Pronitron CR Tablets

(Paroxetine Extended-Release Tablets USP) *

پرونیٹرون سی آر گولیاں

(پیراوکسٹین)

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS: 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. **Pronitron CR Tablets** is not approved for use in pediatric patients.

COMPOSITION:
Each controlled release tablet contains:
Paroxetine HCl USP eq. to Paroxetine ... 12.5mg & 25mg. [USP Specs.]

DESCRIPTION: Pronitron CR Tablets (Paroxetine HCl) is an orally administered psychotropic drug with a chemical structure unrelated to other selective serotonin reuptake inhibitors (SSRIs) or to tricyclic, tetracyclic, or other available antidepressant or antipanic agents.

PHARMACOKINETICS:
Mechanism of action: The mechanism of action of paroxetine in the treatment of major depressive disorder (MDD), panic disorder (PD), social anxiety disorder (SAD), and premenstrual dysphoric disorder (PMDD) is unknown, but is presumed to be linked to potentiation of serotonergic activity in the central nervous system resulting from inhibition of neuronal reuptake of serotonin (5-HT).
Pharmacodynamics: Paroxetine HCl blocks the uptake of serotonin into human platelets. In vitro studies in animals also suggest that paroxetine is a potent and highly selective inhibitor of neuronal serotonin reuptake (SSRI) and has only very weak effects on norepinephrine and dopamine neuronal reuptake.
Pharmacokinetics: Absorption: Paroxetine extended-release tablets are completely absorbed after oral dosing of a solution of the hydrochloride salt. The bioavailability of 25 mg **Pronitron CR Tablets** is not affected by food.
Distribution: Paroxetine distributes throughout the body, including the CNS, with only 1% remaining in the plasma. Approximately 95% and 93% of paroxetine is bound to plasma protein at 100ng/ml and 400ng/ml, respectively. Paroxetine does not alter the in vitro protein binding of phenytoin or warfarin.
Elimination: Metabolism: The mean elimination half-life of paroxetine was 15 to 20 hours throughout a range of single doses of **Pronitron CR Tablets** (12.5mg, 25mg, 37.5mg, and 50mg). During repeated administration of **Pronitron CR Tablets** (25mg once daily), steady state was reached within 2 weeks (i.e., comparable to immediate-release formulations).

INDICATIONS AND USAGE: Pronitron CR Tablets is a selective serotonin reuptake inhibitor (SSRI) indicated in adults for the treatment of: Major Depressive Disorder (MDD), Panic Disorder (PD), Social Anxiety Disorder (SAD) and Premenstrual Dysphoric Disorder (PMDD)

CONTRA-INDICATIONS: Pronitron CR Tablets 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. **Pronitron CR Tablets** is contraindicated in patients taking thioridazine and pimozide. **Pronitron CR Tablets** is contraindicated in patients with hypersensitivity to paroxetine or to any of the inactive ingredients in **Pronitron CR Tablets.**

DOSAGE AND ADMINISTRATION: Administer **Pronitron CR Tablets** as a single daily dose in the morning, with or without food. Swallow tablets whole and do not chew or crush.
Dosage in Patients with Major Depressive Disorder (MDD): The recommended initial dose is 25mg and maximum dose is 62.5mg. In patients with an inadequate response, dosage may be increased in increments of 12.5mg per day at intervals of at least 1 week, depending on tolerability.
Dosage in Patients with Panic Disorder (PD): The recommended initial dose is 12.5mg and maximum dose is 75mg. In patients with an inadequate response, dosage may be increased in increments of 12.5mg per day at intervals of at least 1 week, depending on tolerability.
Dosage in Patients with Social Anxiety Disorder (SAD): The recommended initial dose is 12.5mg and maximum dose is 37.5mg. In patients with an inadequate response, dosage may be increased in increments of 12.5 mg per day at intervals of at least 1 week, depending on tolerability.
Dosage in Patients with Premenstrual Dysphoric Disorder (PMDD): The recommended starting dosage in women with PMDD is 12.5mg per day. **Pronitron CR Tablets** may be administered either continuously or intermittently. Intermittent dosing is repeated with each new cycle. In patients with an inadequate response, the dosage may be increased to the maximum recommended dosage of 25mg per day, depending on tolerability. Institute dosage adjustments at intervals of at least 1 week.
Dosage Modifications for Elderly Patients, Patients with Severe Renal Impairment and Patients with Severe Hepatic Impairment: Dosage should not exceed 50mg per day for MDD or PD and should not exceed 37.5mg per day for SAD.

OVERDOSAGE: The largest known ingestion involved 2000mg of Paroxetine HCl (33 times the maximum recommended daily dose) in a patient who recovered. Commonly reported adverse events associated with Paroxetine HCl overdosage include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. Other notable signs and symptoms observed with overdoses involving Paroxetine HCl (alone or with other substances) include mydriasis, convulsions (including status epilepticus), ventricular dysrhythmias (including torsade de pointes), hypertension, aggressive reactions, syncope, hypotension, stupor, bradycardia, dystonia, rhabdomyolysis, symptoms of hepatic dysfunction (including hepatic failure, hepatic necrosis, jaundice, hepatitis, and hepatic steatosis), serotonin syndrome, manic reactions, myoclonus, acute renal failure, and urinary retention.

**According to USP-42, Extended release tablets is a pharmacopoeia term used interchangeably for Controlled release tablets.*

Rev: 01-21/1 (706039)

DRUG INTERACTIONS: Pronitron CR Tablets is contraindicated in patients taking MAOIs, including MAOIs such as linezolid or intravenous methylene blue. It is contraindicated in patients taking pimozide or thioridazine. The concomitant use of serotonergic drugs with **Pronitron CR Tablets** increases the risk of serotonin syndrome. The concurrent use of an antiplatelet agent or anticoagulant with **Pronitron CR Tablets** may potentiate the risk of bleeding.The concomitant use of **Pronitron CR Tablets** with another drug that is highly bound to plasma protein may increase free concentrations of **Pronitron CR Tablets** or other tightly-bound drugs in plasma. Concomitant use of tamoxifen with **Pronitron CR Tablets** may lead to reduced plasma concentrations of the active metabolite (endoxifen) and reduced efficacy of tamoxifen. Co-administration of fosamprenavir/ritonavir with paroxetine significantly decreased plasma levels of paroxetine.

WARNINGS: Suicidal Thoughts and Behaviors in Adolescents and Young Adults: 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.
Serotonin Syndrome: Serotonin-norepinephrine reuptake inhibitors (SNRIs) and SSRIs, including **Pronitron CR Tablets**, can precipitate serotonin syndrome, a potentially life-threatening condition.
Drug Interactions Leading to QT Prolongation: The CYP2D6 inhibitory properties of paroxetine can elevate plasma levels of thioridazine and pimozide. Therefore, it is contraindicated in combination with thioridazine and pimozide.
Embryofetal and Neonatal Toxicity: Pronitron CR Tablets can cause fetal harm when administered to a pregnant woman.
Increased Risk of Bleeding: Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs. (NSAIDS), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk.
Activation of Mania or Hypomania: In patients with bipolar disorder, treating a depressive episode with **Pronitron CR Tablets** or another antidepressant may precipitate a mixed/manic episode.
Seizures: Pronitron CR Tablets should be prescribed with caution in patients with a seizure disorder.
Angle-Closure Glaucoma: Avoid use of antidepressants, including **Pronitron CR Tablets**, in patients with untreated anatomically narrow angles.
Hyponatremia: In patients with symptomatic hyponatremia, discontinue **Pronitron CR Tablets** and institute appropriate medical intervention.
Reduction of Efficacy of Tamoxifen: When tamoxifen is used for the treatment or prevention of breast cancer, prescribers should consider using an alternative antidepressant.
Bone Fracture: Bone fracture risk during exposure to some antidepressants, including SSRIs, have reported an association between antidepressant treatment and fractures.

PRECAUTIONS: Paroxetine HCl Tablet should be used cautiously in patients with a history of mania and seizures. It should be discontinued in any patient who develops seizures. Discontinuation of Paroxetine HCl Tablet (particularly when abrupt), include the following: Dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations and tinnitus), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. It is uncertain whether the coadministration of Paroxetine and tamoxifen has a significant adverse effect on the efficacy of tamoxifen. The use of Paroxetine or other SSRIs has been associated with the development of akathisia. This is most likely to occur within the first few weeks of treatment. Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Paroxetine HCl Tablet. SSRIs and SNRIs, including Paroxetine, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, and other anticoagulants may add to this risk.

Nursing Mothers: Like many other drugs, Paroxetine is secreted in human milk, and caution should be exercised when Paroxetine HCl Tablet is administered to a nursing woman.
Pediatric Use: Safety and effectiveness in the pediatric population have not been established.

ADVERSE REACTIONS: The following reactions have been identified during post approval use of Paroxetine HCL. 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, priapism, syndrome of inappropriate ADH secretion (SIADH), prolactinemia and galactorrhea; extrapyramidal symptoms which have included akathisia, bradykinesia, cogwheel rigidity, dystonia, hypertonia, trismus; 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), and vasculitic syndromes (such as Henoch-Schönlein purpura).

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Pronitron CR Tablets (Paroxetine HCl) is supplied as controlled-release tablet in pack sizes of 10's and 30's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

PHARMA
Manufactured by:
NABIQASIM INDUSTRIES (PVT) LTD.
17/24, Korangi Industrial Area, Karachi-Pakistan.

Rev: 01-21/1 (706039)