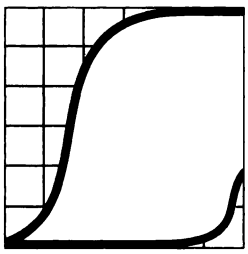
CUT IT OUT

A new window of opportunity

is opening in the treatment of schizophrenia, with the promise of substantial improvements to the quality of patients' lives.

Serdolect® is a novel limbic-selective anti-psychotic. Pre-clinical studies have shown that it inhibits the number of spontaneously active dopamine neurones in the mesolimbic ventral tegmental area without affecting dopamine neurones in the substantia nigra. Furthermore, it has been found to be more selective than certain other atypical drugs.[1] This indicates that Serdolect® may have a lower potential for producing extra-pyramidal side-effects across the therapeutic range.



Serdolect® opens the window of opportunity for your patients

- Effective against positive and negative symptoms[2,3]
- Placebo-level EPS at all doses tested[2,3]
- Sedation at placebo level[4]
- No clinically significant changes in haematological parameters[4]
- Mean serum prolactin levels maintained within normal limits[4]
- Once daily dosage
- One price for all routine maintenance doses

Thankfully, such a profile not only extends your choice, it also opens the window of opportunity for your patients.

Serdolect®

sertindole

Separates efficacy from EPS

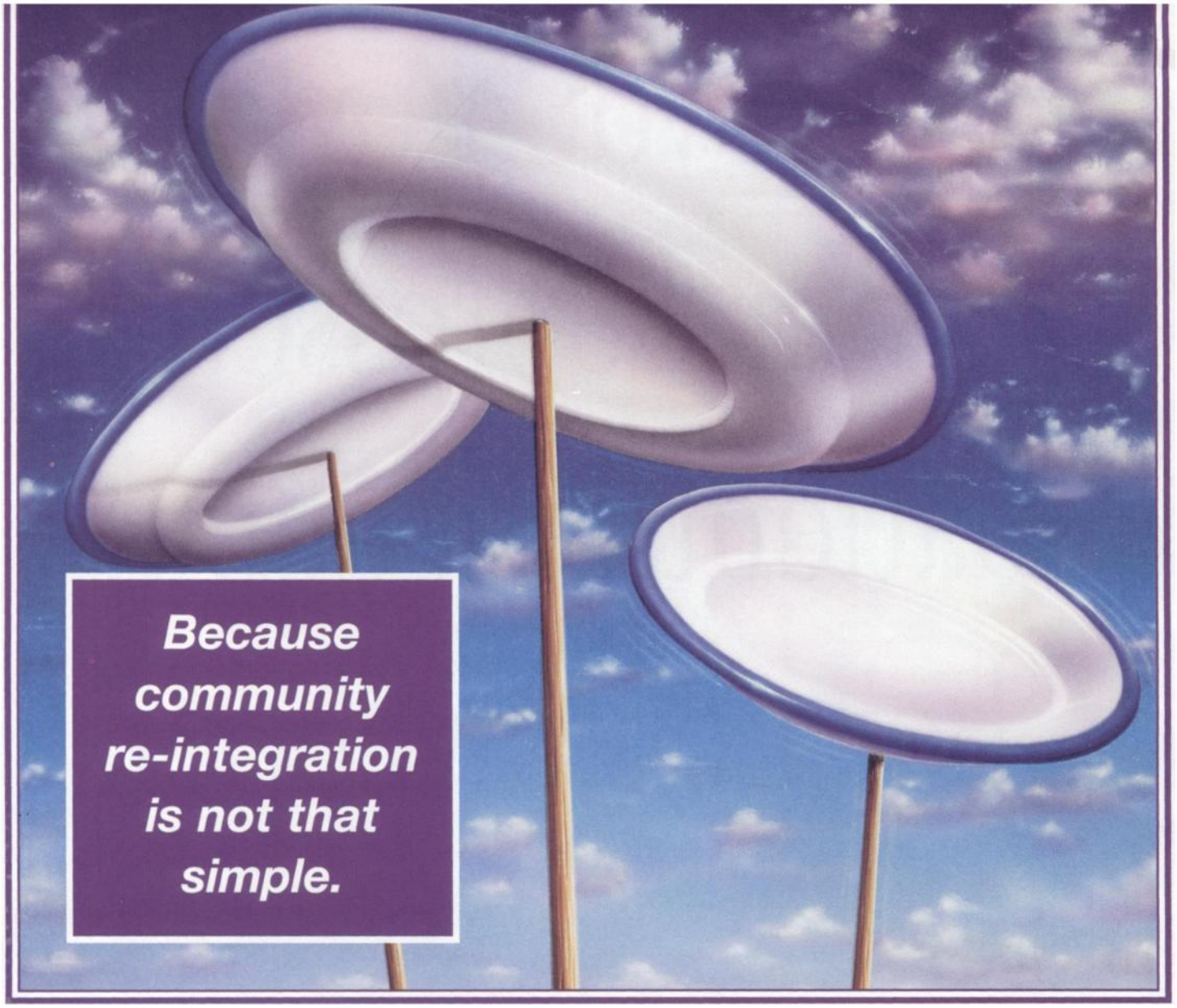
monitoring on treatment. Serdolect should not be initiated or should be discontinued if the QTC2 interval exceeds 520 msec. Hypokalaemia and hypomagnesaemia should be corrected and maintained within normal limits during treatment. If signs and symptoms of tardive dyskinesia appear, consider dose reduction or discontinuation. **Drug interactions:** (Also see contra-indications). Combined use of agents known to inhibit hepatic isoenzymes may necessitate lower maintenance doses. Combined use of agents known to induce hepatic isoenzymes may necessitate maintenance doses toward the upper dose range. **Adverse events:** Most commonly (>1 % of patients): nasal congestion, decreased ejaculatory volume, dizziness, dry mouth, postural hypotension, weight gain, peripheral oedema, dyspnoea, paraesthesia and prolonged QT interval. Incidence of EPS adverse events similar to placebo. **Overdosage:** Symptoms have included somnolence, slurred speech, tachycardia, hypotension and transient prolongation of QT interval. There is no specific antidote. Treatment is supportive and symptomatic. Epinephrine and dopamine should not be used (may exacerbate hypotension). Cardiovascular monitoring recommended. Administration of activated charcoal and laxative should be considered. **Package quantities and basic NHS price:** 4mg tablets, £36.63 for 30 tablet pack. 12mg tablets, £102.55 for 28 tablet calendar pack. 16mg tablets, £102.55 for 28 tablet calendar pack. 20mg tablets, £102.55 for 28 tablet calendar pack. **Legal category:** POM. **Product Licence numbers:** 4mg: 13761/0001. 12mg: 13761/0003. 16mg: 13761/0004. 20mg: 13761/0005. **Date of last review:** November 1996. Further information is available on request from Lundbeck Limited, Sunningdale House, Caldecotte Lake Business Park, Caldecotte, Milton Keynes, MK7 8LF. Serdolect® is a registered trademark of H. Lundbeck A/S.

References: 1. Arnt J *et al.* Poster presented at the 34th ACNP Meeting, December 1995, Puerto Rico. 2. Zborowski J *et al.* Poster presented at 148th APA Meeting, May 1995, Miami, Florida. 3. Daniel DG *et al.* J Psych: In Press. 4. Data on file, H. Lundbeck A/S.

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 patient tolerance. **Contra-indications:** Hypersensitivity to the compound or its constituents. Use in pregnancy/lactation. **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 co-administered with macrolide antibiotics, fluvoxamine, azole anti-fungal agents. Caution when co-administered with drugs 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



Antipsychotic Efficacy for First-line Use

ZYPREXA Olanzapine

Making Community Re-integration the Goal

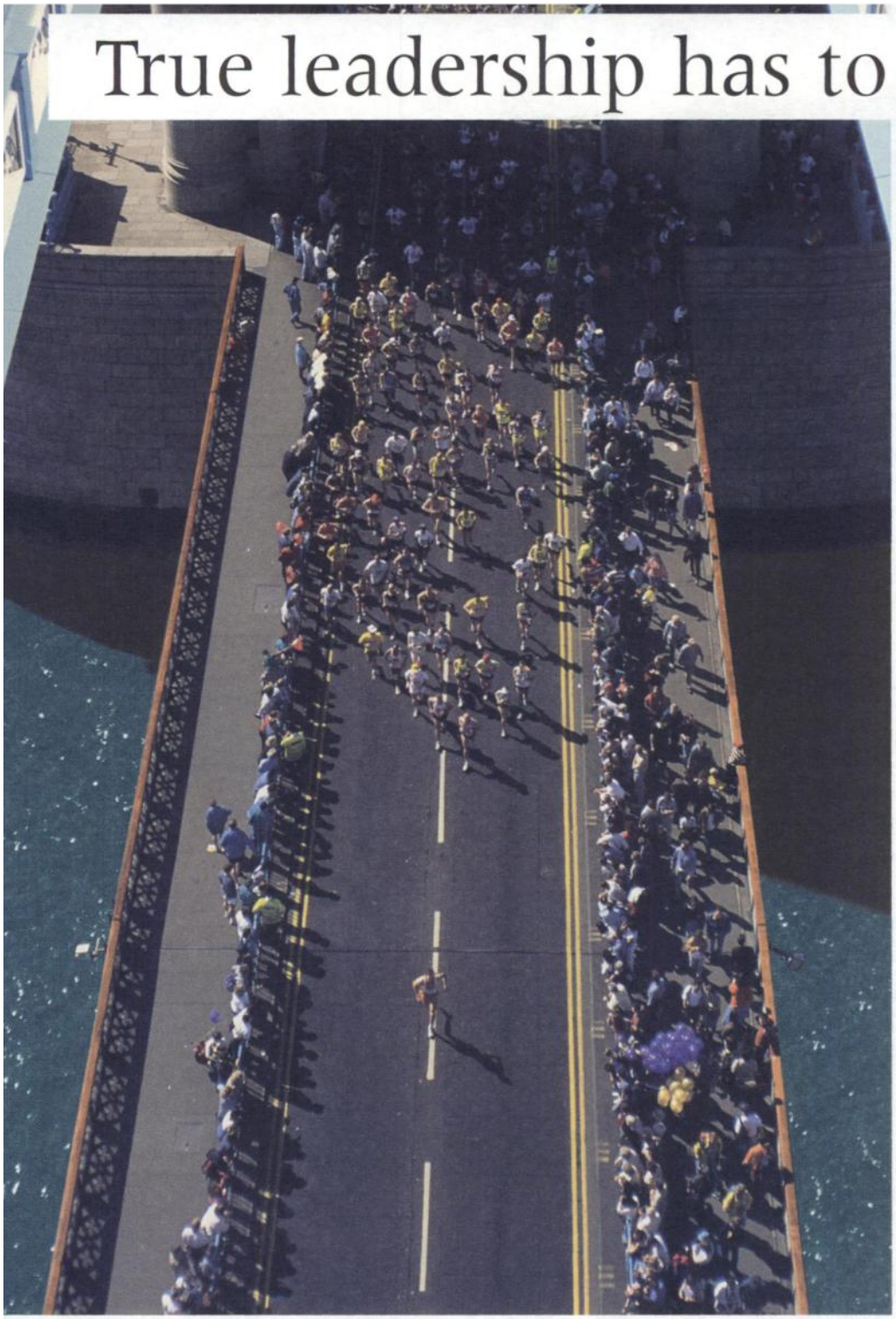
ABBREVIATED PRESCRIBING INFORMATION: **Presentation:** Coated tablets containing 5mg, 7.5mg or 10mg of olanzapine. The tablets also contain lactose. **Uses:** Schizophrenia, both as initial therapy and for maintenance of response. **Further Information:** In studies of patients with schizophrenia and 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 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 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 perpack 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.

'ZYPREXA' is a Lilly trademark.

Lilly PSYCHIATRY

Improving lives, restoring hope

True leadership has to be earned.



ASSOCIATED ANXIETY

Prozac has a proven record of efficacy in depression,[1,2,3] with a confirmed indication in depression with or without associated anxiety symptoms.[4]

A possible reason why Prozac has earned its status around the world.

PROZAC fluoxetine

The World's No.1 prescribed antidepressant brand.[1]

'PROZAC' ABBREVIATED PRESCRIBING INFORMATION (FLUOXETINE HYDROCHLORIDE)
Presentation Capsules containing 20mg or 60mg fluoxetine, as the hydrochloride. Liquid containing 20mg fluoxetine, as the hydrochloride, per 5ml syrup. **USES** Depression: TREATMENT OF THE SYMPTOMS OF DEPRESSIVE ILLNESS, WITH OR WITHOUT ASSOCIATED ANXIETY SYMPTOMS *Obsessive-compulsive disorder. Bulimia nervosa:* For the reduction of binge-eating and purging activity. **Dosage and Administration** (For full information, see data sheet.) For oral administration to adults only. *Depression, with or without associated anxiety symptoms - adults and the elderly:* A dose of 20mg/day is recommended. *Obsessive-compulsive disorder:* 20mg/day to 60mg/day. A dose of 20mg/day is recommended as the initial dose. *Bulimia - adults and the elderly:* A dose of 60mg/day is recommended. Because of the long elimination half-lives of the parent drug (1-3 days after acute administration; may be prolonged to 4-6 days after chronic administration) and its major metabolite (average 9.3 days), active drug substance will persist in the body for several weeks after dosing is stopped. The capsule and liquid dosage forms are bioequivalent. *Children:* Not recommended. *Patients with renal and/or hepatic dysfunction:* See 'Contra-indications' and 'Precautions' sections. **Contra-indications** Hypersensitivity to fluoxetine. Prozac should not be administered to patients with severe renal failure (GFR <10ml/min). *Usage in nursing mothers:* Prozac should not be prescribed to nursing mothers. *Monoamine oxidase inhibitors:* At least 14 days should elapse between discontinuation of an MAOI and initiation of treatment with Prozac. At least five weeks should elapse between discontinuation of Prozac and initiation of therapy with an MAOI. Serious, sometimes fatal reactions (including hyperthermia, rigidity, myoclonus, autonomic instability and mental status changes that include extreme agitation, progressing to delirium and coma) have been reported with concomitant use or when fluoxetine had been recently discontinued and an MAOI started. Some cases presented with features resembling neuroleptic malignant syndrome. **Warnings** *Rash and allergic reactions:* Angioneurotic oedema, urticaria and other allergic reactions have been reported. Upon appearance of rash, or of other allergic phenomena for which an alternative aetiology cannot be identified, Prozac should be discontinued. *Pregnancy:* Use of Prozac should be avoided unless there is no safer alternative. **Precautions** Prozac should be discontinued in any patient who develops seizures. Prozac should be avoided in patients with unstable epilepsy; patients with controlled epilepsy should be carefully monitored. There have been rare reports of prolonged seizures in patients on fluoxetine receiving ECT treatment. A lower dose of Prozac, eg, alternate day dosing, is recommended in patients with significant hepatic dysfunction or mild to moderate renal failure (GFR 10-50ml/min). Caution is advisable when Prozac is used in patients with acute cardiac disease. Prozac may cause weight loss which may be undesirable in underweight depressed patients. In diabetics, fluoxetine may alter glycaemic control. There have been reports of abnormal bleeding in several patients, but causal relationship to fluoxetine and clinical importance are unclear. *Drug interactions:* Increased (with lithium toxicity) or decreased lithium levels have been reported. Lithium levels should be monitored. Because fluoxetine's metabolism involves the hepatic cytochrome P450IID6 isoenzyme system, concomitant therapy with other drugs also metabolised by this system, and which have a narrow therapeutic index (eg, carbamazepine, tricyclic antidepressants), should be initiated at or adjusted to the low end of their dose range. Greater than 2-fold increases of previously stable plasma levels of cyclic antidepressants have been observed when Prozac has been administered in combination. Agitation, restlessness and gastro-intestinal symptoms have been reported in a small number of patients receiving fluoxetine in combination with tryptophan. Patients on stable phenytoin doses have developed elevated plasma concentrations and clinical phenytoin toxicity after starting fluoxetine. *For further information, see data sheet.* **Adverse Effects** Asthenia, fever, nausea, diarrhoea, dry mouth, appetite loss, dyspepsia, vomiting, rarely abnormal LFTs, headache, nervousness, insomnia, drowsiness, anxiety, tremor, dizziness, fatigue, decreased libido, seizures, hypomania or mania, dyskinesia, movement disorders, neuroleptic malignant syndrome-like events, pharyngitis, dyspnoea, pulmonary events (including inflammatory processes and/or fibrosis), rash, urticaria, vasculitis, excessive sweating, arthralgia, myalgia, serum sickness, anaphylactoid reactions, hair loss, sexual dysfunction. The following have been reported in association with fluoxetine but no causal relationship has been established: aplastic anaemia, cerebral vascular accident, confusion, ecchymoses, eosinophilic pneumonia, gastro-intestinal haemorrhage, hyperprolactinaemia, immune-related haemolytic anaemia, pancreatitis, pancytopenia, suicidal ideation, thrombocytopenia, thrombocytopenic purpura, vaginal bleeding after drug withdrawal and violent behaviour. Hyponatraemia (including serum sodium below 110mmol/l) has been rarely reported. This appears to be reversible upon discontinuation. **Overdosage** On the evidence available, fluoxetine has a wide margin of safety in overdose. Since introduction, reports of death, attributed to overdosage of fluoxetine alone, have been extremely rare. One patient who reportedly took 3000mg of fluoxetine experienced 2 grand mal seizures that remitted spontaneously. **Legal Category** POM **Product Licence Numbers** 0006/0195 0006/0198 0006/0272 **Basic NHS Cost** £20.77per pack of 30 capsules (20mg). £67.85 per pack of 98 capsules (20mg). £62.31 per pack of 30 capsules (60mg). £19.39 per 70ml bottle. **Date of Preparation or Last Review** October 1996. **Full Prescribing Information is Available From** Dista Products Limited, Dextra Court, Chapel Hill, Basingstoke, Hampshire, RG21 5SY. Telephone: Basingstoke (01256) 52011
'PROZAC' is a Dista trademark

References:1. Data on file, Dista Products Ltd. 2. Tignol J. *J Clin Psychopharm* 1993; **13** (6, suppl. 2): 18S-22S. 3. Bennie EH, Mullin JM, Martindale JJ. *J Clin Psychiatry* 1995; **56**: 229-237. 4. Prozac Data Sheet 24M.

Date of preparation: May 1997 PZ 906

Lilly PSYCHIATRY
Improving lives, restoring hope

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Patient with schizophrenia exercises *self* esteem by going downhill

The SDA effect of Risperdal can mean a huge difference to the lives of patients with schizophrenia.

Because SDA is the action of Serotonin and Dopamine Antagonism in a single drug. In positive and negative symptoms. In first episode and acute presentations, and in chronic patients. Risperdal continues to provide this SDA effect to give high efficacy, with low levels of extrapyramidal side-effects, to more and more patients.

Helping them keep out of hospitals while enhancing their appreciation of, and participation in, community and family life.

The word is on the street.

Risperdal™
RISPERIDONE

A routine route out

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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 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 3.0×10^9/L and/or the absolute neutrophil count drops below 1.5×10^9/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 3.5×10^9/L and/or a neutrophil count between 1.5 and 2.0×10^9/L, with a view to discontinuing CLOZARIL. Any further fall in white blood/neutrophil count below 1.0×10^9/L and/or 0.5×10^9/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 1.0×10^9/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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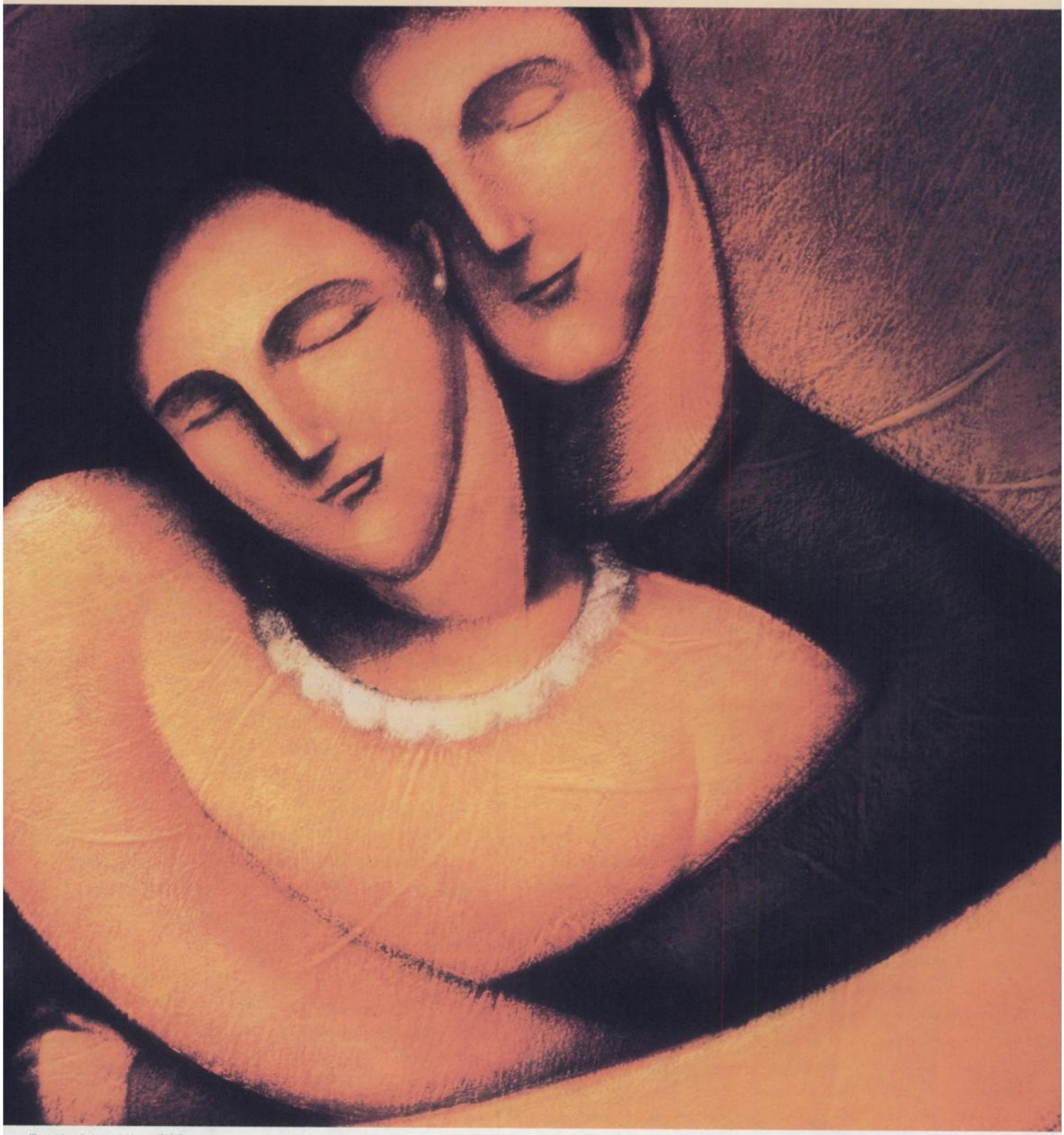

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Tender loving care and SEROXAT

PAROXETINE

'Seroxat' helps get depressed patients back to normal, liberating them from everyday stresses and anxiety.

For all those depressed patients who need a helping hand to face life again, make 'Seroxat' your first-choice prescription for depression.

Rebuilding the lives of anxious depressed patients

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Changing thinking in schizophrenia?

'SEROQUEL' (quetiapine)

Prescribing Notes. Consult Summary of Product Characteristics before prescribing. Special reporting to the CSM required.

Use: Treatment of schizophrenia.
Presentation: Tablets containing 25 mg, 100 mg and 200 mg of quetiapine.

Dosage and Administration: 'Seroquel' should be administered twice daily. Adults: The total daily dose for the first 4 days of therapy is 50 mg (Day 1), 100 mg (Day 2), 200 mg (Day 3) and 300 mg (Day 4). From day 4 onwards, titrate to usual effective range of 300 to 450 mg/day. Dose may be adjusted within the range 150 to 750 mg/day according to clinical response and tolerability. Elderly patients: Use with caution, starting with 25 mg/day and increasing daily by 25 to 50 mg to an effective dose. Children and adolescents: Safety and efficacy not evaluated. Renal and hepatic impairment: Start with 25 mg/day increasing daily by 25 to 50 mg to an effective dose. Use with caution in patients with hepatic impairment.

Contra-indications: Hypersensitivity to any component of the product.
Precautions: Caution in patients with cardiovascular disease, cerebrovascular disease or other conditions predisposing to hypotension and patients with a history of seizures. Caution in combination with drugs known to prolong the QTc interval, especially in the elderly. Caution in combination with other centrally acting drugs and alcohol, and on co-administration with thioridazine, phenytoin or other hepatic enzyme inducers, potent inhibitors of CYP3A4 such as systemic ketoconazole or erythromycin. If signs and symptoms of tardive dyskinesia appear, consider dosage reduction or discontinuation of 'Seroquel'. In cases of neuroleptic malignant syndrome, discontinue 'Seroquel' and give appropriate medical treatment. 'Seroquel' should only be used during pregnancy if benefits justify the potential risks. Avoid breastfeeding whilst taking 'Seroquel'. Patients should be cautioned about operating hazardous machines, including motor vehicles.

Undesirable events: Somnolence, dizziness, constipation, postural hypotension, dry mouth, asthenia, rhinitis, dyspepsia, limited weight gain, orthostatic hypotension (associated with dizziness), tachycardia and in some patients syncope. Occasional seizures and rarely possible neuroleptic malignant syndrome. Transient leucopenia and/or neutropenia and occasionally eosinophilia. Asymptomatic, usually reversible elevations in serum transaminase or gamma - GT levels. Small elevations in non-fasting serum triglyceride levels and total cholesterol. Decreases in thyroid hormone levels, particularly total T4 and free T4 usually reversible on cessation. Prolongation of the QTc interval (in clinical trials this was not associated with a persistent increase).

Legal category: POM

Product licence numbers:

25 mg tablet: 12619/0112
100 mg tablet: 12619/0113
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.

'Seroquel' is a trademark, the property of **Zeneca Limited.**

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.

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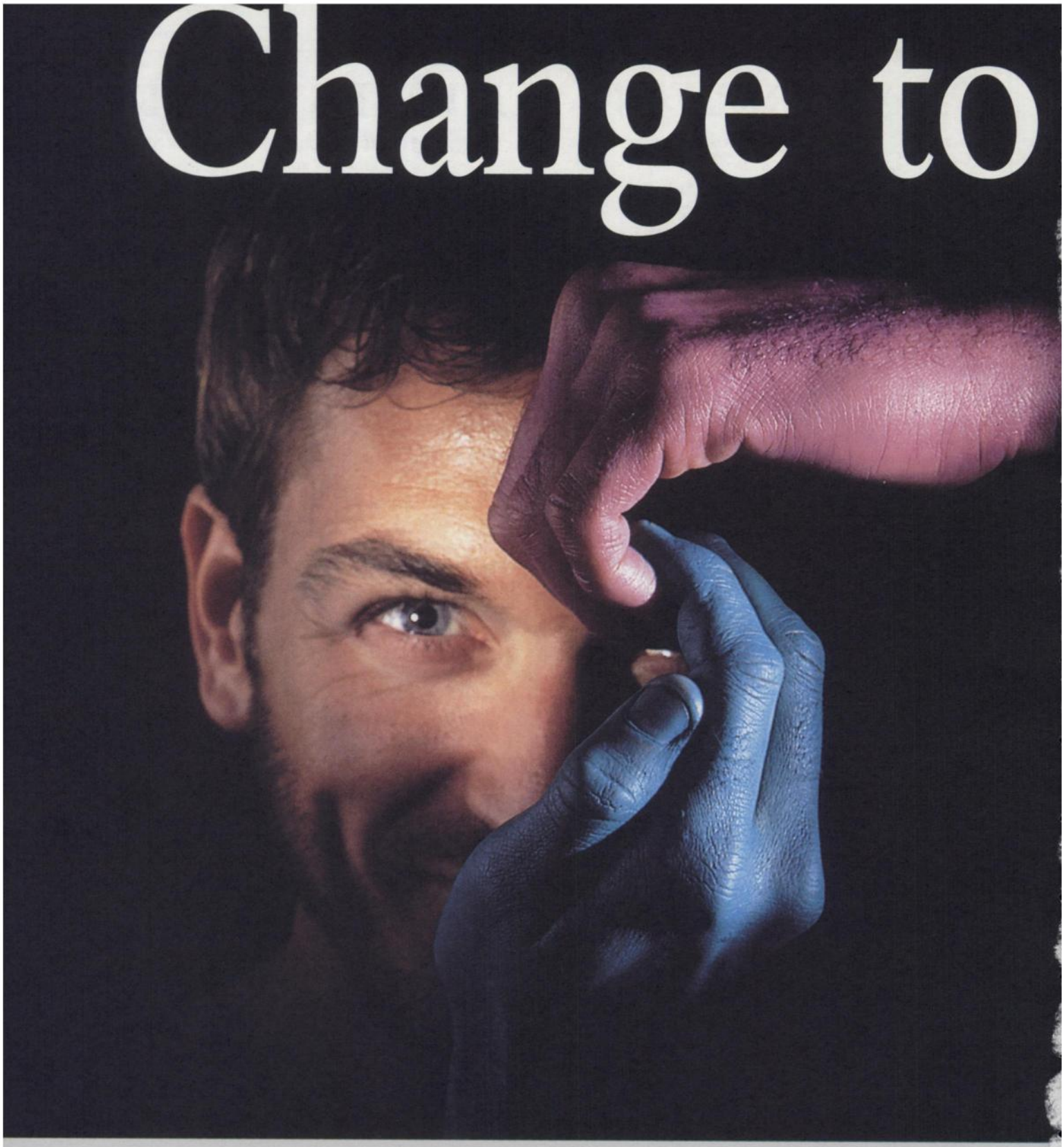

'SEROQUEL' (quetiapine)

Prescribing Notes.
Consult Summary of Product Characteristics before prescribing.
Special reporting to the CSM required.

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Presentation: Tablets containing 25 mg, 100 mg and 200 mg of quetiapine.

Dosage and Administration: 'Seroquel' should be administered twice daily. Adults: The total daily dose for the first 4 days of therapy is 50 mg (Day 1), 100 mg (Day 2), 200 mg (Day 3) and 300 mg (Day 4). From day 4 onwards, titrate to usual effective range of 300 to 450 mg/day. Dose may be adjusted within the range 150 to 750 mg/day

Elderly patients: Use with caution, starting with 25 mg/day and increasing daily by 25 to 50 mg to an effective dose. Children and adolescents: Safety and efficacy not evaluated. Renal and hepatic impairment: Start with 25 mg/day increasing daily by 25 to 50 mg to an effective dose. Use with caution in patients with hepatic impairment.

Contra-indications: Hypersensitivity to any component of the product.

Precautions: Caution in patients with cardiovascular disease, cerebrovascular disease or other conditions predisposing to hypotension and patients with a history of seizures. Caution in combination with drugs known to prolong the QTc interval, especially in the elderly. Caution in combination with other centrally acting drugs and alcohol, and on co-administration with thioridazine, phenytoin or other hepatic

systemic ketoconazole or erythromycin. If signs and symptoms of tardive dyskinesia appear, consider dosage reduction or discontinuation of 'Seroquel'. In cases of neuroleptic malignant syndrome, discontinue 'Seroquel' and give appropriate medical treatment. 'Seroquel' should only be used during pregnancy if benefits justify the potential risks. Avoid breastfeeding whilst taking 'Seroquel'. Patients should be cautioned about operating hazardous machines, including motor vehicles.

Undesirable events: Somnolence, dizziness, constipation, postural hypotension, dry mouth, asthenia, rhinitis, dyspepsia, limited weight gain, orthostatic hypotension (associated with dizziness), tachycardia and in some patients syncope. Occasional seizures and rarely possible neuroleptic malignant syndrome. Transient leucopenia and/or neutropenia and occasionally eosinophilia. Asymptomatic, usually reversible

Seroquel
quetiapine

- Effective in positive and negative symptoms[1-4] and improving mood*[5] in patients with schizophrenia
- Incidence of EPS no different from placebo across the full dose range[1-4]
- Rate of withdrawals due to adverse events no different from placebo[6]
- No requirement for routine blood, BP or ECG monitoring[7]

Seroquel
quetiapine

Changing thinking in schizophrenia.

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

Small elevations in non-fasting serum triglyceride levels and total cholesterol. Decreases in thyroid hormone levels, particularly total T4 and free T4 usually reversible on cessation. Prolongation of the QTc interval (in clinical trials this was not associated with a persistent increase).

Legal category: POM

Product licence numbers:

25 mg tablet: 12619/0112
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'Seroquel' is a trademark, the property of **Zeneca Limited.**

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.

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5. Data on File, Zenaca Pharmaceuticals.
6. Data on File, Zeneca Pharmaceuticals.
7. 'Seroquel' Summary of Product Characteristics.

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