SERTRALINE 50 MG TABLETS AND SERTRALINE 100 MG TABLETS

PL 27583/0002-3

UKPAR

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SERTRALINE 50 MG TABLETS AND SERTRALINE 100 MG TABLETS

PL 27583/0002-3

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Marketing Authorisations (licences) for the medicinal products Sertraline 50 mg tablets and Sertraline 100 mg tablets (PL 27583/0002-3). These tablets are available by prescription only and are used to treat depression, obsessive compulsive disorder (OCD) or post traumatic stress disorder (PTSD) in adults. Sertaline is also used to treat OCD in children of 6 six years old and older.

Sertraline 50 mg tablets and Sertraline 100 mg tablets contain the active ingredient sertraline hydrochloride, which acts on nerve cells in the brain helping to control the behaviour associated with depression, OCD or PTSD.

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

SERTRALINE 50 MG TABLETS AND SERTRALINE 100 MG TABLETS

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Marketing authorisations for Sertraline 50 mg tablets and Sertraline 100 mg tablets (PL 24590/0001-2) were granted to Reg Europe Sarl on 19 September 2006. Following a change of ownership on 11 April 2007, these licences were transferred to Apotex Europe B.V. and the product licence numbers were consequently changed to PL 27583/0003 for the Sertraline 50 mg tablets and PL 27583/0002 for Sertraline 100 mg tablets.

These applications were submitted as generic applications according to Article 10.1 of EC Directive 2001/83. The cross reference product is Lustral 50 mg and 100 mg tablets (PL 00057/0308-9), marketed by Pfizer Ltd and granted a marketing authorisation on 19 November 1990.

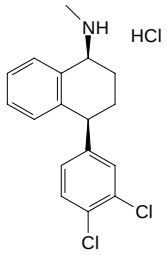
No new data was submitted, nor was it necessary for these standard applications as the data is identical to that of the previously granted cross-reference products. As the cross-reference products were licensed prior to the introduction of current legislation, no Public Assessment Reports (PAR) were generated for them.

PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

Sertraline Hydrochloride

Structure:



INN: Sertraline hydrochloride (Form-II)

Chemical names:

i. (1*S*-*cis*)-4-(3,4-chlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthalenamine hydrochloride
ii. *cis*-(1*S*,4*S*)-*N*-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenamine hydrochloride
iii. *cis*-(1S)-*N*-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenamine hydrochloride
iv. 1-naphthalenamine, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl, hydrochloride, (1*S*-*cis*)-
v. (1*S*,4*S*)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthylamine hydrochloride

Description: White or almost white crystalline powder

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

Relative molecular mass: 342.7

Polymorphism: Form I, II, III and IV
Characterised by X-ray powder diffraction and DSC)

Chiralty: (+)-enantiomer

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated in accordance with ICH guidelines and are satisfactory for ensuring compliance with the relevant specifications.

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

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

The drug substance is packed in suitable containers. Relevant specifications and certificates of analysis have been provided for the packaging components. Suitable documentation has been provided that demonstrates the compliance of the primary packaging material with the food contact requirements of Directive 2002/72/EC.

Appropriate stability data have been generated under ICH conditions, supporting a retest period of 3 years.

DRUG PRODUCT

Sertraline 50mg tablets are bluish purple, oval, scored film-coated tablets, engraved with 'APO' on one side and 'SE' bisect '50' on the other side.

Sertraline 100mg tablets are yellow, oval, scored film-coated tablets, engraved with 'APO' on one side, and 'SER' bisect '100' on the other side.

As well as the active substance, the tablets contain pharmaceutical excipients, namely microcrystalline cellulose M102, methylcellulose A15LV, colloidal anhydrous silica, magnesium stearate, hypromellose 2910 E5, hydroxypropylcellulose LF, Macrogol 8000 and titanium dioxide (E171). The 50 mg tablets also contain the colouring agent FD&C Blue #2 Aluminium Lake (E132) and the 100 mg tablets contain the colouring agent Ferric Oxide (Yellow Iron Oxide) (E172). Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeial monograph, with the exception of colouring agent E132, which complies with an in-house specification and ferric oxide, which complies with the US Pharmacopoieal monograph (in the absence of a Ph Eur monograph, this is acceptable). Satisfactory certificates of analysis have been provided for all excipients.

Confirmation that the colouring agents E132 and E172 comply with the EC Directive 95/45/EC has been provided.

Dissolution and impurity profiles

Dissolution and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

Manufacture

A flow diagram detailing the manufacturing process and in-process control testing has been provided. A written summary of the process has been included.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. 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
Both 50mg and 100mg tablets are proposed to be packed in aluminium/PVC/PVDC blisters or HDPE bottles. Specifications and certificates of compliance stating that the packaging components conform to the food contact requirements in 2002/72/EC and are controlled to Ph Eur monograph are provided.

Certificates of analysis for the packaging materials have been provided.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 36 months has been set, which is satisfactory. There are no special precautions for storage.

Conclusions and advice
Marketing authorisations can be granted.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

INDICATIONS

The applicant has proposed the following indications:

"Sertraline is indicated for the treatment of symptoms of depressive illness, including accompanying symptoms of anxiety. Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes, including accompanying symptoms of anxiety. Sertraline is also indicated for the treatment of obsessive compulsive disorder (OCD). Following initial response, Sertraline has been associated with sustained efficacy, safety and tolerability in up to two years treatment of OCD.
Sertraline 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 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 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 in the treatment of children and adolescents with Major Depressive Disorder."

These indications are consistent with those of the innovator product and are satisfactory.

DOSE & DOSE SCHEDULE

The applicant has proposed the following:

"Posology and method of administration
Sertraline 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. 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 has been established in paediatric OCD patients (aged 6-17). The administration of Sertraline 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 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 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 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. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.
Sertraline tablets are for oral administration only."

These dosage details are satisfactory.

TOXICOLOGY

No new data were submitted and none are necessary for an application of this kind.

CLINICAL PHARMACOLOGY

The applicant submitted a comparative, randomised, 2-way crossover bioavailability study of the applicant's proposed Sertraline 100mg tablets and Pfizer's Lustral 100 mg tablets under fasting conditions. Twenty-four subjects completed the study.

The T/R ratios of the least-squares means (with 90% confidence intervals) of the log-transformed AUC_t, C_{max} and AUC_I were 100.5% (95.8-105.4%), 99.0% (93.1-105.3%) and 100.1% (95.6-104.8%), respectively. The median t_{max} values were 7.00 hours for both the proposed product and the reference product.

These results demonstrate bioequivalence between the test and reference products.

EFFICACY
No new data presented and none are needed for an application of this kind.

SAFETY
No new data presented and none are needed for an application of this kind.

EXPERT REPORTS
A clinical summary by an appropriately qualified person has been submitted.

PATIENT INFORMATION LEAFLET (PIL)
This PIL for these products is satisfactory.

LABELLING
All labelling is medically satisfactory

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is satisfactory and fully consistent with cross-reference product

DISCUSSION
The applicant has satisfactorily demonstrated comparative bioequivalence and hence essential similarity to the reference brand leader product.

MEDICAL CONCLUSION
Marketing authorisation is recommended

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of the products 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 an application of this type.

EFFICACY

The efficacy of sertraline has been well documented in the past. No new or unexpected safety concerns arise from these applications.

The SPCs, PILs and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

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

SERTRALINE 50 MG TABLETS AND SERTRALINE 100 MG TABLETS

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation applications on 25 May 2005
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 28/09/2005
3	Following assessment of the applications the MHRA requested information relating to the dossiers on 17 January 2006. The applicant responded to the MHRA's requests, providing further information the dossiers on 17 January 2006.
4	Following assessment of the response the MHRA requested information relating to the dossiers on 19 May 2006. The applicant responded to the MHRA's requests, providing further information the dossiers on 21 June 2006
5	Following assessment of the response the MHRA requested information relating to the dossiers on 21 June 2006. The applicant responded to the MHRA's requests, providing further information the dossiers on 21 June 2006
6	Marketing Authorisations were granted on 19 September 2006
7	A change of ownership of these products from Reg Europe Sarl to Apotex Europe B.V. on 11 April 2007 was granted.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sertraline 50 mg tablets and Sertraline 100 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains Sertraline hydrochloride equivalent to 50 mg or 100 mg sertraline.
For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
50mg Bluish purple oval scored film coated tablets engraved “APO” on one side, “SE” bisect “50” on the other side.
100mg Yellow oval scored film coated tablets engraved “APO” on one side, “SER” bisect “100” on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Sertraline is indicated for the treatment of symptoms of depressive illness, including accompanying symptoms of anxiety. Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes, including accompanying symptoms of anxiety.
Sertraline is also indicated for the treatment of obsessive compulsive disorder (OCD). Following initial response, Sertraline has been associated with sustained efficacy, safety and tolerability in up to two years treatment of OCD.
Sertraline 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 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 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 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 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. 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 has been established in paediatric OCD patients (aged 6-17). The administration of Sertraline 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 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 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 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. 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 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 should not be used in combination with a MAOI. Sertraline 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 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 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 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 should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Sertraline 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 and ECT, caution is advisable.

Mania: Sertraline should be used with caution in patients with a history of mania/hypomania. Sertraline 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. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Use in Children and adolescents under the age of 18:
Sertraline should not be used in the treatment of children and adolescents under the age of 18 years. 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.

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

Monoamine oxidase inhibitors: See 'Contra-indications'.

Centrally active medication: Caution is advised if Sertraline 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 coadministration. 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 (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 and alcohol in depressed patients is not recommended.

Lithium and Tryptophan: In placebo-controlled trials in normal volunteers, the co-administration of Sertraline and lithium did not significantly alter lithium pharmacokinetics.
Co-administration of Sertraline 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 antiobsessional drugs to Sertraline. Care and prudent medical judgement 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, 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 is bound to plasma proteins, the potential of Sertraline to interact with other plasma protein bound drugs should be borne in mind. Formal drug interaction studies have been performed with Sertraline. Co-administration of Sertraline (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 had no effect on the beta-adrenergic blocking ability of atenolol. No interaction with Sertraline (200mg daily) was observed with

glibenclamide or digoxin.

Co-administration of Sertraline (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 therapy is initiated or stopped.

Sertraline (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 during human pregnancy has not been established. As with all drugs Sertraline 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 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 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 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, 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 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. Common symptoms include dizziness, paraesthesia, headache, anxiety and nausea. Abrupt discontinuation of treatment with Sertraline should be avoided. The majority of symptoms experienced on withdrawal of Sertraline 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 has a wide margin of safety in overdose. Overdoses of Sertraline alone of up to 8g have been reported. Deaths involving overdoses of Sertraline 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. 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

ATC code: N06A B06

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 has not been observed to produce physical or psychological dependence.

Sertraline 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.

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

Microcrystalline Cellulose M102
Methylcellulose A15LV
Colloidal Anhydrous Silica
Magnesium Stearate
Hypromellose 2910 E5
Hydroxypropylcellulose LF
Macrogol 8000, Titanium Dioxide (E171)

50 mg tablets: FD&C Blue #2 Aluminium Lake (E132)
100 mg tablets: Ferric Oxide (Yellow Iron Oxide) (E172).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

6.4. Special precautions for storage

No special precautions for storage.

6.5. Nature and contents of container

Boxes of 4, 28, 30, 56, 60, 84, 90, 100, 112 or 120 for Aluminium/PVC/PVDC blisters
Boxes of 30, 100 or 1000 HDPE bottles.

6.6. Instruction for use and handling (, and disposal)

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Apotex Europe B.V.

Archimedesweg 2
2333 CN Leiden
Postbus 408
2300AK Leiden
The Netherlands

8. MARKETING AUTHORISATION NUMBER

50 mg PL 27583/0003
100 mg PL 27583/0002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 September 2006

10. DATE OF REVISION OF THE TEXT

November 2006

PATIENT INFORMATION LEAFLET

Patient Information Leaflet

SERTRALINE 50 and 100 mg Tablets

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 further questions, please ask your doctor or pharmacist. This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

IT IS PARTICULARLY IMPORTANT TO READ THE SECTION 'HOW SHOULD YOU TAKE SERTRALINE 50 and 100 mg Tablets BEFORE TAKING THIS MEDICINE.

1. WHAT IS IN YOUR TABLETS?

Active ingredient

The active ingredient in SERTRALINE 50 and 100 mg Tablets is Sertraline hydrochloride.
SERTRALINE 50 mg Tablets are bluish purple oval scored film coated tablets engraved "APO" on one side, "SE" bisect "50" on the other side.
SERTRALINE 100 mg Tablets are yellow oval scored film coated tablets engraved "APO" on one side, "SER" bisect "100" on the other side.

Other ingredients

Microcrystalline Cellulose M102, Methylcellulose A15LV, Colloidal Anhydrous Silica, Magnesium Stearate, Hypromellose 2910 E5, Hydroxypropylcellulose LF, Macrogol 8000, Titanium Dioxide (E171),
50 mg tablets: FD&C Blue #2 Aluminium Lake (E132)
100 mg tablets: Ferric Oxide (Yellow Iron Oxide) (E172).
SERTRALINE 50mg and 100mg Tablets are supplied in blister packs of 28 tablets.

2. HOW DO YOUR TABLETS WORK?

This medicine is one of a group of antidepressant or antiobsessional drugs called the Selective Serotonin Re-uptake Inhibitors (SSRIs).

SERTRALINE TABLETS are used to treat depression, Obsessive Compulsive Disorder (OCD) or Post Traumatic Stress Disorder (PTSD). It is also used to treat OCD in children 6 years of age and over. The tablets are not sleeping tablets or tranquillizers. Your doctor has decided that this medicine is suitable for treating your illness.

Depression is a clinical illness. If you have been feeling sad, tearful, unable to sleep properly or to enjoy life as you used to, SERTRALINE TABLETS may help you to feel better. It may also help treat the anxiety which may accompany your depression. If you are not sure why you are on these tablets, ask your doctor.

SERTRALINE tablets should not be used to treat depression in children and adolescents under 18 years old. Please see the section at the end of this leaflet called **' Use in Children and Adolescents under 18 years of age '** for further information
OCD is an illness linked to anxiety. If you have been constantly troubled by persistent ideas (obsessions) that make you carry out repetitive rituals (compulsions) SERTRALINE tablets may help you. If you are not sure why you are on these tablets, ask your doctor.

PTSD is a condition that can occur after a very emotionally traumatic experience, and has some symptoms that are similar to depression and anxiety. If you suffer from PTSD, SERTRALINE tablets may help you.

3. WHO MAKES AND DISTRIBUTES YOUR MEDICINE?

Katwijk Farma BV, Bioscience Bio Science Park, Archimedesweg 2, 2333 CN Leiden,
The Netherlands.
The Marketing Authorisation Holder is Apotex Europe B.V., Archimedesweg 2, 2333 CN Leiden, The Netherlands
SERTRALINE tablets are distributed in the UK by Apotex UK ltd, Rowan House, 41 London Street, RG1 4PS Reading, Berkshire, United Kingdom.

4. WHAT IS SERTRALINE TABLETS FOR?

SERTRALINE TABLETS is used to treat depression, Obsessive Compulsive Disorder (OCD) or Post Traumatic Stress Disorder (PTSD). It is also used to treat OCD in children 6 years of age and over. The tablets are not sleeping tablets or tranquillizers. Your doctor has decided that this medicine is suitable for treating your illness.

Depression is a clinical illness. If you have been feeling sad, tearful, unable to sleep properly or to enjoy life as you used to, SERTRALINE TABLETS may help you to feel better. It may also help treat the anxiety which may accompany your depression. If you are not sure why you are on these tablets, ask your doctor.

SERTRALINE tablets should not be used to treat depression in children and adolescents under 18 years old. Please see the section at the end of this leaflet called 'Use of SERTRALINE tablets in Children and Adolescents' for further information
OCD is an illness linked to anxiety. If you have been constantly troubled by persistent ideas (obsessions) that make you carry out repetitive rituals (compulsions) SERTRALINE tablets may help you. If you are not sure why you are on these tablets, ask your doctor.

PTSD is a condition that can occur after a very emotionally traumatic experience, and has some symptoms that are similar to depression and anxiety. If you suffer from PTSD, SERTRALINE tablets may help you.

5. ARE THERE PATIENTS WHO SHOULD NOT TAKE SERTRALINE TABLETS?

If the answer is YES to any of the questions below - DO NOT TAKE SERTRALINE TABLETS.

- Have you ever had an allergic reaction to SERTRALINE TABLETS?
- Do you have liver problems?
- Are you taking, or have you taken in the last two weeks, any medicines called monoamine oxidase inhibitors (MAOIs for short)?
- Are you a child under 6 years old who suffers from obsessive-compulsive disorder symptoms?
- Are you under 18 years old and suffering from depression?
- Are you taking a medicine called pimozide?

If the answer is YES to any of the following questions - tell your doctor immediately.

- Are you pregnant or think you might be pregnant?
- Are you breast-feeding?
- Do you have liver problems?
- Do you have kidney problems?
- Are you diabetic?
- Have you ever had an epileptic fit?
- Are you a child under 16 years old who suffers from panic symptoms?
- Are you being treated with electroconvulsive therapy (ECT)?
- Do you intend to drink alcohol when taking this medicine?
- Do you intend to drive or use machinery whilst taking this medicine?
- Are you being treated with any other medication for your illness, e.g. lithium, or another antidepressant or antiobsessional drug?
- Are you taking tryptophan, sumatriptan, fenfluramine, warfarin, diazepam, tolbutamide or cimetidine?
- Are you taking aspirin or other pain killers known as NSAIDs (Non-Steroidal Anti-inflammatory Drugs) or another stronger painkiller called Tramadol?
- Do you have a history of bleeding disorders?

Your doctor may want you to have blood tests if you are taking lithium or warfarin.

The herbal remedy St John's Wort (Hypericum perforatum) should not be taken at the same time as this medicine. If you already take a St John's Wort preparation, stop taking the St John's Wort and mention it to your doctor at your next visit.

How to take your medicine

Your medicine 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.

- 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.

6. WHAT ELSE SHOULD YOU KNOW BEFORE TAKING SERTRALINE TABLETS?

Your doctor should not make a change to your dose more than once a week.
What if you take too many tablets?
Too many tablets at once can be dangerous. If you take too many tablets tell your doctor. If you are unable to contact your doctor go to your local hospital casualty department at once.
What if you miss a tablet?
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.
How quickly will the treatment start to work?

- You may need to take SERTRALINE TABLETS for up to 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

7. WHAT UNWANTED EFFECTS COULD SERTRALINE TABLETS HAVE?

Your medicine may cause some undesirable effects:

- 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

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. 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 rarely.
- 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 a doctor immediately.
Tell your doctor straight away if you get any of these effects, or any other discomfort you do not understand.
Use in Children and Adolescents under 18 years of age
SERTRALINE tablets should normally not be used for children and adolescents under 18 years. Also you should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. Despite this, your doctor may prescribe SERTRALINE tablets for patients under 18 because he/she decides that this is in their best interest. If your doctor has prescribed SERTRALINE tablets for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform, you doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking SERTRALINE tablets.
Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of SERTRALINE tablets in this age group have not yet been demonstrated.

8. HOW SHOULD YOUR TABLETS BE KEPT?

Keep your tablets out of the reach of children.
No special storage conditions are required for this medicine.
Do not put the tablets into another container; they might get mixed up. Do not remove the tablets from the blister pack until you are ready to take the medicine.
Do not take the tablets after the expiry date, which is clearly marked on the carton, wallet and blister.

REMEMBER: This medicine is for you. Do not share it with anyone else. It may not suit them.
Leaflet prepared in October 2006

APOTEX UK LTD.

LABELLING

Sertraline 50 mg tablets

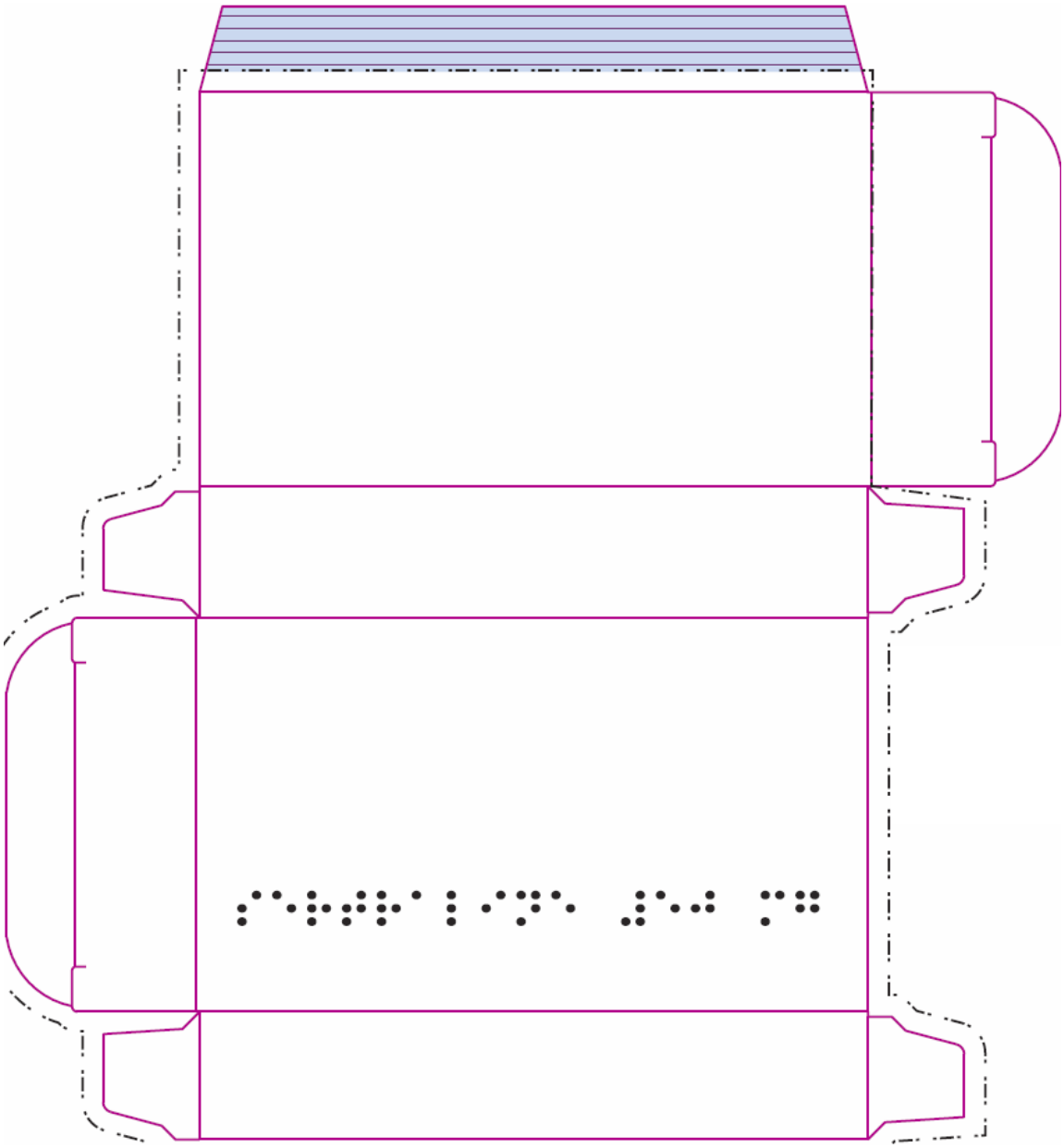
Bilster label:

Bottle label:

Carton:


Sertraline 50 mg Tablets
28 Tablets
5 060129 470219
For dispensing label
BN:
EXP: MMM YYYY
245538
Sertraline 50 mg Tablets
28 Tablets
MA Holder: Apotex Europe BV, Archimedesweg 2,
2333 CN Leiden, The Netherlands
Distributed by: Apotex UK ltd, Rowan House, 41 London Street,
Reading, Berkshire, RG1 4PS, United Kingdom
PL 27583/0003
POM
28 Tablets
Sertraline 50 mg Tablets
For oral use
APOTEX UK LTD.
245538
Sertraline 50 mg Tablets
28 Tablets
Each film-coated tablet contains the equivalent of 50 mg sertraline. Please read the enclosed leaflet carefully. Use as directed by medical practitioner. There are no special storage instructions. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

Carton with Braille:



Sertraline 100 mg tablets

Blister label:

Bottle label:

Carton:


Sertraline 100 mg Tablets
28 Tablets
5 060129 470233
For dispensing label
BN:
EXP: MMM YYYY
242819
Sertraline 100 mg Tablets
28 Tablets
MA Holder: Apotex Europe BV, Archimedesweg 2,
2333 CN Leiden, The Netherlands
Distributed by: Apotex UK ltd, Rowan House, 41 London Street,
Reading, Berkshire, RG1 4PS, United Kingdom
PL 27583/0002
POM
28 Tablets
Sertraline 100 mg Tablets
For oral use
APOTEX UK LTD.
Each film-coated tablet contains the equivalent of 100 mg sertraline. Please read the enclosed leaflet carefully. Use as directed by medical practitioner. There are no special storage instructions. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
242819
Sertraline 100 mg Tablets
28 Tablets

Carton with Braille: