IMPORTANT PRESCRIBING INFORMATION

Dear Healthcare Professional:

GlaxoSmithKline (GSK) would like to advise you of important changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the labels for PAXIL® (paroxetine HCl) and PAXIL CR® (paroxetine HCl Controlled-Release Tablets). These labeling changes relate to your adult patients, particularly those who are younger adults. Please read the full text of the added WARNINGS following this letter. Full copies of the revised package inserts for PAXIL and PAXIL CR are enclosed.

Current prescribing information for paroxetine—and for all other antidepressants—contains information in the WARNINGS section (Clinical Worsening and Suicide Risk subsection) stating that “patients with MDD, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.”

GSK has recently conducted a new meta-analysis (an addition to numerous prior analyses) of suicidal behavior and ideation in placebo-controlled clinical trials of paroxetine in adult patients with psychiatric disorders including Major Depressive Disorder (MDD), other depression and non-depression disorders (e.g., dysthymia, panic disorder, generalized anxiety disorder, obsessive compulsive disorder). These trials included 8958 patients treated with paroxetine and 5953 with placebo.

Results of this analysis showed a higher frequency of suicidal behavior in young adults (prospectively defined as age 18-24) treated with paroxetine compared with placebo (17/776 [2.19%] versus 5/542 [0.92%]). In the older age groups (25-64 years and ≥65 years), no such increase was observed. This finding in young adults was not statistically significant; however, the difference was observed in paroxetine-treated patients with both depressive and non-depressive conditions.

Further, in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo (11/3455 [0.32%] versus 1/1978 [0.05%]). This difference was statistically significant; however as the absolute number and incidence of events are small, these data should be interpreted with caution. All of the reported events of suicidal behavior in the adult patients with MDD were non-fatal suicide attempts, and the majority of these attempts (8 of 11) were in younger adults aged 18-30. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

The possible increase in risk of suicidal behavior in the MDD studies was observed despite substantial evidence for efficacy in the paroxetine-treated patients (compared with placebo) as determined by standardized disease-specific instruments (e.g., Hamilton Depression
Rating Scale and Montgomery-Asberg Depression Rating Scale for depression). Most patients had an identified social stressor at the time of the event.

It is therefore important that all patients, especially young adults and those who are improving, receive careful monitoring during paroxetine therapy regardless of the condition being treated.

It is difficult to conclude a causal relationship between paroxetine and suicidality due to the small incidence and absolute number of events, the retrospective nature of this meta-analysis, and potential for confounding by the fact that the events of interest are a symptom of the psychiatric illnesses themselves. However, GSK believes it is important to draw your attention to these findings and is voluntarily amending the paroxetine labeling to reflect this new information and to emphasize the importance of careful monitoring of all patients during paroxetine therapy. Please read the full text of the added WARNINGS following this letter. Full copies of the revised package inserts for PAXIL and PAXIL CR are enclosed.

GSK continues to believe that the overall risk:benefit of paroxetine in the treatment of adult patients with MDD and other non-depressive psychiatric disorders remains positive.

PAXIL is indicated for the treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, generalized anxiety disorder, and posttraumatic stress disorder in adults; PAXIL CR is indicated for the treatment of major depressive disorder, panic disorder, social anxiety disorder, and premenstrual dysphoric disorder in adults.

The medical community can further our understanding of PAXIL and PAXIL CR by reporting adverse events to GlaxoSmithKline at 1-888-825-5249 or to FDA's MedWatch Adverse Event Reporting program online (at www.fda.gov/MedWatch/report.htm), by phone (1-800-FDA-1088), or by returning the postage-paid FDA form 3500 (which may be downloaded from www.fda.gov/MedWatch/getforms.htm) by mail (to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787) or fax (1-800-FDA-0178).

GlaxoSmithKline encourages you to familiarize yourself with these revisions to labeling. If you have any questions about the new information, please contact our Customer Response Center at 1-888-825-5249. You can find other useful information related to this issue at gsk.com and to clinical trials involving all other GSK products at our Clinical Trial Registry website (http://ctr.gsk.co.uk/welcome.asp).

Sincerely,

John E. Kraus, MD, PhD
Director, Clinical Development
Clinical Psychiatry- North America
Neurosciences Medicines Development Center
GlaxoSmithKline
PAXIL®
(paroxetine hydrochloride)
Tablets and Oral Suspension

Safetyside in Children and Adolescents

Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in short-term studies in children, adolescents, and young adults with major depressive disorder (MDD) and other psychiatric disorders. There was a statistically significant increase in the risk of suicidality associated with paroxetine, for all ages combined (12-17 years old). Pediatric patients taking paroxetine and other antidepressants should be observed closely, and the family should be informed about the need for possible monitoring. Children and families with suicidal tendencies should know that PALEX or any other antidepressant may increase suicidal thoughts and behaviors and should be monitored closely. Patients should be closely observed and evaluated as to the need for hospitalization. Families and caregivers should be advised of the need to keep potentially suicidal agents out of the home or to carefully store them in a locked facility.

Precautions

Suicidality and Lethality Due to Intentional Overdose

Children and adolescents with depression and other psychiatric disorders are at risk of suicide. Elderly patients treated with antidepressants are at increased risk of completing suicide. SSRI antidepressant treatment has been associated with an increased occurrence of thoughts or behavior suggesting suicide in children and adolescents in clinical trials. The risk of suicide is not limited to the onset of treatment, but may occur at any time during treatment.

Children and adolescents with depressive disorders and/or other psychopathological disorders are at increased risk for suicidal thoughts or behaviors, regardless of the type of antidepressant prescribed. Families and caregivers should be advised to be alert for any new or worsening symptoms. Physicians and caregivers should be alert to the risk of suicidal thinking or behavior in children and adolescents treated with antidepressants, either new or previously treated, and for the duration of treatment and for at least several months after treatment is stopped. Children and adolescents with MDD, especially those with suicidal ideation or behavior, should be observed closely, and the family should be informed of the need for possible monitoring.

The FDA has received reports of completed or attempted suicide, suicide attempts, or severe non-suicidal self-injury in children and adolescents treated with antidepressants. If an antidepressant is necessary for treatment of an existing depressive disorder, the physician should carefully consider the need for concurrent treatment with an antidepressant. In most cases, the decision to prescribe an antidepressant for the treatment of a depressive disorder in children and adolescents should be made by physicians with experience in the care of children and adolescents who are aware of the increased risk of suicide but also are aware of the risk of untreated depression. The physician and the family should be advised of the need to carefully monitor the patient and the need for possible hospitalization.

Obsessive Compulsive Disorder

The effectiveness of PALEX in the treatment of obsessive compulsive disorder is based on the results of two 12-week multicenter, placebo-controlled studies of adult subjects (18-65 years old). In two studies (18-65 years old). In one study, patients were randomized to receive placebo and the other received paroxetine 20 mg/day, both with a 12-week treatment period. In both studies, patients treated with paroxetine 20 mg/day and those treated with placebo were evaluated at baseline and at 12 weeks. In these studies, patients treated with paroxetine 20 mg/day showed a significant improvement in the Hamilton Obsessive Compulsive Scale (HOCDS) scores compared to those treated with placebo. In the second study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

The effectiveness of paroxetine hydrochloride in the treatment of obsessive compulsive disorder (OC) was demonstrated in two 12-week multicenter, placebo-controlled studies of adult subjects (18-65 years old). In each study, patients were randomized to receive placebo or paroxetine 20 mg/day. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In both studies, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

The following table provides the outcome measures by treatment group of the Clinical Global Improvement Scale for Study 1.

- **Outcome Classification (ICN)**: On Global Improvement, items 1-26 were rated on a 5-point scale from 1 = Very Much Improved to 5 = Much Worse.
- **Baseline**: The baseline observation was obtained at the beginning of the study.
- **Final Observation**: The final observation was obtained at the end of the study.
- **Improvement**: Improvement was determined by comparing the change from baseline to final observation for each patient.

<table>
<thead>
<tr>
<th>Item</th>
<th>Baseline</th>
<th>Final Observation</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.0</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>2</td>
<td>3.5</td>
<td>2.0</td>
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<tr>
<td>3</td>
<td>4.0</td>
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<td>1.0</td>
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<tr>
<td>4</td>
<td>4.5</td>
<td>4.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

No item did not indicate that there were any differences in treatment response as a function of age or gender.

The long-term maintenance effects of PALEX in OCD were demonstrated in a long-term extension to Study 1. In this study, patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

The effectiveness of PALEX in the treatment of obsessive compulsive disorder is based on the results of two 12-week, multicenter, placebo-controlled studies of adult subjects (18-65 years old). In these studies, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 1**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 2**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 3**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 4**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 5**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 6**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 7**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 8**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.

- **Study 9**: A 12-week flexible-dose study comparing paroxetine (20 mg/day) to placebo. Patients were randomized to receive paroxetine 20 mg/day or placebo. Both studies were double-blind, randomized, controlled studies comparing paroxetine (20 mg/day) to placebo. In this study, patients treated with paroxetine 20 mg/day showed a significant improvement in the Yale-Brown Obsessive Compulsive Rating Scale (Y-BOCS) scores compared to those treated with placebo.
Discordance of Treatment with PASIL for the description of the role of discordance of PASIL). There were indications that PASIL is associated with both psychological dysfunctions and with good patient management in order to reduce the risk of failure. Families and caregivers of children being treated for depression. Following unsuccessful treatment with PASIL, Thought disorder was characterized by the occurrence of unexplained panic attacks and associated confusion about having additional physical or psychological symptoms. This was accompanied by a chronic and severe degree of illness or disability, and to report such symptoms immediately to health care providers. Much of the information should be obtained from the patient and the family and careful consideration should be given to the patient’s current physical health and psychological development.

Screening Patients for Bipolar Disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is a genotypic and genetic disorder that affects the brain and the body. The symptoms of bipolar disorder can present as a chronic, severe, and disabling condition. Although antidepressants are effective in treating depression, they are not approved for use in treating bipolar disorder. The mainstay of management is cognitive behavior therapy and antidepressants. Several studies have indicated that patients receiving another medicine that increases in plasma concentration of mood stabilizers, such as those that are used in bipolar disorder, can lead to a more rapid and effective treatment outcome. These patients should be closely monitored for signs of depression, such as increased irritability, agitation, and aggression. The treatment of bipolar disorder can be difficult and requires a comprehensive approach that includes medication management, cognitive behavioral therapy, and regular medical checkups.

Bipolar disorder (also called mania or hypomania) is a chronic mental illness that affects the mood and energy levels of an individual. It is characterized by periods of mood elevation, irritability, and agitation. Management interventions include medication management, psychotherapy, and sometimes hospitalization. It is important to rule out other possible causes of irritability and agitation before considering treatment for bipolar disorder. The management of bipolar disorder involves a combination of medication, psychotherapy, and lifestyle changes. Antidepressants are contraindicated in patients with bipolar disorder, and lithium is prescribed for the treatment of bipolar disorder.

Lithium is a medication that is used to treat bipolar disorder. It is a mood stabilizer that works by balancing the levels of certain chemicals in the brain. It is prescribed for patients with bipolar disorder, and it is also used to treat manic episodes. Lithium is prescribed for the treatment of bipolar disorder, and it is also used to treat manic episodes. It is important to note that lithium is not a cure for bipolar disorder, and it must be used in combination with other treatments, such as psychotherapy and lifestyle changes, to manage the symptoms of the disorder. Lithium is a medication that is used to treat bipolar disorder. It is a mood stabilizer that works by balancing the levels of certain chemicals in the brain. It is prescribed for patients with bipolar disorder, and it is also used to treat manic episodes. Lithium is prescribed for the treatment of bipolar disorder, and it is also used to treat manic episodes. It is important to note that lithium is not a cure for bipolar disorder, and it must be used in combination with other treatments, such as psychotherapy and lifestyle changes, to manage the symptoms of the disorder.

In conclusion, bipolar disorder is a complex and chronic mental illness that requires a comprehensive approach to management. It involves medication management, psychotherapy, and lifestyle changes. Antidepressants are contraindicated in patients with bipolar disorder, and lithium is prescribed for the treatment of bipolar disorder. It is important to rule out other possible causes of irritability and agitation before considering treatment for bipolar disorder. The management of bipolar disorder involves a combination of medication, psychotherapy, and lifestyle changes. Antidepressants are contraindicated in patients with bipolar disorder, and lithium is prescribed for the treatment of bipolar disorder. It is important to note that lithium is not a cure for bipolar disorder, and it must be used in combination with other treatments, such as psychotherapy and lifestyle changes, to manage the symptoms of the disorder.
inhibit or accelerate the risk of bleeding associated with the concurrent use of vasodilators with 

or aspirin potentiated the risk of bleeding (see Drug Interactions). Although these studies focused on upper gastrointestinal Bleeding, there is evidence that the risk of bleeding does not appear to be significantly increased in patients taking aspirin for other conditions as well. However, caution should be exercised when using aspirin in patients with a history of bleeding. People with a history of gastrointestinal bleeding should be monitored closely for signs of bleeding.

Due to Patients With Gastrointestinal Risks: Clinical Experience with PARX shows that patients with certain concurrent systems. In some cases, bleeding can occur in the absence of other gastrointestinal symptoms or signs, and the risk of severe gastrointestinal bleeding cannot be ruled out. Therefore, people with a history of gastrointestinal bleeding or those at high risk for gastrointestinal bleeding should be monitored closely for signs of bleeding.

The Dose of PARX should be reduced in patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) or severe hepatic impairment (Child-Pugh class C). In patients with severe renal impairment, the dose of PARX should be reduced to 10 mg twice daily. In patients with severe hepatic impairment, the dose of PARX should be reduced to 10 mg once daily.

Increased plasma concentrations of PARX occur in patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) or severe hepatic impairment (Child-Pugh class C). Information for Patients: PARX is not recommended for patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) or severe hepatic impairment (Child-Pugh class C) because the risk of adverse effects may be increased. People with severe renal impairment should be monitored closely for signs of bleeding.

Thrombocytopenia: Severe thrombocytopenia (platelet count < 50,000/mm³) has been reported in patients receiving PARX. Patients with severe thrombocytopenia should be monitored closely for signs of bleeding.

Thrombophilia: Patients with thrombophilia should be monitored closely for signs of bleeding.

Hemorrhage: Patients taking PARX should be monitored closely for signs of bleeding.

Bone Marrow: Bone marrow suppression has been reported in patients taking PARX. Patients should be monitored closely for signs of bleeding.

Alcohol: PARX should be used with caution in patients taking alcohol.

Pregnancy: PARX should be used with caution in pregnant women.

Lactation: The safety and efficacy of PARX in breast-feeding women have not been established.

Pediatric Use: The safety and efficacy of PARX in children have not been established.

Adverse Effects: The most common adverse effects associated with the use of PARX are bleeding, ulcers, and dermatologic events. Patients should be monitored closely for signs of bleeding.

FAXIS* (paroxetine hydrochloride) Tablets and Oral Suspension

At study sites, when the EXPERT PATHWAY is essentially exhausted, precautionary clearance is generalized by alternative PARX pathways. Patients should be monitored closely for signs of bleeding.

Drug Metabolism: Cytochrome P450 2D6 (CYP2D6) is involved in the metabolism of PARX. In vitro studies have shown that CYP2D6 is responsible for the metabolism of PARX. In vivo studies have shown that CYP2D6 is responsible for the metabolism of PARX. Therefore, the use of CYP2D6 inhibitors should be avoided in patients taking PARX. The use of CYP2D6 substrates should be avoided in patients taking PARX. The use of CYP2D6 inhibitors and substrates should be avoided in patients taking PARX.

Drug-Drug Interactions: The use of CYP2D6 inhibitors and substrates should be avoided in patients taking PARX. The use of CYP2D6 inhibitors and substrates should be avoided in patients taking PARX. The use of CYP2D6 inhibitors and substrates should be avoided in patients taking PARX.

Right-sided Heart Failure: Because PARX is highly bound to plasma proteins, administration of PARX to a patient taking another drug that is highly bound protein may cause increased concentrations of the other drug, potentially leading to adverse effects. The use of PARX in patients with heart failure should be avoided.

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Table 4. Treatment- Emergent Adverse Experience Incidence in a Comparative Clinical Trial of the Treatment of Major Depression Disorder (continued)

<table>
<thead>
<tr>
<th>Body System/Preferred Term</th>
<th>Placebo</th>
<th>PAXIL</th>
<th>PAXIL vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in total adverse events</td>
<td>109</td>
<td>118</td>
<td>19%</td>
</tr>
<tr>
<td>Change in mild adverse events</td>
<td>60</td>
<td>65</td>
<td>8%</td>
</tr>
<tr>
<td>Change in moderate adverse events</td>
<td>49</td>
<td>55</td>
<td>12%</td>
</tr>
</tbody>
</table>

Table 5. Incidence of Adverse Events in Clinical Trials (continued)

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo</th>
<th>PAXIL</th>
<th>Placebo vs PAXIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>120</td>
<td>126</td>
<td>5%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>109</td>
<td>114</td>
<td>5%</td>
</tr>
</tbody>
</table>

Adaptation to Certain Adverse Events: One 4- to 6-week period, there was evidence of adaptation to some adverse events, most notably with cardiovascular effects. In 33% of patients, a decrease in blood pressure was noted. Overall, the incidence of adverse events decreased with increasing doses of PAXIL.

Patients with prior psychiatric history had a higher incidence of adverse events, but the incidence was similar between patients with and without a history of prior depression.

Laboratory findings: In the trials conducted in 1992 and 1993, laboratory values were within the normal range, and there were no significant changes in laboratory values that were attributed to PAXIL treatment.

Safety and Tolerability: The incidence of adverse events was similar between patients treated with placebo and those treated with PAXIL. The most common adverse events were somnolence, dizziness, and nausea. These events were generally mild to moderate in severity and were not associated with discontinuation of treatment.

Overall, PAXIL was well-tolerated and generally well-tolerated in the trials conducted in 1992 and 1993. The incidence of adverse events was similar between patients treated with placebo and those treated with PAXIL. The most common adverse events were somnolence, dizziness, and nausea. These events were generally mild to moderate in severity and were not associated with discontinuation of treatment.

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such maintenance (see CLINICAL PHARMACOLOGY—Clinical Risk; Newborns, patients should be periodically reassessed to determine the need for maintenance treatment.

Prolactin or other SSRI or SNRI in the third trimester have developed complications requiring hormonal adjustments, psychiatric support, and close supervision (see WARNINGS). When treating pregnant women with paroxetine during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider stopping paroxetine in the third trimester.

Disorders for Anxiety or Related Disorders, and Patients With Severe Renal or Hepatic Impairment: The recommended initial dose is 10 mg once daily for patients, female patients, and patients with severe renal or hepatic impairment. Maximum enhancement may be achieved in 1-2 weeks. Dosage should not exceed 40 mg/day.

Switching Patients in or from a Monotherapy Outpatient Habitual at least 14 days should elapse during discontinuation of an MAOI and initiation of therapy with PARL. Similarly, at least 14 days should elapse after stopping PARL before starting or switching patients on MAOIs.

Disorder of Treatment With PARL: Symptoms associated with discontinuation of PARL have been reported (see PRECAUTIONS). Patients should be monitored for these symptoms when discontinuing treatment, regardless of the indication for which PARL was being prescribed. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

- Fatigue, dizziness, headache, blurry vision, and drowsiness follow a decrease in the dose or upon discontinuation of treatment. When resuming the previously prescribed dose may be considered. Subsequently, the physician may continue increasing the dose at a more gradual rate.

MISCELLANEOUS:

NOW SUPPLIED

Tablet forms and oral solution as follows:

- 10 mg yellow, scored tablets scored on the front with PARL and on the back with 10.
- 20 mg blue, scored tablets scored on the front with PARL and on the back with 20.
- 40 mg blue, scored tablets scored on the front with PARL and on the back with 40.

- 10 mg white, scored tablets scored on the front with PARL and on the back with 10.
- 20 mg white, scored tablets scored on the front with PARL and on the back with 20.
- 40 mg white, scored tablets scored on the front with PARL and on the back with 40.

- Oral Suspension—Orange-flavored, 15 mg/mL, 15 mL. In 35 mL and 60 mL bottles.
- Oral Suspension—Orange-flavored, 15 mg/mL, 65 mL. In 35 mL and 60 mL bottles.

PARL is a registered trademark of GlaxoSmithKline.

Medication Guide

PARL (paroxetine hydrochloride) Tablets and Oral Suspension

About Using Antidepressants in Children and Teenagers

What is the most important information I should know if my child is being prescribed an antidepressant?

Parents or caregivers need to think about 4 important things when their child is prescribed an antidepressant:

1. There is a risk of suicidal thoughts or actions.
2. There is a risk of suicidal thoughts or actions.
3. You should watch for certain signs if your child is taking an antidepressant.
4. There is a risk of suicidal thoughts or actions.

1. There is a Risk of Suicidal Thoughts or Actions

Children and teenagers sometimes think about suicide, and many report trying to kill themselves.

- Antidepressants increase suicidal thoughts and actions in some children and teenagers. But suicidal thoughts and actions can also be caused by depression, a serious medical condition that can be treated with antidepressants. Learning about killing yourself or trying to kill yourself is called suicidality or being suicidal.

A large study combined the results of 14 different studies of children and teenagers with depression or other illnesses. In these studies, patients either took paroxetine (10 mg or 20 mg) or no paroxetine (placebo) for 12 weeks. The study compared patients with and without depression. The results showed that patients who took paroxetine had higher levels of suicidal thoughts or actions than those who took placebo. However, there was no evidence of any increase in suicidal thoughts or actions in patients with depression. The study also showed that patients who took paroxetine had higher levels of suicidal thoughts or actions than those who took placebo. However, there was no evidence of any increase in suicidal thoughts or actions in patients with depression.

For some children and teenagers, the increased risk of suicide may be especially high. These include patients with:

- Bipolar disorder (sometimes called manic-depressive illness)
- A family history of bipolar disorder
- A history of self-harm or suicide
- A history of sudden loss of appetite
- A history of frequent hospitalization

If any of these are present, make sure you talk to your healthcare provider before your child takes an antidepressant.

2. How to Try to Prevent Suicidal Thoughts or Actions

To try to prevent suicidal thoughts and actions in your child, you can:

- Encourage your child to make the most of his or her time at school, work, or elsewhere.
- Make your child aware of the importance of keeping any appointments or doing things that your child finds important.
- Make sure your child has someone to talk to who can help your child in times of need (such as friends, family members, or teachers).
- Help your child talk to his or her healthcare provider or other professionals about any problems that your child may be having.
- Help your child think about ways to cope with stressful situations (such as school, work, or social situations).
- Help your child think about ways to handle difficult situations (such as arguments, conflict, or other problems).
- Help your child find ways to feel better (such as talking to someone, writing, or doing something that your child enjoys).
- Help your child think about ways to handle emotions (such as anger, sadness, or other emotions).
- Help your child find ways to handle stress (such as exercise, meditation, or other activities).
- Help your child think about ways to handle loneliness (such as talking to someone, writing, or doing something that your child enjoys).
- Help your child think about ways to handle depression (such as talking to someone, writing, or doing something that your child enjoys).
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**PAXIL CR® (paroxetine hydrochloride) Controlled-Release Tablets**

**SUBSTITUTIBILITY IN CHILDREN AND ADOLESCENTS**

Antidepressants may increase the risk of suicidal thinking and behavior (suicidality) in short-term trials of children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Postmarketing monitoring suggests a risk of suicide in such patients. Prescribers, caregivers, and patients should be aware of the need for follow-up and monitoring and should report suicidal thoughts and behaviors to the prescribing healthcare professional immediately, regardless of whether they are considered to be life-threatening. All patients treated with antidepressants should be observed closely for clinical worsening and emergence of suicidality, especially at the start of therapy and at intervals thereafter. suicidality and an increased risk of self-harm have been observed in short-term trials of children and adolescents with MDD and other psychiatric disorders treated with antidepressants. Close monitoring of pediatric patients is particularly important. Prescribers should carefully consider the selection of treatment for a patient with a MANDELINE3-2.5, 2.5-methylene- deuteration (3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)-3H-deuterated (5H-3H)
Fenofibrate is often used in the treatment of hypertriglyceridemia, and a recent study has shown that it may also be effective in reducing the risk of cardiovascular disease. The study, published in the Journal of the American College of Cardiology, examined the effects of fenofibrate on cardiovascular outcomes in patients with hypertriglyceridemia and high blood pressure.

The study randomly assigned 1,000 patients with hypertriglyceridemia and high blood pressure to receive either fenofibrate or a placebo. The patients were followed for an average of 5 years. The results showed that fenofibrate significantly reduced the risk of cardiovascular events, including heart attacks, strokes, and other serious cardiovascular events, compared to the placebo group. The risk reduction was seen across all subgroups of patients, including those with diabetes and those with high blood pressure.

The benefits of fenofibrate were most pronounced in patients with very high triglycerides. In this subgroup, fenofibrate reduced the risk of cardiovascular events by 35% compared to the placebo group. The study also found that fenofibrate was well tolerated, with a similar incidence of side effects to the placebo group.

In conclusion, the study suggests that fenofibrate may be a useful addition to the treatment of hypertriglyceridemia and high blood pressure. The results support the use of fenofibrate in reducing the risk of cardiovascular events, especially in patients with very high triglycerides. However, further studies are needed to confirm these findings and to determine the optimal dosing and duration of treatment. 

References:

Figure 1: Flowchart of the study design. 

Figure 2: Kaplan-Meier curve showing the cumulative incidence of cardiovascular events in the fenofibrate and placebo groups. 

Figure 3: Forest plot comparing the effect of fenofibrate on cardiovascular events in different subgroups of patients.
AXXAL, CHP (paraxanthine hydrochloride) Controlled-Release Tablets

following the use of an SSRI and sumatriptan. If concomitant treatment with a tricyclic antidepressant and an SSRI is planned, the patient's ECG should be monitored for arrhythmia, particularly during the initiation of treatment and for a total of 2 weeks. If a patient experiences any symptoms of cardiac arrhythmia, such as palpitations, dizziness, or syncope, the SSRI should be discontinued immediately.

Concomitant therapy with beta blockers and antihypertensive agents is not recommended as it may result in severe hypotension, bradycardia, and death. Concurrent use of MAO inhibitors and certain over-the-counter cold remedies or herbal supplements is contraindicated due to the risk of serotonin syndrome.

Patients with a history of seizures or a family history of seizures should be monitored closely for any signs of increased seizure activity. Patients with a history ofQT prolongation or a family history of QT prolongation should be monitored closely for any signs of QT prolongation during treatment.

The use of paroxetine in patients with a history of or a risk of developing glaucoma should be avoided as it may lead to increased intraocular pressure.

In general, paroxetine should not be used in patients with a history of or a risk of developing liver disease, as it may lead to increased liver enzyme levels and potentially severe liver injury.

Contraindications:

1. Known hypersensitivity to paroxetine or any of its components
2. Active suicidal ideation or behavior as a contraindication
3. Hypersensitivity reactions such as angioedema, anaphylaxis, or Stevens-Johnson syndrome
4. Severe hepatic impairment
5. May reduce the anticoagulant effect of warfarin
6. Prolonged QT interval or other QT prolongation
7. Congestive heart failure

Warnings:

1. Risk of suicidality: Close monitoring of patients, particularly adolescents and young adults, is recommended for signs of worsening depression, suicidality, or unusual changes in behavior.
2. Risk of sexual dysfunction: Patients may experience decreased libido, decreased orgasmic function, and decreased sexual desire.
3. Risk of QT prolongation and torsades de pointes: Paroxetine may cause QT prolongation, especially in patients with congestive heart failure or bradycardia, and may increase the risk of torsades de pointes.
4. Risk of hepatic impairment: Patients with hepatic impairment may require dose adjustments or monitoring for adverse events.

Precautions:

1. Paroxetine should be used cautiously in patients with a history of or a risk of developing gastrointestinal disorders.
2. Paroxetine should be used with caution in patients with a history of or a risk of developing cardiovascular disease.
3. Paroxetine should be used with caution in patients with a history of or a risk of developing renal impairment.
4. Paroxetine should be used with caution in patients with a history of or a risk of developing pulmonary hypertension.

Adverse Reactions:

1. Nausea, vomiting, constipation, dry mouth, headache, and dizziness
2. Anxiety, irritability, agitation, and insomnia
3. Nervousness, tremor, and weight gain
4. Sexual dysfunction
5. Bradycardia, QT prolongation, and torsades de pointes

Drug Interactions:

1. Paroxetine should be used with caution in combination with other medications that may cause QT prolongation or torsades de pointes.
2. Paroxetine should be used with caution in combination with other medications that may cause hepatic impairment.
3. Paroxetine should be used with caution in combination with other medications that may cause gastrointestinal symptoms.

Dosage and Administration:

1. The recommended dosage for adults is 20 mg once daily, with or without meals.
2. The dosage may be increased to 40 mg once daily after 1 week, if the patient tolerates the initial dosage.

Concomitant Medications:

1. Paroxetine should be used with caution in combination with other medications that may cause QT prolongation or torsades de pointes.
2. Paroxetine should be used with caution in combination with other medications that may cause hepatic impairment.
3. Paroxetine should be used with caution in combination with other medications that may cause gastrointestinal symptoms.

Geriatric Use:

1. Paroxetine should be used with caution in elderly patients, as they may be more sensitive to the effects of paroxetine.
2. The dosage should be reduced in elderly patients or in patients with impaired renal function.

Pediatric Use:

1. Paroxetine should be used with caution in pediatric patients, as they may be more sensitive to the effects of paroxetine.
2. The dosage should be reduced in pediatric patients or in patients with impaired renal function.

Pregnancy:

1. Paroxetine should be used with caution in pregnant women, as animal studies have shown that paroxetine may cause harm to the fetus.
2. Women who are planning to become pregnant should inform their healthcare provider before starting paroxetine.

Lactation:

1. Paroxetine should be used with caution in breastfeeding women, as it is not known if paroxetine is excreted in breast milk.

Emergence of depression symptoms: Paroxetine treatment should be initiated in a setting where close monitoring is possible, such as a hospital or other inpatient setting.

In the event of an adverse reaction, patients should be instructed to discontinue the medication and seek medical attention. Patients should be advised to contact their healthcare provider if they experience any serious adverse reactions, such as suicidal ideation or behavior, worsening depression, or any symptoms of hepatic impairment.

Additional Information:

1. Paroxetine should be taken at the same time each day to maintain consistent levels in the bloodstream.
2. Paroxetine should be swallowed whole and should not be crushed, chewed, or divided.
3. Paroxetine may cause drowsiness, so patients should avoid driving or engaging in other activities that require alertness.

References:

<table>
<thead>
<tr>
<th>Body System/Adverse Event</th>
<th>PAXIL CR</th>
<th>Placebo</th>
<th>% Reporting Event</th>
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<tr>
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<td>10%</td>
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<tr>
<td>Anorexia</td>
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<tr>
<td>Back Pain</td>
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<tr>
<td>Pruritus</td>
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<tr>
<td><strong>Alavage Reaction</strong></td>
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<tr>
<td><strong>Cardiovascular System</strong></td>
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<tr>
<td>Tachycardia</td>
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<tr>
<td>Vasodilation</td>
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<tr>
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<tr>
<td>Vomits</td>
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<tr>
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1. Adverse events for which the PAXIL CR reporting incidence was less than or equal to the placebo incidence are not included. These events are: Abnormal dreams, anxiety, arthralgia, ataxia, peripheral edema, abnormal vision, peripheral edema, pruritus, rash, respiratory disorder, urticaria, urinary frequency, and weight gain. 2. 2% means greater than zero and less than 1%. 3. Mostly MILD. 4. 4. A wide variety of injuries with no obvious pattern. 5. Pain in a variable location with no obvious pattern. 6. Most frequent somnolence. 7. Idiosyncratic. 8. Mostly Mild. 9. Based on the number of males and females. 10. Mostly anergic or delayed ejaculation. 11. Mostly anergic or delayed orgasm.

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</tbody>
</table>

1. 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, anxiety, arthralgia, peripheral edema, abnormal vision, peripheral edema, pruritus, rash, respiratory disorder, urticaria, urinary frequency, and weight gain. 2. <1% means greater than zero and less than 1%. 3. Mostly MILD. 4. Mostly mild. 5. Mostly severe. 6. Mostly blurred vision. 7. Based on the number of males and females. 8. Mostly anergic or delayed ejaculation. 9. Based on the number of males and females. 10. Mostly anergic or delayed ejaculation.
Table 5. Treatment-Emergent Adverse Events Occurring in 31% or More of Patients Treated With PAXIL CR or in a Pool of 3 Prenatal Depressive Disorder Studies With Continuous Easing or in 1 Prenatal Depressive Disorder Study With Low-Dose Placebo Control1

<table>
<thead>
<tr>
<th>Body System/Adverse Event</th>
<th>Continuous Placebo (PAXIL CR)</th>
<th>Low-Dose Placebo (PAXIL CR)</th>
<th>% Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td>17%</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Headache</td>
<td>15%</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4%</td>
<td>8%</td>
<td>1%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Digestive System</td>
<td>17%</td>
<td>12%</td>
<td>2%</td>
</tr>
<tr>
<td>Bladder</td>
<td>12%</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>Urogenital System</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Metabolic and Nutritional Disorders</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Anemia</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Respiratory System</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Skin</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Allergic Reactions</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Abnormal Vision</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Genitourinary System</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervousness</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Absence of Depression</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Treatment Efficacy</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Placebo</td>
<td>12%</td>
<td>10%</td>
<td>1%</td>
</tr>
</tbody>
</table>

1. Adverse events for which the rate of PAXIL CR was less than or equal to placebo rate and not included in the events for which the rate of PAXIL CR was greater than or equal to placebo rate. The events for which PAXIL CR was greater than or equal to placebo rate included the following: Abdominal pain, back pain, fatigue, dry mouth, weight gain, myalgia, peripheral edema, sinusitis, rhinitis, tooth pain, upper respiratory tract infections, pharyngitis, cough, nasopharyngitis, otitis media, urinary tract infections, headache, fatigue, insomnia, depression, anxiety, nausea, vomiting, diarrhoea, constipation, bronchitis, and sinusitis. The percentage of patients reporting gastrointestinal symptoms in the pooled placebo-controlled trials is less than 1%.

Efficacy and Safety Analysis: The percentage of patients experiencing gastrointestinal symptoms in the pooled placebo-controlled trials is less than 1%.

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