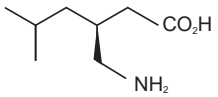
Gabica™

(PREGABALIN CAPSULES)

Capsules 50mg, 75mg, 100mg, 150mg, 300mg.

DESCRIPTION
GABICA (Pregabalin) is an analogue of the neurotransmitter gamma-aminobutyric acid (GABA). It has analgesic and anticonvulsant activity. Chemically pregabalin is described as (S)-3-(aminomethyl)-5-methylhexanoic acid and the molecular formula is $C_8H_{17}NO_2$ and the structural formula is:



Pregabalin

QUALITATIVE & QUANTITATIVE COMPOSITION
GABICA (Pregabalin) is available for oral administration as:

1. GABICA Capsules 50mg
   Each capsule contains:
   Pregabalin…50mg
2. GABICA Capsules 75mg
   Each capsule contains:
   Pregabalin…75mg
3. GABICA Capsules 100mg
   Each capsule contains:
   Pregabalin…100mg
4. GABICA Capsules 150mg
   Each capsule contains:
   Pregabalin…150mg
5. GABICA Capsules 300mg
   Each capsule contains:
   Pregabalin…300mg

CLINICAL PHARMACOLOGY
Mechanism of Action
Pregabalin reduces neuronal calcium currents by binding to the alpha-2-delta subunit of voltage gated calcium channels in CNS tissues and this particular mechanism may be responsible for effects in neuropathic pain, anxiety and other pain syndromes. 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
Absorption and Distribution:
Following oral administration of pregabalin capsules under fasting conditions, peak plasma concentrations occur within 1.5 hours. Pregabalin oral bioavailability is •90% and is independent of dose. Following single (25 to 300mg) and multiple-dose (75 to 900mg/day) administration, maximum plasma concentrations (C_{max}) and area under the plasma concentration-time curve (AUC) values increase linearly. Following repeated administration, steady state is achieved within 24 to 48 hours.
Pregabalin does not bind to plasma proteins. The apparent volume of distribution of pregabalin following oral administration is approximately 0.5L/kg.

Metabolism and Elimination:
Pregabalin undergoes negligible metabolism in humans. About 98% of the dose is excreted in the urine as unchanged drug. The N-methylated derivative of pregabalin, found in urine, accounted for 0.9% of the dose.
Pregabalin mean elimination half-life is 6.3 hours and is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Pregabalin is removed by hemodialysis.

Special Populations
Renal Insufficiency
Pregabalin plasma clearance and renal clearance are directly proportional to creatinine clearance. Pregablin clearance is reduced in patients with impaired renal function. Dose adjustments are required in patients with renal impairment (CL_{Cr} ≤60L/min). Pregabalin is effectively removed by hemodialysis (following 4 hour hemodialysis treatment plasma pregabalin concentrations are reduced by approximately 50%). Dose adjustments are required for patients on hemodialysis.

Elderly (Over 65 years of age):
Pregabalin clearance tends to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with decreases in creatinine clearance associated with increasing age. Reduction of pregabalin dose may be required in patients who have age related compromised renal function.

THERAPEUTIC INDICATIONS
GABICA (Pregabalin) is indicated:
- For the management of neuropathic pain associated with diabetic peripheral neuropathy.
- For the management of postherpetic neuralgia.
- As adjunctive therapy in adults with partial seizures with or without secondary generalization.
- For the treatment of Generalized Anxiety Disorder (GAD) in adults.
- For the treatment of fibromyalgia syndrome (FMS).

DOSAGE AND ADMINISTRATION
GABICA (Pregabalin) is given orally with or without food.
When discontinuing GABICA (Pregabalin), taper gradually over a minimum of 1 week irrespective of the indication.

Neuropathic Pain Associated with Diabetic Peripheral Neuropathy
GABICA (Pregabalin) treatment can be started at a dose of 150mg per day, given as 2-3 divided doses. Based on individual patient response and tolerability, the dosage may be increased to 300mg per day, given as 2 divided doses, after an interval of 3 to 7 days, and if needed, to a maximum dose of 600mg per day after an additional 7day interval.

Postherpetic Neuralgia
The recommended dose of GABICA (Pregabalin) is 75 to 150mg two times a day or 50 to 100mg three times a day (150 to 300mg/day). Dosing should begin at 75mg two times a day or 50mg three times a day (150mg/day) and may be increased to 300mg/day within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300mg/day and who are able to tolerate GABICA (Pregabalin), may be treated with up to 300mg two times a day (600mg/day).

Adjunctive therapy in adults with partial seizure with or without secondary generalization.
GABICA (Pregabalin) treatment can be started with a dose of 150mg per day given as 2-3 divided doses. Based on individual patient response and tolerability, the dosage may be increased to 300mg per day after 1 week. The maximum dosage of 600mg per day may be achieved after an additional week. Pregabalin does not alter the pasma concentrations of other commonly used anti-convulsant drugs. Similarly, commonly used anti-convulsant drugs do not alter plasma concentrations of pregabalin.

General Anxiety Disorder
The dose range is 150 to 600mg/day given as two or three divided doses. The need for treatment should be reassessed regularly. Pregabalin treatment can be started with a dose of 150mg/day given as 2-3 divided doses. Based on individual patient response and tolerability, the dosage may be increased to 300mg/day after 1 week. Following an additional week the dosage may be increased to 450mg/day. The maximum dosage of 600mg/day may be achieved after an additional week.

Fibromyalgia Syndrome (FMS)
The recommended dose of GABICA (Pregabalin) for fibromyalgia is 300 to 450mg/day. Dosing should begin at 75mg two times a day or 50mg three times a day (150mg/day) and may be increased to 300mg/day within 1 week based on on efficacy and tolerability. Patients who do not experience sufficient benefit with 300mg/day may be further increased to 225mg two times a day (450mg/day).

Renally Impaired Patients
As pregabalin clearance is directly proportional to creatinine clearance, dosage reduction in patients with compromised renal function must be individualised according to creatinine clearance, as indicated in table below determined using the following formula:

$$\text{Creatinine Clearance (mL/min)} = \frac{\text{Weight (kg) x (140 - age)}}{\text{72 x serum creatinine (mg/dL)}} \text{ (x 0.85 for female patients)}$$

Creatinine Clearance (CL_{cr}) (mL/min)	Total Pregabalin Daily dose *		Dose Regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
• 60	150	600	BID or TID
• 30 - <60	75	300	BID or TID
• 15 - <30	25 - 50	150	Once Daily or BID
< 15	25	75	Once Daily
Supplementary dosage following hemodialysis (mg)			
	25	100	Single 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.

ADVERSE REACTIONS
Very common: dizziness, drowsiness, somnolence.

Common: appetite increased, euphoric mood, confusion, irritability, libido decreased, ataxia, coordination abnormal, tremor, dysarthria, memory impairment, disturbance in attention, paresthesia, vision blurred, diplopia, vertigo, vomiting, dry mouth, constipation, flatulence, erectile dysfunction, gait abnormal, feeling drunk, fatigue, edema peripheral, weight increased.

Uncommon: anorexia, hallucination, panic attack, restlessness, agitation, depression, depressed mood, mood swings, depersonalization, insomnia exacerbated, word finding difficulty, abnormal dreams, libido increased, anorgasmia, apathy, syncope, stupor, myoclonus, psychomotor hyperactivity, visual field defect, ageusia, dyskinesia, dizziness postural, intention tremor,

nystagmus, cognitive disorder, speech disorder, hyporeflexia, hypoesthesia, amnesia, hyperaesthesia, burning sensation, eye swelling, visual acuity reduced, eye pain, asthenopia, dry eye, lacrimation increased, tachycardia, flushing, hot flushes, dyspnea, nasal dryness, abdominal distension, gastroesophageal reflux disease, salivary hypersecretion, hypoesthesia, rash papular, sweating, muscle twitching, joint swelling, muscle cramp, myalgia, arthralgia, back pain, pain in limb, muscle stiffnesss, urinary incontinence, dysuria, ejaculation delayed, sexual dysfunction, fall, chest tightness, asthenia, thirst, blood creatine phosphokinase increased, alanine aminotransferase increased, aspartate aminotransferase increased, platelet count decreased .

Rare: neutropenia, hypoglycemia, disinhibition, elevated mood, hypokinesia, parosmia, dysgraphia, peripheral vision loss, oscillopsia, altered visual depth perception, photopsia, eye irritation, mydriasis, strabismus, visual brightness, hyperacusis, atrioventricular block first degree, sinus tachycardia, sinus arrhythmia, sinus bradycardia, hypotension, hypertension, peripheral coldness, epistaxis, throat tightness, nasopharyngitis, cough, nasal congestion, rhinitis, snoring, ascites, pancreatitis, dysphagia, urticaria, cold sweat, rhabdomyolysis, cervical spasm, neck pain, renal failure, oliguria, amenorrhea, breast discharge, breast pain, dysmenorrhea, hypertrophy breast, anasarca, pyrexia, rigors, pain exacerbated, blood glucose increased, blood potassium decreased, white blood cell count decreased, blood creatinine increased, weight decreased.

Unknown Frequency: hypersensitivity, angioedema, allergic reaction, loss of consciousness, mental impairment, headache, congestive heart failure, swollen tongue, diarrhea, nausea, pruritus, urinary retention, Stevens Johnson syndrome, keratitis, face edema.

CONTRAINDICATIONS
- Pregabalin is contraindicated in patients with a known hypersensitivity to pregabalin or any of its components.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

PRECAUTIONS
Withdrawal of Antiepileptic Drugs (AEDs)
As with all AEDs, pregabalin should be withdrawn gradually to minimize the potential of increased seizure frequency in patients with seizure disorders. If pregabalin is discontinued this should be done gradually over a minimum of 1 week.

Angioedema
Pregabalin should be discontinued immediately if symptoms of angioedema, such as facial, perioral or upper airway swelling occur.

Weight Gain
Pregabalin associated weight gain is related to dose and duration of exposure. Some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycemic medications.

Discontinuation
After discontinuation of short-term and long-term treatment with pregabalin withdrawal symptoms have been observed in some patients. The following events have been mentioned: insomnia, headache, nausea and diarrhea, flu syndrome, nervousness, depression, pain, sweating and dizziness.

Creatinine Kinase Elevation
Pregabalin should be discontinued if myopathy is diagnosed or suspected or if markedly elevated creatine kinase levels occur.

Congestive Heart Failure
There have been reports of congestive heart failure in some patients receiving pregabalin. These reactions are mostly seen in elderly cardiovascular compromised patients during pregabalin treatment for a neuropathic indication. Pregabalin should be used with caution in these patients. Discontinuation of pregabalin may resolve the reaction.

Alcohol
Patients should be told to avoid consuming alcohol while on pregabalin, as it may potentiate the impairment of motor skills and sedation of alcohol.

Effects on Ability to Drive and Use Machines and Injuries
Pregabalin may cause dizziness and somnolence and therefore may have an influence on the ability to drive or use machines or may increase the occurrence of accidental injuries especially in the elderly population.

Pediatrics
Pregabalin is not recommended for use in children below the age of 12 years and adolescents (12-17 years) due to insufficient data on safety and efficacy.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Pregabalin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether pregabalin is excreted into human milk. Because many drugs are excreted in human milk, caution should be exercised when pregabalin is administered to a nursing woman.

Drug Interactions:
- Patients who require concomitant treatment with CNS depressants such as opiates or benzodiazepines should be informed that they may experience additive CNS side effects such as somnolence.
- Pregabalin may potentiate the effects of ethanol and lorazepam. There are also some reports of respiratory failure and coma in patients taking pregabalin and other CNS depressant medications.
- Pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.

STORAGE
Store below 30°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
1. GABICA (Pregabalin) Capsules 50mg are available in blister pack of 14's and 35's.
2. GABICA (Pregabalin) Capsules 75mg are available in blister pack of 14's and 35's.
3. GABICA (Pregabalin) Capsules 100mg are available in blister pack of 14's and 35's.
4. GABICA (Pregabalin) Capsules 150mg are available in blister pack of 14's and 35's.
5. GABICA (Pregabalin) Capsules 300mg is available in blister pack of 14's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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