Gablo

50mg
75mg
100mg
Capsules

(P r e g a b a l i n)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Gablo 50mg Capsules
Each capsule contains:
Pregabalin.....50mg

Gablo 75mg Capsules
Each capsule contains:
Pregabalin.....75mg

Gablo 100mg Capsules
Each capsule contains:
Pregabalin.....100mg

DESCRIPTION

Pregabalin is a white to off-white, crystalline solid with a pKa1 of 4.2 and a pKa2 of 10.6. It is freely soluble in water and both basic and acidic aqueous solutions. The log of the partition coefficient (n-octanol/0.05M phosphate buffer) at pH 7.4 is – 1.35. Pregabalin capsules are administered orally and are supplied as imprinted hard-shell capsules.

CLINICAL PHARMACOLOGY

Mechanism of Action: Pregabalin binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues. Pregabalin is a structural derivative of the inhibitory neurotransmitter gamma aminobutyric acid (GABA), it does not bind directly to GABAA, GABAB, or benzodiazepine receptors. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline reuptake.

Pharmacokinetics: Pregabalin is well absorbed after oral administration, is eliminated largely by renal excretion, and has an elimination half-life of about 6 hours.

Absorption and Distribution: Following oral administration of pregabalin capsules under fasting conditions, peak plasma concentrations occur within 1.5 hours. Pregabalin oral bioavailability is greater than or equal to 90% and is independent of dose. The rate of pregabalin absorption is decreased when given with food, resulting in a decrease in Cmax of approximately 25% to 30% and an increase in Tmax to approximately 3 hours. However, administration of pregabalin with food has no clinically relevant effect on the total absorption of pregabalin. Therefore, pregabalin can be taken with or without food. Pregabalin does not bind to plasma proteins. The apparent volume of distribution of pregabalin following oral administration is approximately 0.5 L/kg. Pregabalin is a substrate for system L transporter which is responsible for the transport of large amino acids across the blood brain barrier. Although there is no data in humans.

Metabolism and Elimination: Pregabalin undergoes negligible metabolism in humans. Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half-life of 6.3 hours in subjects with normal renal function. Pregabalin elimination is nearly proportional to creatinine clearance (CLcr).

Pharmacodynamics: Multiple oral doses of pregabalin were co-administered with oxycodone, lorazepam, or ethanol. Although no pharmacokinetic interactions were seen, additive effects on cognitive and gross motor functioning were seen when pregabalin was co-administered with these drugs. No clinically important effects on respiration were seen.

INDICATIONS AND USAGE

Gablo is indicated for:

Management of neuropathic pain associated with diabetic peripheral neuropathy(DPN).

Management of postherpetic neuralgia(PHN).

Adjunctive therapy for adult patients with partial onset seizures.

Management of fibromyalgia.

Management of neuropathic pain associated with spinal cord injury.

For the treatment of Generalised anxiety disorder (GAD) in adults.

CONTRAINDICATIONS

Pregabalin is contraindicated in patients with known hypersensitivity to pregabalin or any of its components.

Angioedema and hypersensitivity reactions have occurred in patients receiving pregabalin therapy.

INTERACTIONS

There are no pharmacokinetic interactions between pregabalin and the following antiepileptic drugs: carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital, and topiramate and also with commonly used antiepileptic drugs. Pharmacokinetics of Gabapentin, oral contraceptive(norethindrone and ethynyl estradiol)are unaltered by pregabalin coadministration.

Central nervous system influencing medical products: Pregabalin may potentiate the effects of ethanol and lorazepam. In controlled clinical trials, multiple oral doses of pregabalin co-administered with oxycodone, lorazepam, or ethanol did not result in clinically important effects on respiration. In the postmarketing experience, there are reports of respiratory failure and coma in patients taking pregabalin and other central nervous system (CNS) depressant medicinal products. Pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.

Diuretics, oral hypoglycemics, and insulin: No clinically significant effect on pregabalin clearance with the concomitant use of diuretics, oral hypoglycemics, and insulin.

Thiazolidinedione Antidiabetic Agents: Higher frequencies of weight gain and peripheral edema were observed in patients taking both pregabalin and a thiazolidinedione antidiabetic agent compared to patients taking either drug alone.

USE IN SPECIFIC POPULATION

Pregnancy: There are no adequate and well-controlled studies with pregabalin in pregnant women.

Lactation: Small amounts of pregabalin have been detected in the milk of lactating women. Advise nursing mothers that breastfeeding is not recommended during treatment with pregabalin.

Pediatric Use: The safety and efficacy in children and adolescents (under 18years of age) has not been established and therefore, pregabalin should not be used in this age group.

Geriatric Use: Pregabalin is eliminated primarily by renal excretion, adjust the dose for elderly patients with renal impairment as there is risk of toxic reactions to pregabalin.

Hepatic impairment: No dose adjustment is required for patients with hepatic impairment.

PRECAUTIONS

Angioedema: There have been postmarketing reports of angioedema in patients during initial and chronic treatment with pregabalin. Specific symptoms included swelling of the face, mouth (tongue, lips, and gums), and neck (throat and larynx). **Hypersensitivity:** Skin redness, blisters, hives, rash, dyspnea, and wheezing may occur. Discontinue pregabalin immediately in patients with these symptoms.

Withdrawal of antiepileptic drugs (AEDs): Withdrawal of pregabalin have potential to increase seizure frequency in patients with seizure disorders. If pregabalin is discontinued, taper the drug gradually over a minimum of 1 week.

Suicidal behavior and ideation: Antiepileptic drugs (AEDs), including pregabalin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication.

Peripheral edema: Pregabalin treatment may cause peripheral edema.

Dizziness and somnolence: Pregabalin may cause dizziness and somnolence.

Weight gain: Pregabalin treatment may cause weight gain.

Abrupt or rapid discontinuation: Following abrupt or rapid discontinuation of pregabalin, some patients reported symptoms including insomnia, nausea, headache, anxiety, hyperhidrosis, and diarrhea.

Tumorigenic potential: Tumorigenic potential is present.

Ophthalmological Effects: It causes blurred vision.

Creatine kinase elevations: Pregabalin treatment is associated with creatine kinase elevations.

Decreased platelet Count: Pregabalin treatment is associated with a decrease in platelet count.

PR Interval prolongation: Pregabalin treatment is associated with PR interval prolongation.

CNS depressants: Care should be taken with CNS depressants as they may cause somnolence.

Alcohol: Avoid consuming alcohol while taking pregabalin, as it may potentiate the impairment of motor skills and sedating effects of alcohol.

Lactation: Advise nursing mothers that breastfeeding is not recommended during treatment with pregabalin.

Male Fertility: Inform men being treated with pregabalin who plan to father a child of the potential risk of male-mediated teratogenicity.

Dermatopathy: Diabetic patients should pay particular attention to skin integrity while being treated with pregabalin.

Driving and using machines: Avoid to drive, operate complex machinery and engage in other potentially hazardous activities.

Lactose intolerant patients: Pregabalin contains lactose monohydrate. Care must be taken for lactose intolerant patients.

Congestive heart failure: Congestive heart failure in some patients receiving pregabalin is reported.

Encephalopathy: Cases of encephalopathy have been reported.

Reduced lower gastrointestinal tract function: Intestinal obstruction, paralytic ileus, constipation have been reported when pregabalin was co-administered with medications that have the potential to produce constipation, such as opioid analgesics.

ADVERSE REACTIONS

The overall adverse event profile of pregabalin was similar between women and men.

Body as a whole: Abdominal pain, allergic reaction, fever.

Cardiovascular system: Deep thrombophlebitis, heart failure, hypotension, postural hypotension, retinal vascular disorder, syncope.

Digestive system: Gastroenteritis, increased appetite, nausea, diarrhea.

Hemic and lymphatic System: Ecchymosis, anemia, eosinophilia, hypochromic anemia, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia.

Metabolic and nutritional disorders: Glucose tolerance decreased, urate crystalluria.

Musculoskeletal system: Arthralgia, leg cramps, myalgia, myasthenia.

Nervous system: Anxiety, depersonalization, hypertonia, hypoesthesia, libido decreased, nystagmus, paresthesia.

Respiratory system: Rarely apnea, atelectasis, bronchiolitis, hiccup, laryngismus, lung edema, lung fibrosis.

Skin and appendages: Pruritus, alopecia, dry skin, eczema, hirsutism, skin ulcer, urticaria, vesiculobullous rash.

Special senses: Conjunctivitis, diplopia, otitis media, tinnitus.

Urogenital system: Anorgasmia, impotence, urinary frequency, urinary incontinence.

Reproductive system and breast disorders: Gynecomastia, breast enlargement.

SIDE EFFECTS

Headache, dizziness, sleepiness, blurred vision, dry mouth, swelling of the extremities, weight gain, trouble concentrating, lack of energy, muscle weakness, constipation, and forgetfulness.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: Pregabalin is a schedule V controlled substance.

Misuse and abuse: Cases of misuse, abuse and dependence have been reported.

Dependence: Abrupt or rapid discontinuation of pregabalin can lead to insomnia, nausea, headache or diarrhea, consistent with physical dependence, anxiety and hyperhidrosis.

DOSAGE AND ADMINISTRATION

Pregabalin is given orally with or without food. When discontinuing pregabalin, taper gradually over a minimum of 1 week. For all indications, begin dosing at 150mg/day in divided doses. Doses for adult over 18 years are as follows:

Indication	Dosing Regimen	Maximum Dose
DPN Pain	3 divided doses per day	Begin dosing at 50mg TID or 75mg BID (150mg/day). Dose maybe increased to 300mg/day (100mg TID) within 1 week based on efficacy and tolerability (in patients with CLcr of atleast 60ml/min).
PHN	2 or 3 divided doses per day	Recommended dose is 75-150mg BID or 50-100mg TID (150 to 300mg/day) in patients with CLcr of atleast 60ml/min. Begin dosing at 75mg BID or 50mg TID(150mg/day). Dose maybe increased to 300mg/day (100mg TID) within 1 week based on efficacy and tolerability Incase of insufficient pain relieve following 2 to 4 weeks with 300mg/day, and who are able to tolerate pregabalin , maybe treated with 300mg BID or 200mg TID(600mg/day). Maximum dose is 600mg/day.
Adjunctive Therapy for Adult Patients with Partial Onset Seizures	2 or 3 divided doses per day	Doses of 150 to 600mg/day is effective.Starting daily dose is 75mg BID or 50mg TID not greater than 150mg/day. Maximum dose is 600mg/day.
Fibromyalgia	2 divided doses per day	Recommended dose is 300 to 450mg/day. Begin dosing at 75mg BID(150mg/day). Dose may be increased to 150mg BID (300mg/day) within 1 week based on efficacy and tolerability. Incase of insufficient benefit with 300mg/day, it is increased to 225mgBID (450mg/day). Maximum dose is 450mg/day.
Neuropathic Pain Associated with Spinal Cord Injury	2 divided doses per day	Recommended dose is 150 to 600mg/day. Starting dose is 75mg BID (150mg/day). Dose maybe increased to 150mg BID (300mg/day) within 1 week based on efficacy and tolerability. Incase of insufficient pain relief after 2 to 3 weeks of treatment with 150mg BID, maybe treated with upto 300mg BID. Maximum dose is 600mg/day.
Generalized Anxiety Disorder	2 or 3 divided doses per day	Initially 150mg daily, increased if necessary at 7-day intervals in steps of 150mg daily; maximum 600mg daily in 2-3 divided doses.

Patients with Renal Impairment: For patients having reduced renal function or undergoing hemodialysis, adjust the pregabalin daily dose based on renal function. In addition to the daily dose adjustment, administer a supplemental dose immediately following every 4-hour hemodialysis treatment.

Pregabalin Dosage Adjustment Based on Renal Function

Creatinine Clearance (CLcr ml/min)	Total Pregabalin Daily Dose (mg/day)*				Dose Regimen
≥60	150	300	450	600	BID or TID
30-60	75	150	225	300	BID or TID
15-30	25-50	75	100-150	150	QD or BID
<15	25	25-50	50-75	75	QD
Supplementary dosage following hemodialysis(mg)+					
Patients on the 25mg QD regimen: take one supplemental dose of 25mg or 50mg Patients on the 25-50mg QD regimen: take one supplemental dose of 50mg or 75mg Patients on the 50-75mg QD regimen: take one supplemental dose of 75mg or 100mg Patients on the 75mg QD regimen: take one supplemental dose of 100mg or 150mg					

TID=Three divided doses; BID=Two divided doses; QD=Single daily dose.

*Total daily dose(mg/day) should be divided as indicated by dose regimen to provide mg/dose.

+ Supplementary dose is a single additional dose.

Overdosage: The most commonly reported adverse events observed when pregabalin was taken in overdose (dose range from 800 mg/day up to 11,500 mg as a single dose) included affective disorder, somnolence, confusional state, depression, agitation, and restlessness. Seizures were also reported.

Treatment or management of overdose: There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; observe usual precautions to maintain the airway.

Missed dose: If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, just skip the missed dose. Take the next dose at your regular time. Do not take two doses at the same time.

STORAGE

Store at 25°C, excursions permitted to 15°C to 30°C.
Protect from sunlight and moisture.

PRESENTATION

Gablo(Pregabalin) Capsules 50mg are available in Alu-Alu blister pack of 14 capsules with leaflet.

Gablo(Pregabalin) Capsules 75mg are available in Alu-Alu blister pack of 14 capsules with leaflet.

Gablo(Pregabalin) Capsules 100mg are available in Alu-Alu blister pack of 14 capsules with leaflet.

For detailed information please contact:

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