SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

SEROXAT 10 mg film-coated tablets.
SEROXAT 20 mg film-coated tablets.
SEROXAT 30 mg film-coated tablets.
SEROXAT 20 mg/10 ml oral suspension.

DEROXAT 10 mg film-coated tablets.
DEROXAT 20 mg film-coated tablets.
DEROXAT 20 mg/10 ml oral suspension.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg/20 mg/30 mg paroxetine (as paroxetine hydrochloride hemihydrate).

Each 10 ml of oral suspension contains 20 mg paroxetine (as paroxetine hydrochloride hemihydrate).
Excipients with known effect – each 10 ml of oral suspension contains:

- 20 mg methyl parahydroxybenzoate
- 6 mg propyl parahydroxybenzoate
- 0.9 mg sunset yellow FCF (E110)
- 4 g sorbitol (E420).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.
Oral suspension.

<10 mg tablet>
<White to pinkish-white, film-coated, oval tablets, debossed FC1 and break bar on one side and debossed GS and break bar on the other side.>

<The 10 mg tablet can be divided into equal doses if required.>

<20 mg tablet>
<White, film-coated tablet, oval shaped biconvex tablets debossed with “SEROXAT 20”, “DEROXAT 20”, “AROPAX 20” or “20” on one side and a break bar on the other.
Note: Choice of debossing described is dependent on the combination of market/brand name and original or copy/duplicate licence.>

<The 20 mg tablet can be divided into equal doses if required.>

<30 mg tablet>
<Blue, oval shaped biconvex tablets debossed with “SEROXAT 30”, “AROPAX 30” or “30” on one side and a break bar on the other. The break bar is only to facilitate breaking for ease of swallowing and not to divide into equal doses.
Note: Choice of debossing described is dependent on the combination of market/brand name and original or copy/duplicate licence.>

<Oral Suspension>
<A bright orange fairly viscous suspension having an odour of oranges, free from foreign matter.>

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of
- Major Depressive Episode
- Obsessive Compulsive Disorder
- Panic Disorder with and without agoraphobia
- Social Anxiety Disorders/Social phobia
- Generalised Anxiety Disorder
- Post-Traumatic Stress Disorder

4.2 **Posology and method of administration**

Posology

MAJOR DEPRESSIVE EPISODE

The recommended dose is 20 mg daily. In general, improvement in patients starts after one week but may only become evident from the second week of therapy.
As with all antidepressant medicinal products, dosage should be reviewed and adjusted if necessary within 3 to 4 weeks of initiation of therapy and thereafter as judged clinically appropriate. In some patients, with insufficient response to 20 mg, the dose may be increased gradually up to a maximum of 50 mg a day in 10 mg steps according to the patient's response.

Patients with depression should be treated for a sufficient period of at least 6 months to ensure that they are free from symptoms.

OBSESSIVE COMPULSIVE DISORDER

The recommended dose is 40 mg daily. Patients should start on 20 mg/day and the dose may be increased gradually in 10 mg increments to the recommended dose. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60 mg/day.
Patients with OCD should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer (see section 5.1 Pharmacodynamic properties).

PANIC DISORDER

The recommended dose is 40 mg daily. Patients should be started on 10 mg/day and the dose gradually increased in 10 mg steps according to the patient's response up to the recommended dose. A low initial starting dose is recommended to minimise the potential worsening of panic symptomatology, which is generally recognised to occur early in the treatment of this disorder. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60 mg/day.
Patients with panic disorder should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer (see section 5.1 Pharmacodynamic properties).

SOCIAL ANXIETY DISORDER/SOCIAL PHOBIA

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic properties).

GENERALISED ANXIETY DISORDER

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic properties).

POST-TRAUMATIC STRESS DISORDER

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic properties).

GENERAL INFORMATION

WITHDRAWAL SYMPTOMS SEEN ON DISCONTINUATION OF PAROXETINE
Abrupt discontinuation should be avoided (see section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects). The taper phase regimen used in clinical trials involved decreasing the daily dose by 10 mg at weekly intervals. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

Special Populations:

- **Older people**

Increased plasma concentrations of paroxetine occur in elderly subjects, but the range of concentrations overlaps with that observed in younger subjects. Dosing should commence at the adult starting dose. Increasing the dose might be useful in some patients, but the maximum dose should not exceed 40 mg daily.

- **Children and adolescents (7-17 years)**

Paroxetine should not be used for the treatment of children and adolescents as controlled clinical trials have found paroxetine to be associated with increased risk for suicidal behaviour and hostility. In addition, in these trials efficacy has not been adequately demonstrated (see section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects).

- **Children aged below 7 years**

The use of paroxetine has not been studied in children less than 7 years. Paroxetine should not be used, as long as safety and efficacy in this age group have not been established.

- **Renal/hepatic impairment**

Increased plasma concentrations of paroxetine occur in patients with severe renal impairment (creatinine clearance less than 30 ml/min) or in those with hepatic impairment. Therefore, dosage should be restricted to the lower end of the dosage range.

<u>Method of administration</u>

It is recommended that paroxetine is administered once daily in the morning with food.
<The tablet should be swallowed rather than chewed.>
<Shake bottle before use.>

[To be completed nationally]

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1
Paroxetine is contraindicated in combination with monoamine oxidase inhibitors (MAOIs). In exceptional circumstances, linezolid (an antibiotic which is a reversible non-selective MAOI) can be given in combination with paroxetine provided that there are facilities for close observation of symptoms of serotonin syndrome and monitoring of blood pressure (see section 4.5).
Treatment with paroxetine can be initiated:

- two weeks after discontinuation of an irreversible MAOI, or
- at least 24hrs after discontinuation of a reversible MAOI (e.g. moclobemide, linezolid, methylthioninium chloride (methylene blue; a preoperative visualising agent which is a reversible non-selective MAOI)).

At least one week should elapse between discontinuation of paroxetine and initiation of therapy with any MAOI.

Paroxetine should not be used in combination with thioridazine, because, as with other drugs which inhibit the hepatic enzyme CYP450 2D6, paroxetine can elevate plasma levels of thioridazine (see section 4.5 Interactions with other medicinal products and other forms of interaction). Administration of thioridazine alone can lead to QTc interval prolongation with associated serious ventricular arrhythmia such as torsades de pointes, and sudden death.

Paroxetine should not be used in combination with pimozide (see section 4.5 Interactions with other medicinal products and other forms of interaction).

4.4 Special warnings and precautions for use

Treatment with paroxetine should be initiated cautiously two weeks after terminating treatment with an irreversible MAOI or 24 hours after terminating treatment with a reversible MAO inhibitor. Dosage of paroxetine should be increased gradually until an optimal response is reached (see section 4.3 Contraindications and section 4.5 Interactions with other medicinal products and other forms of interaction).

Paediatric population
Paroxetine 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.

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

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

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or

suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old (see also section 5.1).

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

Akathisia/psychomotor restlessness
The use of paroxetine has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Serotonin Syndrome/Neuroleptic Malignant Syndrome
On rare occasions development of a serotonin syndrome or neuroleptic malignant syndrome-like events may occur in association with treatment of paroxetine, particularly when given in combination with other serotonergic and/or neuroleptic drugs. As these syndromes may result in potentially life-threatening conditions, treatment with paroxetine should be discontinued if such events (characterised by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. Paroxetine should not be used in combination with serotonin-precursors (such as L-tryptophan, oxitriptan) due to the risk of serotonergic syndrome.
(See Sections 4.3 Contraindications and 4.5 Interactions with other medicinal products and other forms of interaction).

Mania
As with all antidepressants, paroxetine should be used with caution in patients with a history of mania. Paroxetine should be discontinued in any patient entering a manic phase.

Renal/hepatic impairment
Caution is recommended in patients with severe renal impairment or in those with hepatic impairment (see section 4.2 Posology and method of administration).

Diabetes
In patients with diabetes, treatment with an SSRI may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted. Additionally, there have been studies suggesting that an increase in blood glucose levels may occur when paroxetine and pravastatin are co-administered (see section 4.5).

Epilepsy
As with other antidepressants, paroxetine should be used with caution in patients with epilepsy.

Seizures
Overall the incidence of seizures is less than 0.1% in patients treated with paroxetine. The drug should be discontinued in any patient who develops seizures.

Electroconvulsive therapy (ECT)
There is little clinical experience of the concurrent administration of paroxetine with ECT.

Glaucoma
As with other SSRIs, paroxetine can cause mydriasis and should be used with caution in patients with narrow angle glaucoma or history of glaucoma.

Cardiac Conditions
The usual precautions should be observed in patients with cardiac conditions.

Hyponatraemia
Hyponatraemia has been reported rarely, predominantly in the elderly. Caution should also be exercised in those patients at risk of hyponatraemia e.g. from concomitant medications and cirrhosis. The hyponatraemia generally reverses on discontinuation of paroxetine.

Haemorrhage
There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs. Other haemorrhagic manifestations e.g. gastrointestinal and gynaecological haemorrhage have been reported. Elderly patients may be at an increased risk for non-menses related events of bleeding.

Caution is advised in patients taking SSRIs concomitantly with oral anticoagulants, drugs known to affect platelet function or other drugs that may increase risk of bleeding (e.g. atypical antipsychotics such as clozapine, phenothiazines, most TCAs, acetylsalicylic acid, NSAIDs, COX-2 inhibitors) as well as in patients with a history of bleeding disorders or conditions which may predispose to bleeding (see section 4.8).

Interaction with tamoxifen
Paroxetine, a potent inhibitor of CYP2D6, may lead to reduced concentrations of endoxifen, one of the most important active metabolites of tamoxifen. Therefore, paroxetine should whenever possible be avoided during tamoxifen treatment (see Section 4.5).

<Drugs affecting gastric pH>
<In patients receiving oral suspension, the paroxetine plasma concentration may be influenced by gastric pH. *In vitro* data have shown that an acidic environment is required for release of the active drug from the suspension, hence absorption may be reduced in patients with a high gastric pH or achlorhydria, such as after the use of certain drugs (antacid drugs, histamine H2-receptor antagonists, proton pump inhibitors), in certain disease states (e.g. atrophic gastritis, pernicious anemia, chronic *Helicobacter pylori* infection), and after surgery (vagotomy, gastrectomy). The pH dependency should be taken into account when changing paroxetine formulation (e.g. the plasma paroxetine concentration may decrease after changing from tablet to oral suspension in patients with a high gastric pH). Caution is therefore recommended in patients when initiating or ending treatment with drugs increasing gastric pH. Dose adjustments may be necessary in such situations.>

Withdrawal symptoms seen on discontinuation of paroxetine treatment

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8 Undesirable effects). In clinical trials adverse events seen on treatment discontinuation occurred in 30% of patients treated with paroxetine compared to 20% of patients treated with placebo. The occurrence of withdrawal symptoms is not the same as the drug being addictive or dependence producing.
The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction.
Dizziness, sensory disturbances (including paraesthesia, electric shock sensations and tinnitus), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported. Generally these symptoms are mild to moderate; however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within two weeks, though in some individuals they may be prolonged (two - three months or more). It is therefore advised that paroxetine should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient’s needs (see "Withdrawal Symptoms Seen on Discontinuation of Paroxetine", Section 4.2 Posology and method of administration).

<Warnings for excipients>
<Parabens>
<Paroxetine oral suspension contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) (parabens), which are known to cause urticaria, generally delayed-type reactions, such as contact dermatitis, but rarely immediate reaction with bronchospasm.>

<Sunset Yellow Colouring Agent>
<Paroxetine oral suspension contains the colouring agent sunset yellow FCF (E110), which may cause allergic reactions.>

<Sorbitol E420>
<Paroxetine oral suspension contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine.>

4.5 Interaction with other medicinal products and other forms of interaction

Serotonergic drugs
As with other SSRIs, co-administration with serotonergic drugs may lead to an incidence of 5-HT associated effects (serotonin syndrome: see Section 4.4 Special warnings and precautions for use). Caution should be advised and a closer clinical monitoring is required when serotonergic drugs (such as L-tryptophan, triptans, tramadol, linezolid, methylthioninium chloride (methylene blue)), SSRIs, lithium, pethidine and St. John's Wort – *Hypericum perforatum* – preparations) are combined with paroxetine. Caution is also advised with fentanyl used in general anaesthesia or in the treatment of chronic pain. Concomitant use of paroxetine and MAOIs is contraindicated because of the risk of serotonin syndrome (see Section 4.3 Contraindications).

Pimozide
Increased pimozide levels of on average 2.5 times have been demonstrated in a study of a single low dose pimozide (2 mg) when co-administered with 60 mg paroxetine. This may be explained by the known CYP2D6 inhibitory properties of paroxetine. Due to the narrow therapeutic index of pimozide and its known ability to prolong QT interval, concomitant use of pimozide and paroxetine is contraindicated (see Section 4.3 Contraindications).

Drug metabolising enzymes
The metabolism and pharmacokinetics of paroxetine may be affected by the induction or inhibition of drug metabolising enzymes.
When paroxetine is to be co-administered with a known drug metabolising enzyme inhibitor, consideration should be given to using paroxetine doses at the lower end of the range.
No initial dosage adjustment is considered necessary when the drug is to be co-administered with known drug metabolising enzyme inducers (e.g. carbamazepine, rifampicin, phenobarbital, phenytoin) or with fosamprenavir/ritonavir. Any paroxetine dosage adjustment (either after initiation or following discontinuation of an enzyme inducer) should be guided by clinical effect (tolerability and efficacy).

Neuromuscular Blockers
SSRIs may reduce plasma cholinesterase activity resulting in a prolongation of the neuromuscular blocking action of mivacurium and suxamethonium.

Fosamprenavir/ritonavir: Co-administration of fosamprenavir/ritonavir 700/100 mg twice daily with paroxetine 20 mg daily in healthy volunteers for 10 days significantly decreased plasma levels of paroxetine by approximately 55%. The plasma levels of fosamprenavir/ritonavir during co-administration of paroxetine were similar to reference values of other studies, indicating that paroxetine had no significant effect on metabolism of fosamprenavir/ritonavir. There are no data available about the effects of long-term co-administration of paroxetine and fosamprenavir/ritonavir exceeding 10 days.

Procyclidine: Daily administration of paroxetine increases significantly the plasma levels of procyclidine. If anti-cholinergic effects are seen, the dose of procyclidine should be reduced.

Anticonvulsants: carbamazepine, phenytoin, sodium valproate. Concomitant administration does not seem to show any effect on pharmacokinetic/dynamic profile in epileptic patients.

CYP2D6 inhibitory potency of paroxetine
As with other antidepressants, including other SSRIs, paroxetine inhibits the hepatic cytochrome P450 enzyme CYP2D6. Inhibition of CYP2D6 may lead to increased plasma concentrations of co-administered drugs metabolised by this enzyme. These include certain tricyclic antidepressants (e.g. clomipramine, nortriptyline, and desipramine), phenothiazine neuroleptics (e.g. perphenazine and thioridazine, see section 4.3 Contraindications), risperidone, atomoxetine, certain Type 1c antiarrhythmics (e.g. propafenone and flecainide) and metoprolol. It is not recommended to use paroxetine in combination with metoprolol when given in cardiac insufficiency, because of the narrow therapeutic index of metoprolol in this indication.

Pharmacokinetic interaction between CYP2D6 inhibitors and tamoxifen, showing a 65-75% reduction in plasma levels of one of the more active forms of tamoxifen, i.e. endoxifen, has been reported in the literature. Reduced efficacy of tamoxifen has been reported with concomitant usage of some SSRI antidepressants in some studies. As a reduced effect of tamoxifen cannot be excluded, co-administration with potent CYP2D6 inhibitors (including paroxetine) should whenever possible be avoided (see section 4.4).

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

Oral anticoagulants
A pharmacodynamic interaction between paroxetine and oral anticoagulants may occur. Concomitant use of paroxetine and oral anticoagulants can lead to an increased anticoagulant activity and haemorrhagic risk. Therefore, paroxetine should be used with caution in patients who are treated with oral anticoagulants (see section 4.4 Special warnings and precautions for use).

NSAIDs and acetylsalicylic acid, and other antiplatelet agents
A pharmacodynamic interaction between paroxetine and NSAIDs/acetylsalicylic acid may occur. Concomitant use of paroxetine and NSAIDs/acetylsalicylic acid can lead to an increased haemorrhagic risk (see section 4.4 Special warnings and precautions for use).
Caution is advised in patients taking SSRIs, concomitantly with oral anticoagulants, drugs known to affect platelet function or increase risk of bleeding (e.g. atypical antipsychotics such as clozapine, phenothiazines, most TCAs, acetylsalicylic acid, NSAIDs, COX-2 inhibitors) as well as in patients with a history of bleeding disorders or conditions that may predispose to bleeding.

Pravastatin
An interaction between paroxetine and pravastatin has been observed in studies suggesting that co-administration of paroxetine and pravastatin may lead to an increase in blood glucose levels. Patients with diabetes mellitus receiving both paroxetine and pravastatin may require dosage adjustment of oral hypoglycaemic agents and/or insulin (see section 4.4).

<Drugs affecting gastric pH>
<*In vitro* data have shown that dissociation of paroxetine from the oral suspension is pH-dependant. Therefore, drugs that alter gastric pH (such as antacid drugs, proton pump inhibitors or histamine H2-receptor antagonists) may affect plasma paroxetine concentrations in patients taking the oral suspension (see section 4.4).>

4.6 Fertility,pregnancy and lactation

Pregnancy
Some epidemiological studies suggest an increased risk of congenital malformations, particularly cardiovascular (e.g. ventricular and atrial septum defects), associated with the use of paroxetine during the first trimester. The mechanism is unknown. The data suggest that the risk of having an infant with a cardiovascular defect following maternal paroxetine exposure is less than 2/100 compared with an expected rate for such defects of approximately 1/100 in the general population.

Paroxetine should only be used during pregnancy when strictly indicated. The prescribing physician will need to weigh the option of alternative treatments in women who are pregnant or are planning to become pregnant. Abrupt discontinuation should be avoided during pregnancy (see "Withdrawal Symptoms Seen on Discontinuation of Paroxetine", section 4.2 Posology and method of administration).

Neonates should be observed if maternal use of paroxetine continues into the later stages of pregnancy, particularly the third trimester.

The following symptoms may occur in the neonate after maternal paroxetine use in later stages of pregnancy: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty in sleeping. These symptoms could be due to either serotonergic effects or withdrawal symptoms. In a majority of instances the complications begin immediately or soon (<24 hours) after delivery.

Epidemiological data have suggested that the use of SSRIs in pregnancy, particularly in late pregnancy, may have an increased risk of persistent pulmonary hypertension of the newborn (PPHN). The observed risk was approximately five cases per 1000 pregnancies. In the general population one to two cases of PPHN per 1000 pregnancies occur.

Animal studies showed reproductive toxicity, but did not indicate direct harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see Section 5.3 Preclinical Safety Data).

Breast-feeding
Small amounts of paroxetine are excreted into breast milk. In published studies, serum concentrations in breast-fed infants were undetectable (<2 nanograms/ml) or very low (<4 nanograms/ml), and no signs of drug effects were observed in these infants. Since no effects are anticipated, breast-feeding can be considered.

Fertility
Animal data have shown that paroxetine may affect sperm quality (see section 5.3). *In vitro* data with human material may suggest some effect on sperm quality; however, human case reports with some SSRIs (including paroxetine) have shown that an effect on sperm quality appears to be reversible. Impact on human fertility has not been observed so far.

4.7 Effects on ability to drive and use machines

Clinical experience has shown that therapy with paroxetine is not associated with impairment of cognitive or psychomotor function. However, as with all psychoactive drugs, patients should be cautioned about their ability to drive a car and operate machinery.
Although paroxetine does not increase the mental and motor skill impairments caused by alcohol, the concomitant use of paroxetine and alcohol is not advised.

4.8 Undesirable effects

Some of the adverse drug reactions listed below may decrease in intensity and frequency with continued treatment and do not generally lead to cessation of therapy. Adverse drug reactions are

listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, <1/10), uncommon (≥ 1/1,000, <1/100), rare (≥ 1/10,000, <1/1,000), very rare (<1/10,000), including isolated reports.

Blood and lymphatic system disorders
Uncommon: abnormal bleeding, predominantly of the skin and mucous membranes (including ecchymosis and gynaecological bleeding).
Very rare: thrombocytopenia.

Immune system disorders
Very rare: severe and potentially fatal allergic reactions (including anaphylactoid reactions and angioedema).

Endocrine disorders
Very rare: syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Metabolism and nutrition disorders
Common: increases in cholesterol levels, decreased appetite.
Uncommon: altered glycaemic control has been reported in diabetic patients (see section 4.4).
Rare: hyponatraemia.
Hyponatraemia has been reported predominantly in elderly patients and is sometimes due to syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Psychiatric disorders
Common: somnolence, insomnia, agitation, abnormal dreams (including nightmares).
Uncommon: confusion, hallucinations.
Rare: manic reactions, anxiety, depersonalisation, panic attacks, akathisia (see section 4.4).
Frequency not known: suicidal ideation, suicidal behaviour, aggression.

Cases of suicidal ideation and suicidal behaviour have been reported during paroxetine therapy or early after treatment discontinuation (see section 4.4).
Cases of aggression were observed in post marketing experience.

These symptoms may also be due to the underlying disease.

Nervous system disorders
Common: dizziness, tremor, headache, concentration impaired.
Uncommon: extrapyramidal disorders.
Rare: convulsions, restless legs syndrome (RLS).
Very rare: serotonin syndrome (symptoms may include agitation, confusion, diaphoresis, hallucinations, hyperreflexia, myoclonus, shivering, tachycardia and tremor).
Reports of extrapyramidal disorder including oro-facial dystonia have been received in patients sometimes with underlying movement disorders or who were using neuroleptic medication.

Eye disorders
Common: blurred vision.
Uncommon: mydriasis (see section 4.4 Special warnings and precautions for use).
Very rare: acute glaucoma.

Ear and labyrinth disorders
Frequency not known: tinnitus.

Cardiac disorders
Uncommon: sinus tachycardia.
Rare: bradycardia.

Vascular disorders
Uncommon: transient increases or decreases in blood pressure, postural hypotension.
Transient increases or decreases of blood pressure have been reported following treatment with paroxetine, usually in patients with pre-existing hypertension or anxiety.

Respiratory, thoracic and mediastinal disorders
Common: yawning.

Gastrointestinal disorders
Very common: nausea.
Common: constipation, diarrhoea, vomiting, dry mouth.
Very rare: gastrointestinal bleeding.

Hepato-biliary disorders
Rare: elevation of hepatic enzymes.
Very rare: hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure).
Elevation of hepatic enzymes have been reported. Post-marketing reports of hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure) have also been received very rarely. Discontinuation of paroxetine should be considered if there is prolonged elevation of liver function test results.

Skin and subcutaneous tissue disorders
Common: sweating.
Uncommon: skin rashes, pruritus
Very rare: severe cutaneous adverse reactions (including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis), urticaria, photosensitivity reactions.

Renal and urinary disorders
Uncommon: urinary retention, urinary incontinence.

Reproductive system and breast disorders
Very common: sexual dysfunction.
Rare: hyperprolactinaemia/galactorrhoea, menstrual disorders (including menorrhagia, metrorrhagia, amenorrhoea, menstruation delayed and menstruation irregular).
Very rare: priapism.

Musculoskeletal and connective tissue disorders
Rare: arthralgia, myalgia

Epidemiological studies, mainly conducted in patients 50 years of age and older, show an increased risk of bone fractures in patients receiving SSRIs and TCAs. The mechanism leading to this risk is unknown.

General disorder and administration site conditions
Common: asthenia, body weight gain
Very rare: peripheral oedema.

WITHDRAWAL SYMPTOMS SEEN ON DISCONTINUATION OF PAROXETINE TREATMENT

Common: dizziness, sensory disturbances, sleep disturbances, anxiety, headache.
Uncommon: agitation, nausea, tremor, confusion, sweating, emotional instability, visual disturbances, palpitations, diarrhoea, irritability.
Discontinuation of paroxetine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia, electric shock sensations and tinnitus), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating,

headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported.
Generally these events are mild to moderate and are self-limiting; however, in some patients they may be severe and/or prolonged. It is therefore advised that when paroxetine treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see section 4.2 Posology and method of administration and section 4.4 Special warnings and precautions for use).

ADVERSE EVENTS FROM PAEDIATRIC CLINICAL TRIALS
The following adverse events were observed:
Increased suicidal related behaviours (including suicide attempts and suicidal thoughts), self-harm behaviours and increased hostility. Suicidal thoughts and suicide attempts were mainly observed in clinical trials of adolescents with Major Depressive Disorder. Increased hostility occurred particularly in children with obsessive compulsive disorder, and especially in younger children less than 12 years of age.
Additional events that were seen are: decreased appetite, tremor, sweating, hyperkinesia, agitation, emotional lability (including crying and mood fluctuations), bleeding related adverse events, predominantly of the skin and mucous membranes.
Events seen after discontinuation/tapering of paroxetine are: emotional lability (including crying, mood fluctuations, self-harm, suicidal thoughts and attempted suicide), nervousness, dizziness, nausea and abdominal pain (see section 4.4 Special warnings and precautions for use).
See section 5.1 for more information on paediatric clinical trials.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms and Signs
A wide margin of safety is evident from available overdose information on paroxetine.
Experience of paroxetine in overdose has indicated that, in addition to those symptoms mentioned under section 4.8 "Undesirable effects", fever and involuntary muscle contractions have been reported. Patients have generally recovered without serious sequelae even when doses of up to 2000 mg have been taken alone. Events such as coma or ECG changes have occasionally been reported and, very rarely with a fatal outcome, but generally when paroxetine was taken in conjunction with other psychotropic drugs, with or without alcohol.

Treatment
No specific antidote is known.
The treatment should consist of those general measures employed in the management of overdose with any antidepressant. Administration of 20-30 g activated charcoal may be considered if possible within a few hours after overdose intake to decrease absorption of paroxetine. Supportive care with frequent monitoring of vital signs and careful observation is indicated. Patient management should be as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidepressants – selective serotonin reuptake inhibitors, ATC code: N06A B05

Mechanism of Action
Paroxetine is a potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake and its antidepressant action and effectiveness in the treatment of OCD, Social Anxiety disorder/Social Phobia, General Anxiety Disorder, Post-Traumatic Stress Disorder and Panic Disorder is thought to be related to its specific inhibition of 5-HT uptake in brain neurones.
Paroxetine is chemically unrelated to the tricyclic, tetracyclic and other available antidepressants.
Paroxetine has low affinity for muscarinic cholinergic receptors and animal studies have indicated only weak anticholinergic properties.
In accordance with this selective action, *in vitro* studies have indicated that, in contrast to tricyclic antidepressants, paroxetine has little affinity for alpha1, alpha2 and beta-adrenoceptors, dopamine (D2), 5-HT1 like, 5-HT2 and histamine (H1) receptors. This lack of interaction with post-synaptic receptors *in vitro* is substantiated by *in vivo* studies which demonstrate lack of CNS depressant and hypotensive properties.

Pharmacodynamic Effects
Paroxetine does not impair psychomotor function and does not potentiate the depressant effects of ethanol.
As with other selective 5-HT uptake inhibitors, paroxetine causes symptoms of excessive 5-HT receptor stimulation when administered to animals previously given monoamine oxidase (MAO) inhibitors or tryptophan.
Behavioural and EEG studies indicate that paroxetine is weakly activating at doses generally above those required to inhibit 5-HT uptake. The activating properties are not "amphetamine-like" in nature.
Animal studies indicate that paroxetine is well tolerated by the cardiovascular system. Paroxetine produces no clinically significant changes in blood pressure, heart rate and ECG after administration to healthy subjects.
Studies indicate that, in contrast to antidepressants which inhibit the uptake of noradrenaline, paroxetine has a much reduced propensity to inhibit the antihypertensive effects of guanethidine.
In the treatment of depressive disorders, paroxetine exhibits comparable efficacy to standard antidepressants.
There is also some evidence that paroxetine may be of therapeutic value in patients who have failed to respond to standard therapy.
Morning dosing with paroxetine does not have any detrimental effect on either the quality or duration of sleep. Moreover, patients are likely to experience improved sleep as they respond to paroxetine therapy.

Adult suicidality analysis
A paroxetine-specific analysis of placebo controlled trials of adults with psychiatric disorders showed a higher frequency of suicidal behaviour in young adults (aged 18-24 years) treated with paroxetine compared with placebo (2.19% vs 0.92%). In the older age groups, no such increase was observed. In adults with major depressive disorder (all ages), there was an increase in the frequency of suicidal behaviour in patients treated with paroxetine compared with placebo (0.32% vs 0.05%); all of the events were suicide attempts. However, the majority of these attempts for paroxetine (8 of 11) were in younger adults (see also section 4.4).

Dose response
In the fixed dose studies there is a flat dose response curve, providing no suggestion of advantage in terms of efficacy for using higher than the recommended doses. However, there are some clinical data suggesting that up-titrating the dose might be beneficial for some patients.

Long-term efficacy
The long-term efficacy of paroxetine in depression has been demonstrated in a 52-week maintenance study with relapse prevention design: 12% of patients receiving paroxetine (20-40mg daily) relapsed, versus 28% of patients on placebo.

The long-term efficacy of paroxetine in treating obsessive compulsive disorder has been examined in three 24-week maintenance studies with relapse prevention design. One of the three studies achieved a

significant difference in the proportion of relapsers between paroxetine (38%) compared to placebo (59%).

The long-term efficacy of paroxetine in treating panic disorder has been demonstrated in a 24-week maintenance study with relapse prevention design: 5% of patients receiving paroxetine (10-40mg daily) relapsed, versus 30% of patients on placebo. This was supported by a 36-week maintenance study.

The long-term efficacy of paroxetine in treating social anxiety disorder and generalised anxiety disorder and Post-Traumatic Stress Disorder has not been sufficiently demonstrated.

Adverse Events from Paediatric Clinical Trials
In short-term (up to 10-12 weeks) clinical trials in children and adolescents, the following adverse events were observed in paroxetine-treated patients at a frequency of at least 2% of patients and occurred at a rate at least twice that of placebo: increased suicidal related behaviours (including suicide attempts and suicidal thoughts), self-harm behaviours and increased hostility. Suicidal thoughts and suicide attempts were mainly observed in clinical trials of adolescents with Major Depressive Disorder. Increased hostility occurred particularly in children with obsessive compulsive disorder, and especially in younger children less than 12 years of age. Additional events that were more often seen in the paroxetine compared to placebo group were: decreased appetite, tremor, sweating, hyperkinesia, agitation, emotional lability (including crying and mood fluctuations).

In studies that used a tapering regimen, symptoms reported during the taper phase or upon discontinuation of paroxetine at a frequency of at least 2% of patients and occurred at a rate at least twice that of placebo were: emotional lability (including crying, mood fluctuations, self-harm, suicidal thoughts and attempted suicide), nervousness, dizziness, nausea and abdominal pain (see section 4.4 Special Warnings and Precautions for use).

In five-parallel group studies with a duration of eight weeks up to eight months of treatment, bleeding related adverse events, predominantly of the skin and mucous membranes, were observed in paroxetine-treated patients at a frequency of 1.74% compared to 0.74% observed in placebo-treated patients.

5.2 Pharmacokinetic properties

Absorption
Paroxetine is well absorbed after oral dosing and undergoes first-pass metabolism. Due to first-pass metabolism, the amount of paroxetine available to the systemic circulation is less than that absorbed from the gastrointestinal tract. Partial saturation of the first-pass effect and reduced plasma clearance occur as the body burden increases with higher single doses or on multiple dosing. This results in disproportionate increases in plasma concentrations of paroxetine and hence pharmacokinetic parameters are not constant, resulting in non-linear kinetics. However, the non-linearity is generally small and is confined to those subjects who achieve low plasma levels at low doses.
Steady state systemic levels are attained by 7 to 14 days after starting treatment with immediate or controlled release formulations and pharmacokinetics do not appear to change during long-term therapy.

Distribution
Paroxetine is extensively distributed into tissues and pharmacokinetic calculations indicate that only 1% of the paroxetine in the body resides in the plasma.
Approximately 95% of the paroxetine present is protein bound at therapeutic concentrations.
No correlation has been found between paroxetine plasma concentrations and clinical effect (adverse experiences and efficacy).

Biotransformation
The principal metabolites of paroxetine are polar and conjugated products of oxidation and methylation which are readily cleared. In view of their relative lack of pharmacological activity, it is most unlikely that they contribute to paroxetine's therapeutic effects.
Metabolism does not compromise paroxetine's selective action on neuronal 5-HT uptake.

Elimination
Urinary excretion of unchanged paroxetine is generally less than 2% of dose whilst that of metabolites is about 64% of dose. About 36% of the dose is excreted in faeces, probably via the bile, of which unchanged paroxetine represents less than 1% of the dose. Thus paroxetine is eliminated almost entirely by metabolism.
Metabolite excretion is biphasic, being initially a result of first-pass metabolism and subsequently controlled by systemic elimination of paroxetine.
The elimination half-life is variable but is generally about one day.

Special Patient Populations

Older people and Renal/Hepatic Impairment
Increased plasma concentrations of paroxetine occur in elderly subjects and in those subjects with severe renal impairment or in those with hepatic impairment, but the range of plasma concentrations overlaps that of healthy adult subjects.

5.3 Preclinical safety data

Toxicology studies have been conducted in rhesus monkeys and albino rats; in both, the metabolic pathway is similar to that described for humans. As expected with lipophilic amines, including tricyclic antidepressants, phospholipidosis was detected in rats. Phospholipidosis was not observed in primate studies of up to one-year duration at doses that were six times higher than the recommended range of clinical doses.
Carcinogenesis: In two-year studies conducted in mice and rats, paroxetine had no tumorigenic effect.
Genotoxicity: Genotoxicity was not observed in a battery of *in vitro* and *in vivo* tests.
Reproduction toxicity studies in rats have shown that paroxetine affects male and female fertility by reducing fertility index and pregnancy rate. In rats, increased pup mortality and delayed ossification were observed. The latter effects were likely related to maternal toxicity and are not considered a direct effect on the foetus/neonate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

<10 mg tablet>
<Tablet core:
Dibasic calcium phosphate dihydrate (E341)
Sodium starch glycolate (Type A)
Magnesium stearate (E470b).

Tablet coating:
Hypromellose (E464)
Macrogol 400
Polysorbate 80 (E433)
Titanium dioxide (E171)
Iron oxide red (E172).>

<20 mg tablet>
<Tablet core:
Dibasic calcium phosphate dihydrate (E341)
Sodium starch glycolate (Type A)
Magnesium stearate (E470b).

Tablet coating:
Hypromellose (E464)
Macrogol 400
Polysorbate 80 (E433)
Titanium dioxide (E171).>

<30 mg tablet>
<Tablet core:
Dibasic calcium phosphate dihydrate (E341)
Sodium starch glycolate (Type A)
Magnesium stearate (E470b).

Tablet coating:
Hypromellose (E464)
Macrogol 400
Polysorbate 80 (E433)
Titanium dioxide (E171)
Indigo carmine (E132).>

<Oral suspension>
<Polacrilin potassium
Dispersible cellulose (E460)
Propylene glycol
Glycerol (E422)
Sorbitol (E420)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Sodium citrate dihydrate (E331)
Citric acid anhydrate (E330)
Sodium saccharin (E954)
Natural orange flavour
Natural lemon flavour
Colouring agent sunset yellow FCF (E110)
Simethicone emulsion
Purified water.>

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

<10/20/30 mg tablet>
<3 years.>

<Oral suspension>
<2 years (1 month after opening).>

6.4 Special precautions for storage

<10/20/30 mg tablet>
<Do not store above 30ºC.
<Store in the original package in order to protect from light.>

<Oral suspension>
<Do not store above 25ºC.>

6.5 Nature and contents of container

<10 mg tablet>
<Blister packs comprising opaque polyvinyl (PVC) backed with aluminium foil.

Pack sizes: 14 and 28 tablets.

Not all pack sizes may be marketed.>

<20 mg tablet>
< Child-resistant blister packs comprising opaque polyvinyl chloride (PVC) backed with aluminium foil laminated with paper. Plastic containers (bottles) made of polypropylene, with polyethylene closures, may also be used.

Pack sizes: 50 x 1 tablet or 4, 10, 14, 20, 28, 30, 50, 56, 60, 98, 100, 250 and 500 tablets.

Not all pack sizes may be marketed.>

<30 mg tablet>
<Child-resistant blister packs comprising opaque polyvinyl chloride (PVC) backed with aluminium foil laminated with paper. Plastic containers (bottles) made of polypropylene, with polyethylene closures, may also be used.

Pack sizes: 28, 30, 56 and 60 tablets.

Not all pack sizes may be marketed.>

<Oral suspension>
<Amber glass bottle sealed with polypropylene child-resistant cap lined with a polyethylene wad.

A polypropylene measuring cup is included.

Pack size: 150 ml.>

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: [to be completed nationally]
Date of renewal of authorisation: 27 September 2010.

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 10 mg film-coated tablets
Paroxetine GSK 10 mg tablet
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 10 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 film-coated tablets
28 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 30ºC
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 10 mg film-coated tablets
Paroxetine GSK 10 mg tablet
Paroxetine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 20 mg film-coated tablets
Paroxetine 20 mg GSK
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 20 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

50 x 1 film-coated tablet
4 film-coated tablets
10 film-coated tablets
14 film-coated tablets
20 film-coated tablets
28 film-coated tablets
30 film-coated tablets
50 film-coated tablets
56 film-coated tablets
60 film-coated tablets
98 film-coated tablets
100 film-coated tablets
250 film-coated tablets
500 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 30ºC
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 20 mg film-coated tablets
Paroxetine 20 mg GSK
Paroxetine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 20 mg film-coated tablets
Paroxetine 20 mg GSK
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 20 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

4 film-coated tablets
10 film-coated tablets
14 film-coated tablets
20 film-coated tablets
28 film-coated tablets
30 film-coated tablets
50 film-coated tablets
56 film-coated tablets
60 film-coated tablets
98 film-coated tablets
100 film-coated tablets
250 film-coated tablets
500 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 30ºC
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 30 mg film-coated tablets
Paroxetine Ratiopharm
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 30 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
30 film-coated tablets
56 film-coated tablets
60 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 30ºC
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 30 mg film-coated tablets
Paroxetine Ratiopharm
Paroxetine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 30 mg film-coated tablets
Paroxetine Ratiopharm
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 30 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
30 film-coated tablets
56 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 30ºC
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON AND BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

SEROXAT 2 mg/ml oral suspension
Paroxetine 2 mg/ml suspension GSK
Paroxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each 10 ml of oral suspension contains 20 mg paroxetine (as paroxetine hydrochloride hemihydrate)

3. LIST OF EXCIPIENTS

Contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) (parabens), colouring agent sunset yellow FCF (E110) and sorbitol (E420) – see package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

150 ml of oral suspension

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use
Shake before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC
Keep your medicine in the original bottle
Discard the contents of the bottle one month after opening

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

PACKAGE LEAFLET

Package leaflet: Information for the patient

'TRADENAME' 10 mg film-coated tablets
'TRADENAME' 20 mg film-coated tablets
'TRADENAME' 30 mg film-coated tablets

Paroxetine (as the hydrochloride hemihydrate)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What 'Tradename' is and what it is used for

'TRADENAME' is a treatment for adults with depression and/or anxiety disorders. The anxiety disorders that 'TRADENAME' is used to treat are: obsessive compulsive disorder (repetitive, obsessive thoughts with uncontrollable behaviour), panic disorder (panic attacks, including those caused by agoraphobia, which is a fear of open spaces), social anxiety disorder (fear or avoidance of social situations), post traumatic stress disorder (anxiety caused by a traumatic event) and generalised anxiety disorder (generally feeling very anxious or nervous).
'TRADENAME' is one of a group of medicines called SSRIs (selective serotonin reuptake inhibitors). Everyone has a substance called serotonin in their brain. People who are depressed or anxious have lower levels of serotonin than others. It is not fully understood how 'TRADENAME' and other SSRIs work but they may help by increasing the level of serotonin in the brain. Treating depression or anxiety disorders properly is important to help you get better.

2. What you need to know before you take 'Tradename'

Do not take 'TRADENAME'...
- **If you are taking medicines called monoamine oxidase inhibitors** (MAOIs, including moclobemide and methylthioninium chloride (methylene blue)), or have taken them at any time within the last two weeks. Your doctor will advise you how you should begin taking 'TRADENAME' once you have stopped taking the MAOI.
- **If you are taking an anti-psychotic** called thioridazine or an anti-psychotic called pimozide.
- **If you are allergic** to paroxetine or any of the other ingredients of this medicine (listed in section 6).

If any of these apply to you, tell your doctor without taking 'TRADENAME'.

Warnings and precautions
Talk to your doctor or pharmacist before taking 'Tradename'
- Are you taking any other medicines (see *Taking other medicines and 'TRADENAME'*, inside this leaflet)?

- Are you taking tamoxifen to treat breast cancer <or fertility problems>? 'TRADENAME' may make tamoxifen less effective, so your doctor may recommend you take another antidepressant.
- Do you have kidney, liver or heart trouble?
- Do you have epilepsy or have a history of fits or seizures?
- Have you ever had episodes of mania (overactive behaviour or thoughts)?
- Are you having electro-convulsive therapy (ECT)?
- Do you have a history of bleeding disorders, or are you taking other medicines that may increase the risk of bleeding (these include medicines used to thin the blood, such as warfarin, antipsychotics such as perphenazine or clozapine, tricyclic antidepressants, medicines used for pain and inflammation called non-steroidal anti-inflammatory drugs or NSAIDs, such as acetylsalicylic acid, ibuprofen, celecoxib, etodolac, diclofenac, meloxicam)?
- Do you have diabetes?
- Are you on a low sodium diet?
- Do you have glaucoma (pressure in the eye)?
- Are you pregnant or planning to get pregnant (see *Pregnancy, breast-feeding and 'TRADENAME'*, inside this leaflet)?
- Are you under 18 years old (see *Children and adolescents under 18*, inside this leaflet)?

If you answer YES to any of these questions, and you have not already discussed them with your doctor, **go back to your doctor and ask what to do about taking 'TRADENAME'.**

Children and adolescents under 18

'TRADENAME' should not be used for children and adolescents under 18 years. Also, 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 'TRADENAME'. If your doctor has prescribed 'TRADENAME' for you (or your child) and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when you (or your child) are taking 'TRADENAME'. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of 'TRADENAME' in this age group have not yet been demonstrated.

In studies of 'TRADENAME' in under 18s, common side effects that affected less than 1 in 10 children/adolescents were: an increase in suicidal thoughts and suicide attempts, deliberately harming themselves, being hostile, aggressive or unfriendly, lack of appetite, shaking, abnormal sweating, hyperactivity (having too much energy), agitation, changing emotions (including crying and changes in mood) and unusual bruising or bleeding (such as nose bleeds). These studies also showed that the same symptoms affected children and adolescents taking sugar pills (placebo) instead of 'TRADENAME', although these were seen less often.

Some patients in these studies of under 18s had withdrawal effects when they stopped taking 'TRADENAME'. These effects were mostly similar to those seen in adults after stopping 'TRADENAME' (see Section 3, *How to take 'TRADENAME'*, inside this leaflet). In addition, patients under 18 also commonly (affecting less than 1 in 10) experienced stomach ache, feeling nervous and changing emotions (including crying, changes in mood, trying to hurt themselves, thoughts of suicide and attempting suicide).

Thoughts of suicide and worsening of your depression or anxiety disorder

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

You may be more likely to think like this:

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

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

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

Important side effects seen with 'TRADENAME'
Some patients who take 'TRADENAME' develop something called akathisia, where they **feel restless and feel like they can't sit or stand still**. Other patients develop something called **serotonin syndrome or neuroleptic malignant syndrome,** where they have some or all of the following symptoms: feeling very agitated or irritable, feeling confused, feeling restless, feeling hot, sweating, shaking, shivering, hallucinations (strange visions or sounds), muscle stiffness, sudden jerks of the muscles or a fast heartbeat. The severity can increase, leading to loss of consciousness. If you notice any of these symptoms, **contact your doctor.** For more information on these or other side effects of 'TRADENAME', see Section 4, *Possible Side Effects*, inside this leaflet.

Other medicines and 'TRADENAME'
Some medicines can affect the way 'TRADENAME' works, or make it more likely that you'll have side effects. 'TRADENAME' can also affect the way some other medicines work. These include:
- Medicines called **monoamine oxidase inhibitors** (MAOIs, including moclobemide and methylthioninium chloride (methylene blue)) – see *Do not take 'TRADENAME'*, inside this leaflet.
- Thioridazine or pimozide, which are **anti-psychotics** – see *Do not take 'TRADENAME'*, inside this leaflet.
- Acetylsalicylic acid, ibuprofen or other medicines called NSAIDs (non-steroidal anti-inflammatory drugs) like celecoxib, etodolac, diclofenac and meloxicam, used for **pain and inflammation**
- Tramadol and pethidine, **painkillers**
- Medicines called triptans, such as sumatriptan, used to treat **migraine**
- Other **antidepressants** including other SSRIs and tricyclic antidepressants like clomipramine, nortriptyline and desipramine
- A **dietary supplement** called tryptophan
- Mivacurium and suxamethonium (used in anaesthesia)
- Medicines such as lithium, risperidone, perphenazine, clozapine (called anti-psychotics) used to treat some **psychiatric conditions**
- Fentanyl, used in **anaesthesia** or to treat **chronic pain**
- A combination of fosamprenavir and ritonavir, which is used to treat **Human Immunodeficiency Virus (HIV) infection**
- St John's Wort, a herbal remedy for **depression**
- Phenobarbital, phenytoin, sodium valproate or carbamazepine, used to treat **fits** or **epilepsy**
- Atomoxetine which is used to treat **attention deficit hyperactivity disorder (ADHD)**
- Procyclidine, used to relieve tremor, especially in **Parkinson's Disease**
- Warfarin or other medicines (called anticoagulants) used to **thin the blood**
- Propafenone, flecainide and medicines used to treat an **irregular heartbeat**
- Metoprolol, a beta-blocker used to treat **high blood pressure** and **heart problems**
- Pravastatin, used to treat **high cholesterol**
- Rifampicin, used to treat **tuberculosis (TB)** and **leprosy**
- Linezolid, an **antibiotic**
- Tamoxifen, which is used to **treat breast cancer** <or **fertility problems>.**

If you are taking or have recently taken any of the medicines in this list, and you have not already discussed these with your doctor, **go back to your doctor and ask what to do.** The dose may need to be changed or you may need to be given another medicine.
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

‘TRADENAME’ with food, drink and alcohol
Do not drink alcohol while you are taking ‘TRADENAME’. Alcohol may make your symptoms or side effects worse. Taking ‘TRADENAME’ in the morning with food will reduce the likelihood of you feeling sick (nausea).

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. In babies whose mothers took ‘TRADENAME’ during the first few months of pregnancy, there have been some reports showing an increased risk of birth defects, in particular those affecting the heart. In the general population, about 1 in 100 babies are born with a heart defect. This increased to up to 2 in 100 babies in mothers who took ‘TRADENAME’. You and your doctor may decide that it is better for you to change to another treatment or to gradually stop taking ‘TRADENAME’ while you are pregnant. However, depending on your circumstances, your doctor may suggest that it is better for you to keep taking ‘TRADENAME’.

Make sure your midwife or doctor knows you’re taking ‘TRADENAME’. When taken during pregnancy, particularly late pregnancy, medicines like ‘TRADENAME’ may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN). In PPHN, the blood pressure in the blood vessels between the baby’s heart and the lungs is too high. If you take ‘TRADENAME’ during the last 3 months of pregnancy, your newborn baby might also have other conditions, which usually begin during the first 24 hours after birth. Symptoms include:
- trouble with breathing
- a blue-ish skin or being too hot or cold
- blue lips
- vomiting or not feeding properly
- being very tired, not able to sleep or crying a lot
- stiff or floppy muscles
- tremors, jitters or fits
- exaggerated reflexes.

If your baby has any of these symptoms when it is born, or you are concerned about your baby’s health, **contact your doctor or midwife who will be able to advise you.**

‘TRADENAME’ may get into breast milk in very small amounts. If you are taking ‘TRADENAME’, go back and talk to your doctor before you start breast-feeding. You and your doctor may decide that you can breast-feed while you're taking 'TRADENAME'.

Paroxetine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.

Driving and using machines
Possible side effects of ‘TRADENAME’ include dizziness, confusion, feeling sleepy or blurred vision. If you do get these side effects, do not drive or use machinery.

3. How to take ‘Tradename’

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
Sometimes you may need to take more than one tablet or half a tablet. This table will show you how many tablets to take.

Dose	Number of tablets to take
10 mg	<One white to pinkish-white tablet **or** Half a white tablet>
20 mg	<One white tablet **or** Two white to pinkish-white tablets>
30 mg	<One blue tablet **or** One-and-a-half white tablets **or** One white tablet + one white to pinkish-white tablet **or** Three white to pinkish-white tablets>
40 mg	<Two white tablets **or** One blue tablet + one white to pinkish-white tablet **or** Four white to pinkish-white tablets>
50 mg	<One blue tablet + one white tablet **or** Two-and-a-half white tablets **or** Two white tablets + one white to pinkish-white tablet **or** Five white to pinkish-white tablets>
60 mg	<Two blue tablets **or** Three white tablets **or** Six white to pinkish-white tablets>

The usual doses for different conditions are set out in the table below.

	Starting dose	Recommended daily dose	Maximum daily dose
Depression	20 mg	20 mg	50 mg
Obsessive Compulsive Disorder	20 mg	40 mg	60 mg
Panic Disorder	10 mg	40 mg	60 mg
Social Anxiety Disorder	20 mg	20 mg	50 mg
Post Traumatic Stress Disorder	20 mg	20 mg	50 mg
Generalised Anxiety Disorder	20 mg	20 mg	50 mg

Your doctor will advise you what dose to take when you first start taking ‘TRADENAME’. Most people start to feel better after a couple of weeks. If you don’t start to feel better after this time, talk to your doctor, who will advise you. He or she may decide to increase the dose gradually, 10 mg at a time, up to a maximum daily dose.

Take your tablets in the morning with food.

Swallow them with a drink of water.

Do not chew.

Your doctor will talk to you about how long you will need to keep taking your tablets. This may be for many months or even longer.

Older people
The maximum dose for people over 65 is 40 mg per day.

Patients with liver or kidney disease
If you have trouble with your liver or severe kidney disease, your doctor may decide that you should have a lower dose of 'TRADENAME' than usual.

If you take more 'TRADENAME' than you should
Never take more tablets than your doctor recommends. If you take too many 'TRADENAME' tablets (or someone else does), tell your doctor or a hospital straight away. Show them the pack of tablets.
Someone who has taken an overdose of 'TRADENAME' may have any one of the symptoms listed in section 4, *Possible side effects*, or the following symptoms: fever, uncontrollable tightening of the muscles.

If you forget to take 'TRADENAME'
Take your medicine at the same time every day.
If you do forget a dose, and you remember before you go to bed, take it straight away. Carry on as usual the next day.
If you only remember during the night, or the next day, leave out the missed dose. You may possibly get withdrawal effects, but these should go away after you take your next dose at the usual time.
Do not take a double dose to make up for a forgotten dose.

What to do if you're feeling no better
'TRADENAME' will not relieve your symptoms straight away – all antidepressants take time to work. Some people will start to feel better within a couple of weeks, but for others it may take a little longer. Some people taking antidepressants feel worse before feeling better. If you don't start to feel better after a couple of weeks, go back to your doctor who will advise you. Your doctor should ask to see you again a couple of weeks after you first start treatment. Tell your doctor if you haven't started to feel better.

If you stop taking 'TRADENAME'
Do not stop taking 'TRADENAME' until your doctor tells you to.
When stopping 'TRADENAME', your doctor will help you to reduce your dose slowly over a number of weeks or months – this should help reduce the chance of withdrawal effects. One way of doing this is to gradually reduce the dose of 'TRADENAME' you take by 10 mg a week. Most people find that any symptoms on stopping 'TRADENAME' are mild and go away on their own within two weeks. For some people, these symptoms may be more severe, or go on for longer.

If you get withdrawal effects when you are coming off your tablets your doctor may decide that you should come off them more slowly. If you get severe withdrawal effects when you stop taking 'TRADENAME', please see your doctor. He or she may ask you to start taking your tablets again and come off them more slowly.

If you do get withdrawal effects, you will still be able to stop 'TRADENAME'.

<u>Possible withdrawal effects when stopping treatment</u>

Studies show that 3 in 10 patients notice one or more symptoms on stopping 'TRADENAME'. Some withdrawal effects on stopping occur more frequently than others.

Common side effects, likely to affect up to 1 in 10 people:
- Feeling dizzy, unsteady or off-balance
- Feelings like pins and needles, burning sensations and (less commonly) electric shock sensations, including in the head, and buzzing, hissing, whistling, ringing or other persistent noise in the ears (tinnitus)

- Sleep disturbances (vivid dreams, nightmares, inability to sleep)
- Feeling anxious
- Headaches.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- Feeling sick (nausea)
- Sweating (including night sweats)
- Feeling restless or agitated
- Tremor (shakiness)
- Feeling confused or disorientated
- Diarrhoea (loose stools)
- Feeling emotional or irritable
- Visual disturbances
- Fluttering or pounding heartbeat (palpitations).

Please see your doctor if you are worried about withdrawal effects when stopping 'TRADENAME'.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Side effects are more likely to happen in the first few weeks of taking 'TRADENAME'.

<u>See the doctor if you get any of the following side effects during treatment.</u>

You may need to contact your doctor or go to a hospital straight away.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- **If you have unusual bruising or bleeding**, including vomiting blood or passing blood in your stools, **contact your doctor or go to a hospital straight away**.
- **If you find that you are not able to pass water, contact your doctor or go to a hospital straight away.**

Rare side effects, likely to affect up to 1 in every 1,000 people:
- **If you experience seizures** (fits), **contact your doctor or go to a hospital straight away.**
- **If you feel restless and feel like you can't sit or stand still,** you may have something called akathisia. Increasing your dose of 'TRADENAME' may make these feelings worse. If you feel like this, **contact your doctor.**
- **If you feel tired, weak or confused and have achy, stiff or uncoordinated muscles** this may be because your blood is low in sodium. If you have these symptoms, **contact your doctor.**

Very rare side effects, likely to affect up to 1 in every 10,000 people:
- **Allergic reactions, which may be severe to 'TRADENAME'.**
  If you develop a red and lumpy skin rash, swelling of the eyelids, face, lips, mouth or tongue, start to itch or have difficulty breathing (shortness of breath) or swallowing and feel weak or lightheaded resulting in collapse or loss of consciousness, **contact your doctor or go to a hospital straight away.**
- **If you have some or all of the following symptoms** you may have something called **serotonin syndrome or neuroleptic malignant syndrome.** The symptoms include: feeling very agitated or irritable, feeling confused, feeling restless, feeling hot, sweating, shaking, shivering, hallucinations (strange visions or sounds), muscle stiffness, sudden jerks of the muscles or a fast heartbeat. The severity can increase, leading to loss of consciousness. If you feel like this **contact your doctor.**
- **Acute glaucoma.**

If your eyes become painful and you develop blurred vision, **contact your doctor.**

Frequency unknown
- Some people have had thoughts of harming or killing themselves while taking 'TRADENAME' or soon after stopping treatment (see Section 2, *Before you take 'TRADENAME'*).
- Some people have experienced aggression while taking 'TRADENAME'.
  If you experience these side effects, contact your doctor.

<u>Other possible side effects during treatment</u>

Very common side effects, likely to affect more than 1 in 10 people:
- Feeling sick (nausea). Taking your medicine in the morning with food will reduce the chance of this happening.
- Change in sex drive or sexual function. For example, lack of orgasm and, in men, abnormal erection and ejaculation.

Common side effects, likely to affect up to 1 in 10 people:
- Increases in the level of cholesterol in the blood
- Lack of appetite
- Not sleeping well (insomnia) or feeling sleepy
- Abnormal dreams (including nightmares)
- Feeling dizzy or shaky (tremors)
- Headache
- Difficulty in concentrating
- Feeling agitated
- Feeling unusually weak
- Blurred vision
- Yawning, dry mouth
- Diarrhoea or constipation
- Vomiting
- Weight gain
- Sweating.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- A brief increase in blood pressure, or a brief decrease that may make you feel dizzy or faint when you stand up suddenly
- A faster than normal heartbeat
- Lack of movement, stiffness, shaking or abnormal movements in the mouth and tongue
- Dilated pupils
- Skin rashes
- Itching
- Feeling confused
- Having hallucinations (strange visions or sounds)
- An inability to urinate (urinary retention) or an uncontrollable, involuntary passing of urine (urinary incontinence).
- If you are a diabetic patient you may notice a loss of control of your blood sugar levels whilst taking 'TRADENAME'. Please speak to your doctor about adjusting the dosage of your insulin or diabetes medications.

Rare side effects, likely to affect up to 1 in every 1000 people:
- Abnormal production of breast milk in men and women
- A slow heartbeat
- Effects on the liver showing up in blood tests of your liver function
- Panic attacks
- Overactive behaviour or thoughts (mania)
- Feeling detached from yourself (depersonalisation)
- Feeling anxious

- Irresistible urge to move the legs (Restless Legs Syndrome)
- Pain in the joints or muscles
- Increase in a hormone called prolactin in the blood
- Menstrual period disorders (including heavy or irregular periods, bleeding between periods and absence or delay of periods).

Very rare side effects, likely to affect up to 1 in every 10,000 people:
- Skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) called erythema multiforme
- A widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome)
- A widespread rash with blisters and skin peeling on much of the body surface (toxic epidermal necrolysis)
- Liver problems that make the skin or whites of the eyes go yellow
- Syndrome of inappropriate antidiuretic hormone production (SIADH) which is a condition in which the body develops an excess of water and a decrease in sodium (salt) concentration, as a result of improper chemical signals. Patients with SIADH may become severely ill, or may have no symptoms at all
- Fluid or water retention (which may cause swelling of the arms or legs)
- Sensitivity to sunlight
- Painful erection of the penis that won't go away
- Low blood platelet count.

Some patients have developed buzzing, hissing, whistling, ringing or other persistent noise in the ears (tinnitus) when they take 'TRADENAME'.

An increased risk of bone fractures has been observed in patients taking this type of medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store 'Tradename'

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the blister or bottle and the carton. The expiry date refers to the last day of that month.
Do not store above 30ºC.
Store in the original package in order to protect from light.
If you are using half tablets, be careful to keep them safely in the pack.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What 'TRADENAME' contains

- 10 mg film-coated tablet
  The active substance is paroxetine (10 mg), as the hydrochloride hemihydrate.
  20 mg film-coated tablet
  The active substance is paroxetine (20 mg), as the hydrochloride hemihydrate.
  30 mg film-coated tablet

The active substance is paroxetine (30 mg), as the hydrochloride hemihydrate.

- The other ingredients are
  10 mg film-coated tablet
  in the tablet core: dibasic calcium phosphate dihydrate (E341), magnesium stearate (E470b) and sodium starch glycolate (Type A).
  in the tablet coat: hypromellose (E464), titanium dioxide (E171), macrogol 400, polysorbate 80 (E433) and iron oxide red (E172).
  20 mg film-coated tablet
  in the tablet core: dibasic calcium phosphate dihydrate (E341), magnesium stearate (E470b) and sodium starch glycolate (Type A).
  in the tablet coat: hypromellose (E464), titanium dixoide (E171), macrogol 400 and polysorbate 80 (E433).
  30 mg film-coated tablet
  in the tablet core: dibasic calcium phosphate dihydrate (E341), magnesium stearate (E470b) and sodium starch glycolate (Type A).
  In the tablet coat: hypromellose (E464), titanium dioxide (E171), macrogol 400, polysorbate 80 (E433) and indigo carmine (E132).

What 'TRADENAME' looks like and contents of the pack

'TRADENAME' 10 mg film-coated tablets are white to pinkish-white, oval-shaped tablets, marked 'FC1' on one side and 'GS' on the other side. The tablets have a break bar on both sides. Each pack of 'TRADENAME' contains blisters of 14 or 28 tablets.
20 mg film-coated tablet
'TRADENAME' 20 mg film-coated tablets are white, oval-shaped tablets, marked <'SEROXAT 20'><'DEROXAT 20'><'AROPAX 20'><'20'> on one side, and with a break bar on the other side. Each pack of 'TRADENAME' contains child-resistant blisters of 50 x 1 tablet or 4, 10, 14, 20, 28, 30, 50, 56, 60, 98, 100, 250 or 500 tablets.
30 mg film-coated tablet
'TRADENAME' 30 mg film-coated tablets are blue, oval-shaped tablets, marked <'SEROXAT 30'><'AROPAX 30'><'30'> on one side, and with a break bar on the other side. The break bar is only to facilitate breaking for ease of swallowing and not to divide into equal doses. Each pack of 'TRADENAME' contains child-resistant blisters of 28, 30, 56 or 60 tablets.
Not all packs may be available.

Marketing Authorisation Holder and Manufacturer

<[To be completed nationally]>

This medicinal product is authorised in the Member States of the EEA under the following names:
Licence number 566/04, 10 mg film-coated tablets:

Greece	Seroxat
Iceland	Seroxat
Ireland	Seroxat 10 mg film-coated tablets
Lithuania	Seroxat
The Netherlands	Seroxat 10 mg tablet
Norway	Seroxat
Slovakia	Seroxat 10 mg
United Kingdom	Seroxat

Licence number 566/01, 20 mg film-coated tablets:

Austria	Seroxat 20 mg - Filmtabletten
Belgium	Seroxat
Cyprus	Seroxat
Czech Republic	Seroxat 20mg
Denmark	Seroxat

Estonia	Seroxat
Finland	Seroxat
France	Deroxat
Germany	Seroxat 20 mg Filmtabletten
Greece	Seroxat
Hungary	Seroxat 20 mg filmtabletta
Iceland	Seroxat
Ireland	Seroxat 20 mg film-coated tablets
Italy	Seroxat
Latvia	Seroxat 20mg film-coated tablets
Lithuania	Seroxat
Luxemburg	Seroxat
Malta	Seroxat
The Netherlands	Seroxat 20 mg tablet
Norway	Seroxat 20 mg
Poland	Seroxat
Portugal	Seroxat
Slovakia	Seroxat 20 mg
Slovenia	Seroxat 20 mg
Spain	Seroxat
Sweden	Seroxat
United Kingdom	Seroxat

Licence number 566/02, 30 mg film-coated tablets:	
Belgium	Seroxat
Czech Republic	Seroxat 30 mg
Denmark	Seroxat
Greece	Seroxat
Ireland	Seroxat 30 mg film-coated tablets
Lithuania	Seroxat
Luxemburg	Seroxat
The Netherlands	Seroxat 30 mg tablet
Slovakia	Seroxat 30 mg
Slovenia	Seroxat
United Kingdom	Seroxat

Licence number 567/04, 10 mg film-coated tablets:	
The Netherlands	Paroxetine GSK 10 mg tablet
Spain	Paroxetina GSK

Licence number 567/01, 20 mg film-coated tablets:	
France	Paroxétine Biogaran
Hungary	Paroxat 20 mg
Italy	Eutimil
The Netherlands	Paroxetine GSK 20 mg
Slovenia	Paroxat 20mg
Spain	Frosinor

Licence number 567/02, 30 mg film-coated tablets:	
The Netherlands	Paroxetine GSK 30 mg
Slovenia	Paroxat 30mg

Licence number 568/01, 20 mg film-coated tablets:	
France	Paroxétine Isomed
The Netherlands	Paroxetine 20 mg tablet GSK
Spain	Motivan

Licence number 568/02, 30 mg film-coated tablets:	
The Netherlands	Paroxetine GSK 30mg

Licence number 569/01, 20 mg film-coated tablets:	
Austria	Paroxetin Allen 20 mg - Filmtabletten
France	Paroxétine RPG
Germany	Paroxetin GSK 20 mg Filmtabletten
The Netherlands	Paroxetine 20 mg GSK
Portugal	Paroxetina Ilf 20 mg comprimidos revestidos

Licence number 570/01, 20 mg film-coated tablets:	
The Netherlands	Paroxetine 20 mg Focus, filmomhulde tabletten

Licence number 591/01, 20 mg film-coated tablets:	
The Netherlands	Paroxetine SKB 20 mg

Licence number 591/02, 30 mg film-coated tablets:	
The Netherlands	Paroxetine SKB 30 mg

Licence number 592/01, 20 mg film-coated tablets:	
The Netherlands	Paroxetine GlaxoSmithKline 20 mg
Spain	Paroxetina Mundogen

You may find it helpful to contact a self-help group, or patient organisation, to find out more about your condition. Your doctor will be able to give you details.

This leaflet was last revised in: to be completed nationally

Package leaflet: Information for the patient

'TRADENAME' 2 mg/ml oral suspension

Paroxetine (as the hydrochloride hemihydrate)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What 'Tradename' is and what it is used for

'TRADENAME' is a treatment for adults with depression and/or anxiety disorders. The anxiety disorders that 'TRADENAME' is used to treat are: obsessive compulsive disorder (repetitive, obsessive thoughts with uncontrollable behaviour), panic disorder (panic attacks, including those caused by agoraphobia, which is a fear of open spaces), social anxiety disorder (fear or avoidance of social situations), post traumatic stress disorder (anxiety caused by a traumatic event) and generalised anxiety disorder (generally feeling very anxious or nervous).
'TRADENAME' is one of a group of medicines called SSRIs (selective serotonin reuptake inhibitors). Everyone has a substance called serotonin in their brain. People who are depressed or anxious have lower levels of serotonin than others. It is not fully understood how 'TRADENAME' and other SSRIs work but they may help by increasing the level of serotonin in the brain. Treating depression or anxiety disorders properly is important to help you get better.

2. What you need to know before you take 'Tradename'

Do not take 'TRADENAME'…
- **If you are taking medicines called monoamine oxidase inhibitors** (MAOIs, including moclobemide and methylthioninium chloride (methylene blue)), or have taken them at any time within the last two weeks. Your doctor will advise you how you should begin taking 'TRADENAME' once you have stopped taking the MAOI.
- **If you are taking an anti-psychotic** called thioridazine or an anti-psychotic called pimozide.
- **If you are allergic** to paroxetine or any of the other ingredients of 'this medicine' (listed in section 6).

If any of these apply to you, tell your doctor without taking 'TRADENAME'.

Warnings and precautions
Talk to your doctor or pharmacist before taking 'Tradename'
- Are you taking any other medicines (see *Taking other medicines and 'TRADENAME'*, inside this leaflet)?
- Are you taking tamoxifen to treat breast cancer <or fertility problems>? 'TRADENAME' may make tamoxifen less effective, so your doctor may recommend you take another antidepressant.

- Do you have kidney, liver or heart trouble?
- Do you have epilepsy or have a history of fits or seizures?
- Have you ever had episodes of mania (overactive behaviour or thoughts)?
- Are you having electro-convulsive therapy (ECT)?
- Do you have a history of bleeding disorders, or are you taking other medicines that may increase the risk of bleeding (these include medicines used to thin the blood, such as warfarin, antipsychotics such as perphenazine or clozapine, tricyclic antidepressants, medicines used for pain and inflammation called non-steroidal anti-inflammatory drugs or NSAIDs, such as acetylsalicylic acid, ibuprofen, celecoxib, etodolac, diclofenac, meloxicam)?
- Do you have diabetes?
- Are you on a low sodium diet?
- Do you have glaucoma (pressure in the eye)?
- Are you pregnant or planning to get pregnant (see *Pregnancy, breast-feeding and 'TRADENAME'*, inside this leaflet)?
- Are you under 18 years old (see *Children and adolescents under 18*, inside this leaflet)?

If you answer YES to any of these questions, and you have not already discussed them with your doctor, **go back to your doctor and ask what to do about taking 'TRADENAME'.**

Children and adolescents under 18

'TRADENAME' should not be used for children and adolescents under 18 years. Also, 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 'TRADENAME'. If your doctor has prescribed 'TRADENAME' for you (or your child) and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when you (or your child) are taking 'TRADENAME'. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of 'TRADENAME' in this age group have not yet been demonstrated.

In studies of 'TRADENAME' in under 18s, common side effects that affected less than 1 in 10 children/adolescents were: an increase in suicidal thoughts and suicide attempts, deliberately harming themselves, being hostile, aggressive or unfriendly, lack of appetite, shaking, abnormal sweating, hyperactivity (having too much energy), agitation, changing emotions (including crying and changes in mood) and unusual bruising or bleeding (such as nose bleeds). These studies also showed that the same symptoms affected children and adolescents taking sugar pills (placebo) instead of 'TRADENAME', although these were seen less often.

Some patients in these studies of under 18s had withdrawal effects when they stopped taking 'TRADENAME'. These effects were mostly similar to those seen in adults after stopping 'TRADENAME' (see Section 3, *How to take 'TRADENAME'*, inside this leaflet). In addition, patients under 18 also commonly (affecting less than 1 in 10) experienced stomach ache, feeling nervous and changing emotions (including crying, changes in mood, trying to hurt themselves, thoughts of suicide and attempting suicide).

Thoughts of suicide and worsening of your depression or anxiety disorder

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

You may be more likely to think like this:

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

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

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

Important side effects seen with 'TRADENAME'
Some patients who take 'TRADENAME' develop something called akathisia, where they **feel restless and feel like they can't sit or stand still**. Other patients develop something called **serotonin syndrome or neuroleptic malignant syndrome,** where they have some or all of the following symptoms: feeling very agitated or irritable, feeling confused, feeling restless, feeling hot, sweating, shaking, shivering, hallucinations (strange visions or sounds), muscle stiffness, sudden jerks of the muscles or a fast heartbeat. The severity can increase, leading to loss of consciousness. If you notice any of these symptoms, **contact your doctor.** For more information on these or other side effects of 'TRADENAME', see Section 4, *Possible Side Effects*, inside this leaflet.

Other medicines and 'TRADENAME'
Some medicines can affect the way 'TRADENAME' works, or make it more likely that you'll have side effects. 'TRADENAME' can also affect the way some other medicines work. These include:
- Medicines called **monoamine oxidase inhibitors** (MAOIs, including moclobemide and methyl thioninium chloride (methylene blue)) – see *Do not take 'TRADENAME'*, inside this leaflet.
- Thioridazine or pimozide, which are **anti-psychotics** – see *Do not take 'TRADENAME'*, inside this leaflet.
- Acetylsalicylic acid, ibuprofen or other medicines called NSAIDs (non-steroidal anti-inflammatory drugs) like celecoxib, etodolac, diclofenac and meloxicam, used for **pain and inflammation**
- Tramadol and pethidine, **painkillers**
- Medicines called triptans, such as sumatriptan, used to treat **migraine**
- Other **antidepressants** including other SSRIs and tricyclic antidepressants like clomipramine, nortriptyline and desipramine
- A **dietary supplement** called tryptophan
- Mivacurium and suxamethonium (used in anaesthesia)
- Medicines such as lithium, risperidone, perphenazine, clozapine (called anti-psychotics) used to treat some **psychiatric conditions**
- Fentanyl, used in **anaesthesia** or to treat **chronic pain**
- A combination of fosamprenavir and ritonavir, which is used to treat **Human Immunodeficiency Virus (HIV) infection**
- St John's Wort, a herbal remedy for **depression**
- Phenobarbital, phenytoin, sodium valproate or carbamazepine, used to treat **fits** or **epilepsy**
- Atomoxetine which is used to treat **attention deficit hyperactivity disorder (ADHD)**
- Procyclidine, used to relieve tremor, especially in **Parkinson's Disease**
- Warfarin or other medicines (called anticoagulants) used to **thin the blood**
- Propafenone, flecainide and medicines used to treat an **irregular heartbeat**
- Metoprolol, a beta-blocker used to treat **high blood pressure** and **heart problems**
- Pravastatin, used to treat **high cholesterol**
- Rifampicin, used to treat **tuberculosis (TB)** and **leprosy**
- Linezolid, an **antibiotic**
- Tamoxifen, which is used to **treat breast cancer** <or **fertility problems>**
- Medicines such as cimetidine or omeprazole, which are used to **reduce the amount of acid in your stomach.**

If you are taking or have recently taken any of the medicines in this list, and you have not already discussed these with your doctor, **go back to your doctor and ask what to do.** The dose may need to be changed or you may need to be given another medicine.
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

'TRADENAME' with food, drink and alcohol
Do not drink alcohol while you are taking 'TRADENAME'. Alcohol may make your symptoms or side effects worse. Taking 'TRADENAME' in the morning with food will reduce the likelihood of you feeling sick (nausea).

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. In babies whose mothers took 'TRADENAME' during the first few months of pregnancy, there have been some reports showing an increased risk of birth defects, in particular those affecting the heart. In the general population, about 1 in 100 babies are born with a heart defect. This increased to up to 2 in 100 babies in mothers who took 'TRADENAME'. You and your doctor may decide that it is better for you to change to another treatment or to gradually stop taking 'TRADENAME' while you are pregnant. However, depending on your circumstances, your doctor may suggest that it is better for you to keep taking 'TRADENAME'.

Make sure your midwife or doctor knows you're taking 'TRADENAME'. When taken during pregnancy, particularly late pregnancy, medicines like 'TRADENAME' may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN). In PPHN, the blood pressure in the blood vessels between the baby's heart and the lungs is too high. If you take 'TRADENAME' during the last 3 months of pregnancy, your newborn baby might also have other conditions, which usually begin during the first 24 hours after birth. Symptoms include:
- trouble with breathing
- a blue-ish skin or being too hot or cold
  blue lips
- vomiting or not feeding properly
- being very tired, not able to sleep or crying a lot
- stiff or floppy muscles
- tremors, jitters or fits
- exaggerated reflexes.

If your baby has any of these symptoms when it is born, or you are concerned about your baby's health, **contact your doctor or midwife who will be able to advise you.**

'TRADENAME' may get into breast milk in very small amounts. If you are taking 'TRADENAME', go back and talk to your doctor before you start breast-feeding. You and your doctor may decide that you can breast-feed while you're taking 'TRADENAME'.

Paroxetine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.

Driving and using machines
Possible side effects of 'TRADENAME' include dizziness, confusion, feeling sleepy or blurred vision. If you do get these side effects, do not drive or use machinery.

'TRADENAME' contains
- This medicine contains the sugar, sorbitol E420. If you have you been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking 'TRADENAME'.
- Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) may cause allergic reactions (possible delayed)
- Sunset yellow FCF (E110) is used as a colouring agent, and may cause allergic reactions.

3. How to take 'Tradename'

Always take this medicine' exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual doses for different conditions are set out in the table below.

	Starting dose	Recommended daily dose	Maximum daily dose
Depression	10 ml	10 ml	25 ml
Obsessive Compulsive Disorder	10 ml	20 ml	30 ml
Panic Disorder	5 ml	20 ml	30 ml
Social Anxiety Disorder	10 ml	10 ml	25 ml
Post Traumatic Stress Disorder	10 ml	10 ml	25 ml
Generalised Anxiety Disorder	10 ml	10 ml	25 ml

Your doctor will advise you what dose to take when you first start taking 'TRADENAME'. Most people start to feel better after a couple of weeks. If you don't start to feel better after this time, talk to your doctor, who will advise you. He or she may decide to increase the dose gradually, 5 ml (10 mg of paroxetine) at a time, up to a maximum daily dose.

Shake the bottle before use.

Take 'TRADENAME' in the morning with food.

Your doctor will talk to you about how long you will need to keep taking your medicine. This may be for many months or even longer.

Older people
The maximum dose for people over 65 is 20 ml (40 mg of paroxetine) per day.

Patients with liver or kidney disease
If you have trouble with your liver or severe kidney disease, your doctor may decide that you should have a lower dose of 'TRADENAME' than usual.

If you take more 'TRADENAME' than you should
Never take more medicine than your doctor recommends. If you take too much 'TRADENAME' (or someone else does), tell your doctor or a hospital straight away. Show them the bottle of medicine. Someone who has taken an overdose of 'TRADENAME' may have any one of the symptoms listed in section 4, *Possible side effects*, or the following symptoms: fever, uncontrollable tightening of the muscles.

If you forget to take 'TRADENAME'
Take your medicine at the same time every day.
If you do forget a dose, and you remember before you go to bed, take it straight away. Carry on as usual the next day.
If you only remember during the night, or the next day, leave out the missed dose. You may possibly get withdrawal effects, but these should go away after you take your next dose at the usual time.
Do not take a double dose to make up for a forgotten dose.

What to do if you're feeling no better
'TRADENAME' will not relieve your symptoms straight away – all antidepressants take time to work. Some people will start to feel better within a couple of weeks, but for others it may take a little longer. Some people taking antidepressants feel worse before feeling better. If you don't start to feel better after a couple of weeks, go back to your doctor who will advise you. Your doctor should ask to see you again a couple of weeks after you first start treatment. Tell your doctor if you haven't started to feel better.

If you stop taking 'TRADENAME'
Do not stop taking 'TRADENAME' until your doctor tells you to.
When stopping 'TRADENAME', your doctor will help you to reduce your dose slowly over a number of weeks or months – this should help reduce the chance of withdrawal effects. One way of doing this is to gradually reduce the dose of 'TRADENAME' you take by 5 ml (10 mg of paroxetine)

a week. Most people find that any symptoms on stopping 'TRADENAME' are mild and go away on their own within two weeks. For some people, these symptoms may be more severe, or go on for longer.

If you get withdrawal effects when you are coming off your medicine your doctor may decide that you should come off them more slowly. If you get severe withdrawal effects when you stop taking 'TRADENAME', please see your doctor. He or she may ask you to start taking your medicine again and come off them more slowly.

If you do get withdrawal effects, you will still be able to stop 'TRADENAME'.

Possible withdrawal effects when stopping treatment

Studies show that 3 in 10 patients notice one or more symptoms on stopping 'TRADENAME'. Some withdrawal effects on stopping occur more frequently than others.

Common side effects, likely to affect up to 1 in 10 people:
- Feeling dizzy, unsteady or off-balance
- Feelings like pins and needles, burning sensations and (less commonly) electric shock sensations, including in the head, and buzzing, hissing, whistling, ringing or other persistent noise in the ears (tinnitus)
- Sleep disturbances (vivid dreams, nightmares, inability to sleep)
- Feeling anxious
- Headaches.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- Feeling sick (nausea)
- Sweating (including night sweats)
- Feeling restless or agitated
- Tremor (shakiness)
- Feeling confused or disorientated
- Diarrhoea (loose stools)
- Feeling emotional or irritable
- Visual disturbances
- Fluttering or pounding heartbeat (palpitations).

Please see your doctor if you are worried about withdrawal effects when stopping 'TRADENAME'.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Side effects are more likely to happen in the first few weeks of taking 'TRADENAME'.

See the doctor if you get any of the following side effects during treatment.

You may need to contact your doctor or go to a hospital straight away.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- **If you have unusual bruising or bleeding**, including vomiting blood or passing blood in your stools, **contact your doctor or go to a hospital straight away**.
- **If you find that you are not able to pass water, contact your doctor or go to a hospital straight away.**

Rare side effects, likely to affect up to 1 in every 1,000 people:
- **If you experience seizures** (fits), **contact your doctor or go to a hospital straight away.**
- **If you feel restless and feel like you can't sit or stand still,** you may have something called *akathisia*. Increasing your dose of 'TRADENAME' may make these feelings worse. If you feel like this, **contact your doctor.**
- **If you feel tired, weak or confused and have achy, stiff or uncoordinated muscles** this may be because your blood is low in sodium. If you have these symptoms, **contact your doctor.**

Very rare side effects, likely to affect up to 1 in every 10,000 people:
- **Allergic reactions, which may be severe to 'TRADENAME'.**
  If you develop a red and lumpy skin rash, swelling of the eyelids, face, lips, mouth or tongue, start to itch or have difficulty breathing (shortness of breath) or swallowing and feel weak or lightheaded resulting in collapse or loss of consciousness, **contact your doctor or go to a hospital straight away.**
- **If you have some or all of the following symptoms** you may have something called **serotonin syndrome or neuroleptic malignant syndrome.** The symptoms include: feeling very agitated or irritable, feeling confused, feeling restless, feeling hot, sweating, shaking, shivering, hallucinations (strange visions or sounds), muscle stiffness, sudden jerks of the muscles or a fast heartbeat. The severity can increase, leading to loss of consciousness. If you feel like this **contact your doctor.**
- **Acute glaucoma.**
  If your eyes become painful and you develop blurred vision, **contact your doctor.**

Frequency unknown
- Some people have had thoughts of harming or killing themselves while taking 'TRADENAME' or soon after stopping treatment (see Section 2, *Before you take 'TRADENAME'*).
- Some people have experienced aggression while taking 'TRADENAME'.
  If you experience these side effects, contact your doctor.

<u>Other possible side effects during treatment</u>

Very common side effects, likely to affect more than 1 in 10 people:
- Feeling sick (nausea). Taking your medicine in the morning with food will reduce the chance of this happening.
- Change in sex drive or sexual function. For example, lack of orgasm and, in men, abnormal erection and ejaculation.

Common side effects, likely to affect up to 1 in 10 people:
- Increases in the level of cholesterol in the blood
- Lack of appetite
- Not sleeping well (insomnia) or feeling sleepy
- Abnormal dreams (including nightmares)
- Feeling dizzy or shaky (tremors)
- Headache
- Difficulty in concentrating
- Feeling agitated
- Feeling unusually weak
- Blurred vision
- Yawning, dry mouth
- Diarrhoea or constipation
- Vomiting
- Weight gain
- Sweating.

Uncommon side effects, likely to affect up to 1 in every 100 people:
- A brief increase in blood pressure, or a brief decrease that may make you feel dizzy or faint when you stand up suddenly

- A faster than normal heartbeat
- Lack of movement, stiffness, shaking or abnormal movements in the mouth and tongue
- Dilated pupils
- Skin rashes
- Itching
- Feeling confused
- Having hallucinations (strange visions or sounds)
- An inability to urinate (urinary retention) or an uncontrollable, involuntary passing of urine (urinary incontinence)
- If you are a diabetic patient you may notice a loss of control of your blood sugar levels whilst taking 'TRADENAME'. Please speak to your doctor about adjusting the dosage of your insulin or diabetes medications.

Rare side effects, likely to affect up to 1 in every 1000 people:
- Abnormal production of breast milk in men and women
- A slow heartbeat
- Effects on the liver showing up in blood tests of your liver function
- Panic attacks
- Overactive behaviour or thoughts (mania)
- Feeling detached from yourself (depersonalisation)
- Feeling anxious
- Irresistible urge to move the legs (Restless Legs Syndrome)
- Pain in the joints or muscles
- Increase in a hormone called prolactin in the blood
- Menstrual period disorders (including heavy or irregular periods, bleeding between periods and absence or delay of periods).

Very rare side effects, likely to affect up to 1 in every 10,000 people:
- Skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) called erythema multiforme
- A widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome)
- A widespread rash with blisters and skin peeling on much of the body surface (toxic epidermal necrolysis)
- Liver problems that make the skin or whites of the eyes go yellow
- Syndrome of inappropriate antidiuretic hormone production (SIADH) which is a condition in which the body develops an excess of water and a decrease in sodium (salt) concentration, as a result of improper chemical signals. Patients with SIADH may become severely ill, or may have no symptoms at all
- Fluid or water retention (which may cause swelling of the arms or legs)
- Sensitivity to sunlight
- Painful erection of the penis that won't go away
- Low blood platelet count.

Some patients have developed buzzing, hissing, whistling, ringing or other persistent noise in the ears (tinnitus) when they take 'TRADENAME'.

An increased risk of bone fractures has been observed in patients taking this type of medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store 'Tradename'

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
Do not store above 25ºC.
Keep your medicine in the original bottle.
Discard the contents of the bottle one month after opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What 'TRADENAME' contains

- The active substance is paroxetine (2 mg/ml), as the hydrochloride hemihydrate.
- The other ingredients are polacrilin potassium, dispersible cellulose (E460), propylene glycol, glycerol (E422), sorbitol (E420), methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium citrate dihydrate (E331), citric acid anhydrate (E330), sodium saccharin (E954), natural orange flavour, natural lemon flavour, colouring agent sunset yellow FCF (E110), simethicone emulsion and purified water.

What 'TRADENAME' looks like and contents of the pack

'TRADENAME' 2 mg/ml oral suspension is an orange liquid with a smell of oranges and a sweet taste. It is available in bottles of 150 ml, with a measuring cup.

Marketing Authorisation Holder and Manufacturer

<[To be completed nationally]>

This medicinal product is authorised in the Member States of the EEA under the following names:

Licence number 566/03:

Austria	Seroxat 2 mg/ml - Suspension
Belgium	Seroxat
Denmark	Seroxat
France	Deroxat
Germany	Seroxat 2 mg/ml Suspension zum Einnehmen
Greece	Seroxat
Ireland	Seroxat 20 mg/10ml oral suspension
Italy	Seroxat
Luxemburg	Seroxat
The Netherlands	Seroxat suspension 2 mg/ml
Portugal	Seroxat
United Kingdom	Seroxat

Licence number 567/03:

Italy	Eutimil
The Netherlands	Paroxetine GSK suspension 2 mg/ml

You may also find it helpful to contact a self-help group, or patient organisation, to find out more about your condition. Your doctor will be able to give you details.

This leaflet was last revised in: to be completed nationally.