REDUCING THE RISK OF DISCONTINUATION SYNDROME[2]

Prozac is rarely associated with unpleasant antidepressant discontinuation symptoms.[2,3,4,5,6,7]

Prozac's long half life may protect against such symptoms.[4,7]

So Prozac makes it easy for you and your patients on stopping treatment[8] or if therapy is interrupted.[1]

Possible reasons 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)

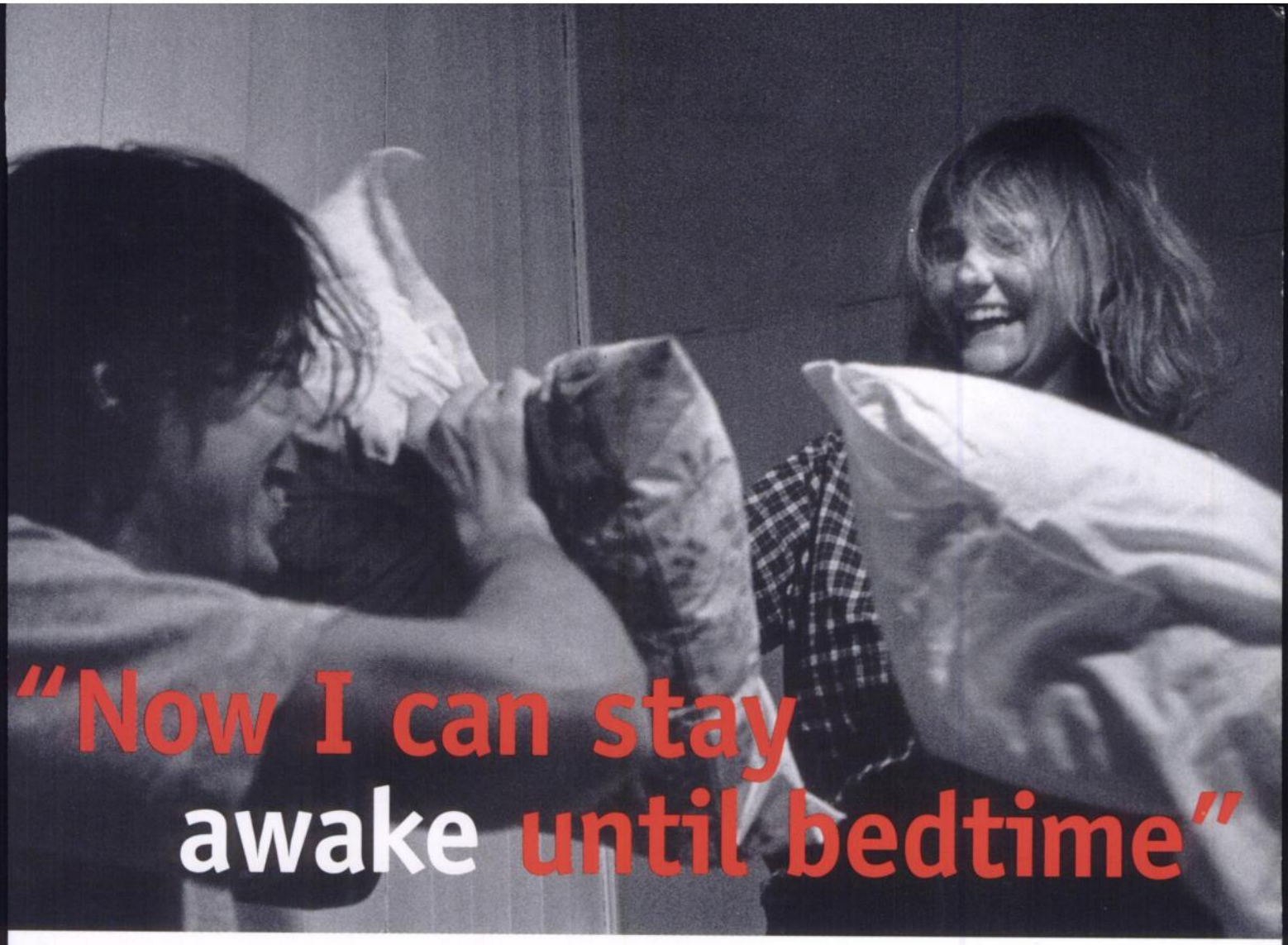
Presentation Capsules containing 20mg or 60mg fluoxetine, as the hydrochloride. Liquid containing 20mg fluoxetine, as the hydrochloride, per 5ml syrup. **Uses** *Depression:* TREATMENT OF THE SYMPTOMS OF DEPRESSIVE ILLNESS, WITH OR WITHOUT ASSOCIATED ANXIETY SYMPTOMS. *Obsessive-compulsive disorder. 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 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 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 **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** £ 20.77 per 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 (internal review August 1997) **Full Prescribing Information is Available From** Dista Products Limited, Dextra Court, Chapel Hill, Basingstoke, Hampshire, RG21 5SY. Telephone: Basingstoke (01256) 352011

'PROZAC' is a Dista trademark.

References: 1. Data on file, Dista Products Ltd. 2. Schatzberg AF. *J Clin Psych* 1997; **58** (Suppl. 7): 5-16. 3. Coupland NJ, Bell CJ, Potokar JP. *J Clin Psychopharmacol* 1996; **16**: 356-362. 4. Price JS. *Pharmacoepid Drug Safety* 1995; **4** (Suppl. 1): 62. 5. Lejoyeux M, *et al. CNS Drugs* 1996; **5** (4): 278-292. 6. Lazowick AL, Levin GM. *Ann Pharmacother* 1995; **29**: 1284-1285. 7. Lane RM. *J Serotonin Res* 1996; **3**: 75-83. 8. Stokes PE. *Clin Therapeutics* 1993; **15** (2): 216-243.

Date of Preparation: November 1997 PZ 938

Lilly PSYCHIATRY



"Now I can stay awake until bedtime"

FOR MOST PATIENTS, SCHIZOPHRENIA IS A LIFELONG DISEASE REQUIRING LIFELONG MEDICATION. SEDATION IS THE MOST COMMON SINGLE SIDE-EFFECT OF ANTIPSYCHOTIC MEDICATIONS[1] AND ITS POTENTIAL IMPACT ON COMPLIANCE AND QUALITY OF DAILY LIFE IS THEREFORE AN IMPORTANT ISSUE TO CONSIDER.

TRIALS WITH SERDOLECT HAVE DEMONSTRATED PLACEBO-LEVEL SEDATION[2]

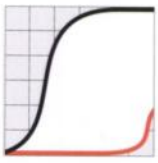
By separating efficacy from sedation, Serdolect gives physicians greater flexibility in patient management - in acute psychotic disturbance, Serdolect may be safely combined with a benzodiazepine[2].

SERDOLECT ADDITIONALLY OFFERS

- Efficacy against positive and negative symptoms of schizophrenia[3,4]
- EPS at placebo level[3]
- Prolactin levels maintained within normal limits[2]
- Once-daily dosage

REFERENCES

1. American Psychiatric Association. Practice Guidelines for the treatment of patients with schizophrenia. Supplement to Am. J. Psychiatry 1997; 154(4)
2. Data on file, H. Lundbeck A/S
3. Zimbroff DL et al. Am. J. Psychiatry 1997;154:782-791
4. Hale A. et al. Poster presented at CINP meeting, June 1996, Melbourne



Serdolect®

sertindole

Success is a long-term achievement

OLECT: ABBREVIATED PRESCRIBING INFORMATION

ntation: Tablets of 4mg, 12mg, 16mg or 20mg sertindole. **Indications:** ent of schizophrenia. Not for urgent relief of symptoms in acutely disturbed ts. **Dosage and administration:** Tablets should be taken orally once daily ut regard for food. Adults: All patients should be started on 4mg/day. The should be increased by 4mg increments after 4-5 days on each dose to the um daily maintenance dose range of 12-20mg. The dose may be increased aximum of 24mg, Re-titration is necessary if dosing is suspended for more ne week. Children: Not recommended. Mild to moderate hepatic impairment: r titration and lower maintenance dose. Elderly: Slower titration and lower enance doses may be required. **Contraindications:** Known prolongation interval or combined use of drugs known to prolong QT interval. Clinically icant cardiac disease or uncorrected hypokalaemia. Combined use of drugs ay induce hypokalaemia. Diuretic therapy may be initiated if required but ssium-sparing agent must be used. Combined use of quinidine or systemic nazole or itraconazole. Severe hepatic impairment. Hypersensitivity to Serdolect is not sedative, however, patients should be advised not to drive or operate machinery until their individual susceptibility is known. History of diabetes, seizures, Parkinson's disease. Symptoms of orthostatic hypotension may occur and blood pressure should be monitored during initial dose titration and in early maintenance phase. In common with other antipsychotic drugs, Serdolect lengthens the QT interval in some patients (<1.7% of patients). Electrolyte imbalance or combined use of other drugs that inhibit Serdolect metabolism can increase the risk of occurrence of prolonged QT interval. An ECG should be performed prior to use with periodic ECG monitoring during treatment. Serdolect should not be initiated or should be discontinued if the QTC_2 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:** (see also contraindications). 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 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:** April 1997. Further information is available on request from Lundbeck Limited, Sunningdale House, Caldecotte Lake Business Park, Caldecotte, Milton Keynes, MK7 8LF. Serdolect®

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