SERTRALINE 50MG TABLETS (PL 20092/0020)
SERTRALINE 100MG TABLETS (PL 20092/0021)

UKPAR

TABLE OF CONTENTS

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 12
Steps taken after authorisation – summary	Page 13
Summary of Product Characteristics	
Product Information Leaflet	
Labelling	

SERTRALINE 50MG TABLETS (PL 20092/0020)
SERTRALINE 100MG TABLETS (PL 20092/0021)

LAY SUMMARY

On 23rd January 2008, the MHRA granted Lupin Europe Limited Marketing Authorisations (licences) for the medicinal products Sertraline 50mg and 100mg Tablets (PL 20092/0020-1). These are prescription only medicines (POM) that are used for the treatment of the following conditions:

- The symptoms of depression (feelings of sadness, tearfulness, inability to sleep or enjoy life as you once used to) and any anxiety you may have at the same time.
- Obsessive-compulsive disorder (OCD). OCD is an illness linked to anxiety in which you can become constantly troubled by persistent ideas (obsessions) that make you carry out repetitive rituals (compulsions).
- Post traumatic stress disorder (PTSD). PTSD can occur after a very emotionally traumatic experience. Some of the symptoms of PTSD are similar to depression and anxiety.

The active ingredient, sertraline, is one of a group of antidepressant or anti-obsessional medicines known as selective serotonin reuptake inhibitors (SSRIs). Low levels of a substance called serotonin in the brain are thought to be a cause of depression and these related disorders. SSRIs work by bringing the level of serotonin back up to normal.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Sertraline 50mg and 100mg Tablets outweigh the risks, hence Marketing Authorisations have been granted.

SERTRALINE 50MG TABLETS (PL 20092/0020)
SERTRALINE 100MG TABLETS (PL 20092/0021)

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 7
Clinical assessment (including statistical assessment)	Page 8
Overall conclusions and risk benefit assessment	Page 11

INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Sertraline 50mg and 100mg Tablets to Lupin (Europe) Limited (PL 20092/0020-1) on 23rd January 2008. The products are prescription-only medicines for the treatment of:

- Symptoms of depressive illness
- Treatment of obsessive compulsive disorder
- Post traumatic stress disorder
- Major depressive disorder

The applications were submitted as abridged applications according to Article 10.1 of Directive 2001/83/EC, as amended, claiming to be a generic medicinal product of Lustral 50mg and 100mg Tablets (PL 00057/0308-9), which have been authorised to Pfizer Limited in the UK since November 1990.

The active ingredient, sertraline, is one of a group of antidepressant or anti-obsessional medicines known as selective serotonin reuptake inhibitors (SSRIs).

PHARMACEUTICAL ASSESSMENT

Active Substance

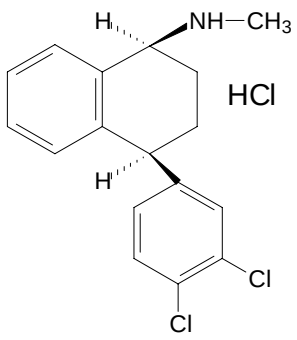
rINN/ BAN Name: Sertraline Hydrochloride

Chemical names:

(1*S*-*cis*)-4-(3,4-chlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthalenamine hydrochloride

(1*S*,4*S*)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthylamine hydrochloride

Structural formula



Molecular formula: $C_{17}H_{17}Cl_2N$, HCl

Molecular weight: 342.73

This is subject to a Drug Master File (DMF). A valid letter of access has been provided.

Synthesis of the drug substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification is provided for the active substance sertraline, with suitable test methods and limits. The methods of testing and limits for residual solvents are in compliance with current guidelines.

Appropriate proof of structure has been supplied for the active pharmaceutical ingredient. All potential known impurities have been identified and characterised. Suitable certificates of analysis have been provided for all reference standards.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated showing the active substance to be a physically and chemically stable drug. The data support a retest period of 12 months

when stored in a transparent polyethylene bag with a cardboard box at 25°C/60%RH. This is acceptable.

Other Ingredients
Other ingredients consist of pharmaceutical excipients calcium hydrogen phosphate anhydrous, microcrystalline cellulose, sodium starch glycollate, hydroxypropyl cellulose, magnesium stearate and water purified.

All excipients are controlled according to their European Pharmacopoeia monograph. Satisfactory certificates of analysis have been provided for all ingredients showing compliance with their respective monograph.

With the exception of magnesium stearate, none of the other ingredients use materials of animal or human origin in their production. A certificate of suitability has been provided by the manufacturers of magnesium stearate showing compliance with current guidelines concerning the minimising of transmission of TSE/BSE.

Pharmaceutical development
The objective of the pharmaceutical development programme was to produce products containing 50mg and 100mg sertraline that are tolerable and which could be considered as generic products to the originator products Lustral 50 and 100 mg Tablets.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

Comparative *in vitro* dissolution profiles have been generated for the proposed and originator products with satisfactory results. Comparative impurity studies have also been undertaken.

Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of both strengths of product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results at pilot-scale.

Finished Product Specification
The finished product specifications proposed for both strengths are acceptable. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container-Closure System
All strengths of tablet are packaged in opaque white PVC/PVDC aluminium blister strips in pack sizes of 28 tablets.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the relevant regulations regarding materials for use in contact with food.

Stability of the product
Stability studies were performed on pilot-scale batches of all strengths of finished product in the packaging proposed for marketing, in accordance with current guidelines. All results from stability studies on pilot batches were within specified limits. These data support a shelf-life of 24 months, with a storage condition “Store below 30 degree C”.

The applicant has committed to providing stability data for the first three production-scale batches of each strength of finished product.

Bioequivalence/bioavailability
Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence study.

SPC, PIL, Labels
The SPC, PIL and Labels are pharmaceutically acceptable.

A 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 it contains.

CONCLUSION
The proposed products have been shown to be generic products of the reference product and have met the requirements with respect to qualitative and quantitative content of the active substance. Similar dissolution profiles have been demonstrated for the proposed and reference products. It is recommended that Marketing Authorisation should be granted for these applications.

PRECLINICAL ASSESSMENT

These applications claim to be generic medicinal products of Lustral 50mg and 100mg Tablets (Pfizer Limited, UK), which have been licensed within the EEA for over 10 years.

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

CLINICAL ASSESSMENT

1. INTRODUCTION AND BACKGROUND

These are National Procedures for tablets containing 50mg and 100mg of Sertraline, as Sertraline Hydrochloride. The applications are submitted under Article 10(1) of Directive 2001/83/EC, as amended, a so-called 'generic' application. The application makes reference to the originator products: Lustral 50 and 100mg tablets, by Pfizer UK Ltd., which have had a license in the UK since 19/11/90.

The application is an abridged dossier. This is appropriate in the case of a generic application. Sertraline is well known, and in the case of a generic product containing a widely used, well known active substance, no further clinical trials are required and none are submitted by the applicant.

The applicant has submitted a single bioequivalence study in support of their application.

Sertraline is a potent and specific inhibitor of neuronal serotonin (5-HT) uptake *in vitro* and *in vivo*, but is without affinity for muscarinic, serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors. Sertraline is devoid of stimulant, sedative or anticholinergic activity or cardiotoxicity in animals.

Sertraline exhibits dose proportional pharmacokinetics over a range of 50-200mg. After oral administration of sertraline in man, peak blood levels occur at about 4.5 - 8.4 hours. Daily doses of sertraline achieve steady state after one week. Sertraline has a plasma half-life of approximately 26 hours with a mean half-life for young and elderly adults ranging from 22-36 hours. Sertraline is approximately 98% bound to plasma proteins. The principal metabolite, N-desmethylsertraline, is inactive in *in vivo* models of depression and has a half-life of approximately 62-104 hours. Sertraline and N-desmethylsertraline are both extensively metabolised in man and the resultant metabolites excreted in faeces and urine in equal amounts. Only a small amount (<0.2%) of unchanged sertraline is excreted in the urine.

2. INDICATIONS

The applicant has submitted the following:

Sertraline Tablets is indicated for the treatment of symptoms of depressive illness, including accompanying symptoms of anxiety. Following satisfactory response, continuation with Sertraline Tablets therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes, including accompanying symptoms of anxiety.

Sertraline Tablets is also indicated for the treatment of obsessive-compulsive disorder (OCD). Following initial response, Sertraline Tablets has been associated with sustained efficacy, safety and tolerability in up to two years treatment of OCD.

Sertraline Tablets is also indicated for the treatment of paediatric patients with OCD.

Clinical trials in PTSD demonstrated efficacy in female patients but no evidence of efficacy was seen in males. Treatment with Sertraline Tablets cannot normally

therefore be recommended for male patients with PTSD. A therapeutic trial in males might on occasion be justified, but treatment should subsequently be withdrawn unless there is clear evidence of therapeutic benefit.

Sertraline Tablets is not indicated for use in children and adolescents under the age of 18 years with Major Depressive Disorder.

In particular, controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline Tablets in the treatment of children and adolescents with Major Depressive Disorder (See sections 4.3, Contra-Indications and 4.8, Undesirable effects).

These are in line with the UK reference product and are satisfactory.

3. DOSE & DOSE SCHEDULE

These are consistent with those of the UK reference product and are therefore satisfactory.

4. CLINICAL PHARMACOLOGY

Randomised, 2-way, single dose, cross-over, bioequivalence study of the test Sertraline 100mg tablets versus the reference Lustral 100mg tablets in healthy adult male subjects under fasting conditions.

Study protocol

Male volunteers aged 18-51 years, were included in this study. Each subject received a single dose (100mg tablet) of one of the sertraline formulations. For each subject there were two dosing periods, with a washout period of 14 days. A randomisation scheme was included in the report. The following formulations were administered:

Test: Sertraline 100mg tablets (Lupin Ltd., Goa, India.)
Reference: Lustral 100mg tablets (Pfizer Ltd., UK.)

The reference is registered in UK. The tablet was administered with 240ml water following a >10hr fast. Standard meals were administered from 4 hours post-dose**.** Blood samples for analysis were taken pre dose and at 1, 2, 3, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 10, 14, 24, 48, 72, 96 and 120 hours following dosing. There followed a 21 day washout period before cross over and repeat.

Plasma samples were analysed for Sertraline concentration using a validated LC/MS/MS method. A validation report has been provided.

$AUC_{(0\text{-}t.)}$, $AUC_{(0\text{-}inf)}$, C_{max}, t_{max} and $t_{½}$ were calculated according normal standard procedures.
Statistical evaluation was performed for $AUC_{(0\text{-}t)}$, AUC_{inf} and C_{max} with ANOVA and the 90% confidence intervals for the ratio of test formulation over the reference formulation were calculated.

The study was conducted in accordance with GCP and GLP. The report is of good quality.

The 90% confidence intervals of the ratios for AUC_{0-t}, infinity and C_{max} were within the accepted limits of 80 – 125%:

Parameters (Units)	Geometric Least Squares Mean			90% Confidence Interval (Parametric)
	Reference Product-A	Test Product-B	Ratio (B / A)%	
C_{max} (ng / mL)	34.406	37.078	107.8	100.31 – 115.78%
AUC_{0-t} (ng.h / mL)	1170.545	1255.968	107.3	100.29 – 114.79%
$AUC_{0-\infty}$ (ng.h / mL)	1275.692	1361.406	106.7	99.98 – 113.92%

One subject (Subject 4) had a pre-dose Sertraline concentration greater than the lower limit of quantification at the start of the second dosing period. However, this was in isolation and there is no reason to suspect that the study protocol was deficient.

The multiple strengths exemption criterion for linear pharmacokinetics over the therapeutic range is met and the results form the bioequivalence study at the 100mg strength can be expected to apply to the 50mg strength tablet also:

a. The pharmacokinetics are linear

b. The qualitative composition is the same

c. The ratio between active substance and the excipients in both strengths of the test product is the same

d. The dissolution rate of the highest strength of the test product in-vitro is similar to that of the lower strength, and the dissolution rate of both of the strengths of the test product in vitro is similar to the dissolution rates of the corresponding strengths of the reference product.

The claim that the test Sertraline product is bioequivalent with the UK reference, Lustral, is accepted

5. EFFICACY

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

6. SAFETY

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

7. EXPERT REPORTS

A satisfactory expert report is provided by an appropriately qualified individual.

8. PATIENT INFORMATION LEAFLET (PIL)

The PIL is satisfactory.

9. LABELLING
Labelling is satisfactory.

10. APPLICATION FORM (MAA)
The MAAs are satisfactory.

11. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The proposed SPCs are in line with that of the UK reference product and are therefore satisfactory.

12. DISCUSSION
Bioequivalence to the reference product has been shown.

13. MEDICAL CONCLUSION
Marketing authorisations should be granted for these products.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Sertraline 50mg and 100mg Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

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

EFFICACY

Bioequivalence has been demonstrated between the applicant's Sertraline 100mg Tablets and the originator products Lustral 100mg Tablets (Pfizer Limited, UK). As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 100mg strength can be extrapolated to the 50mg strength tablets.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Lustral Tablets.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Extensive clinical experience with sertraline is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

SERTRALINE 50MG TABLETS (PL 20092/0020)
SERTRALINE 100MG TABLETS (PL 20092/0021)

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 1st March 2006
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 3rd March 2006
3	Following assessment of the applications, the MHRA requested further information relating to the quality dossiers on 5th July 2006 and 19th April 2007, on clinical dossier 12th September 2007
4	The applicant responded to the MHRA's requests, providing further information on 22nd October 2006 and 30th May 2007 and on the clinical dossier on 12th October 2007
5	The applications were determined on 23rd January 2008

SERTRALINE 50MG TABLETS (PL 20092/0020)
SERTRALINE 100MG TABLETS (PL 20092/0021)

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sertraline 50 mg Tablets
Sertraline 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Sertraline hydrochloride equivalent to 50 mg or 100 mg Sertraline. For Full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet

50 mg are blue coloured, capsule shaped, biconvex, film coated tablets debossed with '50' and breakline on one side and 'LUPIN' on the other side.

100mg are yellow coloured, capsule shaped, biconvex, film coated tablets debossed with '100' on one side and 'LUPIN' on the other side.

Sertraline 50 mg and 100 mg Tablets are designed with breakline; this breakline is only to facilitate breaking for ease of swallowing and not to divide it into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Sertraline Tablets is indicated for the treatment of symptoms of depressive illness, including accompanying symptoms of anxiety. Following satisfactory response, continuation with Sertraline Tablets therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes, including accompanying symptoms of anxiety.

Sertraline Tablets is also indicated for the treatment of obsessive-compulsive disorder (OCD). Following initial response, Sertraline Tablets has been associated with sustained efficacy, safety and tolerability in up to two years treatment of OCD.

Sertraline Tablets is also indicated for the treatment of paediatric patients with OCD.

Clinical trials in PTSD demonstrated efficacy in female patients but no evidence of efficacy was seen in males. Treatment with Sertraline Tablets cannot normally therefore be recommended for male patients with PTSD. A therapeutic trial in males might on occasion be justified, but treatment should subsequently be withdrawn unless there is clear evidence of therapeutic benefit.

Sertraline Tablets is not indicated for use in children and adolescents under the age of 18 years with Major Depressive Disorder.

In particular, controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline Tablets in the treatment of children and adolescents with Major Depressive Disorder (See sections 4.3, Contra-Indications and 4.8, Undesirable effects).

4.2 Posology and method of administration

Sertraline Tablets should be given as a single daily dose. Sertraline Tablets can be administered with or without food.

Adults

Depression (including accompanying symptoms of anxiety): The starting dose is 50mg daily and the usual antidepressant dose is 50mg daily. In some patients, doses higher than 50mg may be required.

Obsessive Compulsive Disorder: The starting dose is 50mg daily, and the therapeutic dose range is 50-200mg daily.

Post-Traumatic Stress Disorder: Treatment for PTSD should be initiated at 25mg/day. After one week, the dose should be increased to 50mg once daily.

PTSD is a heterogeneous illness and some patient groups fulfilling the criteria for PTSD do not appear to be responsive to treatment with Sertraline Tablets. Dosing should be reviewed periodically by the prescribing physician to determine response to therapy and treatment should be withdrawn if there is no clear evidence of efficacy.

Depression (including accompanying symptoms of anxiety), OCD and PTSD: In some patients doses higher than 50mg daily may be required. In patients with incomplete response but good toleration at lower doses, dosage adjustments should be made in 50mg increments over a period of weeks to a maximum of 200mg daily.

Once optimal therapeutic response is achieved the dose should be reduced, depending on therapeutic response, to the lowest effective level. Dosage during prolonged maintenance therapy should be kept at the lowest effective level, with subsequent adjustments depending on therapeutic response. The onset of therapeutic effect may be seen within 7 days, although 2-4 weeks (and even longer in OCD) are usually necessary for full activity. A longer treatment period, even beyond 12 weeks in some cases, may be required in the case of a therapeutic trial in PTSD.

Use in children aged 6-17 years
Treatment should only be *initiated* by specialists. The safety and efficacy of Sertraline Tablets has been established in paediatric OCD patients (aged 6-17). The administration of Sertraline Tablets to paediatric OCD patients (aged 13-17) should commence at 50 mg/day. Therapy for paediatric OCD patients (aged 6-12) should commence at 25mg/day increasing to 50mg/day after 1 week. Subsequent doses may be increased in case of lack of response in 50mg/day increments up to 200mg/day as needed.

However, the generally lower body weights of children compared to adults should be taken into consideration in advancing the dose from 50mg, in order to avoid excessive dosing. Given the 24 hour elimination half-life of sertraline, dose changes should not occur at intervals of less than 1 week.

The efficacy and safety of Sertraline Tablets in children and adolescents under the age of 18 years with Major Depressive Disorder have not been established. Controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline Tablets in the treatment of children and adolescents with Major Depressive Disorder (See sections 4.3, Contra-Indications and 4.8, Undesirable effects).

Children aged less than six years
Sertraline Tablets is not recommended in children under six years of age since safety and efficacy have not been established. See also 'Pharmacological Properties'.

Use in the elderly
No special precautions are required. The usual adult dose is recommended. Several hundred elderly patients have participated in clinical studies with Sertraline Tablets. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Sertraline Tablets are for oral administration only.

4.3 Contraindications
Sertraline Tablets is contra-indicated in patients with a known hypersensitivity to sertraline. Monoamine oxidase inhibitors: Cases of serious and sometimes fatal reactions have been reported in patients receiving an SSRI in combination with a monoamine oxidase inhibitor (MAOI), including the selective MAOI selegiline and the reversible MAOI (RIMA) moclobemide and in patients who have recently discontinued an SSRI and have been started on a MAOI.

Some cases presented with features resembling serotonin syndrome. Symptoms of a drug interaction with a MAOI include: hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes that include confusion, irritability and extreme agitation progressing to delirium and coma.

Sertraline Tablets should not be used in combination with a MAOI. Sertraline Tablets may be started 14 days after discontinuing treatment with an irreversible MAOI and at least one day after discontinuing treatment with the reversible MAOI (RIMA), moclobemide. At least 14 days should elapse after discontinuing Sertraline Tablets treatment before starting a MAOI or RIMA.

Use in hepatic impairment:
There is insufficient clinical experience in patients with significant hepatic dysfunction and accordingly Sertraline Tablets should not be used in such patients.

Concomitant use in patients taking pimozide is contra-indicated (see section 4.5 - Interaction with Other Medicaments and Other Forms of Interaction).

Sertraline
Tablets should not be used in children and adolescents under the age of 18 years with Major Depressive Disorder. (See section 4.8, Undesirable effects).

4.4 Special warnings and precautions for use

Monoamine oxidase inhibitors
See 'Contra-indications'.

Use in patients with renal or hepatic impairment
As with many other medications, sertraline should be used with caution in patients with renal and hepatic impairment (see 'Contra-indications').

Since sertraline is extensively metabolised, excretion of unchanged drug in urine is a minor route of elimination. In patients with mild to moderate renal impairment (creatinine clearance 20-50ml/min) or severe renal impairment (creatinine clearance <20ml/min), single dose pharmacokinetic parameters were not significantly different compared with controls. However, steady state pharmacokinetics of sertraline have not been adequately studied in this patient population and caution is advised when treating patients with renal impairment. Sertraline is extensively metabolised by the liver. A multiple dose pharmacokinetic study in subjects with mild, stable cirrhosis demonstrated a prolonged elimination half-life and approximately three-fold greater AUC and C_{max} in comparison with normal subjects. There were no significant differences in plasma protein binding observed between the two groups. The use of sertraline in patients with hepatic disease should be approached with caution. A lower or less frequent dose should be used in patients with hepatic impairment.

Diabetes
In patients with diabetes, treatment with an SSRI may alter glycaemic control, possibly due to improvement of depressive symptoms. Insulin and/or oral hypoglycaemic dosage may be needed to be adjusted.

Seizures
Seizures are a potential risk with antidepressant or antiobsessional drugs. The drug should be discontinued in any patient who develops seizures. Sertraline Tablets should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Sertraline Tablets should be discontinued if there is an increase in seizure frequency.

Electroconvulsive therapy (ECT)
Since there is little clinical experience of concurrent administration of Sertraline Tablets and ECT, caution is advisable.

Mania

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

Suicide
As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored during this period. The possibility of a suicide attempt is inherent in depression and may persist until significant therapeutic effect is achieved and it is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Haemorrhage
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 tricyclic antidepressants, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs)) as well as in patients with a history of bleeding disorders.

Use in the elderly
Several hundred elderly patients have participated in clinical studies with Sertraline Tablets. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Use in Children more than 250 paediatric
OCD patients have been exposed to Sertraline Tablets in completed and ongoing studies. The safety profile of Sertraline Tablets in these paediatric studies is comparable to that observed in the adult OCD studies. The efficacy of Sertraline Tablets in paediatric patients with depression or panic disorder has not been demonstrated in controlled trials. Safety and effectiveness in paediatric patients below the age of 6 have not been established.

There is limited knowledge with respect to an effect on sexual development in children.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors See 'Contra-indications'.
Centrally active medication Caution is advised if Sertraline Tablets is administered with other centrally active medication. In particular, SSRIs have the potential to interact with tricyclic antidepressants leading to an increase in plasma levels of the tricyclic antidepressant. A possible mechanism for this interaction is the inhibitory effect of SSRIs on the CYP2D6 isoenzyme. There is variability among the SSRIs in the extent to which they inhibit the activity of CYP2D6. The clinical significance of this depends on the extent of inhibition and the therapeutic index of the co-administered drug. In formal interaction studies, chronic dosing with sertraline 50mg daily showed minimal elevation (mean 23-37%) of steady state plasma desipramine levels (a marker of CYP2D6 isoenzyme activity).

Pimozide– Increased pimozide levels have been demonstrated in a study of a single low dose pimozide (2mg) with sertraline co administration. These increased levels were not associated with any changes in ECG. While the mechanism of this interaction is unknown, due to the narrow therapeutic index of pimozide, concomitant of pimozide and sertraline is contra-indicated.

Alcohol In 11 healthy subjects administered Sertraline Tablets (200mg daily) for 9 days, there was no adverse effect on cognitive or psychomotor performance relative to placebo, following a single dose of 500mg/kg alcohol. However, the concomitant use of Sertraline Tablets and alcohol in depressed patients is not recommended.

Lithium and Tryptophan In placebo-controlled trials in normal volunteers, the co-administration of Sertraline Tablets and lithium did not significantly alter lithium pharmacokinetics.

Co-administration of Sertraline Tablets with lithium did result in an increase in tremor relative to placebo, indicating a possible pharmacodynamic interaction. There have been other reports of enhanced effects when SSRIs have been given with lithium or tryptophan and therefore the concomitant use of SSRIs with these drugs should be undertaken with caution.

Serotonergic drugs There is limited controlled experience regarding the optimal timing of switching from other antidepressant or anti-obsessional drugs to Sertraline Tablets. Care and prudent medical judgment should be exercised when switching, particularly from long-acting agents. The duration of washout period which should intervene before switching from one selective serotonin reuptake inhibitor (SSRI) to another has not been established.

Until further data are available, serotonergic drugs, such as tramadol, sumatriptan or fenfluramine, should not be used concomitantly with Sertraline Tablets, due to a possible enhancement of 5-HT associated effects.

St John's Wort Concomitant use of the herbal remedy St John's wort (Hypericum perforatum) in patients receiving SSRIs should be avoided since there is a possibility of serotonergic potentiation.

Drugs that affect platelet function, such as NSAIDs See 'Special warnings and special precautions for use (Haemorrhage)'.

Other drug interactions Since Sertraline Tablets is bound to plasma proteins, the potential of Sertraline Tablets to interact with other plasma protein bound drugs should be borne in mind.

Formal drug interaction studies have been performed with Sertraline Tablets. Co-administration of Sertraline Tablets (200mg daily) with diazepam or tolbutamide resulted in small, statistically significant changes in some pharmacokinetic parameters.

Co-administration with cimetidine caused a substantial decrease in sertraline clearance. The clinical significance of these changes is unknown. Sertraline Tablets had no effect on the beta-adrenergic blocking ability of atenolol. No interaction with Sertraline Tablets (200mg daily) was observed with glibenclamide or digoxin.

Co-administration of Sertraline Tablets (200mg daily) with warfarin resulted in a small but statistically significant increase in prothrombin time, the clinical significance of which is unknown. Accordingly, prothrombin time should be carefully monitored when Sertraline Tablets therapy is initiated or stopped.

Sertraline Tablets (200mg daily), did not potentiate the effects of carbamazepine, haloperidol or phenytoin on cognitive and psychomotor performance in healthy subjects.

4.6 Pregnancy and lactation

Pregnancy

Although animal studies did not provide any evidence of teratogenicity, the safety of Sertraline Tablets during human pregnancy has not been established. As with all drugs Sertraline Tablets should only be used in pregnancy if the potential benefits of treatment to the mother outweigh the possible risks to the developing foetus.

Lactation

Sertraline is known to be excreted in breast milk. Its effects on the nursing infant have not yet been established. If treatment with Sertraline Tablets is considered necessary, discontinuation of breast-feeding should be considered.

4.7 Effects on ability to drive and use machines

Clinical pharmacology studies have shown that Sertraline Tablets has no effect on psychomotor performance. However, since antidepressant or antiobsessional drugs may impair the abilities required to perform potentially hazardous tasks such as driving a car or operating machinery, the patient should be cautioned accordingly. Sertraline Tablets should

not be administered with benzodiazepines or other tranquillizers in patients who drive or operate machinery

4.8 Undesirable effects

Side-effects which occurred significantly more frequently with sertraline than placebo in multiple dose studies were: nausea, diarrhoea/loose stools, anorexia, dyspepsia, tremor, dizziness, insomnia, somnolence, increased sweating, dry mouth and sexual dysfunction (principally ejaculatory delay in males).
The side-effect profile commonly observed in double-blind, placebo-controlled studies in patients with OCD and PTSD was similar to that observed in patients with depression.

In paediatric OCD patients, side effects which occurred significantly more frequently with sertraline than placebo were: headache, insomnia, agitation, anorexia, and tremor. Most were of mild to moderate severity.

Post-marketing spontaneous reports include the following:

Cardiovascular Blood pressure disturbances including postural hypotension, tachycardia.

Eye disorders Abnormal vision.

Gastro-intestinal Vomiting, abdominal pain.

Nervous system Amnesia, headache, drowsiness, movement disorders, paraesthesia, hypoaesthesia, depressive symptoms, hallucinations, aggressive reaction, agitation, anxiety, psychosis, depersonalisation, nervousness, panic reaction and signs and symptoms associated with serotonin syndrome which include fever, rigidity, confusion, agitation, diaphoresis, tachycardia, hypertension and diarrhoea.

There have also been reports of manic reaction, although this phenomenon may be part of the underlying disease.

Convulsions (Seizures) Sertraline Tablets should be discontinued in any patient who develops seizures (See 'Special warnings and special precautions for use').

Musculoskeletal Arthralgia, myalgia.

Hepatic/pancreatic Rarely, pancreatitis and serious liver events (including hepatitis, jaundice and liver failure). Asymptomatic elevations in serum transaminases (SGOT and SGPT) have been reported in association with sertraline administration (0.8 – 1.3%), with an increased risk associated with the 200mg daily dose. The abnormalities usually occurred within the first 1 to 9 weeks of drug treatment and promptly diminished upon drug discontinuation.

Renal & urinary disorders Urinary retention.

Reproductive Hyperprolactinemia, galactorrhoea, menstrual irregularities, anorgasmy.

Skin and allergic reactions Rash (including rare reports of erythema multiforme, photosensitivity), angioedema, ecchymoses, pruritus and anaphylactoid reactions.

Metabolic Rare cases of hyponatremia have been reported and appeared to be reversible when sertraline 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 other medications.

Haematologic There have been rare reports of altered platelet function and/or abnormal clinical laboratory results in patients taking sertraline. While there have been reports of thrombocytopenia, abnormal bleeding or purpura in several patients taking sertraline, it is

unclear whether sertraline had a causative role. See also 'Special warnings and special precautions for use'.

General Malaise.

Other Withdrawal reactions have been reported with Sertraline Tablets. Common symptoms include dizziness, paraesthesia, headache, anxiety and nausea. Abrupt discontinuation of treatment with Sertraline Tablets should be avoided. The majority of symptoms experienced on withdrawal of Sertraline Tablets are non-serious and self-limiting.

Adverse events from paediatric clinical trials
In paediatric clinical trials in depression the following adverse events were reported at a frequency of at least 2% of patients and occurred at a rate of at least twice that of placebo: dry mouth (2.1% vs 0.5%), hyperkinesia (2.6% vs 0.5%), tremor (2.1% vs 0%), diarrhoea (9.5% vs 1.6%), vomiting (4.2% vs 1.1%), agitation (6.3% vs 1.1%), anorexia (5.3% vs 1.1%) and urinary incontinence (2.1% vs 0%).

Suicidal thoughts and suicide attempts were mainly observed in clinical trials with Major Depressive Disorder.

4.9 Overdose

On the evidence available, Sertraline Tablets has a wide margin of safety in overdose. Overdoses of Sertraline Tablets alone of up to 8g have been reported. Deaths involving overdoses of Sertraline Tablets in combination with other drugs and/or alcohol have been reported. Therefore, any overdosage should be treated aggressively.

Symptoms of overdose include serotonin-mediated side effects such as somnolence, gastrointestinal disturbances (such as nausea and vomiting), tachycardia, tremor, agitation and dizziness. Less frequently reported was coma.

No specific therapy is recommended and there are no specific antidotes to Sertraline Tablets. Establish and maintain an airway, ensure adequate oxygenation and ventilation. Activated charcoal, which may be used with sorbitol, may be as or more effective than emesis or lavage, and should be considered in treating overdose. Cardiac and vital signs monitoring is recommended along with general symptomatic and supportive measures. Due to the large volume of distribution of sertraline, forced diuresis, dialysis, haemoperfusion and exchange transfusion are unlikely to be of benefit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Sertraline is a potent and specific inhibitor of neuronal serotonin (5-HT) uptake *in vitro* and *in vivo*, but is without affinity for muscarinic, serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors.

Sertraline is devoid of stimulant, sedative or anticholinergic activity or cardiotoxicity in animals.

Unlike tricyclic antidepressants, no weight gain is observed with treatment for depression.

Sertraline Tablets has not been observed to produce physical or psychological dependence. Sertraline Tablets has been evaluated in paediatric OCD patients aged 6 to 17 in a 12 week placebo-controlled study. Therapy for paediatric OCD patients (aged 6-12) commenced at 25mg/day increasing to 50mg/day after 1 week. Side effects which occurred significantly more frequently with sertraline than placebo were: headache, insomnia, agitation [6-12 years]; insomnia, anorexia, tremor [13-17 years]. There is limited evidence of efficacy and safety beyond 12 weeks of treatment.

5.2 Pharmacokinetic properties

Sertraline exhibits dose proportional pharmacokinetics over a range of 50-200mg. After oral administration of sertraline in man, peak blood levels occur at about 4.5 - 8.4 hours. Daily

doses of sertraline achieve steady state after one week. Sertraline has a plasma half-life of approximately 26 hours with a mean half-life for young and elderly adults ranging from 22-36 hours. Sertraline is approximately 98% bound to plasma proteins. The principal metabolite, N-desmethylsertraline, is inactive in *in vivo* models of depression and has a half-life of approximately 62-104 hours. Sertraline and N-desmethylsertraline are both extensively metabolised in man and the resultant metabolites excreted in faeces and urine in equal amounts. Only a small amount (<0.2%) of unchanged sertraline is excreted in the urine.

The pharmacokinetics of sertraline in paediatric OCD patients have been shown to be comparable with adults (although paediatric patients metabolise sertraline with slightly greater efficiency). However, lower doses may be advisable for paediatric patients given their lower body weights (especially 6-12 years), in order to avoid excessive plasma levels.

A clear relationship between sertraline concentration and the magnitude of therapeutic response has not been established.

The pharmacokinetics of sertraline in elderly patients are similar to younger adults.
Food does not significantly change the bioavailability of Sertraline Tablets tablets.

5.3 Preclinical safety data

Extensive chronic safety evaluation studies in animals show that sertraline is generally well tolerated at doses that are appreciable multiples of those that are clinically effective.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sertraline tablets include the following ingredients:
Tablet cores:
Calcium hydrogen phosphate anhydrous (E 341)
Microcrystalline cellulose (E460)
Hydroxypropylcellulose (E463)
Sodium starch glycolate
Magnesium stearate
Film coating: in 50 mg
- Opadry blue
Hydroxy Propyl methyl cellulose (E464)
Titanium dioxide (E171)
Macragol
Polysorbate 80 (E433)
FD&C Blue#2/Indigo Carmine Aluminum Lake (E132)

Film coating: in 100 mg
- Opadry Yellow
Hydroxy Propyl methyl cellulose (E464)
Titanium dioxide (E171)
Macragol
Iron oxide Yellow (E172)
Polysorbate 80 (E433)

6.2 Incompatibilities

None.

6.3 Shelf life

2 years

6.4 Special precautions for storage

None

6.5 Nature and contents of container

Sertraline Tablets is available as:

Calendar packs of 28 tablets Opaque white PVC/PVDC/ Aluminium blister strips, 14 tablets/strip, and 2 strips in a carton.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Lupin (Europe) Limited
Victoria Court
Bexton Road
Knutsford
Cheshire WA16 0PF
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
Sertraline 50mg Tablets PL 20092 /0020
Sertraline 100mg Tablets PL 20092/0021

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
23/01/2008

10 DATE OF REVISION OF THE TEXT
23/01/2008

PATIENT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET SERTRALINE 50 mg & 100 mg TABLETS

Read all of this leaflet carefully before you start taking this medicine. It is an important source of information about your medicine and how to take it safely.

Even if this medicine is a repeat prescription, some of the information may have changed.

- 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 on this leaflet, please tell your doctor or pharmacist.

Is this leaflet hard for you to see or **read, phone XXXXXX**

In This Leaflet:

1. What Sertraline Tablets are and what they are used for.
2. Before you take Sertraline Tablets.
3. How to take this medicine.
4. Possible side effects.
5. How to store this medicine.
6. Further information.

1. WHAT SERTRALINE TABLETS ARE AND WHAT THEY ARE USED FOR.

The **active** ingredient in Sertraline Tablets is Sertraline. This belongs to a group of medicines of antidepressant or antiobsessional drugs called the Selective Serotonin Re-uptake Inhibitors (SSRIs).

For the **other** ingredients, see Section **6.**

These tablets are prescribed

- To treat depression
- To treat Obsessive Compulsive Disorder (OCD) or Post Traumatic Stress Disorder (PTSD)
- To treat OCD in children 6 years of age & over
- To treat the anxiety, which accompany depression
- To treat PTSD, PTSD is a condition that can occur after a very emotionally traumatic experience, and has some symptoms that are similar to depression and anxiety

2. BEFORE YOU USE SERTRALINE TABLETS

Do not use Sertraline Tablets if:

- you are **allergic** (hypersensitive) to
  - the active substance Sertraline
  - any of the other ingredients, (see Section **6** for a list of these.)
- you have liver problems
- you are or have taken in the last two weeks, any medicines called monoamine oxidase inhibitors (MAOIs for short)?
- you are a child under 6 years old who suffers from obsessive-compulsive disorder symptoms?
- you are under 18 years old and suffering from depression
- you are taking a medicine called pimozide

Check with your doctor if you are not sure.

Take special care with Sertraline Tablets

Make sure your doctor knows if:

- you are pregnant or think you might be pregnant
- you are breast feeding
- you have kidney problems
- you are diabetic
- you ever had an epileptic fit
- you are a child under 16 years old who suffers from panic symptoms
- you are being treated with electroconvulsive therapy (ECT)
- you intend to drink alcohol when taking this medicine
- you intend to drive or use machinery whilst taking this medicine
- you have a history of bleeding disorders

Check with your doctor, if you are not sure.

Using other medicines

Make sure your doctor knows, if you are taking:

- any other medication for your illness, e.g. lithium, or another antidepressant or antiobsessional drug
- Tryptophan, sumatriptan, fenfluramine, warfarin,

diazepam, tolbutamide or cimetidine
- you are taking aspirin or other pain killers known as NSAIDs (Non-Steroidal Anti-inflammatory Drugs) or another stronger painkiller called Tramadol

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

Pregnancy

Do not use Sertraline Tablets if you are pregnant, trying to become pregnant or think you may be pregnant. If you become pregnant while using Sertraline Tablets, **stop** taking them **immediately and contact your doctor.**

Breast-feeding

Do **not** use Sertraline Tablets if you are breast-feeding. If you are breast-feeding while using Sertraline Tablets, **stop** taking them **immediately and contact your doctor.**

Children (under 18 years)

The efficacy and safety of Sertraline Tablets in children and adolescents under the age of 18 years with Major Depressive Disorder have not been established. Controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline Tablets in the treatment of children and adolescents with Major Depressive Disorder.

Children aged less than six years Sertraline Tablets is not recommended in children under six years of age since safety and efficacy have not been established.

The elderly (65 and over)

Use in the elderly No special precautions are required. The usual adult dose is recommended. Several hundred elderly patients have participated in clinical studies with Sertraline Tablets. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Driving and using machinery

Clinical pharmacology studies have shown that Sertraline Tablets have no effect on psychomotor performance. However, since antidepressant or antiobsessional drugs may impair the abilities required to perform potentially hazardous tasks such as driving a car or operating machinery, these should be undertaken with caution. Sertraline Tablets should not be administered with benzodiazepines or other tranquillizers in patients who drive or operate machinery.

3. HOW TO TAKE SERTRALINE TABLETS

Sertraline Tablets should only be taken by mouth.
The usual dose of Sertraline Tablets is 50mg taken once a day.
Doctors sometimes prescribe a higher dose, up to a maximum of 200mg daily. The label on the pack will tell you what dose you should take. If you are still not sure, ask your doctor or pharmacist.
Treatment should only be initiated by specialists.
The safety and efficacy of Sertraline Tablets has been established in paediatric OCD patients (aged 6-17).

- The administration of Sertraline Tablets to paediatric OCD patients (aged 13-17) should commence at 50-mg/day.
- Therapy for paediatric OCD patients (aged 6-12) should commence at 25mg/day increasing to 50mg/day after 1 week. Subsequent doses may be increased in case of lack of response in 50mg/day increments up to 200mg/day as needed.

However, the generally lower body weight of children compared to adults should be taken into consideration in advancing the dose from 50mg, in order to avoid excessive dosing. Given the 24-hour elimination half-life of Sertraline, dose changes should not occur at intervals of less than 1 week.

- Swallow your tablets whole with a drink of water.
- It is best to take them at the same time each day, with or without a meal.
- Do not crush or chew your tablet.
- Keep taking your tablets every day. The day is written on the pack to help you remember.

If you take more Sertraline Tablets than you should

If you take too many TABLETS, tell your doctor **immediately.** If you are unable to contact your doctor go to your local hospital casualty department at once.

If you forget to take Sertraline Tablets

Do not worry. If you forget to take a tablet, do not take that tablet. Just take the next tablet at the right time.
Do not take more tablets at once than your doctor told you.

If you stop taking this medicine

Always check with your doctor before you stop

taking this medicine.

How quickly will the treatment start to work?

- You may need to take Sertraline Tablets for 2-4 weeks before you start to feel better. Your doctor will want to monitor your progress closely during this period.
- You must keep taking Sertraline Tablets to help you get better.
- See your doctor before your tablets run out.
- Even if you begin to feel better, keep taking your tablets. You may need to keep taking them to stay well.

Thoughts of suicide or self harm can be part of your illness and may even occur or increase as you start to get better. This should improve as your treatment continues. Tell your doctor immediately if you have any distressing thoughts or experiences.

What if you do not feel better?

Tell your doctor if - you have taken all your tablets and you still feel unwell: or
- you feel worse

4. POSSIBLE SIDE EFFECTS

SERTRALINE TABLETS may cause some undesirable effects.
Most undesirable effects are usually mild and tend to wear off as you take the tablets for longer.
If they cause you discomfort or are long lasting, check with your doctor or pharmacist.

Undesirable effects are:

- Dry mouth
- Feeling or being sick
- Loss of appetite
- Upset stomach
- Diarrhoea
- Abdominal pain
- Shaky feeling (tremor)
- Sweating
- Change in sex drive or function e.g. ejaculatory delay, inability to experience orgasm.
- Dizziness
- Not being able to sleep
- Excessive sleepiness
- Indigestion

Other effects include:

- Effects on the nervous system, such as headache, tingling, numbness or uncontrollable twitching, jerking or writhing movements (these are more likely if you already experience such effects).
- Convulsions. You should tell your doctor immediately if you experience convulsions.
- Psychological effects, such as confusion, amnesia, agitation, aggression, mania/hypomania, hallucinations, nervousness, panic reaction, reduced ability to react normally to everyday situations, loss of feeling of identity and effects associated with depression: anxiety and crying.
- Cardiovascular effects, including rapid heart beat and changes to blood pressure, including low blood pressure/dizziness on standing.
- Urinary and reproductive effects, such as not being able to pass water, menstrual irregularities and increases in the hormone prolactin, which could lead to symptoms such as abnormal production of breast milk or breast enlargement.
- Effects on the skin, including easy bruising, skin rash, itching and sensitivity to sunlight.

  Other effects include the following: fever, rigidity, abnormal vision, a vague feeling of being unwell, tiredness, joint or muscle pain. Abnormalities in liver function tests and rarely jaundice, inflammation of the pancreas or liver, or liver failure. Also abnormal bleeding and lower sodium content of the blood. Abnormal blood tests have been reported.

- Symptoms such as dizziness, tingling, headache, anxiety and nausea may occur if Sertraline Tablets treatment is stopped too quickly. These symptoms are generally non-serious and disappear within a few days. If you experience symptoms on stopping treatment, contact your doctor.

All medicines can cause allergic reactions. Serious allergic reactions are very rare. Any sudden wheeziness, difficulty in breathing, swelling, rash or itching (especially affecting the whole body) should be reported to the doctor.

Tell your doctor straight away if you get any of these effects, or any other discomfort you do not understand.

Undesirable effects, which occur most commonly in children treated for Obsessive Compulsive disorder, are: headache, anorexia, tremor, insomnia and agitation.

When children and adolescents under 18 years of age with depression have been given Sertraline Tablets in clinical trials the most common side-effects affecting

at least 2 in 100 patients were: dry mouth, hyperactivity, tremor, diarrhoea, vomiting, agitation, loss of appetite and loss of bladder control. Thoughts of suicide and attempting suicide were mainly seen in the trials involving children and adolescents who were depressed.

5. HOW TO STORE SERTRALINE TABLETS

Keep all medicines out of the reach and sight of children. Store below 30°C.

Disposal

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.

6. FURTHER INFORMATION

What Sertraline Tablets contain

The active ingredient is Sertraline 50 mg and 100 mg. Sertraline tablets include the following ingredients:

Tablet cores:

Calcium hydrogen phosphate anhydrous (E 341)
Microcrystalline cellulose (E460)
Hydroxypropylcellulose (E463)
Sodium starch glycolate
Magnesium stearate

Film coating in 50 mg

Opadry blue

- Hydroxy Propyl methyl cellulose (E464)
- Titanium dioxide (E171)
- Macragol
- Polysorbate 80 (E433)
- FD&C Blue#2/Indigo Carmine Aluminum Lake (E132)

Film coating in 100 mg

Opadry yellow

- Hydroxy Propyl methyl cellulose (E464)
- Titanium dioxide (E171)
- Macragol
- Iron oxide (E172)
- Polysorbate 80 (E433)

What Sertraline Tablets look like and the contents of the pack

Sertraline Tablets are available in two strengths.

- Sertraline 50 mg Tablets (Blue coloured)
- Sertraline 100 mg Tablets (Yellow coloured)

Sertraline Tablets is available in blister (calendar) packs of 28 tablets.

Product Licence Holder and supplier of your medicine:
Lupin (Europe) Limited,
Victoria Court,
Bexton Road,
Knutsford, Cheshire, WA16 OPF
United Kingdom
Tel.: + 44 (0) 1565 751378.

Manufacturer

The Manufacturer is:
LUPIN LIMITED,
15 B, Phase 1A,
Verna Industrial Area, Verna,
Goa 403722,
India.

This leaflet was last approved in

How can you obtain more information about Sertraline Tablets?

This leaflet gives you only some of the most important information about Sertraline Tablets. If you have any questions after you have read it, ask your doctor or pharmacist, who will give you further information.

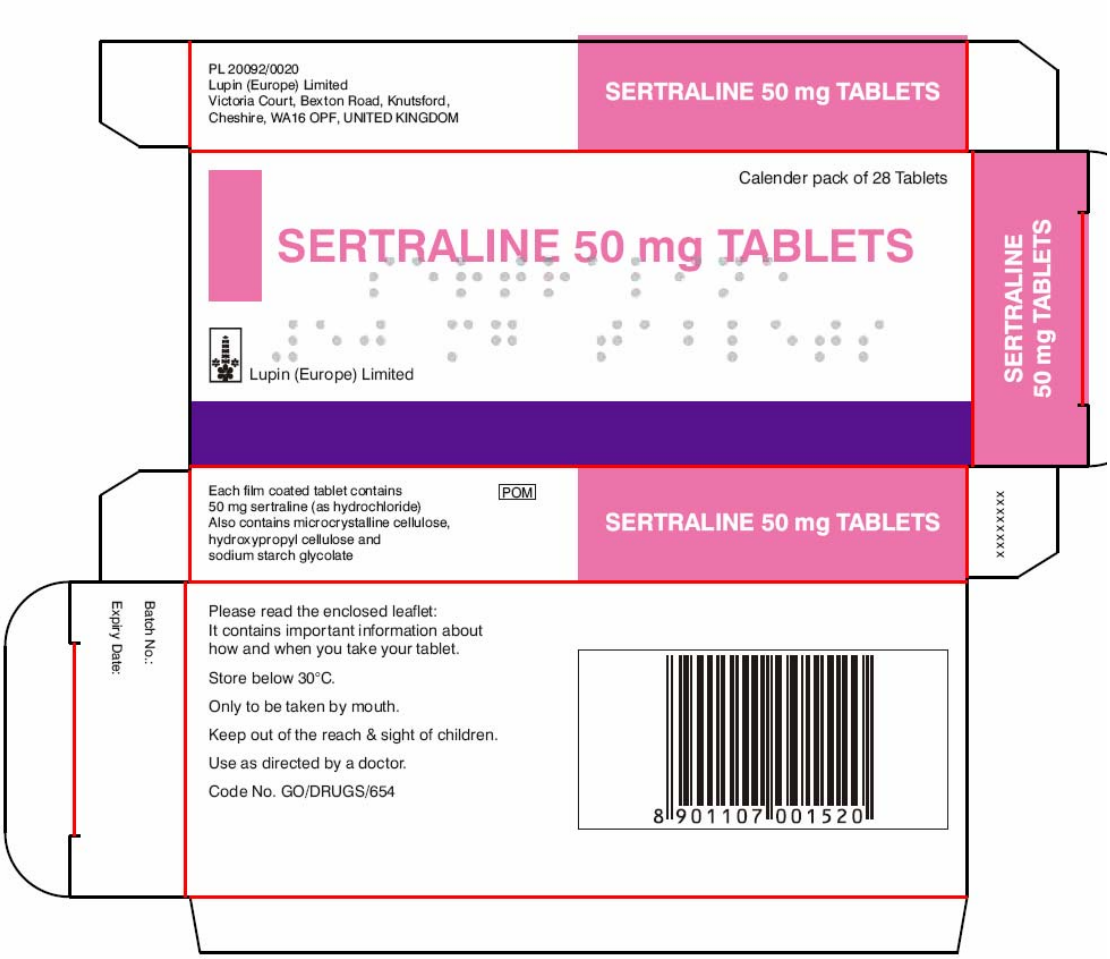
Further information and advice is also available from the following organisations:

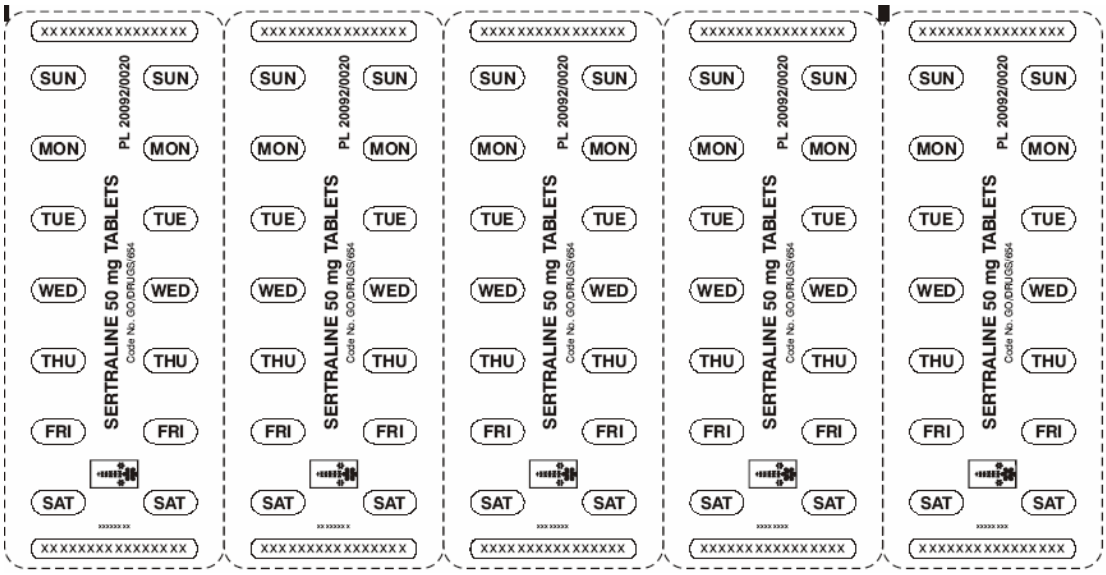
United Kingdom:

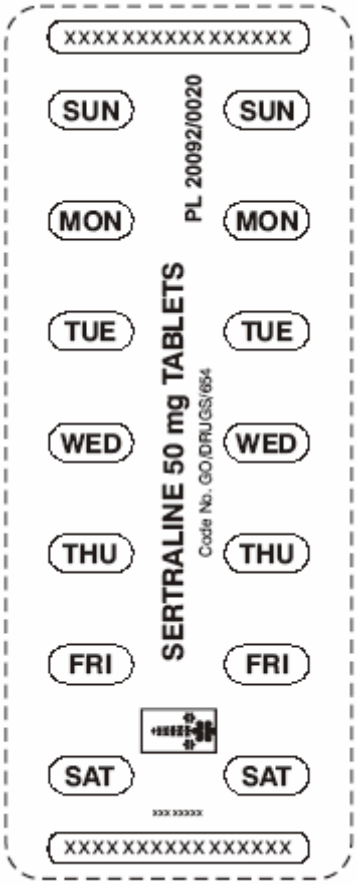
Lupin (Europe) Limited,
Victoria Court,
Bexton Road,
Knutsford,
Cheshire, WA16 OPF
United Kingdom.
Telephone: 01565 751378

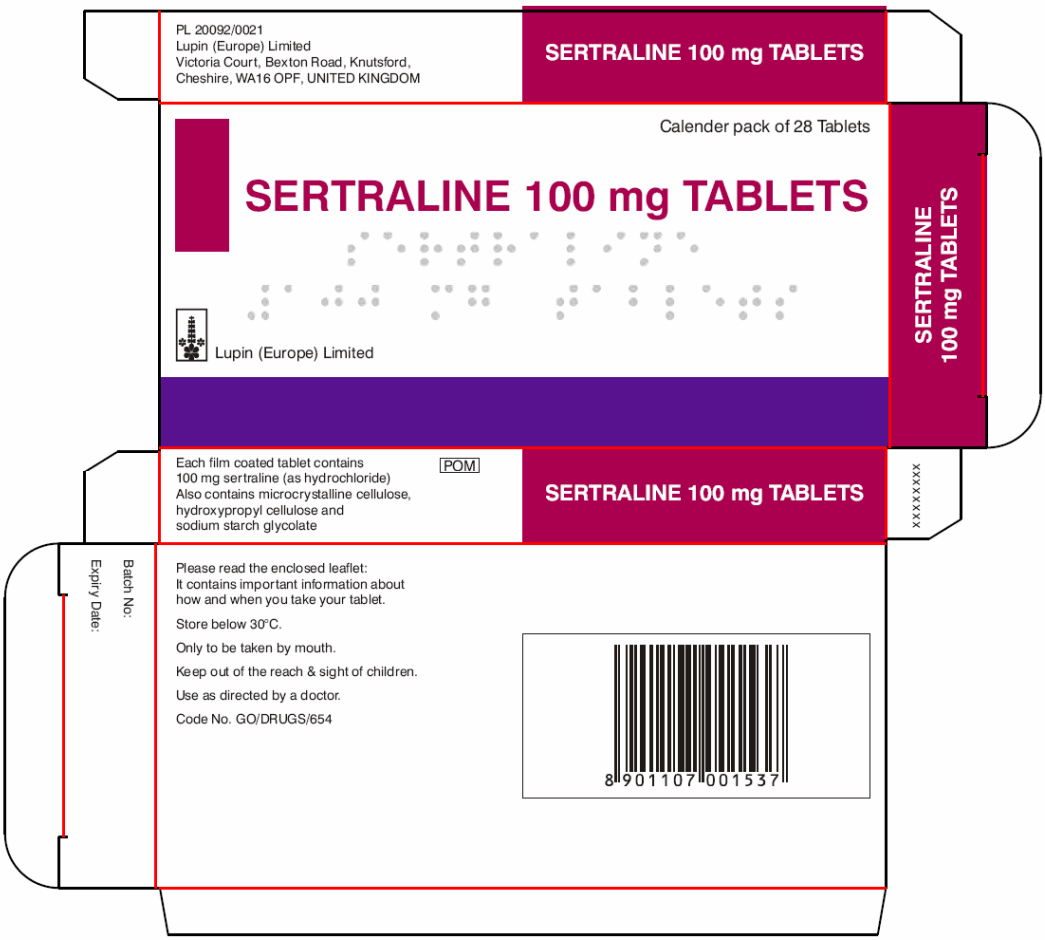
Date of preparation: December 2007.

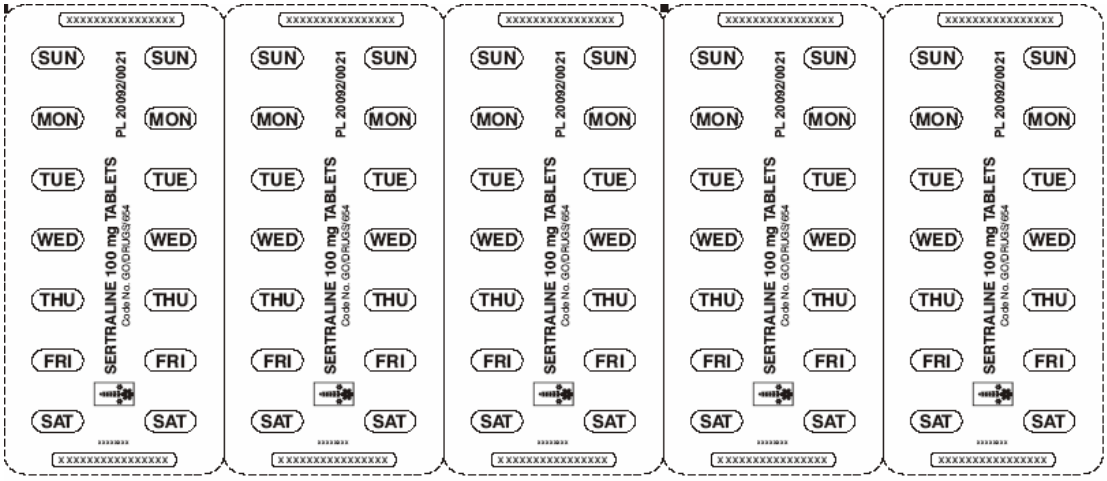
LABELLING

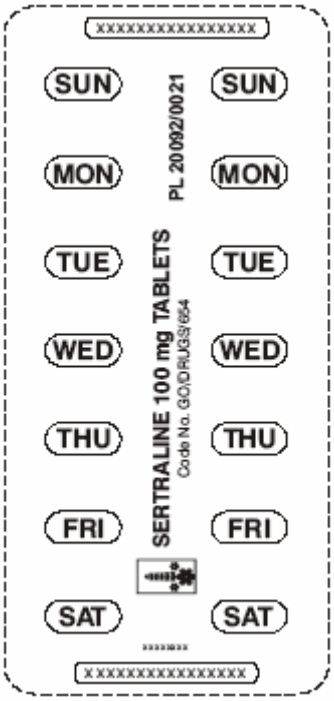

PL 20092/0020
Lupin (Europe) Limited
Victoria Court, Bexton Road, Knutsford,
Cheshire, WA16 OPF, UNITED KINGDOM
SERTRALINE 50 mg TABLETS
Calender pack of 28 Tablets
SERTRALINE 50 mg TABLETS
Lupin (Europe) Limited
SERTRALINE 50 mg TABLETS
Each film coated tablet contains
50 mg sertraline (as hydrochloride)
Also contains microcrystalline cellulose,
hydroxypropyl cellulose and
sodium starch glycolate
POM
SERTRALINE 50 mg TABLETS
xxxxxxxx
Batch No.:
Expiry Date:
Please read the enclosed leaflet:
It contains important information about
how and when you take your tablet.
Store below 30°C.
Only to be taken by mouth.
Keep out of the reach & sight of children.
Use as directed by a doctor.
Code No. GO/DRUGS/654
8 901107 001520


xxxxxxxxxxxxxxx
SUN
MON
TUE
WED
THU
FRI
SAT
PL 20092/0020
SERTRALINE 50 mg TABLETS
Code No. GO/DRUGS/654


XXXXXXXXXXXXXXXX
SUN
MON
TUE
WED
THU
FRI
SAT
SERTRALINE 50 mg TABLETS
PL 20092/0020
Code No. GO/DRUGS/654
SUN
MON
TUE
WED
THU
FRI
SAT
XXXXXXXXXXXXXXXX


PL 20092/0021
Lupin (Europe) Limited
Victoria Court, Bexton Road, Knutsford,
Cheshire, WA16 OPF, UNITED KINGDOM
SERTRALINE 100 mg TABLETS
Calender pack of 28 Tablets
SERTRALINE 100 mg TABLETS
Lupin (Europe) Limited
SERTRALINE
100 mg TABLETS
Each film coated tablet contains
100 mg sertraline (as hydrochloride)
Also contains microcrystalline cellulose,
hydroxypropyl cellulose and
sodium starch glycolate
POM
SERTRALINE 100 mg TABLETS
xxxxxxxx
Batch No:
Expiry Date:
Please read the enclosed leaflet:
It contains important information about
how and when you take your tablet.
Store below 30°C.
Only to be taken by mouth.
Keep out of the reach & sight of children.
Use as directed by a doctor.
Code No. GO/DRUGS/654
8 901107 001537


SUN
MON
TUE
WED
THU
FRI
SAT
PL 20092/0021
SERTRALINE 100 mg TABLETS
Code No. GO/DRUGS/654


xxxxxxxxxxxxxxxx
SUN
MON
TUE
WED
THU
FRI
SAT
SERTRALINE 100 mg TABLETS
Code No. GO/DRUGS/654
PL 20092/0021
SUN
MON
TUE
WED
THU
FRI
SAT
xxxxxxxxxxxxxxxx