HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PAXIL safely and effectively. See full prescribing information for PAXIL.

PAXIL (paroxetine) tablets, for oral use
PAXIL (paroxetine) oral suspension
Initial U.S. Approval: 1992

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
See full prescribing information for complete boxed warning.

Increased risk of suicidal thoughts and behavior in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. PAXIL is not approved for use in pediatric patients. (5.1, 8.4)

----------INDICATIONS AND USAGE----------
PAXIL is a selective serotonin reuptake inhibitor (SSRI) indicated in adults for the treatment of (1):

- Major Depressive Disorder (MDD)
- Obsessive Compulsive Disorder (OCD)
- Panic Disorder (PD)
- Social Anxiety Disorder (SAD)
- Generalized Anxiety Disorder (GAD)
- Posttraumatic Stress Disorder (PTSD)

----------DOSAGE AND ADMINISTRATION----------

- Shake oral suspension well before administration (2.1)
- Recommended starting and maximum daily dosage for MDD, OCD, PD, and PTSD: (2.2)

Indication	Starting Daily Dose	Maximum Daily Dose
MDD	20 mg	50 mg
OCD	20 mg	60 mg
PD	10 mg	60 mg
PTSD	20 mg	50 mg

- Recommended starting dosage for SAD and GAD is 20 mg daily. (2.3)
- Elderly patients, patients with severe renal impairment or severe hepatic impairment: Starting dosage is 10 mg daily. Maximum dosage is 40 mg daily. (2.4)
- When discontinuing PAXIL, reduce dosage gradually. (2.6, 5.7)

----------DOSAGE FORMS AND STRENGTHS----------

- Extended-release tablets: 10 mg, scored; 20 mg, scored; 30 mg; and 40 mg tablets. (3)
- Oral suspension: 10 mg/5 mL. (3)

----------CONTRAINDICATIONS----------

- Concomitant use of monoamine oxidase inhibitors (MAOIs) or use within 14 days of discontinuing a MAOI. (4, 5.3, 7)
- Concomitant use of pimozide or thioridazine. (4, 5.3,7)
- Known hypersensitivity to paroxetine or to any of the inactive ingredients in PAXIL. (4)

----------WARNINGS and PRECAUTIONS----------

- *Serotonin Syndrome:* Increased risk when co-administered with other serotonergic agents (e.g., SSRI, SNRI, triptans), but also when taken alone. If occurs, discontinue PAXIL and initiate supportive measures. (5.2)
- *Embryofetal and Neonatal Toxicity:* Can cause fetal and neonatal harm. Increased risk of cardiovascular malformations with exposure during the first trimester. Exposure in late pregnancy may lead to an increased risk for persistent pulmonary hypertension of the newborn. (5.4, 8.1)
- *Increased Risk of Bleeding*: Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, other antiplatelet drugs, warfarin, and other anticoagulant drugs may increase risk. (5.5)
- *Activation of Mania/Hypomania*: Screen patients for bipolar disorder. (5.6)
- *Seizures*: Use with caution in patients with seizure disorders. (5.8)
- *Angle-Closure Glaucoma*: Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants. (5.9)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥5% and at least twice placebo) are abnormal ejaculation, , asthenia, constipation, decreased appetite, diarrhea, dizziness, dry mouth, female genital disorder, impotence, infection, insomnia, libido decreased, male genital disorder, nausea, nervousness, somnolence, sweating, tremor, yawn. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Apotex Corp. at 1-800-706-5575 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- *Drugs Highly Bound to Plasma Protein*: Monitor for adverse reactions and reduce dosage of PAXIL or other protein-bound drugs (e.g., warfarin) as warranted. (7)
- *Drugs Metabolized by CYP2D6*: Reduce dosage of drugs metabolized by CYP2D6 as warranted. (7)
- *Concomitant use with tamoxifen*: Consider use of an alternative antidepressant with little or no CYP2D6 inhibition. (5.11, 7)

----------USE IN SPECIFIC POPULATIONS----------

- *Pregnancy*: Can cause fetal and neonatal harm. Advise women of potential risk to the fetus. (8.1)
- *Nursing Mothers*: Discontinue drug or nursing, taking into consideration importance of drug to mother. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 2/2021

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FULL PRESCRIBING INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors *[see Warnings and Precautions (5.1)]*. PAXIL is not approved for use in pediatric patients *[see Use in Specific Populations (8.4)]*.

1 INDICATIONS AND USAGE

PAXIL is indicated in adults for the treatment of:

- Major depressive disorder (MDD)
- Obsessive compulsive disorder (OCD)
- Panic disorder (PD)
- Social anxiety disorder (SAD)
- Generalized anxiety disorder (GAD)
- Posttraumatic stress disorder (PTSD)

2 DOSAGE AND ADMINISTRATION

2.1 Administration Information

Administer PAXIL as a single daily dose in the morning, with or without food.

Shake the oral suspension well before administration.

2.2 Recommended Dosage for MDD, OCD, PD, and PTSD

The recommended starting dosages and maximum dosages of PAXIL in patients with MDD, OCD, PD, and PTSD are presented in Table 1.

In patients with an inadequate response, increase dosage in increments of 10 mg per day at intervals of at least 1 week, depending on tolerability.

Table 1: Recommended Daily Dosage of PAXIL in Patients with MDD, OCD, PD, and PTSD

Indication	Starting Dose	Maximum Dose
MDD	20 mg	50 mg
OCD	20 mg	60 mg
PD	10 mg	60 mg
PTSD	20 mg	50 mg

2.3 Recommended Dosage for SAD and GAD

SAD

The starting and recommended dosage in patients with SAD is 20 mg daily. In clinical trials the effectiveness of PAXIL was demonstrated in patients dosed in a range of 20 mg to 60 mg daily. While the safety of PAXIL has been evaluated in patients with SAD at doses up to 60 mg daily, available information does not suggest any additional benefit for doses above 20 mg daily *[see Clinical Studies (14.4)]*.

GAD

The starting and recommended dosage in patients with GAD is 20 mg daily. In clinical trials the effectiveness of PAXIL in GAD was demonstrated in patients dosed in a range of 20 mg to 50 mg daily. There is not sufficient evidence to suggest a greater benefit to doses higher than 20 mg daily *[see Clinical Studies (14.5)]*.

In patients with an inadequate response, increase dosage in increments of 10 mg per day at intervals of at least 1 week, depending on tolerability.

2.4 Screen for Bipolar Disorder Prior to Starting PAXIL

Prior to initiating treatment with PAXIL or another antidepressant, screen patients for a personal or family history of bipolar disorder, mania, or hypomania *[see Warnings and Precautions (5.6)]*.

2.5 Recommended Dosage for Elderly Patients, Patients with Severe Renal Impairment, and Patients with Severe Hepatic Impairment

The recommended initial dosage is 10 mg per day for elderly patients, patients with severe renal impairment, and patients with severe hepatic impairment. Dosage should not exceed 40 mg/day.

2.6 Switching Patients to or From a Monoamine Oxidase Inhibitor (MAOI)

At least 14 days must elapse between discontinuation of a monoamine oxidase inhibitor (MAOI and initiation of PAXIL. In addition, at least 14 days must elapse after stopping PAXIL before starting an MAOI antidepressant *[see Contraindications (4), Warnings and Precautions (5.2)]*.

2.7 Discontinuation of Treatment With PAXIL

Adverse reactions may occur upon discontinuation of PAXIL *[see Warnings and Precautions (5.7)]*. Gradually reduce the dosage rather than stopping PAXIL abruptly whenever possible.

3 DOSAGE FORMS AND STRENGTHS

PAXIL tablets are available as:

- 10 mg yellow, scored tablet engraved on the front with “PAXIL” and on the back with “10”.
- 20 mg pink, scored tablet engraved on the front with “PAXIL” and on the back with “20”.
- 30 mg blue tablet engraved on the front with “PAXIL” and on the back with “30”.
- 40 mg green tablet engraved on the front with “PAXIL” and on the back with “40”.

PAXIL oral suspension is available as:

- 10 mg/5 mL orange colored, orange flavored suspension in bottles containing 250 mL.

4 CONTRAINDICATIONS

PAXIL is contraindicated in patients:

- Taking, or within 14 days of stopping, MAOIs (including the MAOIs linezolid and intravenous methylene blue) because of an increased risk of serotonin syndrome *[see Warnings and Precautions (5.2), Drug Interactions (7)]*.

- Taking thioridazine because of risk of QT prolongation *[see Warnings and Precautions (5.3) and Drug Interactions (7)]*

- Taking pimozide because of risk of QT prolongation *[see Warnings and Precautions (5.3), Drug Interactions (7)]*.

- With known hypersensitivity (e.g., anaphylaxis, angioedema, Stevens-Johnson syndrome) to paroxetine or any of the inactive ingredients in PAXIL *[see Adverse Reactions (6.1), (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Suicidal Thoughts and Behaviors in Adolescents and Young Adults

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1000 patients treated are provided in Table 2.

Table 2: Risk Differences of the Number of Patients with Suicidal Thoughts and Behaviors in the Pooled Placebo-Controlled Trials of Antidepressants in Pediatric and Adult Patients

Age Range	Drug-Placebo Difference in Number of Patients with Suicidal Thoughts and Behaviors per 1,000 Patients Treated
	Increases Compared to Placebo
<18 years old	14 additional cases
18-24 years old	5 additional cases
	Decreases Compared to Placebo
25-64 years old	1 fewer case
≥65 years old	6 fewer cases

PAXIL is not approved for use in pediatric patients.

It is unknown whether the risk of suicidal thoughts and behaviors in children, adolescents, and young adults extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with MDD that antidepressants delay the recurrence of depression and that depression itself is a risk factor for suicidal thoughts and behaviors.

Monitor all antidepressant-treated patients for any indication for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing PAXIL, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

5.2 Serotonin Syndrome

SSRIs, including PAXIL, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines and St. John's Wort) and with drugs that impair metabolism of serotonin, i.e., MAOIs *[see Contraindications (4), Drug Interactions (7.1)]*. Serotonin syndrome can also occur when these drugs are used alone.

Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of PAXIL with MAOIs is contraindicated. In addition, do not initiate PAXIL in a patient being treated with MAOIs such as linezolid or intravenous methylene blue. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection) or at lower doses. If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking PAXIL discontinue PAXIL before initiating treatment with the MAOI *[see Contraindications (4), Drug Interactions (7)]*.

Monitor all patients taking PAXIL for the emergence of serotonin syndrome. Discontinue treatment with PAXIL and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of PAXIL with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

5.3 Drug Interactions Leading to QT Prolongation

The CYP2D6 inhibitory properties of paroxetine can elevate plasma levels of thioridazine and pimozide. Since thioridazine and pimozide given alone produce prolongation of the QTc interval and increase the risk of serious ventricular arrhythmias, the use of PAXIL is contraindicated in combination with thioridazine and pimozide *[see Contraindications (4), Drug Interactions (7), Clinical Pharmacology (12.3)]*.

5.4 Embryofetal and Neonatal Toxicity

PAXIL can cause fetal harm when administered to a pregnant woman. Epidemiological studies have shown that infants exposed to paroxetine in the first trimester of pregnancy have an increased risk of cardiovascular malformations. Exposure to paroxetine in late pregnancy may lead to an increased risk for persistent pulmonary hypertension of the newborn (PPNH) and/or neonatal complications requiring prolonged hospitalization, respiratory support, and tube feeding.

If PAXIL is used during pregnancy, or if the patient becomes pregnant while taking PAXIL, the patient should be apprised of the potential hazard to the fetus *[see Use in Specific Populations (8.1)]*.

5.5 Increased Risk of Bleeding

Drugs that interfere with serotonin reuptake inhibition, including PAXIL, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDS), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages.

Inform patients about the increased risk of bleeding associated with the concomitant use of PAXIL and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio.

5.6 Activation of Mania or Hypomania

In patients with bipolar disorder, treating a depressive episode with PAXIL or another antidepressant may precipitate a mixed/manic episode. During controlled clinical trials of PAXIL, hypomania or mania occurred in approximately 1% of PAXIL-treated unipolar patients compared to 1.1% of active-control and 0.3% of placebo-treated unipolar patients. Prior to initiating treatment with PAXIL, screen patients for any personal or family history of bipolar disorder, mania, or hypomania.

5.7 Discontinuation Syndrome

Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible *[see Dosage and Administration (2.7)]*.

During clinical trials of GAD and PTSD, gradual decreases in the daily dose by 10 mg/day at weekly intervals followed by 1 week at 20 mg/day was used before treatment was discontinued. The following adverse reactions were reported at an incidence of 2% or greater for PAXIL and were at least twice that reported for placebo: Abnormal dreams, paresthesia, and dizziness
Adverse reactions have been reported upon discontinuation of treatment with PAXIL in pediatric patients. The safety and effectiveness of PAXIL in pediatric patients have not been established *[see Boxed Warning, Warnings and Precautions (5.1), Use in Specific Populations (8.4)]*.

5.8 Seizures
PAXIL tablets and oral suspension have not been systematically evaluated in patients with seizure disorders. Patients with history of seizures were excluded from clinical studies. During clinical studies, seizures occurred in 0.1% of patients treated with PAXIL. PAXIL should be prescribed with caution in patients with a seizure disorder. Discontinue PAXIL in any patient who develops seizures.

5.9 Angle-Closure Glaucoma
The pupillary dilation that occurs following use of many antidepressant drugs including PAXIL may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Cases of angle-closure glaucoma associated with use of PAXIL have been reported. Avoid use of antidepressants, including PAXIL in patients with untreated anatomically narrow angles.

5.10 Hyponatremia
Hyponatremia may occur as a result of treatment with SSRIs, including PAXIL. Cases with serum sodium lower than 110 mmol/L have been reported. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

In patients with symptomatic hyponatremia, discontinue PAXIL and institute appropriate medical intervention. Elderly patients, patients taking diuretics, and those who are volume-depleted may be at greater risk of developing hyponatremia with SSRIs *[see Use in Specific Populations (8.5)]*.

5.11 Reduction of Efficacy of Tamoxifen
Some studies have shown that the efficacy of tamoxifen, as measured by the risk of breast cancer relapse/mortality, may be reduced with concomitant use of PAXIL as a result of paroxetine's irreversible inhibition of CYP2D6 and lower blood levels of tamoxifen *[see Drug Interactions (7)]*. One study suggests that the risk may increase with longer duration of coadministration. However, other studies have failed to demonstrate such a risk. When tamoxifen is used for the treatment or prevention of breast cancer, prescribers should consider using an alternative antidepressant with little or no CYP2D6 inhibition.

5.12 Bone Fracture
Epidemiological studies on bone fracture risk during exposure to some antidepressants, including SSRIs, have reported an association between antidepressant treatment and fractures. There are multiple possible causes for this observation and it is unknown to what extent fracture risk is directly attributable to SSRI treatment.

6 ADVERSE REACTIONS

The following adverse reactions are included in more detail in other sections of the prescribing information:

- Hypersensitivity reactions to paroxetine *[see Contraindications (4)]*
- Suicidal Thoughts and Behaviors *[see Warnings and Precautions (5.1)]*
- Serotonin Syndrome *[see Warnings and Precautions (5.2)]*
- Embryofetal and Neonatal Toxicity *[see Warnings and Precautions (5.4)]*
- Increased Risk of Bleeding *[see Warnings and Precautions (5.5)]*
- Activation of Mania/Hypomania *[see Warnings and Precautions (5.6)]*
- Discontinuation Syndrome *[see Warnings and Precautions (5.7)]*
- Seizures *[see Warnings and Precautions (5.8)]*
- Angle-closure Glaucoma *[see Warnings and Precautions (5.9)]*
- Hyponatremia *[see Warnings and Precautions (5.10)]*
- Bone Fracture *[see Warnings and Precautions (5.12)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data for PAXIL are from:

- 6-week clinical trials in MDD patients who received PAXIL 20 mg to 50 mg once daily
- 12-week clinical trials in OCD patients who received PAXIL 20 mg to 60 mg once daily
- 10- to 12-week clinical trials in PD patients who received PAXIL 10 mg to 60 mg once daily
- 12-week clinical trials in SAD patients who received PAXIL 20 mg to 50 mg once daily
- 8-week clinical trials in GAD patients who received PAXIL 10 mg to 50 mg once daily
- 12-week clinical trials in PTSD patients who received PAXIL 20 mg to 50 mg once daily

Adverse Reactions Leading to Discontinuation

Twenty percent (1,199/6,145) of patients treated with PAXIL in clinical trials in MDD 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 clinical trials in SAD, OCD, PD, GAD, and PTSD, respectively, discontinued treatment due to an adverse reaction. The most common adverse reactions (≥1%) associated with discontinuation (i.e., those adverse reactions associated with dropout at a rate approximately twice or greater for PAXIL compared to placebo) are presented in Table 3:

Table 3: Adverse Reactions Reported as Leading to Discontinuation (≥1% of PAXIL-Treated Patients and Greater than Placebo) in MDD, OCD, PD, SAD, GAD, and PTSD Trials

	MDD		OCD		PD		SAD		GAD		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	—	—
Gastroin-testinal												
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			—	—
Other												
Asthenia	1.6	0.4	1.9	0.4			2.5	0.6	1.8	0.2	1.6	0.2
Abnormal Ejaculation[a]	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[a]	—		1.5	0							—	—
Libido Decreased							1.0	0			—	—

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

[a.] Incidence corrected for gender.

Most Common Adverse Reactions

The most commonly observed adverse reactions associated with the use of PAXIL (incidence of 5% or greater and at least twice that for placebo) were:

MDD: Asthenia, sweating, nausea, decreased appetite, somnolence, dizziness, insomnia, tremor, nervousness, ejaculatory disturbance, and other male genital disorders.

OCD: Nausea, dry mouth, decreased appetite, constipation, dizziness, somnolence, tremor, sweating, impotence, and abnormal ejaculation.

PD: Asthenia, sweating, decreased appetite, libido decreased, tremor, abnormal ejaculation, female genital disorders, and impotence.

SAD: Sweating, nausea, dry mouth, constipation, decreased appetite, somnolence, tremor, libido decreased, yawn, abnormal ejaculation, female genital disorders, and impotence.

GAD: Asthenia, infection, constipation, decreased appetite, dry mouth, nausea, libido decreased, somnolence, tremor, sweating, and abnormal ejaculation.

PTSD: Asthenia, sweating, nausea, dry mouth, diarrhea, decreased appetite, somnolence, libido decreased, abnormal ejaculation, female genital disorders, and impotence.

Adverse Reactions in Patients with MDD

Table 4 presents the adverse reactions that occurred at an incidence of 1% or more and greater than placebo in clinical trials of PAXIL-treated patients with MDD.

Table 4: Adverse Reactions (≥1% of PAXIL-Treated Patients and Greater than Placebo) in 6-Week Clinical Trials for MDD

Body System/ Adverse Reaction	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[a]	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[b,c]	13	0
Other Male Genital Disorders[b,d]	10	0
Urinary Frequency	3	1
Urination Disorder[e]	3	0
Female Genital Disorders[b,f]	2	0

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

b. Percentage corrected for gender.

c. Mostly "ejaculatory delay."

d. Includes "anorgasmia," "erectile difficulties," "delayed ejaculation/orgasm," and "sexual dysfunction," and "impotence."

e. Includes mostly "difficulty with micturition" and "urinary hesitancy."

f. Includes mostly "anorgasmia" and "difficulty reaching climax/orgasm."

Adverse Reactions in Patients with OCD, PD, and SAD

Table 5 presents adverse reactions that occurred at a frequency of 2% or more in clinical trials in patients with OCD, PD, and SAD.

Table 5. Adverse Reactions (≥2% of PAXIL-Treated Patients and Greater than Placebo) in 10 to 12-Week Clinical Trials for OCD, PD, and SAD

	Obsessive Compulsive Disorder		Panic Disorder		Social Anxiety Disorder	
Body System/Preferred Term	**PAXIL (n = 542) %**	**Placebo (n = 265) %**	**PAXIL (n = 469) %**	**Placebo (n = 324) %**	**PAXIL (n = 425) %**	**Placebo (n = 339) %**
Body as a Whole						
Asthenia	22	14	14	5	22	14
Abdominal Pain	-	-	4	3	—	—
Chest Pain	3	2	-	-	-	-
Back Pain	-	-	3	2	-	-
Chills	2	1	2	1	—	—
Trauma	—	—	—	—	3	1
Cardiovascular						
Vasodilation	4	1	—	—	—	—
Palpitation	2	0	—	—	—	—
Dermatologic						

	Obsessive Compulsive Disorder		Panic Disorder		Social Anxiety Disorder	
Body System/Preferred Term	**PAXIL (n = 542) %**	**Placebo (n = 265) %**	**PAXIL (n = 469) %**	**Placebo (n = 324) %**	**PAXIL (n = 425) %**	**Placebo (n = 339) %**
Sweating	9	3	14	6	9	2
Rash	3	2	—	—	—	—
Gastrointestinal						
Nausea	23	10	23	17	25	7
Dry Mouth	18	9	18	11	9	3
Constipation	16	6	8	5	5	2
Diarrhea	10	10	12	7	9	6
Decreased Appetite	9	3	7	3	8	2
Dyspepsia	-	-	-	-	4	2
Flatulence	-	-	-	-	4	2
Increased Appetite	4	3	2	1	-	-
Vomiting	-	-	-	-	2	1
Musculoskeletal						
Myalgia	—	—	—	—	4	3
Nervous System						
Insomnia	24	13	18	10	21	16
Somnolence	24	7	19	11	22	5
Dizziness	12	6	14	10	11	7
Tremor	11	1	9	1	9	1
Nervousness	9	8	—	—	8	7
Libido Decreased	7	4	9	1	12	1
Agitation	—	—	5	4	3	1
Anxiety	—	—	5	4	5	4

Body System/Preferred Term	Obsessive Compulsive Disorder		Panic Disorder		Social Anxiety Disorder	
	PAXIL (n = 542 %	Placebo (n = 265) %	PAXIL (n = 469) %	Placebo (n = 324) %	PAXIL (n = 425) %	Placebo (n = 339) %
Abnormal Dreams	4	1	—	—	—	—
Concentration Impaired	3	2	—	—	4	1
Depersonalization	3	0	—	—	—	—
Myoclonus	3	0	3	2	2	1
Amnesia	2	1	-	-	-	-
Respiratory System						
Rhinitis	-	-	3	0	-	-
Pharyngitis	—	—	—	—	4	2
Yawn	-	-	-	-	5	1
Special Senses						
Abnormal Vision	4	2	—	—	4	1
Taste Perversion	2	0	-	-	-	-
Urogenital System						
Abnormal Ejaculation[a]	23	1	21	1	28	1
Dysmenorrhea	—	—	—	—	5	4
Female Genital Disorder[a]	3	0	9	1	9	1
Impotence[a]	8	1	5	0	5	1
Urinary Frequency	3	1	2	0	—	—
Urination Impaired	3	0	—	—	—	—
Urinary Tract Infection	2	1	2	1	—	—

a. Percentage corrected for gender.

Adverse Reactions in Patients with GAD and PTSD

Table 6 presents adverse reactions that occurred at a frequency of 2% or more in clinical trials in patients with GAD and PTSD.

Table 6. Adverse Reactions (≥2% of PAXIL-Treated Patients and Greater than Placebo) in 8- to 12-Week Clinical Trials for GAD and PTSD[a]

Body System/Preferred Term	Generalized Anxiety Disorder		Posttraumatic Stress Disorder	
	PAXIL (n = 735) %	Placebo (n = 529) %	PAXIL (n = 676) %	Placebo (n = 504) %
Body as a Whole				
Asthenia	14	6	12	4
Headache	17	14	—	—
Infection	6	3	5	4
Abdominal Pain			4	3
Trauma			6	5
Cardiovascular				
Vasodilation	3	1	2	1
Dermatologic				
Sweating	6	2	5	1
Gastrointestinal				
Nausea	20	5	19	8
Dry Mouth	11	5	10	5
Constipation	10	2	5	3
Diarrhea	9	7	11	5
Decreased Appetite	5	1	6	3
Vomiting	3	2	3	2
Dyspepsia	—	—	5	3
	11	8	12	11
	15	5	16	5
	6	5	6	5
	5	1	4	1
	4	3	—	—
	9	2	5	2

Nervous System			3	
Insomnia				
Somnolence				
Dizziness				
Tremor				
Nervousness				
Libido Decreased				
Abnormal Dreams				
Respiratory System				
Respiratory Disorder	7	5	—	—
Sinusitis	4	3	—	—
Yawn	4	—	2	<1
Special Senses				
Abnormal Vision	2	1	3	1
Urogenital System				
Abnormal Ejaculation[a]	25	2	13	2
Female Genital Disorder[a]	4	1	5	1
Impotence[a]	4	3	9	1

[a.] Percentage corrected for gender.

Dose Dependent Adverse Reactions

MDD

A comparison of adverse reaction rates in a fixed-dose study comparing PAXIL10 mg, 20 mg, 30 mg, and 40 mg once daily with placebo in the treatment of MDD revealed dose dependent adverse reactions, as shown in Table 7:

Table 7. Adverse Reactions (≥5% of PAXIL-Treated Patients and ≥ Twice the Rate of Placebo) (in a Dose-Comparison Trial in the Treatment of MDD

Body System/Preferred Term	Placebo n = 51 %	PAXIL 10 mg n = 102 %	PAXIL 20 mg n = 104 %	PAXIL 30 mg n = 101 %	PAXIL 40 mg n = 102 %
Body as a Whole					
Asthenia	0.0	2.9	10.6	13.9	12.7
Dermatology					
Sweating	2.0	1.0	6.7	8.9	11.8
Gastrointestinal					
Constipation	5.9	4.9	7.7	9.9	12.7
Decreased Appetite	2.0	2.0	5.8	4.0	4.9
Diarrhea	7.8	9.8	19.2	7.9	14.7
Dry Mouth	2.0	10.8	18.3	15.8	20.6
Nausea	13.7	14.7	26.9	34.7	36.3
Nervous System					
Anxiety	0.0	2.0	5.8	5.9	5.9
Dizziness	3.9	6.9	6.7	8.9	12.7
Nervousness	0.0	5.9	5.8	4.0	2.9
Paresthesia	0.0	2.9	1.0	5.0	5.9
Somnolence	7.8	12.7	18.3	20.8	21.6
Tremor	0.0	0.0	7.7	7.9	14.7
Special Senses					
Blurred Vision	2.0	2.9	2.9	2.0	7.8
Urogenital System					
Abnormal Ejaculation	0.0	5.8	6.5	10.6	13.0
Impotence	0.0	1.9	4.3	6.4	1.9
Male Genital Disorders	0.0	3.8	8.7	6.4	3.7

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OCD

In a fixed-dose study comparing placebo and PAXIL 20 mg, 40 mg, and 60 mg in the treatment of OCD, there was no clear relationship between adverse reactions and the dose of PAXIL to which patients were assigned.

PD

In a fixed-dose study comparing placebo and PAXIL 10 mg, 20 mg, and 40 mg in the treatment of PD, the following adverse reactions were shown to be dose-dependent: asthenia, dry mouth, anxiety, libido decreased, tremor, and abnormal ejaculation.

SAD
In a fixed-dose study comparing placebo and PAXIL 20 mg, 40 mg and 60 mg in the treatment of SAD, for most of the adverse reactions, there was no clear relationship between adverse reactions and the dose of PAXIL to which patients were assigned.

GAD
In a fixed-dose study comparing placebo and PAXIL 20 mg and 40 mg in the treatment of GAD, the following adverse reactions were shown to be dose-dependent: asthenia, constipation, and abnormal ejaculation.

PTSD
In a fixed-dose study comparing placebo and PAXIL 20 mg and 40 mg in the treatment of PTSD, the following adverse reactions were shown to be dose-dependent: impotence and abnormal ejaculation.

Male and Female Sexual Dysfunction
Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of SSRI treatment. However, reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and healthcare providers may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in labeling may underestimate their actual incidence.

The percentage of patients reporting symptoms of sexual dysfunction in males and females with MDD, OCD, PD, SAD, GAD, and PTSD are displayed in Table 8.

Table 8. Adverse Reactions Related to Sexual Dysfunction in Patients Treated with PAXIL in Clinical Trials of MDD, OCD, PD, SAD, GAD, and PTSD

	PAXIL	Placebo
n (males)	**1446**	**1042**
	%	**%**
Decreased Libido	6 to15	0 to 5
Ejaculatory Disturbance	13 to 28	0 to 2
Impotence	2 to 9	0 to 3
n (females)	**1822**	**1340**
	%	**%**
Decreased Libido	0 to 9	0 to 2
Orgasmic Disturbance	2 to 9	0 to 1

PAXIL treatment has been associated with several cases of priapism. In those cases with a known outcome, patients recovered without sequelae.

Hallucinations

In pooled clinical trials of PAXIL, hallucinations were observed in 0.2% of PAXIL-treated patients compared to 0.1% of patients receiving placebo.

Less Common Adverse Reactions

The following adverse reactions occurred during the clinical studies of PAXIL and are not included elsewhere in the labeling.

Adverse reactions are categorized by body system and listed in order of decreasing frequency according to the following definitions: Frequent adverse reactions are those occurring on 1 or more occasions in at least 1/100 patients; infrequent adverse reactions are those occurring in 1/100 to 1/1,000 patients; rare adverse reactions are those occurring in fewer than 1/1,000 patients.

Body as a Whole

Infrequent: Allergic reaction, chills, face edema, malaise, neck pain; *rare:* Adrenergic syndrome, cellulitis, moniliasis, neck rigidity, pelvic pain, peritonitis, sepsis, ulcer.

Cardiovascular System

Frequent: Hypertension, tachycardia; *infrequent:* Bradycardia, hematoma, hypotension, migraine, postural hypotension, syncope; *rare:* Angina pectoris, arrhythmia nodal, atrial fibrillation, bundle branch block, cerebral ischemia, cerebrovascular accident, congestive heart failure, heart block, low cardiac output, myocardial infarct, myocardial ischemia, pallor,

phlebitis, pulmonary embolus, supraventricular extrasystoles, thrombophlebitis, thrombosis, varicose vein, vascular headache, ventricular extrasystoles.

Digestive System
Infrequent: Bruxism, colitis, dysphagia, eructation, gastritis, gastroenteritis, gingivitis, glossitis, increased salivation, abnormal liver function tests, rectal hemorrhage, ulcerative stomatitis; *rare:* Aphthous stomatitis, bloody diarrhea, bulimia, cardiospasm, cholelithiasis, duodenitis, enteritis, esophagitis, fecal impactions, fecal incontinence, gum hemorrhage, hematemesis, hepatitis, ileitis, ileus, intestinal obstruction, jaundice, melena, mouth ulceration, peptic ulcer, salivary gland enlargement, sialadenitis, stomach ulcer, stomatitis, tongue discoloration, tongue edema, tooth caries.

Endocrine System
Rare: Diabetes mellitus, goiter, hyperthyroidism, hypothyroidism, thyroiditis.

Hemic and Lymphatic Systems
Infrequent: Anemia, leukopenia, lymphadenopathy, purpura; *rare:* Abnormal erythrocytes, basophilia, bleeding time increased, eosinophilia, hypochromic anemia, iron deficiency anemia, leukocytosis, lymphedema, abnormal lymphocytes, lymphocytosis, microcytic anemia, monocytosis, normocytic anemia, thrombocythemia, thrombocytopenia.

Metabolic and Nutritional
Frequent: Weight gain; infrequent: Edema, peripheral edema, SGOT increased, SGPT increased, thirst, weight loss; rare: Alkaline phosphatase increased, bilirubinemia, BUN increased, creatinine phosphokinase increased, dehydration, gamma globulins increased, gout, hypercalcemia, hypercholesteremia, hyperglycemia, hyperkalemia, hyperphosphatemia, hypocalcemia, hypoglycemia, hypokalemia, hyponatremia, ketosis, lactic dehydrogenase increased, non-protein nitrogen (NPN) increased.

Musculoskeletal System
Frequent: Arthralgia; *infrequent:* Arthritis, arthrosis; *rare:* Bursitis, myositis, osteoporosis, generalized spasm, tenosynovitis, tetany.

Nervous System
Frequent: Emotional lability, vertigo; *infrequent:* Abnormal thinking, alcohol abuse, ataxia, dystonia, dyskinesia, euphoria, hostility, hypertonia, hypesthesia, hypokinesia, incoordination, lack of emotion, libido increased, manic reaction, neurosis, paralysis, paranoid reaction; *rare:* Abnormal gait, akinesia, antisocial reaction, aphasia, choreoathetosis, circumoral paresthesias, convulsion, delirium, delusions, diplopia, drug dependence, dysarthria, extrapyramidal syndrome, fasciculations, grand mal convulsion, hyperalgesia, hysteria, manic-depressive

reaction, meningitis, myelitis, neuralgia, neuropathy, nystagmus, peripheral neuritis, psychotic depression, psychosis, reflexes decreased, reflexes increased, stupor, torticollis, trismus, withdrawal syndrome.

Respiratory System
Infrequent: Asthma, bronchitis, dyspnea, epistaxis, hyperventilation, pneumonia, respiratory flu; *rare:* Emphysema, hemoptysis, hiccups, lung fibrosis, pulmonary edema, sputum increased, stridor, voice alteration.

Skin and Appendages
Frequent: Pruritus; *infrequent:* Acne, alopecia, contact dermatitis, dry skin, ecchymosis, eczema, herpes simplex, photosensitivity, urticaria; *rare:* Angioedema, erythema nodosum, erythema multiforme, exfoliative dermatitis, fungal dermatitis, furunculosis; herpes zoster, hirsutism, maculopapular rash, seborrhea, skin discoloration, skin hypertrophy, skin ulcer, sweating decreased, vesiculobullous rash.

Special Senses
Frequent: Tinnitus; *infrequent:* Abnormality of accommodation, conjunctivitis, ear pain, eye pain, keratoconjunctivitis, mydriasis, otitis media; *rare:* Amblyopia, anisocoria, blepharitis, cataract, conjunctival edema, corneal ulcer, deafness, exophthalmos, eye hemorrhage, glaucoma, hyperacusis, night blindness, otitis externa, parosmia, photophobia, ptosis, retinal hemorrhage, taste loss, visual field defect.

Urogenital System
Infrequent: Amenorrhea, breast pain, cystitis, dysuria, hematuria, menorrhagia, nocturia, polyuria, pyuria, urinary incontinence, urinary retention, urinary urgency, vaginitis; *rare:* Abortion, breast atrophy, breast enlargement, endometrial disorder, epididymitis, female lactation, fibrocystic breast, kidney calculus, kidney pain, leukorrhea, mastitis, metrorrhagia, nephritis, oliguria, salpingitis, urethritis, urinary casts, uterine spasm, urolith, vaginal hemorrhage, vaginal moniliasis.

6.2 Postmarketing Experience
The following reactions have been identified during post approval use of PAXIL. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Acute pancreatitis, elevated liver function tests (the most severe cases were deaths due to liver necrosis, and grossly elevated transaminases associated with severe liver dysfunction), Guillain-Barré syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, syndrome of inappropriate ADH secretion, prolactinemia and galactorrhea; extrapyramidal symptoms which

have included akathisia, bradykinesia, cogwheel rigidity, oculogyric crisis which has been associated with concomitant use of pimozide; status epilepticus, acute renal failure, pulmonary hypertension, allergic alveolitis, anaphylaxis, eclampsia, laryngismus, optic neuritis, porphyria, restless legs syndrome (RLS), ventricular fibrillation, ventricular tachycardia (including torsade de pointes), hemolytic anemia, events related to impaired hematopoiesis (including aplastic anemia, pancytopenia, bone marrow aplasia, and agranulocytosis), vasculitic syndromes (such as Henoch-Schönlein purpura), and premature births in pregnant women. There has been a case report of severe hypotension when PAXIL was added to chronic metoprolol treatment.

7 DRUG INTERACTIONS

Table 9 presents clinically significant drug interactions with PAXIL.

Table 9: Clinically Significant Drug Interactions with PAXIL

Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Impact	The concomitant use of SSRIs, including PAXIL, and MAOIs increases the risk of serotonin syndrome.
Intervention	PAXIL is contraindicated in patients taking MAOIs, including MAOIs such as linezolid or intravenous methylene blue *[see Dosage and Administration (2.5), Contraindications (4), Warnings and Precautions (5.2)]*.
Examples	selegiline, tranylcypromine, isocarboxazid, phenelzine, linezolid, methylene blue
Pimozide and Thioridazine	
Clinical Impact	Increased plasma concentrations of pimozide and thioridazine, drugs with a narrow therapeutic index, may increase the risk of QTc prolongation and ventricular arrhythmias.
Intervention	PAXIL is contraindicated in patients taking pimozide or thioridazine *[see Contraindications (4)]*.
Other Serotonergic Drugs	
Clinical Impact	The concomitant use of serotonergic drugs with PAXIL increases the risk of serotonin syndrome.
Intervention	Monitor patients for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increases. If serotonin syndrome occurs, consider discontinuation of PAXIL and/or concomitant serotonergic drugs *[see Warnings and Precautions (5.2)]*.
Examples	other SSRIs, SNRIs, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort
Drugs that Interfere with Hemostasis (antiplatelet agents and anticoagulants)	

Clinical Impact	The concurrent use of an antiplatelet agent or anticoagulant with PAXIL may potentiate the risk of bleeding.
Intervention	Inform patients of the increased risk of bleeding associated with the concomitant use of PAXIL and antiplatelet agents and anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio *[see Warnings and Precautions (5.5)]*.
Examples	aspirin, clopidogrel, heparin, warfarin
Drugs Highly Bound to Plasma Protein	

Clinical Impact	PAXIL is highly bound to plasma protein. The concomitant use of PAXIL with another drug that is highly bound to plasma protein may increase free concentrations of PAXIL or other tightly-bound drugs in plasma.
Intervention	Monitor for adverse reactions and reduce dosage of PAXIL or other protein-bound drugs as warranted.
Examples	warfarin
Drugs Metabolized by CYP2D6	
Clinical Impact	PAXIL is a CYP2D6 inhibitor *[see Clinical Pharmacology (12.3)]*. The concomitant use of PAXIL with a CYP2D6 substrate may increase the exposure of the CYP2D6 substrate.
Intervention	Decrease the dosage of a CYP2D6 substrate if needed with concomitant PAXIL use. Conversely, an increase in dosage of a CYP2D6 substrate may be needed if PAXIL is discontinued.
Examples	propafenone, flecainide, atomoxetine, desipramine, dextromethorphan, metoprolol, nebivolol, perphenazine, tolterodine, venlafaxine, risperidone.
Tamoxifen	
Clinical Impact	Concomitant use of tamoxifen with PAXIL may lead to reduced plasma concentrations of the active metabolite (endoxifen) and reduced efficacy of tamoxifen
Intervention	Consider use of an alternative antidepressant with little or no CYP2D6 inhibition *[see Warnings and Precautions (5.11)]*.
Fosamprenavir/Ritonavir	
Clinical Impact	Co-administration of fosamprenavir/ritonavir with PAXIL significantly decreased plasma levels of PAXIL.
Intervention	Any dose adjustment should be guided by clinical effect (tolerability and efficacy).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D *[see Warnings and Precautions (5.14)]*

Epidemiological studies have shown that infants exposed to paroxetine in the first trimester of pregnancy have an increased risk of congenital malformations, particularly cardiovascular malformations. If paroxetine is used during pregnancy, or if the patient becomes pregnant while taking paroxetine, advise the patient of the potential hazard to the fetus.

Clinical Considerations

Embryo-Fetal Toxicity
Advise women of the potential risk to the fetus *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1)]*. Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during therapy because of the risk to the fetus.

Nursing
Advise women to notify their healthcare provider if they are breastfeeding an infant *[see Use In Specific Populations (8.3)]*.

Manufactured by: Apotex Inc**.** Toronto, Ontario M9L 1T9

Manufactured for:
Apotex Corp.
Weston, FL 33326

MEDICATION GUIDE
PAXIL® (PAX-il)
(paroxetine)
tablets
oral suspension

What is the most important information I should know about PAXIL?

PAXIL can cause serious side effects, including:

- **Increased risk of suicidal thoughts or actions.** PAXIL and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger, especially within the **first few months of treatment or when the dose is changed**. **PAXIL is not for use in children.**
    - **Depression or other mental illnesses are the most important causes of suicidal thoughts and actions.**

  How can I watch for and try to prevent suicidal thoughts and actions?

  - Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts or feelings or if you develop suicidal thoughts or actions. This is very important when an antidepressant medicine is started or when the does is changed.
  - Call your healthcare provider right away to report new or sudden changes in mood, behavior, thoughts or feelings or if you develop suicidal thoughts or actions.
  - Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

  Call your healthcare provider or get emergency medical help right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

  - attempts to commit suicide
  - acting aggressive or violent
  - new or worse depression
  - feeling agitated, restless, angry, or irritable
  - an increase in activity and talking more than what is normal for you
  - acting on dangerous impulses
  - thoughts about suicide or dying
  - new or worse anxiety or panic attacks
  - trouble sleeping
  - other unusual changes in behavior or mood

What is PAXIL?

PAXIL is a prescription medicine used in adults to treat:

- A certain type of depression called Major Depressive Disorder (MDD)
- Obsessive Compulsive Disorder (OCD)
- Panic Disorder (PD)
- Social Anxiety Disorder (SAD)
- Generalized Anxiety Disorder (GAD)
- Posttraumatic Stress Disorder (PTSD)

Do not take PAXIL if you:

- take a monoamine oxidase inhibitor (MAOI)
- have stopped taking an MAOI in the last 14 days
- are being treated with the antibiotic linezolid or the intravenous methylene blue
- are taking pimozide
- are taking thioridazine

- are allergic to paroxetine or any of the ingredients in PAXIL. See the end of this Medication Guide for a complete list of ingredients in PAXIL.

Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI or one of these medicines, including the antibiotic linezolid or intravenous methylene blue.

Do not start taking an MAOI for at least 14 days after you stop treatment with PAXIL.

Before taking PAXIL, tell your healthcare provider about all your medical conditions, including if you:

- have heart problems
- have or had bleeding problems
- have, or have a family history of, bipolar disorder, mania or hypomania
- have or had seizures or convulsions
- have glaucoma (high pressure in the eye)
- have low sodium levels in your blood
- have bone problems
- have kidney or liver problems
- are pregnant or plan to become pregnant. PAXIL may harm your unborn baby. Talk to your healthcare provider about the risks to your unborn baby if you take PAXIL during pregnancy. Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with PAXIL.
- are breastfeeding or plan to breastfeed. PAXIL passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with PAXIL.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

PAXIL and some other medicines may affect each other causing possible serious side effects. PAXIL may affect the way other medicines work and other medicines may affect the way PAXIL works.

Especially tell your healthcare provider if you take:

- medicines used to treat migraine headaches called triptans
- tricyclic antidepressants
- fentanyl
- lithium
- tramadol
- tryptophan
- buspirone
- amphetamines
- St. John's Wort
- medicines that can affect blood clotting such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin
- diuretics
- tamoxifen
- medicines used to treat mood, anxiety, psychotic, or thought disorders, including selective serontonin reuptake (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs)

Ask your healthcare provider if you are not sure if you are taking any of these medicines. Your healthcare provider can tell you if it is safe to take PAXIL with your other medicines.

Do not start or stop any other medicines during treatment with PAXIL without talking to your healthcare provider first. Stopping PAXIL suddenly may cause you to have serious side effects. See, **"What are the possible side effects of PAXIL?"**

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How should I take PAXIL?

- Take PAXIL exactly as prescribed. Your healthcare provider may need to change the dose of PAXIL until it is the right dose for you.
- Take PAXIL 1 time each day in the morning.
- PAXIL may be taken with or without food.
- If you are taking PAXIL oral suspension, shake the suspension well before taking.
- If you take too much PAXIL, call your poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What are possible side effects of PAXIL?

PAXIL can cause serious side effects, including:

- See, **"What is the most important information I should know about PAXIL?"**
- **Serotonin syndrome.** A potentially life-threatening problem called serotonin syndrome can happen when you take PAXIL with certain other medicines. See, "Who should not take PAXIL?" **Call your healthcare provider or go to the nearest hospital emergency room right away** if you have any of the following signs and symptoms of serotonin syndrome:
  - o agitation
  - o seeing or hearing things that are not real (hallucinations)
  - o confusion
  - o coma
  - o fast heart beat
  - o changes in blood pressure
  - o dizziness
  - o sweating
  - o flushing
  - o high body temperature (hyperthermia)
  - o shaking (tremors), stiff muscles, or muscle twitching
  - o loss of coordination
  - o seizures
  - o nausea, vomiting, diarrhea
- **Eye problems (angle-closure glaucoma).** PAXIL may cause a type of eye problem called angle-closure glaucoma in people with certain other eye conditions. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are. Call your healthcare provider if you have eye pain, changes in your vision, or swelling or redness in or around the eye**.**
- **Medicine interactions.** Taking PAXIL with certain other medicines including thioridazine and pimozide may increase the risk of developing a serious heart problem called QT prolongation**.**
- **Seizures (convulsions).**
- **Manic episodes.** Manic episodes may happen in people with bipolar disorder who take PAXIL. Symptoms may include:
  - o greatly increased energy
  - o racing thoughts
  - o unusually grand ideas
  - o talking more or faster than usual
  - o severe problems sleeping
  - o reckless behavior
  - o excessive happiness or irritability
- **Discontinuation syndrome.** Suddenly stopping PAXIL may cause you to have serious side effects. Your healthcare provider may want to decrease your dose slowly. Symptoms may include:
  - o nausea
  - o sweating
  - o changes in your mood
  - o irritability and agitation
  - o dizziness
  - o electric shock feeling (paresthesia)
  - o tremor
  - o anxiety
  - o confusion
  - o headache
  - o tiredness
  - o problems sleeping
  - o hypomania
  - o ringing in your ears (tinnitus)
  - o seizures
- **Low sodium levels in your blood (hyponatremia).** Low sodium levels in your blood that may be serious and may cause death, can happen during treatment with PAXIL. Elderly people and people who take certain medicines may be at a greater risk for developing low sodium levels in your blood. Signs and symptoms may include:
  - o headache
  - o difficulty concentrating
  - o memory changes

- confusion
- weakness and unsteadiness on your feet which can lead to falls

In more severe or more sudden cases, signs and symptoms include:

- seeing or hearing things that are not real (hallucinations)
- fainting
- seizures
- coma
- stopping breathing (respiratory arrest)

- **Abnormal bleeding.** Taking PAXIL with aspirin, NSAIDs, or blood thinners may increase this risk. Tell your healthcare provider about any unusual bleeding or bruising.
- **Bone fractures.**

The most common side effects of PAXIL include:

- male and female sexual function problems
- constipation
- diarrhea
- dry mouth
- problems sleeping
- nervousness
- sweating
- yawning
- weakness (asthenia)
- decreased appetite
- dizziness
- infection
- nausea
- sleepiness
- shaking (tremor)

These are not all the possible side effects of PAXIL.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store PAXIL?

- Store PAXIL tablets between 59°F to 86°F (15°C to 30°C).
- Store PAXIL oral suspension at or below 77ºF (25ºC).

Keep PAXIL and all medicines out of the reach of children.

General information about the safe and effective use of PAXIL.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not take PAXIL for a condition for which it was not prescribed. Do not give PAXIL to other people, even if they have the same symptoms that you have. It may harm them. You may ask your healthcare provider or pharmacist for information about PAXIL that is written for healthcare professionals.

What are the ingredients in PAXIL?

Active ingredient: paroxetine hydrochloride

Inactive ingredients:

Tablets: dibasic calcium phosphate dihydrate, hypromellose, magnesium stearate, polyethylene glycols, polysorbate 80, sodium starch glycolate, titanium dioxide, and 1 or more of the following: D&C Red No. 30 aluminum lake, D&C Yellow No. 10 aluminum lake, FD&C Blue No. 2 aluminum lake, FD&C Yellow No. 6 aluminum lake

Oral suspension: citric acid (anhydrous), FD&C yellow No. 6, flavorings, glycerin, methylparaben, microcrystalline cellulose and carboxymethylcellulose sodium, polacrilin potassium, propylene glycol, propylparaben, purified water, saccharin sodium, simethicone emulsion and sodium citrate (dihydrate)

Manufactured by: Apotex Inc.,Toronto, Ontario, Canada M9L 1T9
Manufactured for: Apotex Corp.: Weston, Florida USA 33326

For more information about PAXIL call 1-800-706-5575.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 2/2021