Summary of prescribing information for PEXEP PLUS capsules

Active Ingredient: Each film coated capsule of PEXEP PLUS contains: Paroxetine Hydrochloride IP Eq. to Paroxetine (as extended release) + Clonazepam (25mg+0.5mg, 12.5mg+0.5mg). **Indication:** treatment of patients with Co-morbid depression and anxiety. **Dosage:** taken as a single daily dose (preferably in the evening) with or without food, swallowed whole with the aid of little water, and without splitting, crushing or chewing them. Start therapy with one ZAPTRA 25 capsule taken as a single daily dose. If required, dosage is increased by adding ZAPTRA capsules for incremental additions of paroxetine 12.5 mg and clonazepam 0.5 mg per day at least at weekly intervals, up to a maximum of two ZAPTRA 25 capsules and one ZAPTRA 12.5 capsule per day [equivalent to paroxetine (as ER) 62.5 mg and clonazepam 1.5 mg], to complete maximum 6 weeks. Thereafter, taper-off ZAPTRA over next 4 weeks and substitute with paroxetine ER or IR as monotherapy for maintenance. For maintenance therapy, lowest effective dosage of paroxetine should be used and patient periodically reassessed to determine the need for continuous therapy. **Contraindications:** patients with known hypersensitivity to either paroxetine or benzodiazepines or to any other ingredient present in the formulation; patient taking a Monoamine Oxidase Inhibitors (MAOIs), thioridazine, or pimozide; and if having significant liver disease or acute narrow-angle glaucoma. **Warning and precautions:** Clinical Worsening and Suicide Risk. Paroxetine (as ER): Potential for Interaction with MAOIs: should not be used in combination with a MAOI, or within 14 days of discontinuing treatment with a MAOI. History of Mania: should be used with caution in patients with a history of mania. Patients Receiving Oral Anticoagulants. Discontinuation of Treatment: slowly taper-off. Seizures: should be used cautiously in patients with a history of seizures, discontinued in any patient who develops seizures. Clonazepam: Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Impairment of Motor Performance: may impair cognitive and motor performance – patients to be cautioned against driving, operating machinery, or other activities requiring full mental alertness and intact reflexes. Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines. Caution in Renally Impaired Patients. **Pregnancy & Lactation:** Use in pregnant women is not recommended. Breast-feeding should be avoided when administered to a nursing woman. **Interaction:** Paroxetine ER: Drugs Highly Bound to Plasma Protein: Monitor for adverse reactions and reduce dosage of paroxetine or other protein-bound drugs (e.g., warfarin) as warranted. Drugs Metabolized by CYP2D6: Reduce dosage of drugs metabolized by CYP2D6 as warranted. Concomitant use with Tamoxifen: Consider use of an alternative antidepressant with little or no CYP2D6 inhibition. Clonazepam: Clonazepam has the potential to influence concentrations of phenytoin. Cytochrome P450 inducers, such as phenytoin, carbamazepine, lamotrigine, and phenobarbital induce clonazepam metabolism, causing an approximately 38% decrease in plasma clonazepam levels. Inhibitors of VYP3A4 should be used cautiously. **Adverse reactions:** Common adverse events of Paroxetine (as ER): abnormal ejaculation, abnormal vision, asthenia, constipation, decreased appetite, diarrhea, dizziness, dry mouth, female genital disorder, impotence, insomnia, libido decreased, nausea, somnolence, sweating, tremor. Common side effects of clonazepam: somnolence, depression, dizziness, nervousness, ataxia, and reduced intellectual ability. **Overdose:** Paroxetine: symptoms include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. 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 also reported. Overdose Management: No specific antidotes for paroxetine are known. Clonazepam: Symptoms include somnolence, confusion, coma, and diminished reflexes. Overdose Management: monitoring of respiration, pulse and blood pressure, general supportive measures and immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of levarterenol or metaraminol. Dialysis is of no known value. Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in cyclic antidepressant overdose.

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It is recommended to refer full prescribing information before prescription.

For further medical information, please write to: Intas Pharmaceuticals Ltd., Corporate House, Near Sola Bridge, SG highway, Thaltej, Ahmedabad-380054, Gujarat, India. productqueries@intaspharma.com