Size: 135 x 235 mm

Front

Gablin CR™

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

Tablet

گیبلِن سی آر

Controlled-Release Tablets

COMPOSITION:
Gablin CR Tablet 82.5 mg:
Each film coated tablet contains:
Pregabalin ..... 82.5 mg.

Product Specs.: Innovator

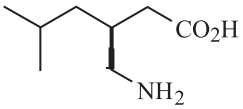
Gablin CR Tablet 165 mg:
Each film coated tablet contains:
Pregabalin ..... 165 mg.

Product Specs.: Innovator

Gablin CR Tablet 330 mg:
Each film coated tablet contains:
Pregabalin ..... 330 mg.

Product Specs.: Innovator

DESCRIPTION:
GABLIN CR (pregabalin controlled-release) tablets are for oral use and contain pregabalin. Pregabalin (GABLIN) is described chemically as (S)-3-(aminomethyl)-5-methylhexanoic acid. The molecular formula is $C_8H_{17}NO_2$ and the molecular weight is 159.23. The chemical structure of pregabalin is:



CLINICAL PHARMACOLOGY:
Pharmacodynamics:
Although no pharmacokinetic interactions were seen, with GABLIN and ethanol, lorazepam, or oxycodone, additive effects on cognitive and gross motor functioning were seen when GABLIN was co-administered with these drugs. No clinically important effects on respiration were seen in studies of GABLIN.
Pharmacokinetics:
GABLIN CR has linear pharmacokinetics with dose-proportional increases in maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve (AUC) from 82.5-660 mg/day. Following repeated administration, steady state is achieved within approximately 48-72 hours. GABLIN CR administered once daily following an evening meal has equivalent AUC and lower C_{max} relative to a comparative dose of administered without food twice daily. Variability in C_{max} and AUC for GABLIN CR is less than or equal to 25%.
Absorption: Pregabalin is absorbed from the small intestine and proximal colon. GABLIN CR absorption is linear and dose proportional. The bioavailability of GABLIN CR is reduced if taken on an empty stomach. The AUC is approximately 30% lower when GABLIN CR is administered fasted relative to following an evening meal. When GABLIN CR is administered following a 600 to 750 calorie (50% carbohydrates, 20% protein, 30% fat) evening meal, peak plasma concentrations occur within approximately 8 to 10 hours and AUC is approximately 93% to 97% relative to a comparative dose of GABLIN. The rate and extent of GABLIN CR absorption is similar when administered following a 400 to 500 calorie, 30% fat or an 800 to 1000 calorie, 15%, 30%, or 50% fat evening meal. When GABLIN CR is administered following an 800 to 1000 calorie (50% carbohydrates, 20% protein, 30% fat) morning meal, peak plasma concentrations occur within approximately 12 hours and AUC is 99% relative to a comparative dose of GABLIN. AUC decreases approximately 13% to 25% when GABLIN CR is administered following a 400 to 500 calorie or 600 to 750 calorie (50% carbohydrates, 20% protein, 30% fat) morning meal relative to the 800 to 1000 calorie meal, while C_{max} remains the same.
Distribution: 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 are no data in humans, pregabalin has been shown to cross the blood brain barrier in mice, rats, and monkeys. In addition, pregabalin has been shown to cross the placenta in rats and is present in the milk of lactating rats.
Elimination:
Metabolism: GABLIN undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 90% of the administered dose was recovered in the urine as unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of the dose. In preclinical studies, pregabalin (S-enantiomer) did not undergo racemization to the R-enantiomer in mice, rats, rabbits, or monkeys.
Excretion: GABLIN 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. Mean renal clearance was estimated to be 67.0 to 80.9 mL/min in young healthy subjects. Because pregabalin is not bound to plasma proteins this clearance rate indicates that renal tubular reabsorption is involved. Pregabalin elimination is nearly proportional to CLcr

INDICATIONS:
GABLIN CR is indicated for the management of:
- Neuropathic pain associated with diabetic peripheral neuropathy.
- Postherpetic neuralgia Efficacy of GABLIN CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures.

DOSAGE AND ADMINISTRATION:
GABLIN CR should be administered once daily after an evening meal. GABLIN CR should be swallowed whole and should not be split, crushed, or chewed. When discontinuing GABLIN CR, taper gradually over a minimum of 1 week. Instruct patients that if they miss taking their dose of GABLIN CR after an evening meal, then they should take their usual dose of GABLIN CR prior to bedtime following a snack. If they miss taking the dose of GABLIN CR prior to bedtime, then they should take their usual dose of GABLIN CR following a morning meal. If they miss taking the dose of GABLIN CR following the morning meal, then they should take their usual dose of GABLIN CR at the usual time that evening following an evening meal.
Neuropathic pain associated with diabetic peripheral neuropathy: Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability. The maximum recommended dose of GABLIN CR is 330 mg once daily. Although GABLIN was studied at 600 mg/day, there was no evidence that this dose conferred additional significant benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions with GABLIN, treatment with doses above 330 mg/day is not recommended for GABLIN CR.
Postherpetic neuralgia: Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 330 mg once daily and who are able to tolerate GABLIN CR, may be treated with up to 660 mg once daily. In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation

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due to adverse reactions, dosing above 330 mg/day should be reserved only for those patients who have on-going pain and are tolerating 330 mg daily. The maximum recommended dose of GABLIN CR is 660 mg once daily.

Patients with renal impairment: Use of GABLIN CR is not recommended for patients with creatinine clearance (CLcr) less than 30 mL/min or who are undergoing hemodialysis. Those patients should receive GABLIN CR. In view of dose-dependent adverse reactions and because pregabalin is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function. Base the dose adjustment in patients with renal impairment on CLcr. To use the dosing tables, an estimate of the patient's CLcr in mL/min is needed. CLcr in mL/min may be estimated from serum creatinine (mg/dL) determination using the Cockcroft and Gault equation:

$$= \frac{\textbf{(140-age) x Lean Body Weight (kg)}}{\textbf{Serum Creatinine (mg/dL) x 72}} \quad \textbf{(x 0.85 if female)}$$

Next, refer to the Dosage and Administration section to determine the recommended total daily dose based on indication, for a patient with normal renal function (CLcr greater than or equal to 60 mL/min). Then refer to Table 2 to determine the corresponding renal adjusted dose. (For example: A patient initiating GABLIN CR therapy for postherpetic neuralgia with normal renal function [CLcr greater than or equal to 60 mL/min], receives a single daily dose of 165 mg/day pregabalin. Therefore, a renal impaired patient with a CLcr of 50 mL/min would receive a single daily dose of 82.5 mg).

WARNINGS & PRECAUTIONS:

Angioedema: Angioedema (e.g., swelling of the face, mouth (tongue, lips, and gums) and neck (throat and larynx)) can occur and may be associated with life-threatening respiratory compromise requiring emergency treatment. Discontinue GABLIN CR immediately in patients with these symptoms.

Hypersensitivity reactions: Hypersensitivity reactions (e.g., hives, dyspnea, and wheezing) can occur. Discontinue GABLIN CR immediately in these patients.

Suicidal behavior and ideation: Antiepileptic drugs, including pregabalin, the active ingredient in GABLIN CR, increase the risk of suicidal thoughts or behavior.

Peripheral edema: May cause peripheral edema. Monitor patients for the development of edema when co-administering GABLIN CR and thiazolidinedione antidiabetic agents.

Dizziness and somnolence: May cause dizziness and somnolence and impair patients ability to drive or operate machinery.

Increased seizure frequency: May occur in patients with seizure disorders if GABLIN CR is rapidly discontinued. Withdraw GABLIN CR gradually over a minimum of 1 week.

SPECIAL POPULATIONS:

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

Lactation: Because of the potential risk of tumorigenicity, breastfeeding is not recommended during treatment with GABLIN CR.

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

Pediatric use: The safety and effectiveness of GABLIN CR in pediatric patients have not been established.

Geriatric use: No overall differences in safety and effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Pregabalin is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

CONTRAINDICATIONS:

GABLIN CR is contraindicated in patients with known hypersensitivity to pregabalin (GABLIN) or any of its components. Angioedema and hypersensitivity reactions have occurred in patients receiving pregabalin therapy.

DRUG INTERACTIONS:

Since pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans (less than 2% of a dose recovered in urine as metabolites), and does not bind to plasma proteins, its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions or protein binding displacement. In vitro studies showed that pregabalin is unlikely to be involved in significant pharmacokinetic drug interactions. The interactions of GABLIN CR with co-administration of other drugs have not been systematically evaluated. Co-administration of the prokinetic drug erythromycin with GABLIN CR did not result in any clinically important changes in the pharmacokinetics of GABLIN CR. Additional studies have been performed with GABLIN. No pharmacokinetic interactions were observed between GABLIN and carbamazepine, gabapentin, lamotrigine, oral contraceptive, phenobarbital, phenytoin, topiramate, and valproic acid. A similar lack of pharmacokinetic interactions would be expected to occur with GABLIN CR.

ADVERSE REACTIONS: Refer to Warnings & Precautions

OVERDOSAGE:

Signs, Symptoms and Laboratory Findings of Acute Overdosage in Humans There is limited experience with overdose of pregabalin. The highest reported accidental overdose of GABLIN during the clinical development program was 8000 mg, and there were no notable clinical consequences. 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. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient. Contact a Certified Poison Control Center for up-to-date information on the management of overdose with pregabalin. Although hemodialysis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal impairment. Standard hemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours).

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight and moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Gablin CR Tablet 82.5 mg	:	Pack of 2 x 7 tablets.
Gablin CR Tablet 165 mg	:	Pack of 2 x 7 tablets.
Gablin CR Tablet 330 mg	:	Pack of 2 x 7 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

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