Pronitron Tablets

(Paroxetine HCl Tablet USP)

پرونیٹرون گولیاں

(پیراوکسٹین ہائیڈروکلورائیڈ)

COMPOSITION: Each film coated tablet contains:
Paroxetine HCl USP eq. to Paroxetine … 20mg. [USP Specs.]

INDICATIONS: Treatment of - Major depressive episode, Obsessive Compulsive Disorder (OCD), Panic disorder with and without agoraphobia, Social anxiety disorders/social phobia, Generalised anxiety disorder, Post-traumatic stress disorder.

CONTRA-INDICATIONS: Hypersensitivity to the paroxetine or to any of the excipients.

PHARMACOLOGY: MECHANISM OF ACTION: Paroxetine is a potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake and its antidepressant action and effectiveness in the treatment of OCD, Social anxiety disorders/social phobia, Generalised anxiety disorder, Post-traumatic stress disorder and Panic disorder is thought to be related to its specific inhibition of 5-HT uptake in brain neurones.

PHARMACOKINETIC: Absorption: Paroxetine is well absorbed after oral dosing and undergoes first-pass metabolism. Due to first-pass metabolism, the amount of Paroxetine available to the systemic circulation is less than that absorbed from the gastrointestinal tract. Partial saturation of the first-pass effect and reduced plasma clearance occur as the body burden increases with higher single doses or on multiple dosing. This results in disproportionate increases in plasma concentrations of Paroxetine and hence pharmacokinetic parameters are not constant, resulting in non-linear kinetics. However, the non-linearity is generally small and is confined to those subjects who achieve low plasma levels at low doses.
Distribution: Paroxetine is extensively distributed into tissues and pharmacokinetic calculations indicate that only 1% of the Paroxetine in the body resides in the plasma. Approximately 95% of the Paroxetine present is protein bound at therapeutic concentrations. No correlation has been found between Paroxetine plasma concentrations and clinical effect (adverse experiences and efficacy).
Biotransformation: The principal metabolites of Paroxetine are polar and conjugated products of oxidation and methylation which are readily cleared. In view of their relative lack of pharmacological activity, it is most unlikely that they contribute to Paroxetine's therapeutic effects. Metabolism does not compromise Paroxetine's selective action on neuronal 5-HT uptake.
Elimination: Urinary excretion of unchanged Paroxetine is generally less than 2% of dose whilst that of metabolites is about 64% of dose. About 36% of the dose is excreted in faeces, probably via the bile, of which unchanged Paroxetine represents less than 1% of the dose. Thus Paroxetine is eliminated almost entirely by metabolism. Metabolite excretion is biphasic, being initially a result of first-pass metabolism and subsequently controlled by systemic elimination of Paroxetine.
The elimination half-life is variable but is generally about 1 day.

DOSAGE AND ADMINISTRATION: Major depressive episodes: The recommended dose is 20mg daily. Improvement but may only become evident from the second week of therapy. In some patients, with insufficient response to 20mg, the dose may be increased gradually up to a maximum of 50mg a day in 10mg steps according to the patient's response. Patients with depression should be treated for a sufficient period of at least 6 months to ensure that they are free from symptoms.
Obsessive Compulsive Disorder (OCD): The recommended dose is 40mg daily. Patients should start on 20mg/day and the dose may be increased gradually in 10mg increments to the recommended dose. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60mg/day. Patients with OCD should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer.
Panic disorder: The recommended dose is 40mg daily. Patients should be started on 10mg/day and the dose gradually increased in 10mg steps according to the patient's response up to the recommended dose. A low initial starting dose is recommended to minimise the potential worsening of panic symptomatology, which is generally recognized to occur early in the treatment of this disorder. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60mg/day. Patients with panic disorder should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer.
Social anxiety disorders/social phobia: The recommended dose is 20mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10mg steps up to a maximum of 50mg/day. Long-term use should be regularly evaluated.
Generalised anxiety disorder: The recommended dose is 20mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10mg steps up to a maximum of 50mg/day. Long-term use should be regularly evaluated.
Post-traumatic stress disorder: The recommended dose is 20mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10mg steps up to a maximum of 50mg/day. Long-term use should be regularly evaluated.
Withdrawal symptoms seen on discontinuation of Paroxetine: Abrupt discontinuation should be avoided. The taper phase regimen used in clinical trials involved decreasing the daily dose by 10mg at weekly intervals. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.
Special populations: Use in elderly: Increased plasma concentrations of Paroxetine occur in elderly subjects. Dosing should commence at the adult starting dose. Increasing the dose might be useful in some patients, but the maximum dose should not exceed 40mg daily.
Paediatric population:
Children and adolescents (7-17 years): Paroxetine should not be used for the treatment of children and adolescents as trials efficacy has not been adequately demonstrated.
Children aged below 7 years: The use of Paroxetine has not been studied in children less than 7 years. Paroxetine should not be used, as long as safety and efficacy in this age group have not been established.
Patients with renal/hepatic impairment: Increased plasma concentrations of Paroxetine occur in patients with severe renal impairment (creatinine clearance less than 30ml/min) or in those with hepatic impairment. Therefore, dosage should be restricted to the lower end of the dosage range.

OVERDOSAGE: A wide margin of safety is evident from available overdose information on Paroxetine. Experience of Paroxetine in overdose has indicated that, in addition to those symptoms mentioned adverse reaction, vomiting, dilated pupils, fever, blood pressure changes, headache, involuntary muscle contractions, agitation, anxiety and tachycardia have been reported. Patients have generally recovered without serious sequalae even when doses of up to 2000mg have been taken alone.
No specific antidote is known. Treatment should be similar to management of overdose with any antidepressant. Supportive care with frequent monitoring of vital signs and careful observation is indicated. Administration of 20-30g activated charcoal may be considered.

WARNINGS & PRECAUTIONS: Use in children and adolescents under 18 years of age: Paroxetine should not be used in the treatment of children and adolescents under the age of 18 years.
Monoamine oxidase inhibitors (MAOIs): Treatment with Paroxetine should be initiated cautiously two weeks after terminating treatment with an irreversible MAOI or 24 hours after terminating treatment with a reversible MAO inhibitor. Dosage of Paroxetine should be increased gradually until an optimal response is reached.

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Suicide/suicidal thoughts or clinical worsening: As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.
Akathisia/psychomotor restlessness: The use of Paroxetine has been associated with the development of akathisia. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.
Serotonin syndrome/Neuroleptic malignant syndrome: Paroxetine should not be used in combination with serotonin-precursors (such as L-tryptophan, oxitriptan) due to the risk of serotonergic syndrome.
Mania: As with all antidepressants, Paroxetine should be used with caution in patients with a history of mania. Paroxetine should be discontinued in any patient entering a manic phase.
Renal/hepatic impairment: Caution is recommended in patients with severe renal impairment or in those with hepatic impairment.
Diabetes: In patients with diabetes, treatment with an Selective Serotonin Reuptake Inhibitor (SSRI) may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.
Epilepsy: As with other antidepressants, Paroxetine should be used with caution in patients with epilepsy.
Seizures: Overall the incidence of seizures is less than 0.1% in patients treated with Paroxetine. The medicinal product should be discontinued in any patient who develops seizures.
Glaucoma: As with other SSRI's, Paroxetine can cause mydriasis and should be used with caution in patients with narrow angle glaucoma or history of glaucoma.
Cardiac conditions: The usual precautions should be observed in patients with cardiac conditions.
Hyponatraemia: Hyponatraemia has been reported rarely, predominantly in the elderly. Caution should also be exercised in those patients at risk of hyponatraemia e.g. from concomitant medications and cirrhosis. The hyponatraemia generally reverses on discontinuation of Paroxetine.
Haemorrhage: There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs. Other haemorrhagic manifestations e.g. gastrointestinal haemorrhage have been reported. Elderly patients may be at an increased risk.
DRUG INTERACTIONS: Drug interactions may occur with the use of following drugs so caution is advised while taking the following medications:
Serotonergic medicinal products: L-tryptophan, triptans, tramadol, linezolid, methylthioninium chloride (methylene blue), SSRIs, lithium, pethidine and St. John's Wort - Hypericumperforatum - preparations,
Pravastatin, Pimozide, Drug metabolizing enzymes: Dosage adjustments are required when taken concomitantly with these drugs (eg.carbamazepine, rifampicin, phenobarbital, phenytoin).
Fosamprenavir/ritonavir: Paroxetine had no significant effect on metabolism of fosamprenavir/ritonavir, however, co-administration of fosamprenavir/ritonavir 700/100 mg twice daily with paroxetine 20 mg daily in healthy volunteers for 10 days significantly decreased plasma levels of Paroxetine by approximately 55%. **Procyclidine:** If anti-cholinergic effects are seen, the dose of procyclidine should be reduced,
Anticonvulsants: Concomitant administration does not seem to show any effect on pharmacokinetic/dynamic profile in epileptic patients.
CYP2D6 inhibitory potency of paroxetine: e.g. clomipramine, nortriptyline and desipramine, perphenazine and thioridazine. risperidone, atomoxetine, certain Type 1c antiarrhythmics (e.g. propafenone and flecainide) and metoprolol should not be used concomitantly with Paroxetine. **Alcohol:** Avoid using alcohol while taking Paroxetine. **Oral anticoagulants.**
NSAIDs and acetylsalicylic acid, and other antiplatelet agents: Concomitant use of Paroxetine and NSAIDs/acetylsalicylic acid can lead to an increased haemorrhagic risk. Caution is advised in patients taking SSRIs, concomitantly with oral anticoagulants. **Tamoxifen:** Paroxetine should whenever possible be avoided during tamoxifen treatment.

FERTILITY, PREGNANCY AND LACTATION: Fertility: In vitro data with human material may suggest some effect on sperm quality; however, human case reports with some SSRIs (including Paroxetine) have shown that an effect on sperm quality appears to be reversible. Impact on human fertility has not been observed so far.
Pregnancy: Some epidemiological studies suggest an increased risk of congenital malformations, particularly cardiovascular (e.g. ventricular and atrial septum defects) associated with the use of Paroxetine during the first trimester. Paroxetine should only be used during pregnancy when strictly indicated on risk versus benefit assessment. Same should be done in women who are planning to become pregnant. Abrupt discontinuation should be avoided during pregnancy. Neonates should be observed if maternal use of Paroxetine continues into the later stages of pregnancy, particularly the third trimester.
Breast-feeding: Small amounts of Paroxetine are excreted into breast milk. Since no effects are anticipated, breast-feeding can be considered.

ADVERSE REACTIONS: Very common side effects: Nausea. Change in sex drive or sexual function.
Common side effects: Increases in the level of cholesterol in the blood, lack of appetite, insomnia or feeling sleepy, abnormal dreams (including nightmares), feeling dizzy or shaky (tremors), headache, difficulty in concentrating, feeling agitated, feeling unusually weak, blurred vision, yawning, dry mouth, diarrhoea or constipation, vomiting, weight gain, sweating.
Uncommon side effects: A brief increase in blood pressure, or a brief decrease that may make you feel dizzy or faint when you stand up suddenly, A faster than normal heartbeat, lack of movement, stiffness, shaking or abnormal movements in the mouth and tongue, dilated pupils, skin rashes, itching. Feeling confused, hallucinations. Urinary retention or urinary incontinence.
Rare side effects: Abnormal production of breast milk in men and women. A slow heartbeat. Effects on the liver. Panic attacks, mania, depersonalisation, feeling anxious. Restless Legs Syndrome, pain in the joints or muscles, increase in prolactin in the blood. Menstrual period disorders (including heavy or irregular periods, bleeding between periods and absence or delay of (periods).

Withdrawal symptoms seen on discontinuation of Paroxetine treatment:
Discontinuation of Paroxetine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia electric shock sensations and tinnitus), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported. Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when Paroxetine treatment is no longer required, gradual discontinuation by dose tapering should be carried out.

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

PRESENTATION: Pronitron Tablets 20mg are available in pack size of 10'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.
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