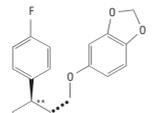


PC-19 PRESCRIBING INFORMATION 733647 PAXIL CR® (paroxetine hydrochloride) Controlled-Release Tablets

Sucidality in Children and Adolescents
Antidepressants increased the risk of suicidal thinking and behavior (sucidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of PAXIL CR in children and adolescents should be aware that these drugs may increase the risk of suicidal thoughts or actions. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PAXIL CR is not approved for use in pediatric patients. (See WARNINGS—Use in Children and Adolescents.)

Controlled Analyses of Short-Term (4 to 16 Weeks) Placebo-Controlled Trials of 9 Antidepressant Drugs (SSRIs and others) in Children and Adolescents with Major Depressive Disorder (MDD), Obsessive Compulsive Disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4,400 patients) have revealed a greater risk of adverse events representing suicidal thoughts or behavior (sucidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2% seen in these trials.

DESCRIPTION
PAXIL CR (paroxetine hydrochloride) is an orally administered psychotropic drug with a chemical structure unrelated to other selective serotonin reuptake inhibitors or to tricyclic, tetracyclic, or other available antidepressant or antianginal agents. It is the hydrochloride salt of a piperidine compound identified chemically as (-)-trans-4-(4-(fluorophenyl)-3-(4-(4-methyleneoxyphenoxy) methyl) piperidine hydrochloride hemihydrate and has the empirical formula $C_{20}H_{21}FNO_2 \cdot HCl \cdot 1.5H_2O$ (molecular weight is 374.8 (352.4 as a free base). The structural formula of paroxetine hydrochloride is:



Paroxetine hydrochloride is a white to off-white powder, having a melting point range of 120° to 130°C and a solubility of 5.4 mg/mL in water. Each enteric, film-coated, controlled-release tablet contains paroxetine hydrochloride equivalent to paroxetine as indicated on the label. The tablets are white to off-white. One layer of the tablet consists of a degradable barrier layer and the other layers the active material in a hydrophilic matrix.

Pharmacokinetics: Paroxetine hydrochloride is completely absorbed after oral dosing of a solution of the hydrochloride salt. The elimination half-life is approximately 15 to 20 hours after a single dose of PAXIL CR. Paroxetine is extensively metabolized and the metabolites are considered to be inactive. Nonlinearly in pharmacokinetics is observed with increasing doses. Paroxetine is metabolized in part by CYP2D6. In vitro radioligand binding studies indicate that paroxetine has a high affinity for muscarinic, alpha₁-, alpha₂-, beta-adrenergic, dopamine (D₁–5-HT₁, 5-HT₂), and histamine (H₁)-receptors; antagonism of muscarinic, histaminergic, and alpha₁-adrenergic receptors has been associated with various anticholinergic, sedative, and antihistaminic effects of paroxetine. Because the relative potencies of paroxetine's major metabolites are at most 1/50 of the parent compound, they are essentially inactive.

Pharmacodynamics: Paroxetine hydrochloride is pharmacodynamically completely absorbed after oral dosing of a solution of the hydrochloride salt. The elimination half-life is approximately 15 to 20 hours after a single dose of PAXIL CR. Paroxetine is extensively metabolized and the metabolites are considered to be inactive. Nonlinearly in pharmacokinetics is observed with increasing doses. Paroxetine is metabolized in part by CYP2D6. In vitro radioligand binding studies indicate that paroxetine has a high affinity for muscarinic, alpha₁-, alpha₂-, beta-adrenergic, dopamine (D₁–5-HT₁, 5-HT₂), and histamine (H₁)-receptors; antagonism of muscarinic, histaminergic, and alpha₁-adrenergic receptors has been associated with various anticholinergic, sedative, and antihistaminic effects of paroxetine. Because the relative potencies of paroxetine's major metabolites are at most 1/50 of the parent compound, they are essentially inactive.

Pharmacokinetics: Paroxetine hydrochloride is pharmacodynamically completely absorbed after oral dosing of a solution of the hydrochloride salt. The elimination half-life is approximately 15 to 20 hours after a single dose of PAXIL CR. Paroxetine is extensively metabolized and the metabolites are considered to be inactive. Nonlinearly in pharmacokinetics is observed with increasing doses. Paroxetine is metabolized in part by CYP2D6. In vitro radioligand binding studies indicate that paroxetine has a high affinity for muscarinic, alpha₁-, alpha₂-, beta-adrenergic, dopamine (D₁–5-HT₁, 5-HT₂), and histamine (H₁)-receptors; antagonism of muscarinic, histaminergic, and alpha₁-adrenergic receptors has been associated with various anticholinergic, sedative, and antihistaminic effects of paroxetine. Because the relative potencies of paroxetine's major metabolites are at most 1/50 of the parent compound, they are essentially inactive.

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(very much improved or less interest) on the Clinical Global Impression (CGI) Global Improvement score, and the CGI Improvement responder criterion. For patients who completed the trial, 64% of patients treated with PAXIL CR compared to 34.7% of patients treated with placebo were CGI Improvement responders.

Other Clinical Studies: In placebo-controlled studies in treatment outcomes as a function of gender. Subgroup analyses of studies utilizing the immediate-release formulation of paroxetine generally did not indicate differences in treatment outcomes as a function of age, race, or gender.

Major Depressive Disorder: The effectiveness of PAXIL CR for the treatment of PMDD utilizing a continuous dosing regimen has been established in 2 placebo-controlled trials. Patients in these trials met DSM-IV criteria for PMDD. In a pool of 1,030 patients treated with daily doses of PAXIL CR 12.5 or 25 mg/day, or placebo the mean duration of the PMDD symptoms was significantly shorter in patients treated with PAXIL CR than in those treated with placebo. In these trials, the efficacy of PAXIL CR in combination with systemic (including oral) hormonal contraceptives for the continuous daily treatment of PMDD is unknown. In both positive studies, patients (N = 672) were treated with 12.5 mg/day or 25 mg/day of PAXIL CR or placebo continuously throughout the menstrual cycle for a period of 3 menstrual cycles. The VAS total score is a patient-rated instrument that mirrors the diagnostic criteria of PMDD as identified in the DSM-IV, and includes assessments for mood, physical symptoms, and other symptoms. 12.5 mg/day and 25 mg/day of PAXIL CR were significantly more effective than placebo as measured by change from baseline to the endpoint on the total phase VAS total score.

In a third study exploring intermittent dosing, patients (N = 366) were treated for 2 weeks prior to the onset of menses (initial phase dosing, also known as intermittent dosing) with 12.5 mg/day or 25 mg/day of PAXIL CR or placebo for a period of 3 months, 12.5 mg/day and 25 mg/day of PAXIL CR, as initial phase dosing, was significantly more effective than placebo as measured by change from baseline total phase VAS total score.

There is insufficient information to determine the effect of race or age on outcome in these studies.

INDICATIONS AND USAGE
Major Depressive Disorder: PAXIL CR is indicated for the treatment of major depressive disorder.

The efficacy of PAXIL CR in the treatment of a major depressive episode was established in two 12-week controlled trials of outpatients whose diagnoses corresponded to the DSM-IV category of major depressive disorder (see CLINICAL PHARMACOLOGY—Clinical Trials).

A major depressive episode (DSM-IV) comprises a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed mood or loss of interest or pleasure in previously enjoyed activities, accompanied by at least four of the following, and includes the presence of at least 5 of the following 9 symptoms during the same 2-week period. Depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt, or suicidal ideation.

The antidepressant action of paroxetine in hospitalized depressed patients has not been adequately evaluated. Paroxetine or other antidepressants during the first trimester of pregnancy have been shown to increase the effectiveness of immediate-release paroxetine hydrochloride in maintaining a response in major depressive disorder for up to 1 year has been demonstrated in a placebo-controlled trial (see CLINICAL PHARMACOLOGY—Clinical Trials). The physician who elects to use PAXIL CR for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Panic Disorder: PAXIL CR is indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-IV. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional panic attacks or the implications or consequences of the attacks, and/or a significant change in behavior of the patient at the attacks. The efficacy of PAXIL CR controlled-release tablets was established in two 10-week trials in panic disorder patients whose diagnoses corresponded to the DSM-IV category of panic disorder (see CLINICAL PHARMACOLOGY—Clinical Trials).

Premenstrual Dysphoric Disorder: The effectiveness of PAXIL CR for a desor of the risks of discontinuation of PAXIL CR was established in a 12-week trial, in adult outpatients with social anxiety disorder (DSM-IV). PAXIL CR has not been studied in children or adolescents with social phobia (see CLINICAL PHARMACOLOGY—Clinical Trials).

Social Anxiety Disorder: PAXIL CR is indicated for the treatment of social anxiety disorder, also known as social phobia, as defined in DSM-IV (2002). Social anxiety disorder is characterized by a marked and persistent fear of 1 or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack. The feared situations are avoided or endured with intense anxiety or discomfort, or the anticipation, or distress, or discomfort associated with the feared situation interferes significantly with the person's normal routine, occupational or academic functioning, or social activities or relationships, or is otherwise markedly distressing about having the phobias. Lesser degrees of performance anxiety or shyness generally do not require pharmacologic treatment.

The efficacy of PAXIL CR, as a treatment for social anxiety disorder has been established, in part, on the basis of extrapolation from studies of paroxetine hydrochloride in bipolar patients. In a subset of patients classified as bipolar, the efficacy of PAXIL CR was established in a 12-week trial, in adult outpatients with social anxiety disorder (DSM-IV). PAXIL CR has not been studied in children or adolescents with social phobia (see CLINICAL PHARMACOLOGY—Clinical Trials).

Serotonin Syndrome: During premarketing testing of immediate-release paroxetine hydrochloride, seizures occurred in 0.1% of paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

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Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

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Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

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symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, PAXIL CR demonstrated statistically significant differences in the following areas: Such symptoms such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that PAXIL CR is not approved for use in treating bipolar depression.

Subgroup Analyses: In placebo-controlled studies in treatment outcomes as a function of gender. Subgroup analyses of studies utilizing the immediate-release formulation of paroxetine generally did not indicate differences in treatment outcomes as a function of age, race, or gender.

Major Depressive Disorder: The effectiveness of PAXIL CR for the treatment of PMDD utilizing a continuous dosing regimen has been established in 2 placebo-controlled trials. Patients in these trials met DSM-IV criteria for PMDD. In a pool of 1,030 patients treated with daily doses of PAXIL CR 12.5 or 25 mg/day, or placebo the mean duration of the PMDD symptoms was significantly shorter in patients treated with PAXIL CR than in those treated with placebo. In these trials, the efficacy of PAXIL CR in combination with systemic (including oral) hormonal contraceptives for the continuous daily treatment of PMDD is unknown. In both positive studies, patients (N = 672) were treated with 12.5 mg/day or 25 mg/day of PAXIL CR or placebo continuously throughout the menstrual cycle for a period of 3 menstrual cycles. The VAS total score is a patient-rated instrument that mirrors the diagnostic criteria of PMDD as identified in the DSM-IV, and includes assessments for mood, physical symptoms, and other symptoms. 12.5 mg/day and 25 mg/day of PAXIL CR were significantly more effective than placebo as measured by change from baseline to the endpoint on the total phase VAS total score.

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The antidepressant action of paroxetine in hospitalized depressed patients has not been adequately evaluated. Paroxetine or other antidepressants during the first trimester of pregnancy have been shown to increase the effectiveness of immediate-release paroxetine hydrochloride in maintaining a response in major depressive disorder for up to 1 year has been demonstrated in a placebo-controlled trial (see CLINICAL PHARMACOLOGY—Clinical Trials). The physician who elects to use PAXIL CR for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Panic Disorder: PAXIL CR is indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-IV. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional panic attacks or the implications or consequences of the attacks, and/or a significant change in behavior of the patient at the attacks. The efficacy of PAXIL CR controlled-release tablets was established in two 10-week trials in panic disorder patients whose diagnoses corresponded to the DSM-IV category of panic disorder (see CLINICAL PHARMACOLOGY—Clinical Trials).

Social Anxiety Disorder: PAXIL CR is indicated for the treatment of social anxiety disorder, also known as social phobia, as defined in DSM-IV (2002). Social anxiety disorder is characterized by a marked and persistent fear of 1 or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack. The feared situations are avoided or endured with intense anxiety or discomfort, or the anticipation, or distress, or discomfort associated with the feared situation interferes significantly with the person's normal routine, occupational or academic functioning, or social activities or relationships, or is otherwise markedly distressing about having the phobias. Lesser degrees of performance anxiety or shyness generally do not require pharmacologic treatment.

The efficacy of PAXIL CR, as a treatment for social anxiety disorder has been established, in part, on the basis of extrapolation from studies of paroxetine hydrochloride in bipolar patients. In a subset of patients classified as bipolar, the efficacy of PAXIL CR was established in a 12-week trial, in adult outpatients with social anxiety disorder (DSM-IV). PAXIL CR has not been studied in children or adolescents with social phobia (see CLINICAL PHARMACOLOGY—Clinical Trials).

Serotonin Syndrome: During premarketing testing of immediate-release paroxetine hydrochloride, seizures occurred in 0.1% of paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with PAXIL CR: Adverse events while discontinuing therapy with PAXIL CR were not systematically monitored. During premarketing testing of immediate-release paroxetine hydrochloride, 9 patients (0.9%) who were paroxetine-treated patients, or similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received PAXIL CR in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, 1 patient (0.1%) experienced a seizure. PAXIL CR should be used cautiously in patients with a history of seizures. It

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reported at an incidence of 5% or greater among elderly patients (ages 60 to 88) treated with PAXIL CR who participated in a short-term (12-week) placebo-controlled trial in major depressive disorder. In the treatment of major depressive disorder, in a range of 12.5 mg/day to 50 mg/day. Table 3 enumerates adverse events reported at an incidence of 1% or greater among patients (19 to 72 years) treated with PAXIL CR who participated in short-term (10-week) placebo-controlled trials in panic disorder in which patients were dosed in a range of 12.5 mg/day to 75 mg/day. Table 4 enumerates adverse events reported at an incidence of 1% or greater among adult patients treated with PAXIL CR who participated in a short-term (12-week), double-blind, placebo-controlled trial in social anxiety disorder in which patients were dosed in a range of 12.5 to 37.5 mg/day. Table 5 enumerates adverse events that occurred at an incidence of 1% or more among patients treated with PAXIL CR who participated in the 12-week, placebo-controlled trials in PMDD in which patients were dosed at 12.5 mg/day or 25 mg/day and in one 12-week placebo-controlled trial in which patients were dosed for 2 weeks prior to the onset of menses (luteal phase dosing) at 12.5 mg/day or 25 mg/day. Reported adverse events were classified using a standard CDSAT-based Dictionary terminology.

The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the side effect incidence rate in the population studied.

Table 1. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Pool of 2 Studies in Major Depressive Disorder^{1,2}

Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 212)	Placebo (n = 211)
Body as a Whole		
Headache	27%	20%
Asthenia	14%	9%
Infection ³	8%	5%
Abdominal Pain	7%	4%
Back Pain	7%	4%
Trauma ⁴	5%	1%
Pain ⁵	3%	1%
Allergic Reaction ⁶	2%	1%
Cardiovascular System		
Tachycardia	1%	0%
Vasodilatation ⁷	2%	0%
Digestive System		
Nausea	22%	10%
Diarrhea	18%	7%
Dry Mouth	15%	6%
Constipation	13%	4%
Flatulence	6%	4%
Decreased Appetite	6%	1%
Vomiting	2%	1%
Nervous System		
Somnolence	22%	8%
Insomnia	14%	9%
Dizziness	14%	4%
Libido Decreased	7%	3%
Tremor	7%	4%
Hypertonia	3%	1%
Paresthesia	3%	1%
Agitation	3%	1%
Confusion	1%	0%
Respiratory System		
Yawn	5%	0%
Rhinitis	2%	1%
Cough Increased	2%	1%
Bronchitis	1%	0%
Skin and Appendages		
Sweating	6%	2%
Photosensitivity	2%	0%
Special Senses		
Abnormal Vision ⁸	5%	1%
Taste Perversion	2%	0%
Urogenital System		
Abnormal Ejaculation ^{9,10}	26%	1%
Female Genital Disorder ^{9,11}	10%	<1%
Impotence ¹²	4%	1%
Urinary Tract Infection	3%	1%
Menstrual Disorder ⁹	2%	<1%
Vaginitis ¹³	2%	0%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Abnormal dreams, allergic reaction, back pain, bronchitis, chest pain, concentration impaired, confusion, cough increased, depression, dizziness, dysmenorrhea, dyspepsia, dyspareunia, dyspareunia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, sinusitis, urinary frequency, and weight gain.
- <1% means greater than zero and less than 1%.
- Mostly flu.
- A wide variety of injuries with no obvious pattern.
- Pain in a variety of locations with no obvious pattern.
- Most frequently seasonal allergic symptoms.
- Usually flushing.
- Mostly blurred vision.
- Based on the number of males or females.
- Mostly anorgasmia or delayed ejaculation.
- Mostly anorgasmia or delayed orgasm.

Table 2. Treatment-Emergent Adverse Events Occurring in >5% of Patients Treated With PAXIL CR in a Study of Elderly Patients With Major Depressive Disorder^{1,2}

Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 104)	Placebo (n = 109)
Body as a Whole		
Headache	17%	13%
Asthenia	15%	14%
Trauma	8%	5%
Infection	6%	2%
Digestive System		
Dry Mouth	18%	7%
Diarrhea	15%	9%
Constipation	13%	3%
Dyspepsia	10%	1%
Decreased Appetite	12%	5%
Flatulence	8%	7%
Nervous System		
Somnolence	21%	12%
Insomnia	10%	8%
Impotence ¹²	8%	2%
Libido Decreased	8%	<1%
Tremor	7%	0%
Skin and Appendages		
Sweating	10%	<1%
Urogenital System		
Abnormal Ejaculation ⁴	17%	3%
Impotence ¹²	9%	3%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo incidence are not included. These events are: Dyspareunia, flatulence, gastroenteritis, hypertension, infection, pain, pharyngitis, rash, respiratory disorder, rhinitis, and vomiting.
- <1% means greater than zero and less than 1%.
- Various physical injuries.
- Mostly blurred vision.
- Mostly anorgasmia or delayed ejaculation.
- Mostly anorgasmia or delayed orgasm.

Table 3. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Pool of 3 Panic Disorder Studies^{1,2}

Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 444)	Placebo (n = 445)
Body as a Whole		
Headache	15%	10%
Abdominal Pain	12%	4%
Trauma ⁴	5%	4%
Digestive System		
Nausea	23%	17%
Dry Mouth	12%	9%
Diarrhea	9%	6%
Constipation	9%	6%
Dyspepsia	8%	6%
Decreased Appetite	9%	6%
Cardiovascular System		
Myocardial Infarction ⁵	2%	<1%
Nervous System		
Somnolence	20%	11%
Insomnia	20%	9%
Libido Decreased	9%	4%
Weight Gain	8%	7%
Tremor	8%	2%
Anxiety	5%	4%
Agitation	5%	4%
Hypertonia ⁵	2%	<1%
Myoclonus ⁵	2%	<1%
Respiratory System		
Sinusitis	8%	5%
Yawn	3%	0%
Skin and Appendages		
Sweating	7%	2%
Special Senses		
Abnormal Vision ⁸	3%	<1%
Urogenital System		
Abnormal Ejaculation ¹⁰	27%	3%
Female Genital Disorders ^{9,11}	10%	1%
Urinary Frequency	2%	<1%
Urinary Impaired	2%	<1%
Vaginitis ¹³	1%	0%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Abnormal dreams, allergic reaction, back pain, bronchitis, chest pain, concentration impaired, confusion, cough increased, depression, dizziness, dysmenorrhea, dyspepsia, dyspareunia, dyspareunia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, sinusitis, urinary frequency, and weight gain.
- <1% means greater than zero and less than 1%.
- Mostly flu.
- A wide variety of injuries with no obvious pattern.
- Pain in a variety of locations with no obvious pattern.
- Most frequently seasonal allergic symptoms.
- Usually flushing.
- Mostly blurred vision.
- Based on the number of males or females.
- Mostly anorgasmia or delayed ejaculation.
- Mostly anorgasmia or delayed orgasm.

Table 4. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Social Anxiety Disorder Study^{1,2}

Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 186)	Placebo (n = 184)
Body as a Whole		
Asthenia	23%	17%
Abdominal Pain	18%	7%
Back Pain	5%	4%
Trauma ⁴	4%	3%
Allergic Reaction ⁶	3%	<1%
Chest Pain	1%	<1%
Cardiovascular System		
Hypertension	2%	0%
Tachycardia	2%	1%
Digestive System		
Nausea	22%	6%
Diarrhea	9%	8%
Constipation	9%	2%
Dry Mouth	5%	2%
Dyspepsia	1%	<1%
Decreased Appetite	1%	<1%
Vomiting	1%	0%
Metabolic/Nutritional Disorders		
Weight Gain	3%	1%
Weight Loss	1%	0%
Nervous System		
Insomnia	9%	4%
Somnolence	9%	1%
Dizziness	8%	1%
Diarrhea	7%	4%
Tremor	4%	2%
Anxiety	4%	1%
Concentration Impaired	2%	0%
Agitation	2%	1%
Hypertonia	1%	<1%
Myoclonus ⁵	1%	<1%
Respiratory System		
Yawn	2%	0%
Skin and Appendages		
Sweating	14%	3%
Eczema	1%	0%
Special Senses		
Abnormal Vision ⁸	2%	0%
Abnormality of Accommodation	2%	0%
Urogenital System		
Abnormal Ejaculation ¹⁰	15%	1%
Female Genital Disorders ^{9,11}	9%	0%
Urinary Frequency	3%	0%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Dyspareunia, flatulence, gastroenteritis, hypertension, infection, pain, pharyngitis, rash, respiratory disorder, rhinitis, and vomiting.
- <1% means greater than zero and less than 1%.
- Various physical injuries.
- Mostly blurred vision.
- Mostly anorgasmia or delayed ejaculation.
- Mostly anorgasmia or delayed orgasm.

Table 5. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Pool of 3 Premenstrual Dysphoric Disorder Studies with Continuous Dosing or in 1 Premenstrual Dysphoric Disorder Study with Luteal Phase Dosing^{1,2}

Body System/Adverse Event	Continuous Dosing		Luteal Phase Dosing	
	PAXIL CR (n = 681)	Placebo (n = 349)	PAXIL CR (n = 246)	Placebo (n = 120)
Body as a Whole				
Asthenia	17%	6%	15%	4%
Headache	12%	4%	-	-
Infection	6%	-	-	-

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Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 444)	Placebo (n = 445)
Cardiovascular System		
Vasodilatation ⁷	3%	2%
Digestive System		
Nausea	23%	17%
Dry Mouth	12%	9%
Diarrhea	9%	6%
Constipation	9%	6%
Dyspepsia	8%	6%
Decreased Appetite	9%	6%
Cardiovascular System		
Myocardial Infarction ⁵	2%	<1%
Nervous System		
Somnolence	20%	11%
Insomnia	20%	9%
Libido Decreased	9%	4%
Weight Gain	8%	7%
Tremor	8%	2%
Anxiety	5%	4%
Agitation	5%	4%
Hypertonia ⁵	2%	<1%
Myoclonus ⁵	2%	<1%
Respiratory System		
Sinusitis	8%	5%
Yawn	3%	0%
Skin and Appendages		
Sweating	7%	2%
Special Senses		
Abnormal Vision ⁸	3%	<1%
Urogenital System		
Abnormal Ejaculation ¹⁰	27%	3%
Female Genital Disorders ^{9,11}	10%	1%
Urinary Frequency	2%	<1%
Urinary Impaired	2%	<1%
Vaginitis ¹³	1%	0%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Abnormal dreams, allergic reaction, back pain, bronchitis, chest pain, concentration impaired, confusion, cough increased, depression, dizziness, dysmenorrhea, dyspepsia, dyspareunia, dyspareunia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, rhinitis, tachycardia, taste perversion, thinking abnormal, urinary tract infection, and vomiting.
- <1% means greater than zero and less than 1%.
- Various physical injuries.
- Mostly flushing.
- Mostly muscle tightness or stiffness.
- Mostly blurred vision.
- Based on the number of male patients.
- Mostly anorgasmia or delayed ejaculation.
- Based on the number of female patients.
- Mostly anorgasmia or delayed orgasm.

Table 6. Treatment-Emergent Adverse Effects Occurring in >1% of Patients Treated With PAXIL CR in a Social Anxiety Disorder Study^{1,2}

Body System/Adverse Event	% Reporting Event	
	PAXIL CR (n = 186)	Placebo (n = 184)
Body as a Whole		
Asthenia	23%	17%
Abdominal Pain	18%	7%
Back Pain	5%	4%
Trauma ⁴	4%	3%
Allergic Reaction ⁶	3%	<1%
Chest Pain	1%	<1%
Cardiovascular System		
Hypertension	2%	0%
Tachycardia	2%	1%
Digestive System		
Nausea	22%	6%
Diarrhea	9%	8%
Constipation	9%	2%
Dry Mouth	5%	2%
Dyspepsia	1%	<1%
Decreased Appetite	1%	<1%
Vomiting	1%	0%
Metabolic/Nutritional Disorders		
Weight Gain	3%	1%
Weight Loss	1%	0%
Nervous System		
Insomnia	9%	4%
Somnolence	9%	1%
Dizziness	8%	1%
Diarrhea	7%	4%
Tremor	4%	2%
Anxiety	4%	1%
Concentration Impaired	2%	0%
Agitation	2%	1%
Hypertonia	1%	<1%
Myoclonus ⁵	1%	<1%
Respiratory System		
Yawn	2%	0%
Skin and Appendages		
Sweating	14%	3%
Eczema	1%	0%
Special Senses		
Abnormal Vision ⁸	2%	0%
Abnormality of Accommodation	2%	0%
Urogenital System		
Abnormal Ejaculation ¹⁰	15%	1%
Female Genital Disorders ^{9,11}	9%	0%
Urinary Frequency	3%	0%

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Abnormal dreams, allergic reaction, back pain, bronchitis, chest pain, concentration impaired, confusion, cough increased, depression, dizziness, dysmenorrhea, dyspepsia, dyspareunia, dyspareunia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, rhinitis, tachycardia, taste perversion, thinking abnormal, urinary tract infection, and vomiting.
- <1% means greater than zero and less than 1%.
- Various physical injuries.
- Mostly flushing.
- Mostly muscle tightness or stiffness.
- Mostly blurred vision.
- Based on the number of male patients.
- Mostly anorgasmia or delayed ejaculation.
- Based on the number of female patients.
- Mostly anorgasmia or delayed orgasm.

Table 7. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Pool of 3 Premenstrual Dysphoric Disorder Studies with Continuous Dosing or in 1 Premenstrual Dysphoric Disorder Study with Luteal Phase Dosing^{1,2}

Body System/Adverse Event	Continuous Dosing		Luteal Phase Dosing	
	PAXIL CR (n = 681)	Placebo (n = 349)	PAXIL CR (n = 246)	Placebo (n = 120)
Body as a Whole				
Asthenia	17%	6%	15%	4%
Headache	12%	4%	-	-
Infection	6%	-	-	-

- Adverse events for which the reporting rate for PAXIL CR was less than or equal to the placebo rate are not included. These events are: Abnormal dreams, allergic reaction, back pain, bronchitis, chest pain, concentration impaired, confusion, cough increased, depression, dizziness, dysmenorrhea, dyspepsia, dyspareunia, dyspareunia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, rhinitis, tachycardia, taste perversion, thinking abnormal, urinary tract infection, and vomiting.
- <1% means greater than zero and less than 1%.
- Various physical injuries.
- Mostly blurred vision.
- Mostly anorgasmia or delayed ejaculation.
- Mostly anorgasmia or delayed orgasm.

Table 8. Treatment-Emergent Adverse Events Occurring in >1% of Patients Treated With PAXIL CR in a Pool of 3 Premenstrual Dysphoric Disorder Studies with Continuous Dosing or in 1 Premenstrual Dysphoric Disorder Study with Luteal Phase Dosing^{1,2}

Body System/Adverse Event	Continuous Dosing		Luteal Phase Dosing	
	PAXIL CR (n = 681)	Placebo (n = 349)	PAXIL CR (n = 246)	Placebo (n = 120)
Body as a Whole				
Asthenia	17%	6%	15%	4%
Headache	12%	4%	-	-
Infection	6%	-	-	-

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Body System/Adverse Event



EAT Phase II Information Panel for DOMESTIC market artwork					
Product Name Paxil CR	Drawing No. 0002458	Scale 100%	Originated on 14 DEC 05	Replaces NA	Proofreader's Check
ECR N/A	Dimensions 628.65x311.15mm	Colors (1) <input checked="" type="checkbox"/> Black <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color <input type="checkbox"/> PMS Color	Originated by Gayle Pallansch	Proof Status P1 / M1	Date
Item/Material Code 733647-PC:119	Component type Leaflet		Site RSCUS, RTP	Amended by N/A	Graphics Check
Edge Code 459/pharma	Market USA		For Production at Cidra	Date Completed 14 DEC 05	Date
Cust. Ref. No. N/A	Code#/Type 385(8)/ 2 of 5				
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Reason for Change: Revisions to PRECAUTIONS, Pregnancy, Teratogenic Effects.					
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