Safeguarding public health

MHRA

Public Assessment Report

Fluoxetine 20mg Capsules

PL 20395/0003

Medicines and Healthcare products Regulatory Agency

FLUOXETINE 20MG CAPSULES

PL 20395/0003

UKPAR

TABLE OF CONTENTS

FLUOXETINE 20MG CAPSULES

PL 20395/0003

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Relon Chem Limited a Marketing Authorisation (licence) for the medicinal product Fluoxetine 20mg Capsules (PL 20395/0003). This is a prescription only medicine [POM] for treating depression, obsessive-compulsive disorder and bulimia nervosa (an eating disorder characterised by binge-eating and purging).

The product contains fluoxetine hydrochloride, which helps to raise the levels of the hormone serotonin.

This is a simple abridged application that cross-refers to a previously granted licence for Fluoxetine 20mg Capsules (PL 16002/0016).

No new or unexpected safety concerns arose from this simple application and it was therefore judged that the benefits of using Fluoxetine 20mg Capsules outweigh the risks, hence a Marketing Authorisation has been granted.

FLUOXETINE 20MG CAPSULES

PL 20395/0003

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Fluoxetine 20mg Capsules (PL 20395/0003) to Relon Chem Limited on 7 June 2006. The product is a prescription only medicine [POM].

This application was submitted as a simple abridged application according to Article 10.1(a)i of Directive 2001/83/EC, cross-referring to Fluoxetine 20mg Capsules (PL 16002/0016, approved on 6 January 2000).

Fluoxetine is a selective serotonin (5-hydroxytryptamine, 5-HT) reuptake inhibitor, whose selectivity is unaltered by its major metabolite.

No new data were submitted for this simple application, nor were any necessary, as the data are identical to that of the previously granted cross-referenced product. As the cross-referenced product was granted prior to the introduction of current legislation, no public assessment report was generated for it.

Fluoxetine 20mg Capsules is indicated for the treatment of the symptoms of depressive illness, with or without associated anxiety symptoms, especially where sedation is not required. It is also used in the treatment of obsessive-compulsive disorder and for the reduction of binge-eating and purging activity in bulimia nervosa.

PHARMACEUTICAL ASSESSMENT

LICENCE No.:	**PL 20395/0003**
PROPRIETARY NAME:	**Fluoxetine 20 mg Capsules**
ACTIVE(S):	**Fluoxetine Hydrochloride**
COMPANY NAME:	**Relon Chem Ltd.**
EC ARTICLE:	**10.1(a)(i)**
LEGAL STATUS:	**POM**

INTRODUCTION

This is a simple national abridged marketing authorisation application for Fluoxetine 20mg Capsules, cross-referring to an existing product on the UK market (PL 16002/0016, granted 6 January 2000 to Pharmafile).

A letter of access is provided by Pharmafile Ltd, authorising the licensing authority to cross-refer to Pharmafile's licence.

COMMENTS

No Part II data is provided and the applicant declares that it has in its possession the Part II data. A pharmaceutical statement is provided by the applicant's Pharmaceutical Expert stating that the proposed product is the same as the reference product in terms of the qualitative and quantitative composition, manufacture and QC.

A letter is provided stating that the manufacturer of the product is willing to manufacture for the applicant (Relon Chem Ltd).

The proposed manufacturing, packaging and QC batch release sites are in line with the sites specified in the PL 16002/0016.

Copies of the manufacturing licences are provided for the batch release, manufacturing and assembly (packing), distribution and storage sites.

The Clinical Expert statement is also provided, indicating that the proposed product is identical to the cross-referenced product.

MAA forms and Part I data were checked against licence PL 16002/0016. The formulation, manufacturing methods, drug substance specification, finished product specification, proposed shelf life and the proposed sites are identical.

MARKETING AUTHORISATION APPLICATION FORM

Satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS, LEAFLET & LABELLING

Satisfactory.

BSE/TSE Compliance

Satisfactory TSE Certificates of Suitability are provided from the suppliers of magnesium stearate and gelatin.

CONCLUSION

Marketing authorisation should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.

OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

The data for this application are consistent with those previously assessed for the cross-referenced product and as such have been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

This application is identical to a previously granted application for Fluoxetine 20mg Capsules.

No new or unexpected safety concerns arose from this application.

The SPC, PIL and labelling are satisfactory and consistent with those of the cross-referenced product.

RISK-BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-referenced product. The risk-benefit assessment is therefore considered to be favourable.

FLUOXETINE 20MG CAPSULES

PL 20395/0003

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application for Fluoxetine 20mg Capsules on 20 June 2003.
2	The MHRA's assessment of the submitted data was completed on 25 September 2003.
3	Further information was requested from the company on 27 October 2003.
4	The applicant's response to further information request was received 28 January 2004.
5	Further information was requested from the company on 16 August 2004.
6	The applicant's response to further information request was received 21 September 2004.
7	Additional information was requested on 22 June 2005.
8	The applicant responded to additional information request in a letter dated 24 August 2005.
9	Further details were provided by the applicant on 11 and 19 April 2006.
10	The MHRA completed its assessment of the application on 5 June 2006.
11	The application was determined on 7 June 2006.

FLUOXETINE 20MG CAPSULES

PL 20395/0003

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fluoxetine 20mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluoxetine 20mg as Fluoxetine Hydrochloride.

For excipients, see section 6.1

3. PHARMACEUTICAL FORM

Hard capsule.

Size 3. Capsule cap is light green opaque. Capsule body is standard yellow opaque. Markings are "F20".

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Depression: Fluoxetine is indicated for the treatment of the symptoms of depressive illness, with or without associated anxiety symptoms, especially where sedation is not required.

Obsessive-compulsive disorder.

Bulimia nervosa: Fluoxetine is indicated for the reduction of binge-eating and purging activity.

4.2. Posology and method of administration

For oral administration to adults only.

Depression with or without associated anxiety symptoms - adults and the elderly: A dose of 20 mg/day is recommended.

Obsessive-compulsive disorder: 20 mg/day to 60 mg/day. A dose of 20 mg/day is recommended as the initial dose. Although there may be an increase in the potential of side-effects at higher doses, a dose increase may be considered after several weeks if there is no response.

Bulimia nervosa - adults and the elderly: A dose of 60 mg/day is recommended.

Children and adolescents under 18 years of age: The use of Fluoxetine in children is not recommended, as safety and efficacy have not been established. The use of fluoxetine in adolescents under 18 years of age is not recommended due to suicidal behaviour.

Patients with renal and/or hepatic dysfunction: Fluoxetine should not be administered to patients with severe renal failure (GFR <10 ml/min). A lower dose, *e.g.* alternate day dosing, is recommended in patients with significant hepatic dysfunction or mild to moderate renal failure (GFR 10-50 ml/min).

4.3. Contraindications

Hypersensitivity to fluoxetine or the ingredients of the preparation.

Fluoxetine should not be administered to patients with severe renal failure (GFR <10 ml/min) because accumulation may occur in these patients during chronic treatment.

Monoamine oxidase inhibitors: At least 14 days should elapse between discontinuation of monoamine oxidase inhibitors (MAOIs) and initiation of treatment with Fluoxetine. At least five weeks (longer if fluoxetine has been prescribed chronically and/or at higher doses) should elapse between discontinuation of Fluoxetine and initiation of therapy with an MAOI.

Serious, sometimes fatal reactions (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that indicate extreme agitation progressing to delirium and coma) have been reported with concomitant use of fluoxetine and MAOI or when fluoxetine had been recently discontinued and an MAOI started. Some cases presented with features resembling neuroleptic malignant syndrome. Cyproheptadine or dantrolene may benefit patients experiencing such reactions.

4.4. Special warnings and precautions for use

Angioneurotic oedema, urticaria and other allergic reactions have been reported. Upon the appearance of rash or of other allergic phenomena for which an alternative aetiology cannot be identified, Fluoxetine should be discontinued.

Fluoxetine should be discontinued in any patient who develops seizures. Fluoxetine 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.

Fluoxetine should be used with caution in patients with significant hepatic dysfunction or mild to moderate renal failure (GFR 10-50 ml/min).

Clinical experience in acute cardiac disease is limited, therefore caution is advisable. However, the ECG of 312 patients who received fluoxetine in double-blind trials were retrospectively evaluated and no conduction abnormalities which resulted in heart block were observed.

Fluoxetine may cause weight loss which may be undesirable in underweight depressed patients. Only rarely have depressed or bulimic patients been discontinued for weight loss when treated with fluoxetine.

In patients with diabetes, fluoxetine may alter glycaemic control. Hypoglycaemia has occurred during therapy with fluoxetine and hyperglycaemia has developed following discontinuation. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.

There have been reports of abnormal bleeding in several patients, but causal relationship to fluoxetine and clinical importance are unclear.

As improvement may not occur during the first two or more weeks of treatment, patients should be closely monitored during this period. The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs.

Use in children and adolescents under 18 years of age
Fluoxetine 20 mg Capsules should not be used in the treatment of children and adolescents under the age of 18 years. Suicide-related behaviours (suicidal attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo. If, based on clinical need, a decision to treat is nevertheless taken, the patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking.

4.5. Interactions with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors (see contraindications).

Caution is advised if the concomitant administration of Fluoxetine and CNS active drugs, including lithium, is required. There have been reports of both increased and decreased lithium levels when used concomitantly with fluoxetine. Cases of lithium toxicity have been reported. Lithium levels should be monitored.

Because fluoxetine's metabolism (like tricyclic anti-depressants and other selective serotonin antidepressants) involves the hepatic cytochrome P450IID6 isoenzyme systems, concomitant therapy with drugs also metabolised by these enzyme systems may lead to drug interactions.

Concomitant therapy with drugs predominantly metabolised by this isoenzyme, and which have a narrow therapeutic index (such as flecainide, encainide, vinblastine, carbamazepine and tricyclic antidepressants), should be initiated at or adjusted to the low end of their dose range. This will also apply if fluoxetine has been taken in the previous 5 weeks.

Greater than two-fold increases of previously stable plasma levels of tricyclic antidepressants have been observed when administered in combination with Fluoxetine.

Patients on stable doses of phenytoin have developed elevated plasma phenytoin concentrations and clinical phenytoin toxicity, following initiation of concomitant fluoxetine treatment.

Fluoxetine binds to plasma protein and concurrent administration may alter plasma concentrations of other plasma protein bound drugs or conversely fluoxetine. In formal testing, no drug interaction of clinical significance has been observed between fluoxetine and chlorothiazide, ethanol, secobarbital and tolbutamide.

No drug interactions of clinical significance have been observed between fluoxetine and warfarin. However, clinicians should be aware (based on experimental data from animal studies) that the effects of nicoumalone and warfarin may be enhanced.

Fluoxetine does not appear to potentiate the effects of alcohol.

Dynamic interactions between fluoxetine and the herbal remedy, St. John's wort (Hypericum perforatum) can occur, resulting in an increase in undesirable effects**.**

The long elimination half-lives should be borne in mind when considering pharmacodynamic or pharmacokinetic drug interactions.

4.6. Pregnancy and lactation

Pregnancy: The safety of fluoxetine in human pregnancy has not been established; accordingly, the drug should be avoided in pregnancy unless there is no safer alternative. There was no evidence of teratogenicity from animal studies but full testing was limited by maternal toxicity.

Lactation: Fluoxetine should not be prescribed to nursing mothers. In one breast milk sample the concentration of fluoxetine, plus norfluoxetine, was 70.4 ng/ml, compared to 295.0 ng/ml in the mother's plasma. No adverse effects on the infant were noted. In another infant the plasma level of fluoxetine was 340 ng/ml and 208 ng/ml of norfluoxetine on the second day of breast feeding from a mother on fluoxetine. This infant developed crying, sleep disturbance, vomiting and watery stools.

4.7. Effects on ability to drive and use machines

Although fluoxetine has been shown not to affect psychomotor performance in healthy volunteers, any psychoactive drug may impair judgement or skills. Therefore patients should be cautioned that their ability to perform potentially hazardous tasks (*e.g.* driving, operating machinery) may be impaired.

4.8. Undesirable effects

Body as a whole: Asthenia, fever

Digestive system: Nausea, diarrhoea, dry mouth, appetite loss, dyspepsia, vomiting. Abnormal liver function tests have been reported rarely.

Nervous system: Headache, nervousness, insomnia, drowsiness, anxiety, tremor, dizziness, fatigue, decreased libido, seizures. Hypomania or mania occurred in approximately one percent of fluoxetine treated trial patients. Dyskinesia (including, for example, a case of buccal-lingual-masticatory syndrome, which resolved following drug discontinuation), movement disorders developing in patients with risk factors (including drugs associated with such events) and worsening of pre-existing movement disorders, and neuroleptic malignant syndrome-like events have been reported. In children and adolescents under 18 years of age, suicide-related behaviours, emotional lability and hostility have been observed.

Respiratory system: Pharyngitis, dyspnoea. Pulmonary events (including inflammatory processes of varying histopathology and/or fibrosis) have been reported rarely. Dyspnoea may be the only preceding symptom.

Skin and appendages: A small percentage of patients developed rash and/or urticaria. Serious systemic reactions, possibly related to vasculitis, have developed in patients with rash, and rare cases death has been reported. Excessive sweating, arthralgia, myalgia, serum sickness and anaphylactoid reactions have also been reported. Hair loss, usually reversible, has been reported.

Urinogenital system: Sexual dysfunction (delayed or inhibited orgasm).

Effects on body chemicals: Hyponatraemia (including serum sodium below 110mmol/l) has been rarely reported and appeared to be reversible when Fluoxetine was discontinued. Some cases were possibly due to the syndrome of inappropriate antidiuretic hormone secretion. The majority of reports were associated with older patients, and patients taking diuretics or otherwise volume depleted.

Others: 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.

4.9. Overdose

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 3000 mg of fluoxetine experienced two grand mal seizures that remitted spontaneously. Nausea and vomiting were prominent in overdoses involving higher fluoxetine doses. Agitation, restlessness, hypomania and other signs of CNS excitation were also observed.

Management: No specific antidote is known.

An airway should be established. Cardiac and vital signs monitoring is recommended, along with general symptomatic and supportive measures.

An extended time for close medical observation may be needed in patients who have taken excessive quantities of a tricyclic antidepressant if they are also taking, or have recently taken, fluoxetine. Accumulation of the parent tricyclic or an active metabolite may increase the possibility of clinically relevant sequelae.

Based on experience with animals, fluoxetine induced seizures which fail to remit spontaneously may respond to diazepam. Due to the large volume of distribution of fluoxetine, forced diuresis, dialysis, haemoperfusion and exchange transfusion are unlikely to be of benefit. Activated charcoal, which may be used with sorbitol, may be as effective if not more effective than emesis or lavage.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC Code: N06A B03 Pharmacotherapuetic group: Antidepressants; Selective Serotonin Reuptake Inhibitors

Fluoxetine is chemically unrelated to tricyclic and tetracyclic antidepressant agents. It is a specific serotonin (5-hydroxytryptamine, 5-HT) reuptake inhibitor, whose specificity is unaltered by its major metabolite. Fluoxetine is a 50:50 mixture of two isomers which have equivalent pharmacological activity in animals. Individuals with reduced P450IID6 isoenzyme activity (3-10% of the normal human population - 'poor metabolisers') were compared to normal metabolisers. The total sum at steady state of the two isomers and their active norfluoxetine metabolites were similar. Thus, net pharmacodynamic activities were essentially the same.

Suicide-related behaviours have been frequently observed in children and adolescents treated with SSRI's. Long-term safety data in children and adolescents are lacking in regards to growth, maturation and cognitive behavioural development.

5.2. Pharmacokinetic properties

Fluoxetine has a half-life of 1 to 3 days after acute administration. The half-life may be prolonged to 4 to 6 days after chronic administration. The active metabolite, norfluoxetine, has a mean half-life of 9.3 days after multiple dosing (range 4 to 16 days). Steady state plasma concentrations are only achieved after continuous dosing for weeks.

When dosing is stopped, active drug substances will persist in the body for weeks. This should be borne in mind when starting or stopping treatment.

Plasma concentrations do not appear to increase without limit because, in addition to metabolism by the hepatic cytochrome P450IID6 isoenzyme system, there are non-saturable pathways. Patients receiving fluoxetine for as long as 3 years exhibited average plasma concentrations, similar to those seen among patients treated for 4 or 5 weeks.

5.3. Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

The capsule also contains:
pregelatinised maize starch
anhydrous colloidal silica
magnesium stearate
talc.

The capsule shell contains:
quinoline yellow E104
erythrosine E127
indigo carmine E132
titanium dioxide E171
gelatin.

The printing ink contains: shellac (E904), black iron oxide (E172), soya lecithin (E322), antifoam DC 1510.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

AL/PVC Blister: Do not store above 25ºC. Store in the original package.
HDPE Bottle: : Do not store above 25ºC. Keep the bottle tightly closed.

6.5. Nature and contents of container

Al/PVC blisters. Pack size 28 or 30 capsules
HDPE bottle with white LDPE snap on cap. Pack size 28 or 30 capsules.

6.6. Instruction for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Relon Chem Limited
27 Old Gloucester Road
London
WC1 3XX

8. MARKETING AUTHORISATION NUMBER

PL 20395/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07/06/2006

10 DATE OF REVISION OF THE TEXT

07/06/2006

Patient Information Leaflet

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Leaflet for bottle

Fluoxetine 20mg Capsules

RelonChem

Patient Information Leaflet

Please read this leaflet carefully before you start to take your medicine. It gives you important information about your medicine. If you want to know more, or you are not sure about anything, ask your pharmacist or doctor. Keep the leaflet until you have finished the medicine.

What's in your medicine

This leaflet refers to the Fluoxetine 20mg Capsules only. Each hard capsule contains 20mg of the active ingredient fluoxetine as fluoxetine hydrochloride.

The capsule also contains: pregelatinised maize starch, talc, anhydrous colloidal silica and magnesium stearate.

The capsule shell contains: E104, E127, E132, E171 and gelatin.

The printing ink contains: shellac, black iron oxide (E172), soya lecithin (E322), antifoam DC1510.

Fluoxetine Capsules are available in pack sizes of 28 or 30.

Your capsules are made by Actavis Ltd., Reykjavikurvegi 78, PO Box 420, IS-222 Hafnarfjordur, Iceland.

The Marketing Authorisation Holder is Relonchem Limited, 27 Old Gloucester Street, London WC1 3XX.

The Marketing Authorisation Number is: PL 20395/0003.

About your medicine

Fluoxetine capsules is one of a group of medicines called antidepressants that will relieve the symptoms of depression. It may also be used to treat the eating disorder, bulimia nervosa and disorders characterised by obsessive-compulsive actions.

Before taking your medicine

Make sure it is safe for you to take Fluoxetine Capsules. If you answer yes to any of the following questions, or you are unsure, talk to your pharmacist or doctor.

- have you ever had an allergic reaction to Fluoxetine capsules or any of the ingredients in the capsule? (An allergic reaction may include a rash, itching or shortness of breath).
- do you have heart, kidney or liver trouble?
- are you pregnant, planning to become pregnant or breast feeding?
- are you taking other medicines, especially monoamine oxidase inhibitors (MAOIs)? MAOIs include phenelzine, tranylcypromine and isocarboxazide. MAOIs and Fluoxetine Capsules do not mix. So if you are taking any MAOI or stopped taking them within the last 2 weeks, you must not take Fluoxetine Capsules.
- do you take any herbal medicines? The herbal remedy St. John's wort (Hypericum perforatum), should not be taken at the same time as this medicine. If you already take a St. John's wort preparation, stop taking the St. John's wort and mention it to your doctor at your next visit.
- do you have epilepsy or diabetes?
- are you taking, or have recently taken, other medicines including lithium, flecainide, encainide, vinblastine, carbamazepine and tricyclic antidepressants
- DO NOT take any MAOIs for at least 5 weeks after stopping Fluoxetine Capsules.

Antidepressants can affect your judgement or co-ordination. Do not drive or use machinery unless you are sure that you are not affected.

- If you are not sure what to do ask your doctor or pharmacist. If you see another doctor or go into hospital, let them know what medicines you are taking.

Taking your medicine

Follow your doctor's instructions. Check the pharmacy label to see how many tablets to take and how often to take them. If you are not sure how to take them ask your pharmacist or doctor.

Usual doses

Depression: One 20mg capsule per day

Bulimia: Three 20mg capsules each day

Obsessive-compulsive disorder: Initially one 20mg capsule per day. Your doctor may increase this to 60mg (three capsules) per day.

Swallow the capsule whole with a drink of water. Antidepressants may not make you feel any better for the first 2 weeks or more. This medicine should be taken for as long as your doctor tells you to, it may be dangerous to stop without their advice.

If you forget to take a dose, take one as soon as you remember. Then go on as before. DO NOT take two doses at the same time. If you are worried ask your pharmacist or doctor for advice.

Do not take more capsules than your doctor tells you to. If you ever take too many go to the nearest hospital casualty unit department or tell your doctor immediately. Take the container and any remaining capsules with you to show to the doctor.

Use in children and adolescents under 18 years of age

Fluoxetine should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicine. Despite this, your doctor may prescribe fluoxetine capsules for patients under

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Leaflet for bottle

18 because he/she decides that this is in their best interests. If your doctor has prescribed fluoxetine capsules for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking fluoxetine. Also the long-term safety effects concerning growth, maturation and cognitive and behavioural development of fluoxetine in this age group have not yet been demonstrated.

While taking your medicine

This medicine sometimes causes unwanted effects in some people. These effects may include:

- *Effects on the digestive system:* feeling or being sick, indigestion, dry mouth, loss of appetite and changes in liver function (detected by blood tests)
- *Effects on the nervous system:* headache, nervousness, anxiety, difficulty sleeping, fatigue, drowsiness, tremor, changes in sexual desire, unusually excited behaviour, suicidal tendencies, hostility and worsening emotional stability, fits, disorders or abnormal movements or worsening of movement disorders. A sensitivity reaction to fluoxetine has been reported and symptoms may include high temperature, fast breathing, drowsiness and restlessness.
- *Effects on the skin:* rash, which may be itchy. Severe skin reactions have also been reported and may be associated with other symptoms such as bruising, ulceration, sweating, muscle pain and joint pain. Hair loss, usually reversible, has also been reported.
- *Effects on the sexual organs:* poor sexual performance.
- *Effects on the lungs:* difficulty breathing, breathlessness, lung damage which can be severe. If you experience any difficulty breathing or breathlessness tell your doctor.
- *General effects:* weakness, fever.
- *Effects on body chemicals:* low blood sodium levels have been reported (detected by blood test).
- *Other effects:* some other side effects have been reported in patients taking fluoxetine but it is not clear whether the effects were caused by the medicine. These effects include: changes in the numbers and types of blood cells, bruising, bleeding in the brain, bleeding in the stomach, vaginal bleeding, pneumonia, high blood levels of pro lactin(a hormone which causes milk secretion), inflammation of the pancreas (pancreatitis), confusion, suicidal thoughts and violent behaviour.
- You may lose a little weight while taking fluoxetine.

If you develop a rash, breathing problems or fits you should speak to your doctor immediately.

If you are concerned about any of these effects or get any other unusual effects, tell your doctor immediately.

Storing your medicine

Do not use the capsules after the expiry (use by) date shown on the product packaging.

Do not store above 25°C. Keep the bottle tightly closed.

KEEP THEM IN A SECURE PLACE WHERE CHILDREN CANNOT GET AT THEM.

REMEMBER, this medicine is for **YOU** only. **NEVER** give it to anyone else. It may harm them, even if their symptoms are the same as yours.

Unless your doctor tells you to, do not keep medicines that you no longer need - give them back to your pharmacist for safe disposal.

Date of revision of leaflet: March 2006 POM

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Leaflet for blisters

Fluoxetine 20mg Capsules

RelonChem

Patient Information Leaflet

Please read this leaflet carefully before you start to take your medicine. It gives you important information about your medicine. If you want to know more, or you are not sure about anything, ask your pharmacist or doctor. Keep the leaflet until you have finished the medicine.

What's in your medicine

This leaflet refers to the Fluoxetine 20mg Capsules only. Each hard capsule contains 20mg of the active ingredient fluoxetine as fluoxetine hydrochloride.

The capsule also contains: pregelatinised maize starch, talc, anhydrous colloidal silica and magnesium stearate.

The capsule shell contains: E104, E127, E132, E171 and gelatin.

The printing ink contains: shellac, black iron oxide (E172), soya lecithin (E322), antifoam DC1510.

Fluoxetine Capsules are available in pack sizes of 28 or 30.

Your capsules are made by Actavis Ltd., Reykjavikurvegi 78, PO Box 420, IS-222, Iceland.

The Marketing Authorisation Holder is Relonchem Limited, 27 Old Gloucester Street, London WC1 3XX.

The Marketing Authorisation Number is: PL 20395/0003.

About your medicine

Fluoxetine capsules is one of a group of medicines called antidepressants that will relieve the symptoms of depression. It may also be used to treat the eating disorder, bulimia nervosa and disorders characterised by obsessive-compulsive actions.

Before taking your medicine

Make sure it is safe for you to take Fluoxetine Capsules. If you answer yes to any of the following questions, or you are unsure, talk to your pharmacist or doctor.

- have you ever had an allergic reaction to Fluoxetine capsules or any of the ingredients in the capsule? (An allergic reaction may include a rash, itching or shortness of breath).
- do you have heart, kidney or liver trouble?
- are you pregnant, planning to become pregnant or breast feeding?
- are you taking other medicines, especially monoamine oxidase inhibitors (MAOIs)? MAOIs include phenelzine, tranylcypromine and isocarboxazide. MAOIs and Fluoxetine Capsules do not mix. So if you are taking any MAOI or stopped taking them within the last 2 weeks, you must not take Fluoxetine Capsules.
- do you take any herbal medicines? The herbal remedy St. John's wort (Hypericum perforatum), should not be taken at the same time as this medicine. If you already take a St. John's wort preparation, stop taking the St. John's wort and mention it to your doctor at your next visit.
- do you have epilepsy or diabetes?
- are you taking, or have recently taken, other medicines including lithium, flecainide, encainide, vinblastine, carbamazepine and tricyclic antidepressants
- DO NOT take any MAOIs for at least 5 weeks after stopping Fluoxetine Capsules.

Antidepressants can affect your judgement or co-ordination. Do not drive or use machinery unless you are sure that you are not affected.

- If you are not sure what to do ask your doctor or pharmacist. If you see another doctor or go into hospital, let them know what medicines you are taking.

Taking your medicine

Follow your doctor's instructions. Check the pharmacy label to see how many tablets to take and how often to take them. If you are not sure how to take them ask your pharmacist or doctor.

Usual doses

Depression: One 20mg capsule per day

Bulimia: Three 20mg capsules each day

Obsessive-compulsive disorder: Initially one 20mg capsule per day. Your doctor may increase this to 60mg (three capsules) per day.

Swallow the capsule whole with a drink of water. Antidepressants may not make you feel any better for the first 2 weeks or more. This medicine should be taken for as long as your doctor tells you to, it may be dangerous to stop without their advice.

If you forget to take a dose, take one as soon as you remember. Then go on as before. DO NOT take two doses at the same time. If you are worried ask your pharmacist or doctor for advice.

Do not take more capsules than your doctor tells you to. If you ever take too many go to the nearest hospital casualty unit department or tell your doctor immediately. Take the container and any remaining capsules with you to show to the doctor.

Use in children and adolescents under 18 years of age

Fluoxetine should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicine. Despite this, your doctor may prescribe fluoxetine capsules for patients under

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Leaflet for blisters

18 because he/she decides that this is in their best interests. If your doctor has prescribed fluoxetine capsules for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking fluoxetine. Also the long-term safety effects concerning growth, maturation and cognitive and behavioural development of fluoxetine in this age group have not yet been demonstrated.

While taking your medicine

This medicine sometimes causes unwanted effects in some people. These effects may include:

- *Effects on the digestive system:* feeling or being sick, indigestion, dry mouth, loss of appetite and changes in liver function (detected by blood tests)
- *Effects on the nervous system:* headache, nervousness, anxiety, difficulty sleeping, fatigue, drowsiness, tremor, changes in sexual desire, unusually excited behaviour, suicidal tendencies, hostility and worsening emotional stability, fits, disorders or abnormal movements or worsening of movement disorders. A sensitivity reaction to fluoxetine has been reported and symptoms may include high temperature, fast breathing, drowsiness and restlessness.
- *Effects on the skin:* rash, which may be itchy. Severe skin reactions have also been reported and may be associated with other symptoms such as bruising, ulceration, sweating, muscle pain and joint pain. Hair loss, usually reversible, has also been reported.
- *Effects on the sexual organs:* poor sexual performance.
- *Effects on the lungs:* difficulty breathing, breathlessness, lung damage which can be severe. If you experience any difficulty breathing or breathlessness tell your doctor.
- *General effects:* weakness, fever.
- *Effects on body chemicals:* low blood sodium levels have been reported (detected by blood test).
- *Other effects:* some other side effects have been reported in patients taking fluoxetine but it is not clear whether the effects were caused by the medicine. These effects include: changes in the numbers and types of blood cells, bruising, bleeding in the brain, bleeding in the stomach, vaginal bleeding, pneumonia, high blood levels of prolactin (a hormone which causes milk secretion), inflammation of the pancreas (pancreatitis), confusion, suicidal thoughts and violent behaviour.
- You may lose a little weight while taking fluoxetine.

If you develop a rash, breathing problems or fits you should speak to your doctor immediately.

If you are concerned about any of these effects or get any other unusual effects, tell your doctor immediately.

Storing your medicine

Do not use the capsules after the expiry (use by) date shown on the product packaging.

Do not store above 25°C. Store in the original package.

KEEP THEM IN A SECURE PLACE WHERE CHILDREN CANNOT GET AT THEM.

REMEMBER, this medicine is for **YOU** only. **NEVER** give it to anyone else. It may harm them, even if their symptoms are the same as yours.

Unless your doctor tells you to, do not keep medicines that you no longer need - give them back to your pharmacist for safe disposal.

Date of revision of leaflet: March 2006 POM

Labelling

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Bottle carton label

Braille - punched on front panel

*Only the marketed pack sizes will be used on the final cartons.

The Batch Number and Expiry Date will be embossed on the actual cartons.

FLUOXETINE 20MG CAPSULES

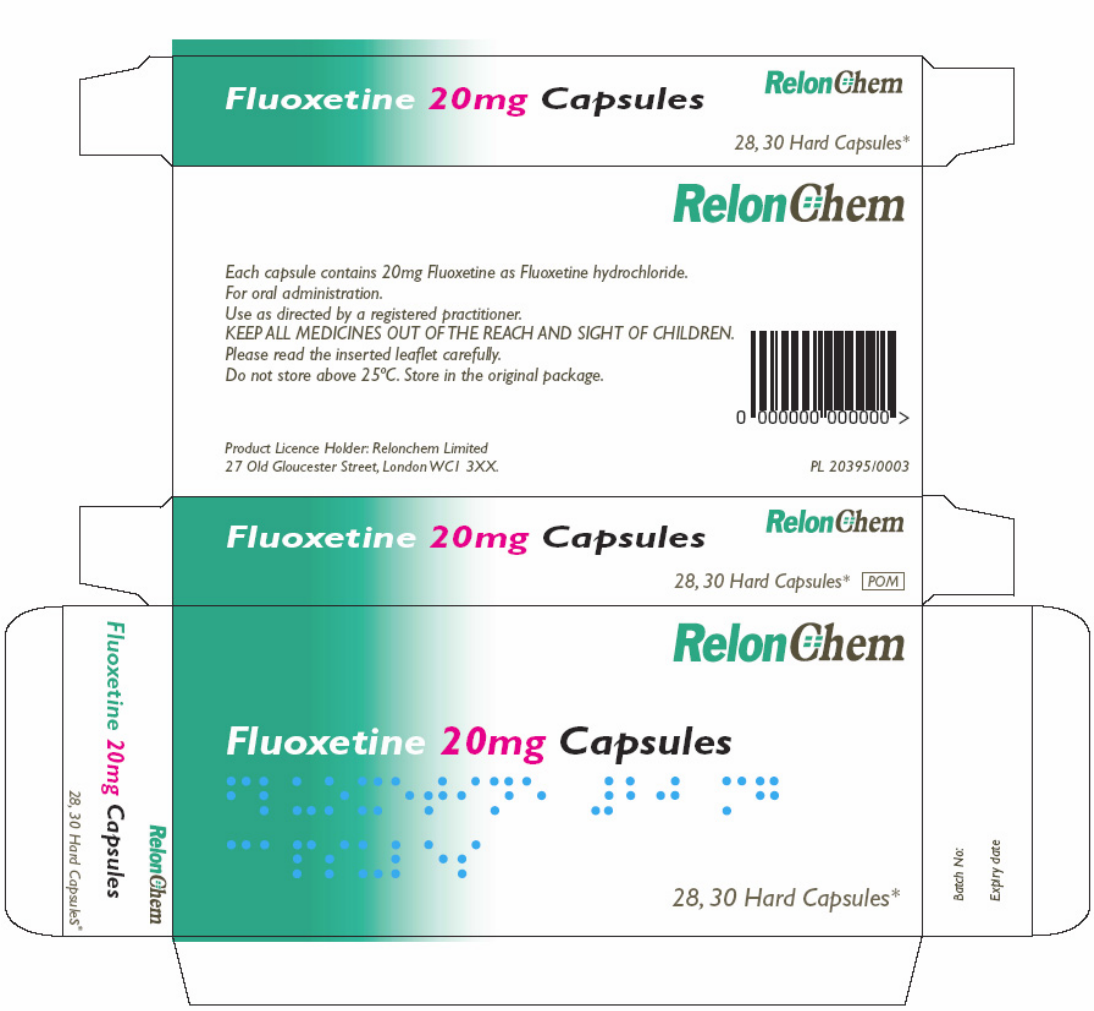
PL 20395/0003

Bottle label

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Blister carton label



Braille - punched on front face

*Only the marketed pack sizes will be used on the final cartons.

The Batch Number and Expiry Date will be embossed on the actual cartons.

FLUOXETINE 20MG CAPSULES

PL 20395/0003

Blister foil label