

**Information for Patients:** Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with PAXIL and should counsel them in its appropriate use. A patient Medication Guide About Using Antidepressants in Children and Teenagers is available for PAXIL. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking PAXIL.

**Clinical Worsening and Suicide Risk:** Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to observe for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

**Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.):** Patients should be cautioned about the concomitant use of paroxetine and NSAIDs, aspirin, or other drugs that affect coagulation since the combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding.

**Interference With Cognitive and Motor Performance:** Any psychoactive drug may impair judgment, thinking, or motor skills. Although in controlled studies PAXIL has not been shown to impair psychomotor performance, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with PAXIL does not affect their ability to engage in such activities.

**Completing Course of Therapy:** While patients may notice improvement with treatment with PAXIL in 1 to 4 weeks, they should be advised to continue therapy as directed.

**Concomitant Medication:** Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions.

**Alcohol:** Although PAXIL has not been shown to increase the impairment of mental and motor skills caused by alcohol, patients should be advised to avoid alcohol while taking PAXIL.

**Pregnancy:** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. (See WARNINGS—Usage in Pregnancy: *Teratogenic and Nonteratogenic Effects*).

**Nursing:** Patients should be advised to notify their physician if they are breast-feeding an infant (see PRECAUTIONS—Nursing Mothers).

**Laboratory Tests:** There are no specific laboratory tests recommended.

**Drug Interactions:** **Tryptophan:** As with other serotonin reuptake inhibitors, an interaction between paroxetine and tryptophan may occur when they are coadministered. Adverse experiences, consisting primarily of headache, nausea, sweating, and dizziness, have been reported when tryptophan was administered to patients taking PAXIL. Consequently, concomitant use of PAXIL with tryptophan is not recommended (see Serotonin Syndrome).

**Monoamine Oxidase Inhibitors:** See CONTRAINDICATIONS and WARNINGS.

**Pimozide:** In a controlled study of healthy volunteers, after PAXIL was titrated to 60 mg daily, co-administration of a single dose of 2 mg pimozide was associated with mean increases in pimozide AUC of 151% and  $C_{max}$  of 62%, compared to pimozide administered alone. Due to the narrow therapeutic index of pimozide and its known ability to prolong the QT interval, concomitant use of pimozide and PAXIL is contraindicated (see CONTRAINDICATIONS).

**Serotonergic Drugs:** Based on the mechanism of action of paroxetine and the potential for serotonin syndrome, caution is advised when PAXIL is coadministered with other drugs or agents that may affect the serotonergic neurotransmitter systems, such as tryptophan, triptans, serotonin reuptake inhibitors, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort (see Serotonin Syndrome).

**Thioridazine:** See CONTRAINDICATIONS and WARNINGS.

**Warfarin:** Preliminary data suggest that there may be a pharmacodynamic interaction (that causes an increased bleeding diathesis in the face of unaltered prothrombin time) between paroxetine and warfarin. Since there is little clinical experience, the concomitant administration of PAXIL and warfarin should be undertaken with caution (see *Drugs That Interfere With Hemostasis*).

**Triptans:** There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment with a triptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline) is clinically warranted, appropriate observation of the patient is advised (see Serotonin Syndrome).

**Drugs Affecting Hepatic Metabolism:** The metabolism and pharmacokinetics of paroxetine may be affected by the induction or inhibition of drug-metabolizing enzymes.

**Cimetidine:** Cimetidine inhibits many cytochrome P<sub>450</sub> (oxidative) enzymes. In a study where PAXIL (30 mg once daily) was dosed orally for 4 weeks, steady-state plasma concentrations of paroxetine were increased by approximately 50% during coadministration with oral cimetidine (300 mg three times daily) for the final week. Therefore, when these drugs are administered concurrently, dosage adjustment of PAXIL after the 20-mg starting dose should be

guided by clinical effect. The effect of paroxetine on cimetidine's pharmacokinetics was not studied.

**Phenobarbital:** Phenobarbital induces many cytochrome P<sub>450</sub> (oxidative) enzymes. When a single oral 30-mg dose of PAXIL was administered at phenobarbital steady state (100 mg once daily for 14 days), paroxetine AUC and T<sub>1/2</sub> were reduced (by an average of 25% and 38%, respectively) compared to paroxetine administered alone. The effect of paroxetine on phenobarbital pharmacokinetics was not studied. Since PAXIL exhibits nonlinear pharmacokinetics, the results of this study may not address the case where the 2 drugs are both being chronically dosed. No initial dosage adjustment of PAXIL is considered necessary when coadministered with phenobarbital; any subsequent adjustment should be guided by clinical effect.

**Phenytoin:** When a single oral 30-mg dose of PAXIL was administered at phenytoin steady state (300 mg once daily for 14 days), paroxetine AUC and T<sub>1/2</sub> were reduced (by an average of 50% and 35%, respectively) compared to PAXIL administered alone. In a separate study, when a single oral 300-mg dose of phenytoin was administered at paroxetine steady state (30 mg once daily for 14 days), phenytoin AUC was slightly reduced (12% on average) compared to phenytoin administered alone. Since both drugs exhibit nonlinear pharmacokinetics, the above studies may not address the case where the 2 drugs are both being chronically dosed. No initial dosage adjustments are considered necessary when these drugs are coadministered; any subsequent adjustments should be guided by clinical effect (see ADVERSE REACTIONS—Postmarketing Reports).

**Drugs Metabolized by CYP2D6:** Many drugs, including most drugs effective in the treatment of major depressive disorder (paroxetine, other SSRIs and many tricyclics), are metabolized by the cytochrome P<sub>450</sub> isozyme CYP2D6. Like other agents that are metabolized by CYP2D6, paroxetine may significantly inhibit the activity of this isozyme. In most patients (>90%), this CYP2D6 isozyme is saturated early during dosing with PAXIL. In 1 study, daily dosing of PAXIL (20 mg once daily) under steady-state conditions increased single dose desipramine (100 mg) C<sub>max</sub>, AUC, and T<sub>1/2</sub> by an average of approximately 2-, 5-, and 3-fold, respectively. Concomitant use of paroxetine with risperidone, a CYP2D6 substrate has also been evaluated. In 1 study, daily dosing of paroxetine 20 mg in patients stabilized on risperidone (4 to 8 mg/day) increased mean plasma concentrations of risperidone approximately 4-fold, decreased 9-hydroxyrisperidone concentrations approximately 10%, and increased concentrations of the active moiety (the sum of risperidone plus 9-hydroxyrisperidone) approximately 1.4-fold. The effect of paroxetine on the pharmacokinetics of atomoxetine has been evaluated when both drugs were at steady state. In healthy volunteers who were extensive metabolizers of CYP2D6, paroxetine 20 mg daily was given in combination with 20 mg atomoxetine every 12 hours. This resulted in increases in steady state atomoxetine AUC values that were 6- to 8-fold greater and in atomoxetine C<sub>max</sub> values that were 3- to 4-fold greater than when atomoxetine was given alone. Dosage adjustment of atomoxetine may be necessary and it is recommended that atomoxetine be initiated at a reduced dose when it is given with paroxetine.

Concomitant use of PAXIL with other drugs metabolized by cytochrome CYP2D6 has not been formally studied but may require lower doses than usually prescribed for either PAXIL or the other drug.

Therefore, coadministration of PAXIL with other drugs that are metabolized by this isozyme, including certain drugs effective in the treatment of major depressive disorder (e.g., nortriptyline, amitriptyline, imipramine, desipramine, and fluoxetine), phenothiazines, risperidone, and Type 1C antiarrhythmics (e.g., propafenone, flecainide, and encainide), or that inhibit this enzyme (e.g., quinidine), should be approached with caution.

However, due to the risk of serious ventricular arrhythmias and sudden death potentially associated with elevated plasma levels of thioridazine, paroxetine and thioridazine should not be coadministered (see CONTRAINDICATIONS and WARNINGS).

At steady state, when the CYP2D6 pathway is essentially saturated, paroxetine clearance is governed by alternative P<sub>450</sub> isozymes that, unlike CYP2D6, show no evidence of saturation (see PRECAUTIONS—*Tricyclic Antidepressants*).

**Drugs Metabolized by Cytochrome CYP3A4:** An in vivo interaction study involving the coadministration under steady-state conditions of paroxetine and terfenadine, a substrate for cytochrome CYP3A4, revealed no effect of paroxetine on terfenadine pharmacokinetics. In addition, in vitro studies have shown ketoconazole, a potent inhibitor of CYP3A4 activity, to be at least 100 times more potent than paroxetine as an inhibitor of the metabolism of several substrates for this enzyme, including terfenadine, astemizole, cisapride, triazolam, and cyclosporine. Based on the assumption that the relationship between paroxetine's in vitro K<sub>i</sub> and its lack of effect on terfenadine's in vivo clearance predicts its effect on other CYP3A4 substrates, paroxetine's extent of inhibition of CYP3A4 activity is not likely to be of clinical significance.

**Tricyclic Antidepressants (TCAs):** Caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with PAXIL, because paroxetine may inhibit TCA metabolism. Plasma TCA concentrations may need to be monitored, and the dose of TCA may need to be reduced, if a TCA is coadministered with PAXIL (see PRECAUTIONS—*Drugs Metabolized by Cytochrome CYP2D6*).

**Drugs Highly Bound to Plasma Protein:** Because paroxetine is highly bound to plasma protein, administration of PAXIL to a patient taking another drug that is highly protein bound may cause increased free concentrations of the other drug, potentially resulting in adverse events. Conversely, adverse effects could result from displacement of paroxetine by other highly bound drugs.

**Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.):** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated

the risk of bleeding. Thus, patients should be cautioned about the use of such drugs concurrently with paroxetine.

**Alcohol:** Although PAXIL does not increase the impairment of mental and motor skills caused by alcohol, patients should be advised to avoid alcohol while taking PAXIL.

**Lithium:** A multiple-dose study has shown that there is no pharmacokinetic interaction between PAXIL and lithium carbonate. However, due to the potential for serotonin syndrome, caution is advised when PAXIL is coadministered with lithium.

**Digoxin:** The steady-state pharmacokinetics of paroxetine was not altered when administered with digoxin at steady state. Mean digoxin AUC at steady state decreased by 15% in the presence of paroxetine. Since there is little clinical experience, the concurrent administration of paroxetine and digoxin should be undertaken with caution.

**Diazepam:** Under steady-state conditions, diazepam does not appear to affect paroxetine kinetics. The effects of paroxetine on diazepam were not evaluated.

**Procyclidine:** Daily oral dosing of PAXIL (30 mg once daily) increased steady-state  $AUC_{0-24}$ ,  $C_{max}$ , and  $C_{min}$  values of procyclidine (5 mg oral once daily) by 35%, 37%, and 67%, respectively, compared to procyclidine alone at steady state. If anticholinergic effects are seen, the dose of procyclidine should be reduced.

**Beta-Blockers:** In a study where propranolol (80 mg twice daily) was dosed orally for 18 days, the established steady-state plasma concentrations of propranolol were unaltered during coadministration with PAXIL (30 mg once daily) for the final 10 days. The effects of propranolol on paroxetine have not been evaluated (see ADVERSE REACTIONS—Postmarketing Reports).

**Theophylline:** Reports of elevated theophylline levels associated with treatment with PAXIL have been reported. While this interaction has not been formally studied, it is recommended that theophylline levels be monitored when these drugs are concurrently administered.

**Fosamprenavir/Ritonavir:** Co-administration of fosamprenavir/ritonavir with paroxetine significantly decreased plasma levels of paroxetine. Any dose adjustment should be guided by clinical effect (tolerability and efficacy).

**Electroconvulsive Therapy (ECT):** There are no clinical studies of the combined use of ECT and PAXIL.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** **Carcinogenesis:** Two-year carcinogenicity studies were conducted in rodents given paroxetine in the diet at 1, 5, and 25 mg/kg/day (mice) and 1, 5, and 20 mg/kg/day (rats). These doses are up to 2.4 (mouse) and 3.9 (rat) times the maximum recommended human dose (MRHD) for major depressive disorder, social anxiety disorder, GAD, and PTSD on a mg/m<sup>2</sup> basis. Because the MRHD for major depressive disorder is slightly less than that for OCD (50 mg versus 60 mg), the doses used in these carcinogenicity studies were only 2.0 (mouse) and 3.2 (rat) times the MRHD for OCD. There was a significantly greater number of male rats in the high-dose group with reticulum cell sarcomas (1/100, 0/50, 0/50, and 4/50 for control, low-, middle-, and high-dose groups,

respectively) and a significantly increased linear trend across dose groups for the occurrence of lymphoreticular tumors in male rats. Female rats were not affected. Although there was a dose-related increase in the number of tumors in mice, there was no drug-related increase in the number of mice with tumors. The relevance of these findings to humans is unknown.

**Mutagenesis:** Paroxetine produced no genotoxic effects in a battery of 5 in vitro and 2 in vivo assays that included the following: Bacterial mutation assay, mouse lymphoma mutation assay, unscheduled DNA synthesis assay, and tests for cytogenetic aberrations in vivo in mouse bone marrow and in vitro in human lymphocytes and in a dominant lethal test in rats.

**Impairment of Fertility:** A reduced pregnancy rate was found in reproduction studies in rats at a dose of paroxetine of 15 mg/kg/day, which is 2.9 times the MRHD for major depressive disorder, social anxiety disorder, GAD, and PTSD or 2.4 times the MRHD for OCD on a mg/m<sup>2</sup> basis. Irreversible lesions occurred in the reproductive tract of male rats after dosing in toxicity studies for 2 to 52 weeks. These lesions consisted of vacuolation of epididymal tubular epithelium at 50 mg/kg/day and atrophic changes in the seminiferous tubules of the testes with arrested spermatogenesis at 25 mg/kg/day (9.8 and 4.9 times the MRHD for major depressive disorder, social anxiety disorder, and GAD; 8.2 and 4.1 times the MRHD for OCD and PD on a mg/m<sup>2</sup> basis).

**Pregnancy:** Pregnancy Category D. See WARNINGS—Usage in Pregnancy: Teratogenic and Nonteratogenic Effects.

**Labor and Delivery:** The effect of paroxetine on labor and delivery in humans is unknown.

**Nursing Mothers:** Like many other drugs, paroxetine is secreted in human milk, and caution should be exercised when PAXIL is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS—Clinical Worsening and Suicide Risk). Three placebo-controlled trials in 752 pediatric patients with MDD have been conducted with PAXIL, and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of PAXIL in a child or adolescent must balance the potential risks with the clinical need.

In placebo-controlled clinical trials conducted with pediatric patients, the following adverse events were reported in at least 2% of pediatric patients treated with PAXIL and occurred at a rate at least twice that for pediatric patients receiving placebo: emotional lability (including self-harm, suicidal thoughts, attempted suicide, crying, and mood fluctuations), hostility, decreased appetite, tremor, sweating, hyperkinesia, and agitation.

Events reported upon discontinuation of treatment with PAXIL in the pediatric clinical trials that included a taper phase regimen, which occurred in at least 2% of patients who received PAXIL and which occurred at a rate at least twice that of placebo, were: emotional lability (including suicidal ideation, suicide attempt, mood changes, and tearfulness), nervousness, dizziness, nausea, and abdominal pain (see Discontinuation of Treatment With PAXIL).

**Geriatric Use:** In worldwide premarketing clinical trials with PAXIL, 17% of patients treated with PAXIL (approximately 700) were 65 years of age or older. Pharmacokinetic studies

revealed a decreased clearance in the elderly, and a lower starting dose is recommended; there were, however, no overall differences in the adverse event profile between elderly and younger patients, and effectiveness was similar in younger and older patients (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION).

#### ADVERSE REACTIONS

**Associated With Discontinuation of Treatment:** Twenty percent (1,199/6,145) of patients treated with PAXIL in worldwide clinical trials in major depressive disorder and 16.1% (84/522), 11.8% (64/542), 9.4% (44/469), 10.7% (79/735), and 11.7% (79/676) of patients treated with PAXIL in worldwide trials in social anxiety disorder, OCD, panic disorder, GAD, and PTSD, respectively, discontinued treatment due to an adverse event. The most common events ( $\geq 1\%$ ) associated with discontinuation and considered to be drug related (i.e., those events associated with dropout at a rate approximately twice or greater for PAXIL compared to placebo) included the following:

	Major Depressive Disorder		OCD		Panic Disorder		Social Anxiety Disorder		Generalized Anxiety Disorder		PTSD	
	PAXIL	Placebo	PAXIL	Placebo	PAXIL	Placebo	PAXIL	Placebo	PAXIL	Placebo	PAXIL	Placebo
	CNS											
Somnolence	2.3%	0.7%	—	—	1.9%	0.3%	3.4%	0.3%	2.0%	0.2%	2.8%	0.6%
Insomnia	—	—	1.7%	0%	1.3%	0.3%	3.1%	0%	—	—	—	—
Agitation	1.1%	0.5%	—	—	—	—	—	—	—	—	—	—
Tremor	1.1%	0.3%	—	—	—	—	1.7%	0%	—	—	1.0%	0.2%
Anxiety	—	—	—	—	—	—	1.1%	0%	—	—	—	—
Dizziness	—	—	1.5%	0%	—	—	1.9%	0%	1.0%	0.2%	—	—
<b>Gastrointestinal</b>												
Constipation	—	—	1.1%	0%	—	—	—	—	—	—	—	—
Nausea	3.2%	1.1%	1.9%	0%	3.2%	1.2%	4.0%	0.3%	2.0%	0.2%	2.2%	0.6%
Diarrhea	1.0%	0.3%	—	—	—	—	—	—	—	—	—	—
Dry mouth	1.0%	0.3%	—	—	—	—	—	—	—	—	—	—
Vomiting	1.0%	0.3%	—	—	—	—	1.0%	0%	—	—	—	—
Flatulence	—	—	—	—	—	—	1.0%	0.3%	—	—	—	—
<b>Other</b>												
Asthenia	1.6%	0.4%	1.9%	0.4%	—	—	2.5%	0.6%	1.8%	0.2%	1.6%	0.2%
Abnormal ejaculation <sup>1</sup>	1.6%	0%	2.1%	0%	—	—	4.9%	0.6%	2.5%	0.5%	—	—
Sweating	1.0%	0.3%	—	—	—	—	1.1%	0%	1.1%	0.2%	—	—
Impotence <sup>1</sup>	—	—	1.5%	0%	—	—	—	—	—	—	—	—
Libido Decreased	—	—	—	—	—	—	—	—	1.0%	0%	—	—

Where numbers are not provided the incidence of the adverse events in patients treated with PAXIL was not  $> 1\%$  or was not greater than or equal to 2 times the incidence of placebo.

1. Incidence corrected for gender.

**Commonly Observed Adverse Events: Major Depressive Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that for placebo, derived from Table 1) were: Asthenia, sweating, nausea, decreased appetite, somnolence, dizziness, insomnia, tremor, nervousness, ejaculatory disturbance, and other male genital disorders.

**Obsessive Compulsive Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that of placebo, derived from Table 2) were: Nausea, dry mouth, decreased appetite, constipation, dizziness, somnolence, tremor, sweating, impotence, and abnormal ejaculation.

**Panic Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that for placebo, derived from Table 2) were: Asthenia, sweating, decreased appetite, libido decreased, tremor, abnormal ejaculation, female genital disorders, and impotence.

**Social Anxiety Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that for placebo, derived from Table 2) were: Sweating, nausea, dry mouth, constipation, decreased appetite, somnolence, tremor, libido decreased, yawn, abnormal ejaculation, female genital disorders, and impotence.

**Generalized Anxiety Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that for placebo, derived from Table 3) were: Asthenia, infection, constipation, decreased appetite, dry mouth, nausea, libido decreased, somnolence, tremor, sweating, and abnormal ejaculation.

**Posttraumatic Stress Disorder:** The most commonly observed adverse events associated with the use of paroxetine (incidence of 5% or greater and incidence for PAXIL at least twice that for placebo, derived from Table 3) were: Asthenia, sweating, nausea, dry mouth, diarrhea, decreased appetite, somnolence, libido decreased, abnormal ejaculation, female genital disorders, and impotence.

**Incidence in Controlled Clinical Trials:** The prescriber should be aware that the figures in the tables following 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 nondrug factors to the side effect incidence rate in the populations studied.

**Major Depressive Disorder:** Table 1 enumerates adverse events that occurred at an incidence of 1% or more among paroxetine-treated patients who participated in short-term (6-week) placebo-controlled trials in which patients were dosed in a range of 20 mg to 50 mg/day. Reported adverse events were classified using a standard COSTART-based Dictionary terminology.

**Table 1. Treatment-Emergent Adverse Experience Incidence in Placebo-Controlled Clinical Trials for Major Depressive Disorder<sup>1</sup>**

Body System	Preferred Term	PAXIL (n = 421)	Placebo (n = 421)
Body as a Whole	Headache	18%	17%
	Asthenia	15%	6%
Cardiovascular	Palpitation	3%	1%
	Vasodilation	3%	1%
Dermatologic	Sweating	11%	2%
	Rash	2%	1%
Gastrointestinal	Nausea	26%	9%
	Dry Mouth	18%	12%
	Constipation	14%	9%
	Diarrhea	12%	8%
	Decreased Appetite	6%	2%
	Flatulence	4%	2%
	Oropharynx Disorder <sup>2</sup>	2%	0%
	Dyspepsia	2%	1%
Musculoskeletal	Myopathy	2%	1%
	Myalgia	2%	1%
	Myasthenia	1%	0%
Nervous System	Somnolence	23%	9%
	Dizziness	13%	6%
	Insomnia	13%	6%
	Tremor	8%	2%
	Nervousness	5%	3%
	Anxiety	5%	3%
	Paresthesia	4%	2%
	Libido Decreased	3%	0%
	Drugged Feeling	2%	1%
	Confusion	1%	0%
Respiration	Yawn	4%	0%
Special Senses	Blurred Vision	4%	1%
	Taste Perversion	2%	0%
Urogenital System	Ejaculatory Disturbance <sup>3,4</sup>	13%	0%
	Other Male Genital Disorders <sup>3,5</sup>	10%	0%
	Urinary Frequency	3%	1%
	Urination Disorder <sup>6</sup>	3%	0%
	Female Genital Disorders <sup>3,7</sup>	2%	0%

1. Events reported by at least 1% of patients treated with PAXIL are included, except the following events which had an incidence on placebo  $\geq$  PAXIL: Abdominal pain, agitation, back pain, chest pain, CNS stimulation, fever, increased appetite, myoclonus, pharyngitis, postural hypotension, respiratory disorder (includes mostly "cold symptoms" or "URI"), trauma, and vomiting.

2. Includes mostly "lump in throat" and "tightness in throat."