FLUOXETINE 20MG CAPSULES
PL 18224/0059

UKPAR

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FLUOXETINE 20MG CAPSULES
PL 18224/0059

LAY SUMMARY

The MHRA granted Karib Kemi-Pharm Limited a Marketing Authorisation (licence) for the medicinal product Fluoxetine 20mg Capsules on 1st October 2007. This product, to be available by prescription only (POM), contains fluoxetine hydrochloride and is used for the treatment of depression and the eating disorder bulimia nervosa.

The active ingredient fluoxetine hydrochloride is part of a group of medicines called selective serotonin reuptake inhibitor (SSRI) antidepressants. These medicines raise the levels of the hormone serotonin.

This application is a duplicate of a previously granted application for Fluoxetine 20mg Capsules (PL 16363/0064), for which the marketing authorisation holder is Milpharm Limited and which was first authorised on 20th September 2002.

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

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Fluoxetine 20mg Capsules to Karib Kemi-Pharm Limited on 1st October 2007. The product is available as a prescription-only medicine (POM).

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Fluoxetine 20mg Capsules (PL 16363/0064), approved on 20th September 2002 to the marketing authorisation holder Milpharm Limited.

No new data were submitted nor were they necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report was generated for it.

The active ingredient fluoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI) antidepressant and is indicated for the following:

- Major depressive disorders/episodes.
- Bulimia nervosa in conjunction with a psychotherapeutic intervention strategy.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 18224/0059
PROPRIETARY NAME: Fluoxetine 20mg Capsules
ACTIVE(S): Fluoxetine hydrochloride
COMPANY NAME: Milpharm Limited
E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC
LEGAL STATUS: POM

1. INTRODUCTION

This is a simple, piggy back application for Fluoxetine 20mg Capsules submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Karib Kemi-Pharm Limited, Karib House, 63-65 Imperial Way, Croydon, CR0 4RR.

The application cross-refers to Fluoxetine 20mg Capsules (PL 16363/0064), approved on 20th September 2002 to the marketing authorisation holder Milpharm Limited.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Fluoxetine 20mg Capsules. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The product contains fluoxetine hydrochloride, equivalent to 20mg. It is to be stored in aluminium/polyvinylchloride/polyvinylidene chloride blister packs in pack sizes of 10, 14, 20, 30, 50, 70 and 100 capsules. The proposed shelf-life (36 months) and storage conditions (store in original package) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the product will be available as a prescription-only medicine (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Karib Kemi-Pharm Limited, Karib House, 63-65 Imperial Way, Croydon, CR0 4RR.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
With the exception of gelatin, no materials of animal or human origin are included in the product. This is consistent with the cross reference product.

The applicant has provided TSE certificates of suitability to show that gelatin is provided by appropriate sources.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet has been prepared in line with the details registered for the cross-reference product.

Carton and blister
The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with the application are acceptable. A 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

As this is a duplicate application, no new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND BENEFIT RISK ASSESSMENT

QUALITY
The data for this application are consistent with that previously assessed for the cross-reference 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 (PL 16363/0064).

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference 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-reference product. Extensive clinical experience with fluoxetine hydrocholoride is considered to have demonstrated the therapeutic value of the compound. The benefit:risk is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 22/02/2006.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 28/02/2006.
3	Following assessment of the application the MHRA requested further information on 12/04/2006, 25/10/2006 and 16/02/2007.
4	The applicant responded to the MHRA's requests, providing further information on 21/10/2006, 06/02/2007 and 23/05/2007
5	The application was determined on 01/10/2007

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

FLUOXETINE 20MG CAPSULES
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Fluoxetine 20mg Capsules.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 22.5mg fluoxetine hydrochloride equivalent to 20mg fluoxetine.

For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM
Capsule, Hard.
Green/Off-white hard gelatin self locked capsules of size '2' imprinted with 'FLX' and 'MIL' on cap / body in black edible ink containing white powder.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Major depressive disorders/episodes.

Bulimia nervosa in conjunction with a psychotherapeutic intervention strategy.

4.2 Posology and method of administration
Fluoxetine capsules are meant for oral administration in adults only. The capsules should be swallowed whole with a glass of water.

Major depressive disorders/episodes - adults: A dose of 20 mg/day is recommended.

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

The maximum daily dose should not exceed 80 mg.

Elderly: There are not enough data available on fluoxetine efficacy and safety in this population. Therefore caution is recommended when increasing the dose which should only rarely exceed 40 mg and never 60 mg.

Children: The use of fluoxetine in children is not recommended, as safety and efficacy have not been established.

Patients with renal and/or hepatic dysfunction: In case of reduced liver and/or kidney function (GFR 10-50 ml/min) the dose should be reduced for example to 20 mg every other day.

4.3 Contraindications
Hypersensitivity to fluoxetine or any of the excipients.

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.

Fluoxetine should not be prescribed to breastfeeding mothers (See 4.6 Pregnancy and Lactation).

Monoamine oxidase inhibitors (MAOI) and L-tryptophan: At least 14 days should elapse between discontinuation of a MAOI and L-tryptophan 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 a MAOI and L-tryptophan (See 4.5 Interaction with other medicinal products and other forms of interaction).

Fluoxetine should not be used in patients with unstable epilepsy or convulsant disorders.

4.4 Special warnings and precautions for use

Rash and allergic reactions: Angioneurotic oedema, urticaria and other allergic reactions have been reported following the use of fluoxetine. Upon the appearance of rash or of other allergic phenomena for which an alternative aetiology cannot be identified,

Fluoxetine capsules should be discontinued. In some cases of rash, life threatening events may occur possibly related to vasculitis involving the lungs, liver and kidneys.

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 reports of prolonged seizures in patients on fluoxetine receiving ECT treatment.

Fluoxetine is extensively metabolised by the liver and excreted by the kidneys. 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).

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; no conduction abnormalities that 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.

Psychosis has been described, and especially in patients with bipolar disorder, mood shifts towards mania have been reported. This may require treatment discontinuation.

Fluoxetine may alter glycaemic control in patients with diabetes. Hypoglycaemia has been reported during therapy with fluoxetine and hyperglycaemia has developed following discontinuation. In such situations, the dosage of insulin and/or oral hypoglycaemic agents may need to be adjusted.

There have been reports of bleeding abnormalities such as ecchymosis or purpura or other haemorrhagic manifestations. Caution is advised in patients taking fluoxetine especially with concomitant use of other drugs known to affect platelet function or coagulation as well as in patients with a history of bleeding disorders.

As with all antidepressant treatment there is a risk of suicide particularly at the beginning of treatment due to the delay between treatment and clinical improvement; as for all antidepressants the full therapeutic effect may not manifest itself for 3-4 weeks. Patients should be closely monitored during this period.

Withdrawal reactions have been reported in association with selective serotonin reuptake inhibitors (SSRIs) including fluoxetine. Common symptoms include dizziness, paraesthesiae, headache, anxiety and nausea. The majority of symptoms experienced on withdrawal of SSRIs are non-serious and self limiting. Avoid abrupt discontinuation of treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors including selegiline:
Serious, sometimes fatal reactions (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, 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 a MAOI started. Some cases presented with features resembling neuroleptic malignant syndrome. Cyproheptadine or dantrolene may benefit patients experiencing such reactions.

At least 14 days should elapse between discontinuation of a MAOI 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 a MAOI.

Caution is advised if the concomitant administration of fluoxetine and CNS active medicinal products, 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 antidepressants and other selective serotonin antidepressants) involves the hepatic cytochrome P45011D6 isoenzyme system, concomitant therapy with medicinal products also metabolised by this enzyme system may lead to medicinal product interactions.

Concomitant therapy with medicinal products 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.

When fluoxetine has been administered in combination with tricyclic antidepressants, greater than two fold increases of previously stable plasma levels have been observed.

Half lives of some benzodiazepines e.g., diazepam may be increased when administered simultaneously with fluoxetine.

As norfluoxetine is an inhibitor of CYP3A4, interactions with CYP3A4 substrates are possible.

Agitation, restlessness and gastro-intestinal symptoms have been reported in a small number of patients receiving fluoxetine in combination with L-tryptophan should not be given 14 days before or for 5 weeks after treatment with fluoxetine.

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

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

The long elimination half lives should be borne in mind (see 5.2 Pharmacokinetic properties) when considering pharmacodynamic or pharmacokinetic medicinal product interactions.

Fluoxetine is highly bound to plasma proteins. Concurrent administration with other plasma protein bound medicinal products (e.g. coumarin derivatives or digitoxin) may alter their plasma concentrations, potentially resulting in adverse effects. Conversely the plasma concentration of fluoxetine may be altered. In formal testing, no medicinal product interaction of clinical significance has been observed between fluoxetine and chlorothiazide, ethanol, secobarbital and tolbutamide.

Caution is advised in patients concomitantly receiving anticoagulants or medicinal products affecting platelet function.

Fluoxetine does not appear to potentiate the effects of alcohol.

4.6 Pregnancy and lactation

Exposure of pregnant women during the first trimester of pregnancy so far has not been associated with malformations in their offspring although an increase in the incidence of minor anomalies has been described. Exposure during late pregnancy could give rise to prematurity, a decrease in birth weight and poor neonatal adaptation.

There is no indication that in utero exposure affects IQ, language and behavioural development in pre-school children. However fluoxetine should only be used in pregnancy if there is no safer alternative.

Fluoxetine is excreted in breast milk (milk/plasma concentration ratio of 1:4) and therefore it should not be used in breastfeeding mothers or breastfeeding should be discontinued.

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 medicinal product may impair judgement or skills. Therefore, patients should be cautioned that their ability to perform potentially hazardous tasks (eg. driving, operating machinery) may be impaired.

4.8 Undesirable effects

Estimated frequency:
Very common: > 10 %
Common: 1-10 %
Uncommon:0.l-l%
Rare:0.0l-0.l %
Very rare: <0.01 %

Gastro-intestinal system:
Very common: nausea, diarrhoea, anorexia weight loss
Uncommon: dry mouth, appetite loss, dyspepsia, vomiting, severe constipation.
Rare: reports of abnormal liver function tests
Also problems with sense of taste have been reported.

Central nervous system:
Common: nervousness, insomnia, drowsiness, anxiety, tremor, dizziness, fatigue.
Uncommon: Headache
Hypomania or mania has been reported to occur in approximately one percent of fluoxetine treated trial patients. Dyskinesia (including, for example, a case of buccal-lingual- masticatory syndrome, which resolved following medicinal product discontinuation), movement disorders developing in patients with risk factors (including medicinal products associated with such events) and worsening of pre-existing movement disorders, and neuroleptic malignant syndrome-like events have been reported.

Respiratory system:
Rare: 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:
Very common: excessive sweating.
Common: urticaria
Rare: rash, anaphylactoid reactions, angiitis, polymorphous erythema
Very rare: Quincke's oedema, Lyell's syndrome and in very rare cases fever, skin eruptions, arthralgia, myalgia associated with serum sickness.
Hair loss, usually reversible, has been reported.

Cardiovascular system:
Uncommon: slight increase in diastolic blood pressure and both tachycardia and bradycardia have been reported.

General:
Uncommon: visual disorders

Other reported side effects:
Urinogenital system: sexual dysfunction (delayed or inhibited orgasm).

Body as a whole: asthenia, fever
Hyponatraemia (including serum sodium below 110 mol/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.

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, hyper- prolactinaemia, immune related haemolytic anaemia, pancreatitis, pancytopenia, suicidal ideation, thrombocytopenia, thrombocytopenic purpura, vaginal bleeding after drug withdrawal and violent behaviour.

4.9 Overdose

The fatal dose is not known. The effects will be potentiated by alcohol taken at the same time. Toxicity is also potentiated by tricyclic antidepressants and MAOIs.

Symptoms

Nausea, vomiting, agitation, tremor, nystagmus and drowsiness may occur. Convulsions have been reported in a small percentage of cases and may not occur until up to ten hours after ingestion. Sinus tachycardia is common. Less frequently bradycardia, hypertension and junctional rhythm may occur.

Rarely features of the "serotonin syndrome" may occur. This includes alteration of mental status, neuromuscular hyperactivity and autonomic instability. There may be hyperpyrexia and elevation of serum creatine kinase. Rhabdomyolysis is rare.

Management

Consider oral activated charcoal if more than 500mg has been ingested by an adult or if more than 5mg/kg has been ingested by a child within one hour. Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: selective serotonin reuptake inhibitor.

ATC CODE: N06AB 03

Fluoxetine is a potent and highly selective serotonin (5-hydroxytryptamine, 5HT) reuptake inhibitor. The antidepressant, antiobsessive -compulsive, and antibulimic actions of fluoxetine are presumed to be linked to this inhibition of neuronal uptake of serotonin in the central nervous system. Fluoxetine is chemically unrelated to tricyclic and tetracyclic antidepressant agents. Fluoxetine is a 50:50 mixture of two isomers which have equivalent pharmacological activity in animals. Individuals with reduced P45011D6 isoenzyme activity (3-10% of the normal human population - ' poor metabolisers') have been compared to normal metabolisers. The total sum at steady state of the two isomers and their active norfluoxetine metabolites was reported to be similar. Thus, net pharmacodynamic activities were essentially the same.

5.2 Pharmacokinetic properties

Fluoxetine is readily absorbed from the gastrointestinal tract with peak plasma concentrations appearing about 6 to 8 hours after administration. Food does not affect the bioavailability of fluoxetine. It is widely distributed throughout the body and is extensively bound to plasma proteins. Fluoxetine is extensively metabolised, by demethylation, in the liver to its primary active metabolite norfluoxetine. 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). Excretion is mainly via the urine. Steady state plasma concentrations are only achieved after continuous dosing for weeks.

When dosing is stopped, active 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 P45011D6 isoenzyme system, there are non-saturable pathways. It has been reported that 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

Fluoxetine has a low acute toxicity. Studies in chronic toxicity have shown that fluoxetine may provoke reversible phospholipidosis as observed in other amphophilic cation substances (e.g. amiodarone, imipramine). The clinical relevance of this effect has not been established. However this should be taken into consideration in case respiratory disease should occur.

In preclinical studies fluoxetine did not show any evidence of mutagenicity, carcinogenicity or teratogenicity.

Fertility studies in rats at dose levels up to 12.5 mg/kg/day showed that fluoxetine had no adverse effects on fertility but that neonatal survival rate was decreased.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised maize starch

Capsule shell components:
gelatin
yellow iron oxide (E172)
titanium dioxide (E171)
brilliant blue (E133)

Printing ink components:
activated charcoal
shellac (E904)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store in the original container.

6.5 Nature and contents of container

10, 14, 20, 30, 50, 70 or 100 Capsules packed in a blister pack containing PVdC coated PVC film with a backing of aluminium foil (coated with heat seal lacquer).

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Karib Kemi Pharm Limited
Karib House
63-65 Imperial Way
Croydon
Surrey CR0 4RR
U. K.

8 MARKETING AUTHORISATION NUMBER(S)

PL 18224/0059

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/10/2007

10 DATE OF REVISION OF THE TEXT

01/10/2007

FLUOXETINE 20MG CAPSULES
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PATIENT INFORMATION LEAFLET

Patient Information leaflet

Fluoxetine 20mg Capsules

Karib Kemi

Read all of this leaflet carefully before you start taking this medicine.

- ***Keep this leaflet. You may need to read it again.***
- ***If you have any further questions ask your doctor or pharmacist***
- ***This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms are the same as yours.***
- ***If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.***

In this leaflet:

1. WHAT FLUOXETINE 20mg CAPSULES ARE AND WHAT THEY ARE USED FOR?

Fluoxetine is one of a group of medicines called selective serotonin re-uptake inhibitors (SSRI) antidepressants.

This medicine is used to treat:

- ***Depression***
- ***The eating disorder bulimia nervosa***

2. BEFORE YOU TAKE FLUOXETINE 20MG CAPSULES

Do not take Fluoxetine 20mg Capsules if:

- you have ever had an allergic reaction (this may include rash, itching, swollen face or
- lips or breathing difficulties) to fluoxetine or any of the capsule ingredients listed in section 6. What Fluoxetine 20mg Capsules contain.
- you are pregnant, intending to become pregnant or breast feeding?
- you have serious kidney problems
- you suffer from epilepsy or convulsant disorders
- you are taking or have recently been taking any medicines known as monoamine oxidase inhibitors (MAOI) (which are used in the treatment of depression) or a drug called tryptophan. Examples of MAOI include phenelzine, tranylcypromine, isocarboxazid, moclobemide (a reversible MAOI [RIMA]) and selegiline (used in treatment of Parkinson's disease) (You should not take Fluoxetine capsules at the same time as or within two weeks of stopping MAO inhibitors or tryptophan. Also do not take MAO inhibitors or tryptophan for at least five weeks after stopping Fluoxetine 20mg capsules).

Take special care with Fluoxetine 20mg Capsules

If you develop seizures you should stop taking Fluoxetine 20mg Capsules.

If you have liver or mild kidney problems, heart disease or diabetes you should talk to your doctor before taking Fluoxetine 20mg Capsules Fluoxetine may cause weight loss.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Fluoxetine 20mg Capsules with food and drink

You should take this medicine with a drink of water during or after meals. Although fluoxetine does not increase the effect of alcohol, the combination of this type of medicine and alcohol is not advisable.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before you take any medicine.

Driving and using machines

Caution should be taken because Fluoxetine may affect your ability to drive or operate machines.

3. HOW TO TAKE FLUOXETINE 20MG CAPSULES

Always take Fluoxetine 20mg Capsules exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The capsules are for adults only and should be swallowed whole with a glass of water. The usual dose for depression is one capsule (20mg) per day. For bulimia nervosa the usual dose is 3 capsules (60mg) per day.

If you take more Fluoxetine 20mg Capsules than you should, contact your doctor or hospital immediately.

If you forget to take Fluoxetine 20mg Capsules do not take a double dose to make up for a forgotten dose. Take the next dose at the normal time and continue regular dosing.

If you stop taking Fluoxetine 20mg Capsules

Do not stop taking Fluoxetine 20mg Capsules until your doctor tells you to. Withdrawal reactions have been reported in association with selective serotonin reuptake inhibitors (SSRIs) including fluoxetine. Common symptoms include dizziness, pins and needles, headache, anxiety and nausea. The majority of symptoms experienced on withdrawal of SSRIs are non-serious and self-limiting. Your doctor will gradually reduce your dose when stopping Fluoxetine to reduce the risk of withdrawal reactions.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Fluoxetine 20mg Capsules can cause side effects, although not everybody gets them.

If you get a rash or allergy reaction such as itching, swollen lips or tongue, or wheezing/shortness of breath stop taking the capsules and contact your doctor or pharmacist immediately.

If your skin becomes red and then starts to blister or peel, contact your doctor immediately. This is very rare.

Some patients have had:

- A combination of symptoms such as unexplained fever, breathing problems, excessive sweating, muscle and joint pain, confusion, excessive agitation and uncontrollable movement.
- Feelings of weakness and drowsiness

If you experience any of these, tell your doctor.

Other side effects include:
Chills, loss of appetite, loss of weight. Diarrhoea and stomach upsets, feeling sick, constipation, dry mouth, changed sense of taste. Headache, nervousness, anxiety, trembling, dizziness, tiredness, problems sleeping, changes to normal behaviour, thoughts of suicide or harming yourself. Breathing difficulties, sore throat. Swelling of different parts of the body, rash and itching. Hair loss that is normally reversible. Decrease or increase in heart rate. Passing urine too frequently, poor sexual performance. Blurred vision, unexplained bruising, joint or muscle pain.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE FLUOXETINE 20MG CAPSULES

Keep your capsules in the original package. Keep them out of the reach and sight of children.
Do not take your capsules after the expiry date on the carton and blister.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6. FURTHER INFORMATION

What Fluoxetine 20mg capsules contains

The active substance is fluoxetine hydrochloride. The other ingredient is pre-gelatinised maize starch. The gelatin capsules are coloured with E172, E133 and E171. The black ink contains shellac and activated charcoal.

What Fluoxetine 20mg capsules looks like and contents of the pack

The capsules are coloured green and off-white and are marked FLX/MIL. Fluoxetine 20mg capsules are available as blister packs containing 10, 14, 20, 30, 50, 70 or 100 capsules.

Marketing Authorisation Holder :

The product licence holder is Karib Kemi Pharm Limited, Karib House, 63-65 Imperial Way, Croydon, Surrey CR0 4RR, U.K.
Manufacturer : Milpharm Limited, Ares, Odyssey Business Park, West End Road, South Ruislip, HA4 6QD, U.K.

This leaflet was last approved in: August 2007

This leaflet is available in large font format or audio format for partially sighted patients. Please contact the Marketing Authorisation Holder at the address given above.

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LABELLING