FLUVOXAMINE 50MG AND 100MG FILM-COATED TABLETS
PL 32019/0035-6

UKPAR

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FLUVOXAMINE 50MG AND 100MG FILM-COATED TABLETS
PL 32019/0035-6

LAY SUMMARY

On 11th May 2010, the MHRA granted Roger Oakes Limited Marketing Authorisations (licences) for Fluvoxamine 50mg and 100mg Film-Coated Tablets (PL 32019/0035-6).

Fluvoxamine 50mg and 100mg Film-Coated Tablets contains fluvoxamine maleate, which belongs to a group of medicines called antidepressants.

Fluvoxamine 50mg and 100mg Film-Coated Tablets is used for:
- Depressive illness (major depressive episodes)
- Obsessive thoughts and obsessive actions (obsessive compulsive disorders).

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Fluvoxamine 50mg and 100mg Film-Coated Tablets outweigh the risks; hence Marketing Authorisations have been granted.
FLUVOXAMINE 50MG AND 100MG FILM-COATED TABLETS
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Fluvoxamine 50mg and 100mg Film-Coated Tablets (PL 32019/0035-6) to Roger Oakes Limited on 11th May 2010.

This prescription only medicine (POM) is indicated for major depressive episodes and Obsessive-Compulsive Disorder (OCD).

This application for Fluvoxamine 50mg and 100mg Film-Coated Tablets is submitted as an abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Fluvoxamine 50mg and 100mg Film-Coated Tablets, which was originally approved and licensed to Tillomed Laboratories Limited (PL 11311/0189-90) on 25th October 2002.

No new data were submitted nor were they necessary for these simple applications, as the data is identical to that of the previously granted cross-reference products.
1. INTRODUCTION
This is a simple, informed consent application for Fluvoxamine 50mg and 100mg Film-Coated Tablets (PL 32019/0035-6) submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Roger Oakes Limited, Allstoe House, Church Lane, Greetham, Rutland, LE15 7NF, United Kingdom.

The application cross-refers to Fluvoxamine 50mg and 100mg Film-Coated Tablets, which was originally approved and licensed to Tillomed Laboratories Limited (PL 11311/0189-90) on 25th October 2002.

The current applications are considered valid.

2. MARKETING AUTHORIZATION APPLICATION FORM
2.1 NAME(S)
The proposed name of the product is Fluvoxamine 50mg and 100mg Film-Coated Tablets. 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 fluvoxamine. The finished product is packaged in blisters made of aluminium and polyvinyl chloride (PVC), or polyvinylidene chloride (PVDC) and aluminium. Pack sizes are 15, 20, 30, 40, 50, 60, 90 and 100 film-coated tablets. Hospital packs contain 250 (5 x 50) film-coated tablets.

The proposed shelf-life (18 months) with storage conditions, ‘Do not store above 25 °C’ and ‘Store in the original package, in order to protect from light and moisture’ are consistent with the details registered for the cross-reference products.

2.3 Legal status
On approval, the product will be available on prescription only (POM).

2.4 Marketing authorization holder/Contact Persons/Company
Roger Oakes Limited, Allstoe House, Church Lane, Greetham, Rutland, LE15 7NF, United Kingdom.

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 products 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 products.

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

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

2.9 Drug substance specification
The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
With the exception of lactose monohydrate, none of the excipients used contain material of animal or human origin.
The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption.
This information is consistent with the cross-reference products.

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 products are identical to the cross-reference products.

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

6. PATIENT INFORMATION LEAFLET/CARTON
PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference products. The package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that they contain.
Labelling

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

7. CONCLUSIONS
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for applications of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with these applications and none are required for applications of this type.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for these applications are consistent with that previously assessed for the cross-reference products and, as such, has been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
These applications are identical to previously granted applications Fluvoxamine 50mg and 100mg Film-Coated Tablets, which was originally approved and licensed to Tillomed Laboratories Limited (PL 11311/0189-90) on 25th October 2002.

No new or unexpected safety concerns arise from these applications.

The SPCs, PIL and labelling are satisfactory and consistent with that for the cross-reference products.

RISK BENEFIT ASSESSMENT
The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s products are identical to the cross-reference products. The risk:benefit is, therefore, considered to be positive.
**FLUVOXAMINE 50MG AND 100MG FILM-COATED TABLETS**

**PL 32019/0035-6**

**STEPS TAKEN FOR ASSESSMENT**

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 27(^{th}) November 2008.</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 4(^{th}) December 2008.</td>
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<td>3</td>
<td>Following assessment of the application, the MHRA requested further information relating to the quality dossier on 18(^{th}) December 2008, 6(^{th}) November 2009 and 1(^{st}) March 2010.</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 4(^{th}) November 2009, 5(^{th}) February 2010 and 15(^{th}) April 2010 for the quality section.</td>
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<td>5</td>
<td>The applications were determined on 11(^{th}) May 2010.</td>
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**FLUVOXAMINE 50MG AND 100MG FILM-COATED TABLETS**
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**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

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<tr>
<th>Date submitted</th>
<th>Application type</th>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Fluvoxamine 50 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One film-coated tablet contains 50 mg fluvoxamine maleate.
Excipients: 1.7 mg lactose /film-coated tablet
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet
Appearance:
50 mg Film-Coated Tablets: white, biconvex, round, scored

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Major depressive episode
Obsessive-Compulsive Disorder (OCD)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Depression
Adults
The recommended starting dose is 50 or 100 mg, given as a single dose in the evening. It is recommended to increase the dose gradually until an effective dose is reached. The usual effective dose is 100 mg per day and should be adjusted on individual patient response. Doses of up to 300 mg per day have been given. Dosages above 150 mg should be given in divided doses.
In agreement with the consensus statement of the WHO, antidepressant medication should be continued for at least 6 months after recovery from a depressive episode. A dose of 100 mg daily may be sufficient for this use.

Use in children and adolescents under 18 years of age
Fluvoxamine film-coated tablets should not be used for the treatment of major depressive episodes in children and adolescents under the age of 18 years (see section 4.4).
The efficacy and safety of Fluvoxamine film-coated tablets have not been established in the treatment of paediatric major depressive episodes (see 4.4).

Obsessive Compulsive Disorder
The recommended starting dose is 50 mg per day for 3-4 days. The effective dose usually lies between 100 mg and 300 mg per day. The dosage should be increased gradually until the effective dose is achieved, with a maximum of 300 mg per day for adults.

Doses up to 150 mg can be given as a single dose, preferably in the evening. It is advisable that a total daily dose of more than 150 mg is given in 2 or 3 divided doses.

If a good therapeutic response has been obtained, treatment can be continued at a dosage adjusted on an individual basis. If no improvement is observed within 10 weeks, treatment with fluvoxamine should be reconsidered. While there are no systematic studies to answer the question of how long to continue fluvoxamine treatment, OCD is a chronic condition and it is reasonable to consider continuation beyond 10 weeks in responding patients. Dosage adjustments should be made carefully on an individual patient basis, to maintain the patient at the lowest effective dose. The need for treatment should be reassessed periodically. Some clinicians advocate concomitant behavioural psychotherapy for patients who have done well on pharmacotherapy.

Children and adolescents under 18 years of age
In children over 8 years and adolescents there is limited data on a dose of up to 100 mg b.i.d. for 10 weeks. The starting dose is 25 mg per day. Increase every 4-7 days in 25 mg increments as tolerated until an effective dose is achieved. The maximum dose in children should not exceed 200 mg/day. (For further details see 5.1) It is advisable that a total daily dose of more than 50 mg
should be given in two divided doses. If the two divided doses are not equal, the larger dose should be given at bedtime.

**Hepatic or renal insufficiency**
Patients suffering from hepatic or renal insufficiency should start on a low dose and be carefully monitored.

**Withdrawal symptoms seen on discontinuation of fluvoxamine**
Abrupt discontinuation should be avoided. When stopping treatment with fluvoxamine the dose should be gradually reduced over a period of at least one or two weeks in order to reduce the risk of withdrawal reactions. (see section 4.4 and section 4.8). If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

**Method of administration**
Fluvoxamine tablets should be swallowed with water and without chewing.

### 4.3 CONTRAINDICATIONS
Fluvoxamine film-coated tablets are contraindicated in combination with monoamine oxidase inhibitors (MAOIs). Treatment with fluvoxamine can be initiated:
- two weeks after discontinuation of an irreversible MAOI, or
- the following day after discontinuation of a reversible MAOI (e.g. moclobemide).
At least one week should elapse between discontinuation of fluvoxamine and initiation of therapy with any MAOI.

- Hypersensitivity to the active substance or to any of the excipients.

### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

**Use in children and adolescents under 18 years of age**
Fluvoxamine film-coated tablets should not be used in the treatment of children and adolescents under the age of 18 years, except for patients over 8 years with Obsessive Compulsive Disorder. Suicide-related behaviours (suicide 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.

**Suicide/suicidal thoughts or clinical worsening**
Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which fluvoxamine is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.
Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients, (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Akathisia/psychomotor restlessness

The use of fluvoxamine has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental and it may be necessary to review the use of fluvoxamine.

Withdrawal symptoms seen on discontinuation of fluvoxamine treatment

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8). In clinical trials adverse events seen on treatment discontinuation occurred in approximately 12% of patients treated with fluvoxamine, a comparative incidence for placebo treated patients is not currently available. The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction.

Dizziness, sensory disturbance (including paraesthesia, visual disturbances and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation and anxiety, irritability, confusion, emotional instability, nausea and/or vomiting and diarrhoea, sweating and palpitations, headache and tremor are the most commonly reported reactions. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that fluvoxamine should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient’s needs (see “Withdrawal Symptoms Seen on Discontinuation of Fluvoxamine”, Section 4.2).

Patients suffering from hepatic or renal insufficiency should start on a low dose and be carefully monitored.

Treatment with fluvoxamine has rarely been associated with an increase in hepatic enzymes, generally accompanied by clinical symptoms. In such cases treatment should be discontinued. Glycaemic control may be disturbed, especially in the early stages of treatment. The dosage of antidiabetic drugs may need to be adjusted.

Although in animal studies fluvoxamine has no proconvulsive properties, caution is recommended when the drug is administered to patients with a history of convulsive disorders. Fluvoxamine should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Treatment with fluvoxamine should be discontinued if seizures occur or if seizure frequency increases.

On rare occasions development of a serotonin syndrome or neuroleptic malignant syndrome-like events have been reported in association with treatment of fluvoxamine, particularly when given in combination with other serotonergic and/or neuroleptic drugs. As these syndromes may result in potentially life-threatening conditions, treatment with fluvoxamine should be discontinued if such events (characterised by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. As with other SSRIs, hyponatremia has been rarely reported, and appears to be reversible when fluvoxamine is discontinued. Some cases were possibly due to the syndrome of inappropriate antidiuretic hormone secretion. The majority of reports were associated with older patients.
There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs. Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g., atypical antipsychotics and phenothiazines, most TCAs, aspirin, NSAIDs) as well as in patients with a history of bleeding or coagulation disorders.

Fluvoxamine should be used with caution in patients with a history of mania/hypomania. Fluvoxamine should be discontinued in any patient entering a manic phase.

When combined with fluvoxamine plasma concentrations of terfenadine, astemizole or cisapride may be increased resulting in an increased risk for QT-prolongation/Torsade de Pointes. Therefore, fluvoxamine should not be co-administered with these drugs.

Due to lack of clinical experience special attention is advised in the situation of post-acute myocardial infarction.

There is limited clinical experience of concomitant administration of fluvoxamine and ECT therefore caution is advisable.

Data in elderly subjects give no indication of clinically significant differences in normal daily dosages compared to younger subjects. However upward dose titration should be done slower in the elderly, and dosing should always be done with caution.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Fluvoxamine should not be used in combination with MAOIs (see also section 4.3).

Fluvoxamine is a potent inhibitor of CYP1A2, and to a lesser extent of CYP2C and CYP3A4. Drugs which are largely metabolised via these isoenzymes are eliminated slower and may have higher plasma concentrations when co-administered with Fluvoxamine. This is particularly relevant for drugs with a narrow therapeutic index. Patients should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

Fluvoxamine has marginal inhibitory effects on CYP2D6 and seems not to affect non-oxidative metabolism or renal excretion.

CYP1A2

An increase in previously stable plasma levels of those tricyclic antidepressants (e.g., clomipramine, imipramine, amitriptyline) and neuroleptics (e.g., clozapine, olanzapine) which are largely metabolised through cytochrome P450 1A2 when given together with fluvoxamine, has been reported. A decrease in the dose of these products should be considered if treatment with fluvoxamine is initiated.

In case of concomitant administration with tizanidine an increasing of the intensity and duration of its effects (33-fold of the AUC of tizanidine) has been reported. It was correlated with decrease in blood pressure and heart rate as well as drowsiness.

Patients co-administered fluvoxamine and CYP1A2 metabolised drugs with a narrow therapeutic index (such as tacrine, theophylline, methadone, mexiletine) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

When given with fluvoxamine, warfarin plasma concentrations were significantly increased and prothrombin times prolonged.

Isolated cases of cardiac toxicity have been reported when fluvoxamine was combined with thioridazine. As plasma concentrations of propranolol are increased in combination with fluvoxamine, the propranolol dose may need to be lowered.

Caffeine plasma levels are likely to be increased during co-administration with fluvoxamine. Thus, patients who consume high quantities of caffeine-containing beverages should lower their intake when fluvoxamine is administered and adverse caffeine effects (like tremor, palpitations, nausea, restlessness, insomnia) are observed.
As plasma concentrations of ropinirol may be increased in combination with fluvoxamine thus increasing the risk of overdose, surveillance and reduction in the posology of ropinirol during fluvoxamine treatment and after its withdrawal may be required.

**CYP2C**

Patients co-administered fluvoxamine and CYP2C metabolised drugs with a narrow therapeutic index (such as phenytoin) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

**CYP3A4**

Terfenadine, astemizole, cisapride: see also section 4.4.

Patients co-administered fluvoxamine and CYP3A4 metabolised drugs with a narrow therapeutic index (such as carbamazepine, ciclosporin) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

The plasma levels of oxidatively metabolised benzodiazepines (e.g. triazolam, midazolam, alprazolam, and diazepam) are likely to be increased when co-administered with fluvoxamine. The dosage of these benzodiazepines should be reduced during co-administration with fluvoxamine.

**Glucuronidation**

Fluvoxamine does not influence plasma concentrations of digoxin.

**Renal excretion**

Fluvoxamine does not influence plasma concentrations of atenolol.

**Pharmacodynamic interactions**

The serotonergic effects of fluvoxamine may be enhanced when used in combination with other serotonergic agents (including triptans, tramadol, SSRIs and St. John's Wort preparations). (See also section 4.4)

Fluvoxamine has been used in combination with lithium in the treatment of severely ill, drug-resistant patients. However, lithium (and possibly also tryptophan) enhances the serotonergic effects of fluvoxamine. The combination should be used with caution in patients with severe, drug-resistant depression.

In patients on oral anticoagulants and fluvoxamine, the risk for haemorrhage may increase and these patients should therefore be closely monitored.

As with other psychotropic drugs patients should be advised to avoid alcohol use while taking fluvoxamine.

4.6 **PREGNANCY AND LACTATION**

Data on a limited number of exposed pregnancies indicate no adverse effects of fluvoxamine on pregnancy. To date, no other relevant epidemiological data are available.

Reproduction studies in animals at high doses revealed no evidence of impaired fertility, reproductive performance or teratogenic effects in the offspring. Caution should be exercised when prescribing to pregnant women.

Isolated cases of withdrawal symptoms in the newborn child have been described after the use of fluvoxamine at the end of pregnancy.

Fluvoxamine is excreted via human milk in small quantities. Therefore, the drug should not be used by women, who breast feed.

4.7 **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**

Fluvoxamine up to 150 mg has no or negligible influence on the ability to drive and use machines. It showed no effect on psychomotor skills associated with driving and operating machinery in healthy volunteers. However, somnolence has been reported during treatment with fluvoxamine. Therefore, caution is recommended until the individual response to the drug has been determined.

4.8 **UNDESIRABLE EFFECTS**

Nausea, sometimes accompanied by vomiting, is the most frequently observed symptom associated with fluvoxamine treatment. This side effect usually diminishes within the first two weeks of
treatment. Other adverse events, observed in clinical studies at frequencies listed below, are often associated with the illness and are not necessarily related to treatment.

**Common (frequency 1-10 %):**
- General disorders: Asthenia, malaise
- Cardiac disorders: Palpitations/tachycardia
- Gastrointestinal disorders: Abdominal pain, anorexia, constipation, diarrhoea, dry mouth, dyspepsia
- Nervous system disorders: Agitation, dizziness, headache, insomnia, nervousness, somnolence, tremor
- Psychiatric disorders: Anxiety
- Skin and subcutaneous tissue disorders: Sweating

**Uncommon (frequency < 1 %):**
- Vascular disorders: (Postural) hypotension
- Musculoskeletal and connective tissue disorders: Arthralgia, myalgia
- Nervous system disorders: Ataxia, extrapyramidal symptoms
- Psychiatric disorders: Confusion, hallucinations
- Reproductive system and breast disorders: Abnormal (delayed) ejaculation
- Skin and subcutaneous tissue disorders: Cutaneous hypersensitivity reactions (incl. rash, pruritus, angioedema)

**Rare (frequency < 0.1 %):**
- Hepatobiliary disorders: Liver function abnormality
- Nervous system disorders: Convulsions
- Psychiatric disorders: Mania
- Reproductive system and breast disorders: Galactorrhoea
- Skin and subcutaneous tissue disorders: Photosensitivity
- Psychomotor restlessness/akathisia (see section 4.4)

**Other adverse events observed during marketing**
- Weight gain or weight loss have been reported.
- Rarely, serotonin syndrome, neuroleptic malignant syndrome-like events, hyponatremia and SIADH have been reported. (see also section 4.4)
- It is possible that withdrawal reactions may occur on stopping therapy with fluvoxamine although the available preclinical and clinical evidence does not suggest that this treatment cause dependence Haemorrhage: (see also section 4.4)
- Very rarely, paresthesia, anorgasmy and taste perversion have been reported.
- Cases of suicidal ideation and suicidal behaviours have been reported during fluvoxamine therapy or early after treatment discontinuation (see section 4.4)

In one 10-week placebo-controlled trial in children and adolescents with OCD, frequently reported adverse events with a higher incidence than placebo, were: insomnia, asthenia, agitation, hyperkinesia, somnolence and dyspepsia. Serious adverse events in this study included: agitation and hypomania. Convulsions in children and adolescents have been reported during use outside clinical trials.

**Withdrawal symptoms seen on discontinuation of fluvoxamine treatment**
Discontinuation of fluvoxamine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbance (including paraesthesia, visual disturbance and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation and anxiety, irritability, confusion, emotional instability, nausea and/or vomiting and diarrhoea, sweating and palpitations, headache and tremor are the most commonly reported reactions. Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when fluvoxamine treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see section 4.2 and section 4.4).

### 4.9 OVERDOSE

**Symptoms**
Symptoms include gastro-intestinal complaints (nausea, vomiting and diarrhoea), somnolence and dizziness. Cardiac events (tachycardia, bradycardia, hypotension), liver function disturbances, convulsions and coma have also been reported.

Fluvoxamine has a wide margin of safety in overdose. Since market introduction, reports of death attributed to overdose of fluvoxamine alone have been extremely rare. The highest documented dose of fluvoxamine ingested by a patient is 12 gram. This patient recovered completely. Occasionally, more serious complications were observed in cases of deliberate overdose of fluvoxamine in combination with other drugs.

Treatment
There is no specific antidote to fluvoxamine. In case of overdose the stomach should be emptied as soon as possible after tablet ingestion and symptomatic treatment should be given. The repeated use of medicinal charcoal, if necessary accompanied by an osmotic laxative, is also recommended. Forced diuresis or dialysis are unlikely to be of benefit.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: Antidepressants, Selective serotonin reuptake inhibitors
ATC code: N06AB08

The mechanism of action of fluvoxamine is thought to be related to selective serotonin re-uptake inhibition in brain neurones. There is minimum interference with noradrenergic processes. Receptor binding studies have demonstrated that fluvoxamine has negligible binding capacity to alpha adrenergic, beta adrenergic, histaminergic, muscarine cholinergic, dopaminergic or serotonergic receptors.

In a placebo-controlled trial in 120 patients with OCD, aged between 8 and 17 years, a statistically significant improvement was seen in the total population in favour of fluvoxamine at 10 weeks. A further subgroup analysis showed improvement on the C-YBOCS rating scale in children whereas no effect was seen in adolescents. The mean dose was respectively 158 mg and 168 mg/day.

5.2 PHARMACOKINETIC PROPERTIES
Absorption
Fluvoxamine is completely absorbed following oral administration. Maximum plasma concentrations occur within 3-8 hours of dosing. The mean absolute bioavailability is 53%, due to first-pass metabolism. The pharmacokinetics of Fluvoxamine film-coated tablets is not influenced by concomitant food intake.

Distribution
In vitro plasma protein binding of fluvoxamine is 80%. Volume of distribution in humans is 25 l/kg.

Metabolism
Fluvoxamine undergoes extensive metabolism in the liver. Although CYP2D6 is in vitro the main isoenzyme involved in fluvoxamine's metabolism, plasma concentrations in poor metabolisers for CYP2D6 are not much higher than those in extensive metabolisers. The mean plasma half-life is approximately 13-15 hours after a single dose, and slightly longer (17-22 hours) during repeated dosing, when steady-state plasma levels are usually achieved within 10-14 days.

Fluvoxamine undergoes extensive hepatic transformation, mainly via oxidative demethylation, into at least nine metabolites, which are excreted by the kidneys. The two major metabolites showed negligible pharmacological activity. The other metabolites are not expected to be pharmacologically active. Fluvoxamine is a potent inhibitor of CYP1A2 and a moderate inhibitor of CYP2C and CYP3A4, with only marginal inhibitory effects on CYP2D6.

Fluvoxamine displays linear single-dose pharmacokinetics. Steady-state concentrations are higher than calculated from single-dose data, and are disproportionally higher at higher daily doses.

Special Patients groups
The pharmacokinetics of fluvoxamine is similar in healthy adults, elderly patients, and patients with renal insufficiency. The metabolism of fluvoxamine is impaired in patients with liver disease.

Steady-state plasma concentrations of fluvoxamine were twice as high in children (aged 6-11) as in adolescents (aged 12-17). Plasma concentrations in adolescents are similar to those in adults.

5.3 PRECLINICAL SAFETY DATA
There is no evidence of carcinogenicity, mutagenicity or impairment of fertility with fluvoxamine.

Reproduction studies in animals at high doses revealed no evidence of impaired fertility, reproductive performance or teratogenic effects in the offspring.

The potential for abuse, tolerance and physical dependence has been studied in a non-human primate model. No evidence of dependency phenomena was found.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
lactose monohydrate
mannitol
maize starch
methylhydroxy propylcellulose
polyethylene glycol 4000
pregelatinized starch
sodium stearyl fumarate
silica colloidal, anhydrous
titanium dioxide (colouring agent E 171)

6.2 INCOMPATIBILITIES
Not applicable.

6.3 SHELF LIFE
The shelf life is 18 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25 °C.
Store in the original package, in order to protect from light and moisture.

6.5 NATURE AND CONTENTS OF CONTAINER
Fluvoxamine 50 mg Film-Coated Tablets
Fluvoxamine 50 mg Film-Coated Tablets are packed in polyvinylchloride/aluminium or polyvinylidene chloride/aluminium blisters inserted into a carton folder.

The original packages contain:
15, 20, 30, 40, 50, 60, 90, and 100 film-coated tablets.
hospital pack containing 250 (5 x 50) film-coated tablets
Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
This medicinal product does not require any special storage conditions.

7 MARKETING AUTHORISATION HOLDER
Roger Oakes Ltd
Allstoe House
Church Lane
Greetham
Rutland
LE15 7NF

8 MARKETING AUTHORISATION NUMBER(S)
PL32019/0035
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
11/05/2010

10 DATE OF REVISION OF THE TEXT
11/05/2010
1 NAME OF THE MEDICINAL PRODUCT
Fluvoxamine 100 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One film-coated tablet contains 100 mg fluvoxamine maleate.
Excipients: 1.7 mg lactose /film-coated tablet
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet
Appearance:
100 mg Film-Coated Tablets: white, biconvex, round, scored

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Major depressive episode
Obsessive-Compulsive Disorder (OCD)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

 Depression
Adults
The recommended starting dose is 50 or 100 mg, given as a single dose in the evening. It is recommended to increase the dose gradually until an effective dose is reached. The usual effective dose is 100 mg per day and should be adjusted on individual patient response. Doses of up to 300 mg per day have been given. Dosages above 150 mg should be given in divided doses.
In agreement with the consensus statement of the WHO, antidepressant medication should be continued for at least 6 months after recovery from a depressive episode. A dose of 100 mg daily may be sufficient for this use.

Use in children and adolescents under 18 years of age
Fluvoxamine film-coated tablets should not be used for the treatment of major depressive episodes in children and adolescents under the age of 18 years (see section 4.4).

The efficacy and safety of Fluvoxamine film-coated tablets have not been established in the treatment of paediatric major depressive episodes (see 4.4).

Obsessive Compulsive Disorder
The recommended starting dose is 50 mg per day for 3-4 days. The effective dose usually lies between 100 mg and 300 mg per day. The dosage should be increased gradually until the effective dose is achieved, with a maximum of 300 mg per day for adults.

Doses up to 150 mg can be given as a single dose, preferably in the evening. It is advisable that a total daily dose of more than 150 mg is given in 2 or 3 divided doses.

If a good therapeutic response has been obtained, treatment can be continued at a dosage adjusted on an individual basis. If no improvement is observed within 10 weeks, treatment with fluvoxamine should be reconsidered. While there are no systematic studies to answer the question of how long to continue fluvoxamine treatment, OCD is a chronic condition and it is reasonable to consider continuation beyond 10 weeks in responding patients. Dosage adjustments should be made carefully on an individual patient basis, to maintain the patient at the lowest effective dose. The need for treatment should be reassessed periodically. Some clinicians advocate concomitant behavioural psychotherapy for patients who have done well on pharmacotherapy.

Children and adolescents under 18 years of age
In children over 8 years and adolescents there is limited data on a dose of up to 100 mg b.i.d. for 10 weeks.
The starting dose is 25 mg per day. Increase every 4-7 days in 25 mg increments as tolerated until an effective dose is achieved. The maximum dose in children should not exceed 200 mg/day. (For further details see 5.1)
It is advisable that a total daily dose of more than 50 mg should be given in two divided doses. If the two divided doses are not equal, the larger dose should be given at bedtime.
Hepatic or renal insufficiency
Patients suffering from hepatic or renal insufficiency should start on a low dose and be carefully monitored.

Withdrawal symptoms seen on discontinuation of fluvoxamine
Abrupt discontinuation should be avoided. When stopping treatment with fluvoxamine the dose should be gradually reduced over a period of at least one or two weeks in order to reduce the risk of withdrawal reactions. (see section 4.4 and section 4.8). If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

Method of administration
Fluvoxamine tablets should be swallowed with water and without chewing.

4.3 CONTRAINDICATIONS
Fluvoxamine film-coated tablets are contraindicated in combination with monoamine oxidase inhibitors (MAOIs). Treatment with fluvoxamine can be initiated:
- two weeks after discontinuation of an irreversible MAOI, or
- the following day after discontinuation of a reversible MAOI (e.g. moclobemide).
At least one week should elapse between discontinuation of fluvoxamine and initiation of therapy with any MAOI.

- Hypersensitivity to the active substance or to any of the excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Use in children and adolescents under 18 years of age
Fluvoxamine film-coated tablets should not be used in the treatment of children and adolescents under the age of 18 years, except for patients over 8 years with Obsessive Compulsive Disorder. Suicide-related behaviours (suicide 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.

Suicide/suicidal thoughts or clinical worsening
Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which fluvoxamine is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients, (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Akathisia/psychomotor restlessness
The use of fluvoxamine has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental and it may be necessary to review the use of fluvoxamine.

**Withdrawal symptoms seen on discontinuation of fluvoxamine treatment**

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8). In clinical trials adverse events seen on treatment discontinuation occurred in approximately 12% of patients treated with fluvoxamine, a comparative incidence for placebo treated patients is not currently available. The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction.

Dizziness, sensory disturbance (including paraesthesia, visual disturbances and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation and anxiety, irritability, confusion, emotional instability, nausea and/or vomiting and diarrhoea, sweating and palpitations, headache and tremor are the most commonly reported reactions. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that fluvoxamine should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient’s needs (see "Withdrawal Symptoms Seen on Discontinuation of Fluvoxamine", Section 4.2).

Patients suffering from hepatic or renal insufficiency should start on a low dose and be carefully monitored. Treatment with fluvoxamine has rarely been associated with an increase in hepatic enzymes, generally accompanied by clinical symptoms. In such cases treatment should be discontinued. Glycaemic control may be disturbed, especially in the early stages of treatment. The dosage of antidiabetic drugs may need to be adjusted. Although in animal studies fluvoxamine has no proconvulsive properties, caution is recommended when the drug is administered to patients with a history of convulsive disorders. Fluvoxamine should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Treatment with fluvoxamine should be discontinued if seizures occur or if seizure frequency increases.

On rare occasions development of a serotonin syndrome or neuroleptic malignant syndrome-like events have been reported in association with treatment of fluvoxamine, particularly when given in combination with other serotonergic and/or neuroleptic drugs. As these syndromes may result in potentially life-threatening conditions, treatment with fluvoxamine should be discontinued if such events (characterised by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated.

As with other SSRIs, hyponatremia has been rarely reported, and appears to be reversible when fluvoxamine is discontinued. Some cases were possibly due to the syndrome of inappropriate antidiuretic hormone secretion. The majority of reports were associated with older patients.

There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs. Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g. atypical antipsychotics and phenothiazines, most TCAs, aspirin, NSAIDs) as well as in patients with a history of bleeding or coagulation disorders.

Fluvoxamine should be used with caution in patients with a history of mania/hypomania. Fluvoxamine should be discontinued in any patient entering a manic phase.

When combined with fluvoxamine plasma concentrations of terfenadine, astemizole or cisapride may be increased resulting in an increased risk for QT-prolongation/Torsade de Pointes. Therefore, fluvoxamine should not be co-administered with these drugs.

Due to lack of clinical experience special attention is advised in the situation of post-acute myocardial infarction.
There is limited clinical experience of concomitant administration of fluvoxamine and ECT therefore caution is advisable.

Data in elderly subjects give no indication of clinically significant differences in normal daily dosages compared to younger subjects. However upward dose titration should be done slower in the elderly, and dosing should always be done with caution.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

### 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Fluvoxamine should not be used in combination with MAOIs (see also section 4.3).

Fluvoxamine is a potent inhibitor of CYP1A2, and to a lesser extent of CYP2C and CYP3A4. Drugs which are largely metabolised via these isoenzymes are eliminated slower and may have higher plasma concentrations when co-administered with Fluvoxamine. This is particularly relevant for drugs with a narrow therapeutic index. Patients should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

Fluvoxamine has marginal inhibitory effects on CYP2D6 and seems not to affect non-oxidative metabolism or renal excretion.

**CYP1A2**

An increase in previously stable plasma levels of those tricyclic antidepressants (e.g., clomipramine, imipramine, amitriptyline) and neuroleptics (e.g., clozapine, olanzapine) which are largely metabolised through cytochrome P450 1A2 when given together with fluvoxamine, has been reported. A decrease in the dose of these products should be considered if treatment with fluvoxamine is initiated.

In case of concomitant administration with tizanidine an increasing of the intensity and duration of its effects (33-fold of the AUC of tizanidine) has been reported. It was correlated with decrease in blood pressure and heart rate as well as drowsiness.

Patients co-administered fluvoxamine and CYP1A2 metabolised drugs with a narrow therapeutic index (such as tacrine, theophylline, methadone, mexiletine) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

When given with fluvoxamine, warfarin plasma concentrations were significantly increased and prothrombin times prolonged.

Isolated cases of cardiac toxicity have been reported when fluvoxamine was combined with thioridazine. As plasma concentrations of propranolol are increased in combination with fluvoxamine, the propranolol dose may need to be lowered.

Caffeine plasma levels are likely to be increased during co-administration with fluvoxamine. Thus, patients who consume high quantities of caffeine-containing beverages should lower their intake when fluvoxamine is administered and adverse caffeine effects (like tremor, palpitations, nausea, restlessness, insomnia) are observed.

As plasma concentrations of ropinirol may be increased in combination with fluvoxamine thus increasing the risk of overdose, surveillance and reduction in the posology of ropinirol during fluvoxamine treatment and after its withdrawal may be required.

**CYP2C**

Patients co-administered fluvoxamine and CYP2C metabolised drugs with a narrow therapeutic index (such as phenytoin) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended.

**CYP3A4**

Terfenadine, astemizole, cisapride: see also section 4.4.
Patients co-administered fluvoxamine and CYP3A4 metabolised drugs with a narrow therapeutic index (such as carbamazepine, ciclosporin) should be carefully monitored and, if necessary, dose adjustment of these drugs is recommended. The plasma levels of oxidatively metabolised benzodiazepines (e.g. triazolam, midazolam, alprazolam, and diazepam) are likely to be increased when co-administered with fluvoxamine. The dosage of these benzodiazepines should be reduced during co-administration with fluvoxamine.

**Glucuronidation**
Fluvoxamine does not influence plasma concentrations of digoxin.

**Renal excretion**
Fluvoxamine does not influence plasma concentrations of atenolol.

**Pharmacodynamic interactions**
The serotonergic effects of fluvoxamine may be enhanced when used in combination with other serotonergic agents (including triptans, tramadol, SSRIs and St. John's Wort preparations). (See also section 4.4) Fluvoxamine has been used in combination with lithium in the treatment of severely ill, drug-resistant patients. However, lithium (and possibly also tryptophan) enhances the serotonergic effects of fluvoxamine. The combination should be used with caution in patients with severe, drug-resistant depression. In patients on oral anticoagulants and fluvoxamine, the risk for haemorrhage may increase and these patients should therefore be closely monitored.

As with other psychotropic drugs patients should be advised to avoid alcohol use while taking fluvoxamine.

### 4.6 PREGNANCY AND LACTATION
Data on a limited number of exposed pregnancies indicate no adverse effects of fluvoxamine on pregnancy. To date, no other relevant epidemiological data are available.

Reproduction studies in animals at high doses revealed no evidence of impaired fertility, reproductive performance or teratogenic effects in the offspring. Caution should be exercised when prescribing to pregnant women.

Isolated cases of withdrawal symptoms in the newborn child have been described after the use of fluvoxamine at the end of pregnancy.

Fluvoxamine is excreted via human milk in small quantities. Therefore, the drug should not be used by women, who breast feed.

### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Fluvoxamine up to 150 mg has no or negligible influence on the ability to drive and use machines. It showed no effect on psychomotor skills associated with driving and operating machinery in healthy volunteers. However, somnolence has been reported during treatment with fluvoxamine. Therefore, caution is recommended until the individual response to the drug has been determined.

### 4.8 UNDESIRABLE EFFECTS
Nausea, sometimes accompanied by vomiting, is the most frequently observed symptom associated with fluvoxamine treatment. This side effect usually diminishes within the first two weeks of treatment. Other adverse events, observed in clinical studies at frequencies listed below, are often associated with the illness and are not necessarily related to treatment.

**Common (frequency 1-10 %):**
- General disorders: Asthenia, malaise
- Cardiac disorders: Palpitations/tachycardia
- Gastrointestinal disorders: Abdominal pain, anorexia, constipation, diarrhoea, dry mouth, dyspepsia
- Nervous system disorders: Agitation, dizziness, headache, insomnia, nervousness, somnolence, tremor
- Psychiatric disorders: Anxiety
- Skin and subcutaneous tissue disorders: Sweating

**Uncommon (frequency < 1 %):**
- Vascular disorders: (Postural) hypotension
- Musculoskeletal and connective tissue disorders: Arthralgia, myalgia
Nervous system disorders: Ataxia, extrapyramidal symptoms
Psychiatric disorders: Confusion, hallucinations
Reproductive system and breast disorders: Abnormal (delayed) ejaculation
Skin and subcutaneous tissue disorders: Cutaneous hypersensitivity reactions (incl. rash, pruritus, angioedema)

Rare (frequency < 0.1 %):
Hepatobiliary disorders: Liver function abnormality
Nervous system disorders: Convulsions
Psychiatric disorders: Mania
Reproductive system and breast disorders: Galactorrhoea
Skin and subcutaneous tissue disorders: Photosensitivity
Psychomotor restlessness/akathisia (see section 4.4)

Other adverse events observed during marketing
Weight gain or weight loss have been reported.
Rarely, serotonin syndrome, neuroleptic malignant syndrome-like events, hyponatremia and SIADH have been reported. (see also section 4.4)
It is possible that withdrawal reactions may occur on stopping therapy with fluvoxamine although the available preclinical and clinical evidence does not suggest that this treatment cause dependence
Haemorrhage: (see also section 4.4)
Very rarely, paresthesia, anorgasmy and taste perversion have been reported.
Cases of suicidal ideation and suicidal behaviours have been reported during fluvoxamine therapy or early after treatment discontinuation (see section 4.4)

In one 10-week placebo-controlled trial in children and adolescents with OCD, frequently reported adverse events with a higher incidence than placebo, were: insomnia, asthenia, agitation, hyperkinesia, somnolence and dyspepsia, Serious adverse events in this study included: agitation and hypomania. Convulsions in children and adolescents have been reported during use outside clinical trials.

Withdrawal symptoms seen on discontinuation of fluvoxamine treatment
Discontinuation of fluvoxamine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbance (including paraesthesia, visual disturbance and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation and anxiety, irritability, confusion, emotional instability, nausea and/or vomiting and diarrhoea, sweating and palpitations, headache and tremor are the most commonly reported reactions. Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when fluvoxamine treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see section 4.2 and section 4.4).

4.9 OVERDOSE

Symptoms
Symptoms include gastro-intestinal complaints (nausea, vomiting and diarrhoea), somnolence and dizziness. Cardiac events (tachycardia, bradycardia, hypotension), liver function disturbances, convulsions and coma have also been reported.
Fluvoxamine has a wide margin of safety in overdose. Since market introduction, reports of death attributed to overdose of fluvoxamine alone have been extremely rare. The highest documented dose of fluvoxamine ingested by a patient is 12 gram. This patient recovered completely. Occasionally, more serious complications were observed in cases of deliberate overdose of fluvoxamine in combination with other drugs.

Treatment
There is no specific antidote to fluvoxamine. In case of overdose the stomach should be emptied as soon as possible after tablet ingestion and symptomatic treatment should be given. The repeated use of medicinal charcoal, if necessary accompanied by an osmotic laxative, is also recommended. Forced diuresis or dialysis are unlikely to be of benefit.

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: Antidepressants, Selective serotonin reuptake inhibitors
ATC code: N06AB08
The mechanism of action of fluvoxamine is thought to be related to selective serotonin re-uptake inhibition in brain neurones. There is minimum interference with noradrenergic processes. Receptor binding studies have demonstrated that fluvoxamine has negligible binding capacity to alpha adrenergic, beta adrenergic, histaminergic, muscarine cholinergic, dopaminergic or serotonergic receptors.

In a placebo-controlled trial in 120 patients with OCD, aged between 8 and 17 years, a statistically significant improvement was seen in the total population in favour of fluvoxamine at 10 weeks. A further subgroup analysis showed improvement on the C-YBOCS rating scale in children whereas no effect was seen in adolescents. The mean dose was respectively 158 mg and 168 mg/day.

5.2 PHARMACOKINETIC PROPERTIES
Absorption
Fluvoxamine is completely absorbed following oral administration. Maximum plasma concentrations occur within 3-8 hours of dosing. The mean absolute bioavailability is 53%, due to first-pass metabolism. The pharmacokinetics of Fluvoxamine film-coated tablets is not influenced by concomitant food intake.

Distribution
In vitro plasma protein binding of fluvoxamine is 80%. Volume of distribution in humans is 25 l/kg.

Metabolism
Fluvoxamine undergoes extensive metabolism in the liver. Although CYP2D6 is in vitro the main isoenzyme involved in fluvoxamine's metabolism, plasma concentrations in poor metabolisers for CYP2D6 are not much higher than those in extensive metabolisers. The mean plasma half-life is approximately 13-15 hours after a single dose, and slightly longer (17-22 hours) during repeated dosing, when steady-state plasma levels are usually achieved within 10-14 days. Fluvoxamine undergoes extensive hepatic transformation, mainly via oxidative demethylation, into at least nine metabolites, which are excreted by the kidneys. The two major metabolites showed negligible pharmacological activity. The other metabolites are not expected to be pharmacologically active. Fluvoxamine is a potent inhibitor of CYP1A2 and a moderate inhibitor of CYP2C and CYP3A4, with only marginal inhibitory effects on CYP2D6. Fluvoxamine displays linear single-dose pharmacokinetics. Steady-state concentrations are higher than calculated from single-dose data, and are disproportionally higher at higher daily doses.

Special Patients groups
The pharmacokinetics of fluvoxamine is similar in healthy adults, elderly patients, and patients with renal insufficiency. The metabolism of fluvoxamine is impaired in patients with liver disease. Steady-state plasma concentrations of fluvoxamine were twice as high in children (aged 6-11) as in adolescents (aged 12-17). Plasma concentrations in adolescents are similar to those in adults.

5.3 PRECLINICAL SAFETY DATA
There is no evidence of carcinogenicity, mutagenicity or impairment of fertility with fluvoxamine. Reproduction studies in animals at high doses revealed no evidence of impaired fertility, reproductive performance or teratogenic effects in the offspring.

The potential for abuse, tolerance and physical dependence has been studied in a non-human primate model. No evidence of dependency phenomena was found.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
lactose monohydrate
mannitol
maize starch
methylhydroxy propylcellulose
polyethylene glycol 4000
pregelatinized starch
sodium stearyl fumarate
silica colloidal, anhydrous
titanium dioxide (colouring agent E 171)

6.2 INCOMPATIBILITIES
Not applicable.

6.3 SHELF LIFE
The shelf life is 18 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25 °C.
Store in the original package, in order to protect from light and moisture.

6.5 NATURE AND CONTENTS OF CONTAINER
Fluvoxamine 100 mg Film-Coated Tablets
Fluvoxamine 100 mg Film-Coated Tablets are packed in polyvinylchloride/aluminium or polyvinylidene chloride/aluminium blisters inserted into a carton folder.

The original packages contain:
15, 20, 30, 40, 50, 60, 90, and 100 film-coated tablets.
hospital pack containing 250 (5 x 50) film-coated tablets

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
This medicinal product does not require any special storage conditions.

7 MARKETING AUTHORISATION HOLDER
Roger Oakes Ltd
Allstoe House
Church Lane
Greetham
Rutland
LE15 7NF

8 MARKETING AUTHORISATION NUMBER(S)
PL32019/0036

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
11/05/2010

10 DATE OF REVISION OF THE TEXT
11/05/2010
UKPAR Fluvoxamine 50mg and 100mg Film-Coated Tablets   PL 32019/0035-6

Fluvoxamine 50mg, 100mg Tablets
(Fluvoxamine maleate)

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 Fluvoxamine 50mg, 100mg Tablets is and what it is used for
2. Before you take Fluvoxamine 50mg, 100mg tablets
3. How to take Fluvoxamine 50mg, 100mg Tablets
4. Possible side effects
5. How to store Fluvoxamine 50mg, 100mg Tablets.
6. Further information

1 What Fluvoxamine 50mg, 100mg Tablets is and what it is used for
Fluvoxamine 50mg, 100mg Tablets is an antidepressant that influences the central nervous system.

Fluvoxamine 50mg, 100mg Tablets is used for:
- depressive illness (major depressive episodes)
- obsessive thoughts and obsessive actions (obsessive compulsive disorders).

2 Before you take Fluvoxamine 50mg, 100mg Tablets
Do not take Fluvoxamine 50mg, 100mg Tablets
- If you are allergic (hypersensitive) to fluvoxamine or any of the other ingredients in the product.
- If you are taking or have recently taken a medicine that belongs to the group of monoamine oxidase (MAO) inhibitors (medicines to treat depression or Parkinson's disease), or if you are going to use such medicine within the next week. Depending on the type of MAO-inhibitor you must wait for up to two weeks before you can start taking Fluvoxamine 50mg, 100mg Tablets (see "Taking other medicines").

Take special care with Fluvoxamine 50mg, 100mg Tablets
- If you have diabetes control of blood sugar may be disturbed, especially in the early stages of treatment. The dose of your insulin or the anti-diabetic medicines that you take by mouth may need to be adjusted.
- If you have reduced liver or kidney function you must tell your doctor, because it may be necessary to prescribe a lower dose for you.
- If you have recently had a heart attack.

patients under 18 are taking Fluvoxamine 50mg, 100mg Tablets. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Fluvoxamine 50mg, 100mg Tablets in this age group have not yet been demonstrated.

Taking other medicines
Certain other medicines can affect or be affected by Fluvoxamine 50mg, 100mg Tablets. Please ask your doctor for advice if you are taking:
- Medicines that belong to the group of MAO inhibitor (MAOI).
  - If your doctor changes your medicine from a MAOI to Fluvoxamine 50mg, 100mg Tablets, there must be an interval of:
    - at least 2 weeks after stopping an irreversible MAOI (e.g. selegiline)
    - one day after stopping a reversible MAOI (e.g. moclobemide)
  - Therapy with any MAOI should not be started for at least 1 week after stopping intake of Fluvoxamine 50mg, 100mg Tablets.
- Other medicine for depression: other serotonin re-uptake inhibitors.
- Medicines containing lithium (antipsychotic) or the dietary supplement tryptophan.
- Medicines against migraine (triptane).
- Tramadol (pain-killer).
- Herbal remedy St.John’s Wort (Hypericum perforatum).

Concomitant use of above mentioned medicinal products may e. g. lead to serotonin syndrome or neuroleptic malignant syndrome (see “Do not take Fluvoxamine 50mg, 100mg Tablets” and “Take special care with Fluvoxamine 50mg, 100mg Tablets”).
If epileptic seizures (convulsions) occur during treatment, Fluvoxamine 50mg, 100mg Tablets should be discontinued. If you already suffer from epilepsy and the frequency of seizures increases during treatment, Fluvoxamine 50mg, 100mg Tablets should also be discontinued.

If you have or have had episodes of overactive behaviour or thoughts (mania).

If you have a history of bleeding disorder e.g. cutaneous bleeding abnormalities, gynaecological or bleeding from the stomach or if you use medicines which possibly increase tendency to bleed (see section "Taking other medicines").

If you are receiving electric shock treatment.

Use of Fluvoxamine 50mg, 100mg Tablets can be connected with the development of a condition of inner restlessness and inability to sit or stand still. This is most likely to occur in the first weeks of treatment. Increasing the dose can worsen such symptoms.

If you develop some or all of the following symptoms: high fever, rigidity, sudden jerks of the muscles, confusion, irritability, extreme agitation, rapid fluctuations in heart beat or breathing rate. If you notice these symptoms, contact your doctor immediately, because you may have something called serotonin-syndrome. Concomitant use of certain other medicines may enhance the risk of this syndrome (see "Taking other medicines").

If you are at risk of a decreased sodium level in the blood (hyponatraemia) e.g. from concomitant medications. Hyponatraemia has been reported rarely during treatment with Fluvoxamine 50mg, 100mg Tablets, predominantly in the elderly.

If you are an elderly patient. Your doctor will increase your dose of Fluvoxamine 50mg, 100mg Tablets more slowly and with extra caution.

**Withdrawal symptoms**

After the end of therapy, withdrawal symptoms commonly occur, particularly if Fluvoxamine 50mg, 100 mg Tablets are discontinued abruptly (see section 4, "Possible side effects"). The risk of withdrawal symptoms may be dependent on several factors including the duration of therapy and dosage and the rate of dose reduction.

Other medicine for depression: tricyclic antidepressants (e.g. clomipramine, imipramine, amitriptyline).

Neuroleptics such as clozapine, olanzapine or thioridazine (used to treat schizophrenia).

Tizanidine for treatment of muscle disorders. The duration and intensity of its effect may be increased, correlated with increased blood pressure and heart rate.

Tacrine (used to treat dementia), Theophylline (used to treat asthma and bronchitis), Methadon (commonly used to treat drug dependence) and Mexiletine (used to treat heart disorders).

Propranolol (against high blood pressure).

Ropinrole (used to treat Parkinson’s Disease).

Caffeine (found in tea or coffee). The consume of high quantities of caffeine-containing beverages should be avoided.

Phenytoin (used to treat epilepsy or certain heart rhythm disorders)

Terfenadine, astemizole (used to treat allergic reaction) or cisapride (for gastrointestinal disorders). Concomitant use with Fluvoxamine 50mg, 100mg Tablets can lead to disorders of heart rate and these medicinal products should therefore not be used simultaneously.

Ciclosporin (used after organ transplant).

Carbamazepine (used to treat epilepsy).

Benzodiazepines such as triazolam, midazolam, alprazolam and diazepam (uses include treatment of anxiety and epilepsy).

Fluvoxamine 50mg, 100mg Tablets may increase the blood levels of above mentioned medicinal products, which can result in adverse effects. Your doctor may need to adjust the dose of the above mentioned products.

Anti-inflammatory medicines/painkillers (e.g. ibuprofen, diclofenac) and acetylsalicylic acid.

Warfarin (to prevent blood clotting) and other medicines known to effect blood clotting, e.g. antipsychotics and tricyclic antidepressants.

Concomitant use of above mentioned medicinal products may lead to increased/prolonged bleeding (see "Take special care with Fluvoxamine 50mg, 100mg Tablets").
Thoughts of suicide and worsening of your depression or anxiety disorder

If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer. You may be more likely to think like this:

- If you have previously had thoughts about killing or harming yourself.
- If you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed or have an anxiety disorder, and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behaviour.

Children and adolescents of less than 18 years of age

Fluvoxamine 50mg, 100mg Tablets should normally not be used for children and adolescents under 18 years, except for patients over 8 years with obsessive compulsive disorders. Also, you should know that patients under 18 have an increased risk of side-effects such suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. Despite this, your doctor may prescribe Fluvoxamine 50mg, 100mg Tablets for patients under 18 because he/she decides that this is in their best interests. If your doctor has prescribed Fluvoxamine 50mg, 100mg Tablets 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

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

Taking Fluvoxamine 50mg, 100mg Tablets with food and drink

Drink: The film-coated tablets should be swallowed with water.

Alcohol: You should avoid consumption of alcohol during therapy with Fluvoxamine 50mg, 100mg Tablets.

Pregnancy and breast-feeding

There is only limited data available regarding use of fluvoxamine in pregnant women. Therefore Fluvoxamine 50mg, 100mg Tablets should be used with caution during pregnancy. If Fluvoxamine 50mg, 100mg Tablets is used at the end of pregnancy the newborn child may suffer from withdrawal symptoms. Always ask your doctor for advice before taking Fluvoxamine 50mg, 100mg Tablets.

Fluvoxamine passes into breast milk. Therefore do not take Fluvoxamine 50mg, 100mg Tablets while breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

In individual cases, the ability to drive and use machines can be reduced.

Fluvoxamine 50mg, 100mg Tablets can cause somnolence as an undesirable effect. Therefore patients should be aware of this at the start of treatment.

Important information about some of the ingredients of Fluvoxamine 50mg, 100mg Tablets

Fluvoxamine 50mg, 100mg Tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

continued....
How to take Fluvoxamine 50mg, 100mg Tablets

Always take Fluvoxamine 50mg, 100mg Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
The film-coated tablets should be swallowed without chewing and with water.

The usual dose is:

Major depressive episodes

**Adults:**

**Starting dose:** 1 or 2 tablets (50mg fluvoxamine maleate) or ½ or 1 tablet (100 mg) taken as a single dose in the evening. Your doctor may increase the dose gradually until an effective dose is reached.

**Usual effective daily dose:** 2 tablets (50 mg fluvoxamine maleate) or 1 tablet (100 mg). Your doctor will adjust the dose to your individual response.
A daily dose in excess of 3 tablets (50mg fluvoxamine maleate) or 1 ½ tablets (100mg) should be divided into several doses.

**Maximum dose:** 6 (50mg fluvoxamine maleate) or 3 tablets (100mg), daily.

Children and adolescents of less than 18 years of age

Fluvoxamine 50mg, 100mg Tablets should **not be used** in children and adolescents of less than 18 years of age (see “Take special care with Fluvoxamine 50mg, 100mg Tablets”).

Obsessive-compulsive disorders

**Adults:**

**Starting dose:** 1 tablet (50mg fluvoxamine maleate) or ½ tablet (100 mg) per day for 3-4 days.
Your doctor may increase the dose gradually until an effective dose is reached.

**Usually effective dose:** 2-6 tablets (50 mg fluvoxamine maleate) or 1-3 tablets (100 mg) per day.

**Maximum daily dose:** 6 tablets (50mg fluvoxamine maleate) or 3 tablets (100mg).
The tablets should be taken preferably in the evening as a single dose. A daily dose in excess of 3 tablets (50 mg fluvoxamine maleate) or 1 ½ tablets (100 mg) should be taken in 2 or 3 divided doses.

Nervous system disorders

**Common:** sleepiness, sleep disturbances, feeling nervous, trembling, headache, dizziness, restlessness

**Uncommon:** movement disorders, difficulty in co-ordinating movement and impaired tension of muscles

**Rare:** convulsions

Cardiac disorders

**Common:** increased heart rate or palpitations

Vascular disorders:

**Uncommon:** low blood pressure (when changing posture from lying to standing)

Gastrointestinal disorders:

**Very common:** nausea

**Common:** abdominal pain, digestive disorders (a feeling of pressure in the stomach, bloating, loss of appetite), constipation, diarrhoea, vomiting, dry mouth

Hepato-biliary disorders:

**Rare:** liver function disorders

Skin and subcutaneous tissue disorders:

**Common:** sweating

**Uncommon:** allergic skin reactions such as rash, itching, swelling

**Rare:** sensitivity to light

Reproductive system and breast disorders:

**Uncommon:** delayed ejaculation

**Rare:** milky secretion from the breast gland (galactorrhea)

Musculoskeletal disorders:

**Uncommon:** joint pain, muscle pain

Other side effects

**weight gain or weight loss,**

**Common:** weakness, feeling sick

**Rare:** serotonin syndrome, neuroleptic-malignant syndrome, hyponatremia and abnormal bleeding (see also “Taking other medicines” and “Take special care with Fluvoxamine 50mg, 100mg Tablets”),

**Very rare:** taste abnormalities, sensation of pins and needles, failure to experience orgasm.
Children and adolescents over 18 years of age
For children over 8 years and adolescents the starting dose is ½ tablet (50 mg fluvoxamine maleate) per day. Your doctor will increase the dose every 4-7 days in ½ tablet (50 mg fluvoxamine maleate) as tolerated until an effective dose is achieved. A total daily dose of more than 1 tablet (50 mg fluvoxamine maleate) or ½ tablet (100mg) should be given in two divided doses. If doses are not equal, the larger dose should be given at bedtime.

**Maximum dose:** 4 tablets (50mg fluvoxamine maleate) or 2 tablets (100mg).

**Patients with hepatic and renal insufficiency** should commence treatment at a low dose.

**Duration of treatment**
The duration depends on the course of the disease and is determined by your doctor.

**Major depressive episodes**
It may take a few weeks or more until you start feeling better. After the symptoms have disappeared treatment should be continued for at least 6 months.

**Obsessive-compulsive disorders**
If no improvement is observed after 10 weeks your doctor may decide to stop prescribing Fluvoxamine for you. If you respond well to Fluvoxamine, your doctor will most likely continue treatment with Fluvoxamine. He/she will then periodically reassess the need for treatment.

**Before terminating treatment,** gradual dose reduction is to be taken into consideration.

**If you take more Fluvoxamine 50mg, 100mg Tablets then you should**
If you have taken too much Fluvoxamine 50mg, 100mg Tablets you should contact your doctor or a hospital.

**Withdrawal symptoms**
after the end of therapy commonly occur, particularly Fluvoxamine 50mg, 100mg Tablets are discontinued abruptly. The risk of withdrawal symptoms may be dependent on the duration of therapy and dosage and the rate of dose reduction. Dizziness, sensory disturbances (including tingling in arms and legs and electric shock sensation), sleep disturbances (including intense dreams), inner restlessness or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported. Most of these symptoms are mild to moderate, however, in some patients they may also be severe in intensity. They usually occur within the first few days of discontinuing treatment. Generally, these symptoms are self-limiting and spontaneously resolve within 2 weeks, though in some individuals they may be prolonged. It is therefore advised to discontinue treatment gradually by stepwise reduction in the dose over a period of several weeks or months.

**How to store Fluvoxamine 50mg, 100mg Tablets**
Keep out of the reach and sight of children.

Do not store above 25 °C.

Keep the blister in the carton, in order to protect from light and moisture.

Do not use Fluvoxamine 50mg, 100mg Tablets after the expiry date which is stated on the carton and the blister. The expiry date refers to the last day of that month.

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 to protect the environment.
Symptoms of overdose:
Nausea, vomiting and diarrhoea, sleepiness, dizziness, rapid heart beat, slow heart beat and low blood pressure, liver function disturbances, seizures and coma.

If you forget to take Fluvoxamine 50mg, 100mg Tablets
Do not take a double dose to make up for a forgotten dose. Continue intake as prescribed by your doctor.

If you stop taking Fluvoxamine 50mg, 100mg Tablets
Please speak with your doctor if you want to terminate or interrupt treatment. Withdrawal symptoms may occur when you stop taking Fluvoxamine 50mg, 100mg Tablets (see section 4 “Possible side effects”). Since the risk of withdrawal symptoms is higher when you stop taking Fluvoxamine 50mg, 100mg Tablets abruptly, your doctor will gradually reduce the dose over a period of at least 1–2 weeks.

If intolerable withdrawal symptoms occur after dose reduction or discontinuation of the medicinal product, inform your doctor. He/she may consider to decrease your dose in smaller steps.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4 Possible side effects
Like all medicines, Fluvoxamine 50mg, 100mg Tablets can cause side effects, although not everybody gets them.
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.

Frequencies are defined as:
Very common: in more than 1 of 10 patients
Common: in more than 1 of 100, but in less than 1 of 10 patients
Uncommon: in more than 1 of 1000, but in less than 1 of 100 patients.
Rare: in more than 1 of 10,000, but less than 1 of 1000 patients
Very rare: in less than 1 of 10,000 patients
Frequency not known: frequency cannot be estimated from the available data

Psychiatric disorders:
Common: anxiety
Uncommon: confusion, hallucinations
Rare: episodes of overactive behaviour or thoughts (mania)
Frequency not known: Suicidal thoughts and thus related behaviour (see section “Take special care with Fluvoxamine 50mg, 100 mg Tablets”)

6 Further information
What Fluvoxamine 50mg, 100mg Tablets contains
- The active substance is 50mg, or 100 mg fluvoxamine maleate in 1 film-coated tablet.
- The other ingredients are:
  Lactose monohydrate, mannitol, maize starch, hypromellose, polyethylene glycol 4000, pregelatinized starch, sodium stearyl fumarate, colloidal anhydrous silica, titanium dioxide (colouring agent E 171)

What Fluvoxamine 50mg, 100mg Tablets look like and contents of the pack
Fluvoxamine 50mg, 100mg Tablets are white, biconvex, round film-coated tablets with a score.
The tablets are packed in blisters in a carton containing 15, 20, 30, 40, 50, 60, 90, and 100 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
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Allstoe House, Church Lane
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Manufacturer
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Product Licence Number:
Fluvoxamine 50mg Tablets:
PL 32019/0035
Fluvoxamine 100mg Tablets:
PL 32019/0036

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