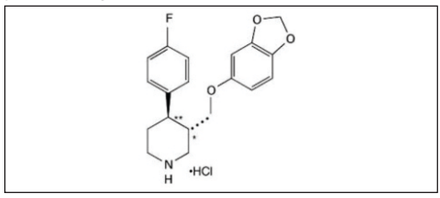
Pariz
Tablets

پیرز ٹیبلٹس

COMPOSITION:
Each Extended Release Tablet contains: Paroxetine (as Hcl)……..…….....12.5 & 25 mg.

Suicidality and Antidepressant Drugs
Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in children, adolescents and young adults. Anyone considering the use of PARIZ or any other antidepressant in a child, adolescent or young adult must balance this risk with the clinical need.Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PARIZ is not approved for use in pediatric patients.

DESCRIPTION:
PARIZ (paroxetine hydrochloride) is an orally administered psychotropic drug with a chemical structure unrelated to other selective serotonin reuptake inhibitors or to tricyclic, tetracyclic, or other available antidepressant or antipanic agents. It is the hydrochloride salt of a phenylpiperidine compound identified chemically as (-)-trans-4R-(4'-fluorophenyl)-3S-[(3',4' methylenedioxyphenoxy) methyl] piperidine hydrochloride hemihydrate and has the empirical formula of C19H20FNO3HCl1/2H2O. The structural formula of paroxetine hydrochloride is:



CLINICAL PHARMACOLOGY:
Pharmacodynamics: The efficacy of paroxetine in the treatment of major depressive disorder, panic disorder, social anxiety disorder, and premenstrual dysphoric disorder (PMDD) is presumed to be linked to potentiation of serotonergic activity in the central nervous system resulting from inhibition of neuronal reuptake of serotonin (5-hydroxy-tryptamine, 5-HT). Paroxetine blocks the uptake of serotonin into human platelets. Paroxetine is a potent and highly selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake.
Pharmacokinetics: Paroxetine hydrochloride is completely absorbed after oral dosing of a solution of the hydrochloride salt. The elimination half-life is approximately 15 to 20 hours after a single dose of PARIZ. Paroxetine is extensively metabolized and the metabolites are considered to be inactive. Nonlinearity in pharmacokinetics is observed with increasing doses. Paroxetine metabolism is mediated in part by CYP2D6, and the metabolites are primarily excreted in the urine and to some extent in the feces. Pharmacokinetic behavior of paroxetine has not been evaluated in patients who are deficient in CYP2D6 (poor metabolizers).
Absorption and Distribution: Tablets of PARIZ contain a degradable polymeric matrix designed to control the dissolution rate of paroxetine over a period of approximately 4 to 5 hours. The bioavailability of 25 mg PARIZ is not affected by food. Paroxetine distributes throughout the body, including the CNS, with only 1% remaining in the plasma.
Metabolism and Excretion: The mean elimination half-life of paroxetine was 15 to 20 hours throughout a range of single doses of PARIZ (12.5 mg, 25 mg).
Paroxetine is extensively metabolized after oral administration. The principal metabolites are polar and conjugated products of oxidation and methylation, which are readily cleared.
The metabolism of paroxetine is accomplished in part by CYP2D6. Saturation of this enzyme at clinical doses appears to account for the nonlinearity of paroxetine kinetics with increasing dose and increasing duration of treatment. The role of this enzyme in paroxetine metabolism also suggests potential drug-drug interactions.

INDICATIONS AND USAGE:
Major Depressive Disorder: PARIZ is indicated for the treatment of major depressive disorder.
Panic Disorder: PARIZ is indicated for the treatment of panic disorder, with or without agoraphobia.Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behavior related to the attacks.
Social Anxiety Disorder: PARIZ is indicated for the treatment of social anxiety disorder, also known as social phobia. Social anxiety disorder is characterized by a marked and persistent fear of 1 or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack.
Premenstrual Dysphoric Disorder: PARIZ is indicated for the treatment of PMDD. The essential features of PMDD, include markedly depressed mood, anxiety or tension, affective lability and persistent anger or irritability. Other features include decreased interest in usual activities, difficulty concentrating, lack of energy, change in appetite or sleep and feeling out of control.

CONTRAINDICATIONS:
The use of MAOIs intended to treat psychiatric disorders with PARIZ or within 14 days of stopping treatment with PARIZ is contraindicated because of an increased risk of serotonin syndrome. The use of PARIZ within 14 days of stopping MAOI intended to treat psychiatric disorders is also contraindicated.
Starting PARIZ in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome.
Concomitant use with thioridazine is contraindicated.
Concomitant use in patients taking pimozide is contraindicated.
PARIZ is contraindicated in patients with a hypersensitivity to paroxetine or to any of the inactive ingredients in PARIZ.

ADVERSE REACTIONS:
Body as a Whole: Infrequent are chills, face edema, fever, flu syndrome, malaise; rare are abscess, anaphylactoid reaction, anticholinergic syndrome, hypothermia; also observed are adrenergic syndrome, neck rigidity, sepsis.
Cardiovascular System: Infrequent are angina pectoris, bradycardia, hematoma, hypertension, hypotension, palpitation, postural hypotension, supraventricular tachycardia and syncope.
Digestive System: Infrequent are bruxism, dysphagia, eructation, gastritis, gastroenteritis, gastroesophageal reflux, gingivitis, hemorrhoids, liver function test abnormal, melena, pancreatitis, rectal hemorrhage, toothache, ulcerative stomatitis; rare are colitis, glossitis and gum hyperplasia.
Endocrine System: Infrequent are ovarian cyst, testes pain; rare were diabetes mellitus, hyperthyroidism.
Hemic and Lymphatic System: Infrequent are anemia, eosinophilia, hypochromic anemia, leukocytosis, leukopenia, lymphadenopathy, purpura; rare are thrombocytopenia.
Metabolic and Nutritional Disorders: Infrequent are generalized edema, hyperglycemia, hypokalemia, peripheral edema, thirst; rare are bilirubinemia, dehydration, hyperkalemia, obesity.
Musculoskeletal System: Infrequent are arthritis, bursitis, tendonitis; rare are myasthenia, myopathy, myositis; also observed are generalized spasm, osteoporosis.
Nervous System: Frequent are depression; infrequent are amnesia, convulsion, depersonalization, dystonia, emotional lability, hallucinations, hyperkinesia, hypesthesia.
Respiratory System: Frequent are pharyngitis; infrequent are asthma, dyspnea, epistaxis, laryngitis, pneumonia; rare are stridor.
Skin and Appendages: Frequent are rash; infrequent are acne, alopecia, dry skin, eczema, pruritus, urticaria; rare are exfoliative dermatitis.
Special Senses: Infrequent are conjunctivitis, earache, keratoconjunctivitis, mydriasis, photophobia, retinal hemorrhage, tinnitus; rare are blepharitis, visual field defect.
Urogenital System: Frequent are dysmenorrhea; infrequent are albuminuria, amenorrhea, breast pain, cystitis, dysuria, prostatitis, urinary retention; rare are breast enlargement,breast neoplasm, female lactation.

Drug Interactions:
Tryptophan: Concomitant use of PARIZ with tryptophan is not recommended.
Pimozide:Due to the narrow therapeutic index of pimozide and its known ability to prolong the QT interval, concomitant use of pimozide and PARIZ is contraindicated.
Thioridazine: Thioridazine administration alone produces prolongation of the QTc interval, which is associated with serious ventricular arrhythmias, such as torsade de pointes–type arrhythmias, and sudden death. This effect appears to be dose related.
Warfarin: There may be pharmacodynamic interaction between paroxetine and warfarin (that causes an increased bleeding diathesis in the face of unaltered prothrombin time) the concomitant administration of PARIZ and warfarin should be undertaken with caution.
Triptans: concomitant use of PARIZ with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.
Drugs Affecting Hepatic Metabolism: The metabolism and pharmacokinetics of paroxetine may be affected by the induction or inhibition of drug-metabolizing enzymes.
Tricyclic Antidepressants (TCAs): Caution is indicated in the co-administration of TCAs with PARIZ, because paroxetine may inhibit TCA metabolism. Plasma TCA concentrations may need to be monitored and the dose of TCA may need to be reduced, if a TCA is coadministered with PARIZ.
Drugs Highly Bound to Plasma Protein: Because paroxetine is highly bound to plasma protein, administration of PARIZ to a patient taking another drug

that is highly protein bound may cause increased free concentrations of the other drug, potentially resulting in adverse events.

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

WARNINGS AND PRECAUTIONS:

Clinical Worsening and Suicide Risk: Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment.

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior and the other symptoms described above, as well as the emergence of suicidality and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers.

Bipolar Disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression. It should be noted that PARIZ is not approved for use in treating bipolar depression.

Serotonin Syndrome: The development of a potentially life-threatening serotonin syndrome is linked with SNRIs and SSRIs, including PARIZ, alone but particularly 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 (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue). 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). Patients should be monitored for the emergence of serotonin syndrome.

The concomitant use of PARIZ with MAOIs intended to treat psychiatric disorders is contraindicated.

If concomitant use of PARIZ with certain other serotonergic drugs, i.e., triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, buspirone, tryptophan, amphetamines and St. John's Wort is clinically warranted, be aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases. Treatment with PARIZ and any concomitant serotonergic agents should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.

Angle-Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressant drugs including PARIZ may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

Akathisia: The use of paroxetine or other SSRIs has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment.

Hyponatremia: Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PARIZ. Discontinuation of PARIZ should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

Abnormal Bleeding: SSRIs and SNRIs, including paroxetine, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin and other anticoagulants may add to this risk.

Bone Fracture: The possibility of a fracture should be considered in patients treated with paroxetine.

Alcohol: Patients should be advised to avoid alcohol while taking PARIZ.

SPECIAL POPULATIONS:

Pediatric Use: Safety and effectiveness in the pediatric population have not been established.

Geriatric Use: SSRIs and SNRIs, including PARIZ, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event.

Pregnancy: Infants exposed to paroxetine in the first trimester of pregnancy have an increased risk of congenital malformations, particularly cardiovascular malformations. Pregnancy Category D.

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

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

DOSAGE AND ADMINISTRATION:

Major Depressive Disorder: PARIZ should be administered as a single daily dose, usually in the morning, with or without food. The recommended initial dose is 25 mg/day. Some patients not responding to a 25-mg dose may benefit from dose increases, in 12.5-mg/day increments, up to a maximum of 62.5 mg/day. Dose changes should occur at intervals of at least 1 week.

Panic Disorder: PARIZ should be administered as a single daily dose, usually in the morning. Patients should be started on 12.5 mg/day. Dose changes should occur in 12.5-mg/day increments and at intervals of at least 1 week. The maximum dosage should not exceed 75 mg/day.

Social Anxiety Disorder: PARIZ should be administered as a single daily dose, usually in the morning, with or without food. The recommended initial dose is 12.5 mg/day. If the dose is increased, this should occur at intervals of at least 1 week, in increments of 12.5 mg/day, up to a maximum of 37.5 mg/day.

Premenstrual Dysphoric Disorder: PARIZ should be administered as a single daily dose, usually in the morning, with or without food. PARIZ may be administered either daily throughout the menstrual cycle or limited to the luteal phase of the menstrual cycle, depending on physician assessment. The recommended initial dose is 12.5 mg/day.

Dose changes should occur at intervals of at least 1 week.

Dosage for Elderly or Debilitated Patients, and Patients With Severe Renal or Hepatic Impairment: The recommended initial dose of PARIZ is 12.5 mg/day for elderly patients, debilitated patients, and/or patients with severe renal or hepatic impairment. Increases may be made if indicated. Dosage should not exceed 50 mg/day.

Overdose: Commonly adverse events associated with paroxetine overdosage include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. Other notable signs and symptoms observed with overdoses involving paroxetine (alone or with other substances) include mydriasis, convulsions (including status epilepticus), ventricular dysrhythmias (including torsade de pointes), hypertension, aggressive reactions, syncope, hypotension.

No specific antidotes for paroxetine are known. Treatment should consist of those general measures employed in the management of overdosage with any drugs effective in the treatment of major depressive disorder. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, or exchange perfusion are unlikely to be of benefit.

STORAGE/PRECAUTIONS: Store in a cool, dry and dark place between 15-30 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners.

PRESENTATION: PARIZ Tablets 12.5 mg and 25 mg are available in packing containing 10 extended release tablets.

خوراک: ڈاکٹر کی ہدایت کے مطابق۔

احتیاط: روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ مستند ڈاکٹر کے نسخہ پر فروخت اور استعمال کریں۔

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