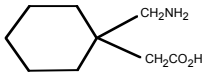
GABIX™
(GABAPENTIN)

گیبکس

100mg & 300mg Capsules

DESCRIPTION
GABIX (Gabapentin) is a new antiepileptic drug that is structurally similar to the neurotransmitter gamma aminobutyric acid (GABA) and the endogenous amino acid L-leucine. Chemically gabapentin is 1-(aminomethyl) cyclohexaneacetic acid. Its molecular formula is $C_9H_{17}NO_2$ and the structural formula is:



Gabapentin

QUALITATIVE & QUANTITATIVE COMPOSITION
GABIX (Gabapentin) is available for oral administration as:

1. GABIX Capsules 100mg
   Each capsule contains:
   Gabapentin USP ...100mg

2. GABIX Capsules 300mg
   Each capsule contains:
   Gabapentin USP...300mg

CLINICAL PHARMACOLOGY
Mechanism of Action
The exact mechanism of gabapentin CNS depressant and anticonvulsant activity is not fully understood. However, the binding site for gabapentin has been identified as the α_2-delta subunit of voltage-gated calcium channels.

Pharmacokinetics
Absorption
Gabapentin is absorbed from the gastrointestinal tract by means of saturable mechanism. Gabapentin bioavailability is not dose proportional i.e. as dose is increased bioavailability is decreased. Absolute bioavailability of 300mg oral dose is approximately 60%. Peak plasma gabapentin concentrations are observed within 2 to 3 hours. Over the recommended dose range of 300mg to 600mg three times a day, the differences in bioavailability are not large, and bioavailability is about 60%. Food, including a high-fat diet, has no clinically significant effect on gabapentin pharmacokinetics.

Distribution
Gabapentin circulates largely unbound (<3%) to plasma proteins and has a volume of distribution equal to 57.7 litres. Gabapentin is distributed into breast milk.

Metabolism
There is no evidence of gabapentin metabolism in humans. Gabapentin does not induce hepatic mixed function oxidase enzymes responsible for drug metabolism.

Excretion
Gabapentin is eliminated from the systemic circulation by renal excretion as unchanged drug. Elimination half-life ($t_{1/2}$) ranges from 5 to 7 hours and is unaltered by dose or following multiple dosing. Gabapentin elimination rate constant, plasma clearance and renal clearance are directly proportional to creatinine clearance.

Special Populations
Renal Impairment
The mean gabapentin half-life ranged from about 6.5 hours (patients with creatinine clearance (CL_{cr}) >60mL/min) to 52 hours (CL_{cr} <30mL/min) and gabapentin renal clearance ranged from 90mL/min (CL_{cr}>60mL/min) to about 10mL/min (CL_{cr} <30mL/min). Gabapentin dosage should be adjusted in patients with compromised renal function.

Patients on Hemodialysis
In anuric patients, the elimination half-life ($t_{1/2}$) of gabapentin on a nondialysis day was about 132 hours; during dialysis the apparent half-life was reduced to 3.8 hours. Thus hemodialysis has a significant effect on gabapentin elimination in anuric patients. Gabapentin dosage should be adjusted in patients undergoing hemodialysis.

Elderly Patients
The apparent oral clearance (CL/F) of gabapentin decreased as age increased, from about 225mL/min in those under 30 years of age to about 125mL/min in those over 70 years of age. Reduction of gabapentin dose may be required in patients who have age related compromised renal function.

THERAPEUTIC INDICATIONS
GABIX (Gabapentin) is indicated for:

Various types of neuropathic pain in adults
- Postherpetic neuralgia (PHN)
- Painful diabetic neuropathy.
- Trigeminal neuralgia.
- Central pain.
- Complex regional pain syndrome.

Epilepsy
- As adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 6 years and above.
- As monotherapy in the treatment of partial seizures with and without secondary generalization in adults and adolescents aged 12 years and above.

DOSAGE AND ADMINISTRATION
GABIX (Gabapentin) can be given with or without food.

Neuropathic Pain (Adults)
GABIX (Gabapentin) therapy may be initiated as a single 300mg dose on Day 1, 600mg/day on Day 2 (divided BID), and 900mg/day on Day 3 (divided TID). The dose can subsequently be titrated up as needed for pain relief to a daily dose of 1800mg (divided TID). Thereafter, based on individual patient response and tolerability, the dose can be further increased in 300mg/day increments every 2-3 days up to a maximum dose of 3600mg/day. The minimum time to reach a dose of 1800mg/day is one week, to reach 2400mg/day is a total of 2 weeks and to reach 3600mg/day is a total of 3 weeks.

Epilepsy
Adults and adolescents
The starting dose is 300mg three times a day. Thereafter, based on individual patient response and tolerability, the dose can be further increased in 300mg/day increments every 2-3 days up to a maximum dose of 3600mg/day. The minimum time to reach a dose of 1800mg/day is one week, to reach 2400mg/day is a total of 2 weeks and to reach 3600mg/day is a total of 3 weeks. The total daily dose should be divided in three single doses, the maximum time interval between the doses should not exceed 12 hours to prevent breakthrough convulsions.

Children aged 6 years and above
The starting dose should range from 10-15mg/kg/day in 3 divided doses and the effective dose reached by upward titration over a period of approximately 3 days. The effective dose of gabapentin in patients 6 years of age and older is 25–35mg/kg/day and given in divided doses (three times a day). The maximum time interval between doses should not exceed 12 hours.

Special Populations
Renal Impaired Patients
A dosage adjustment is recommended in renally impaired patients with neuropathic pain or epilepsy.

Creatinine Clearance (mL/min)	Total Daily Dose[a] (mg/day)
≥ 80	900-3600
50-79	600-1800
30-49	300-900
15-29	150[b]-600
<15[c]	150[b]-300

a. Total daily dose should be administered as three divided doses. Reduced dosages are for patients with renal impairment (creatinine clearance < 79mL/min).
b. To be administered as 300 mg every other day.
c. For patients with creatinine clearance <15mL/min, the daily dose should be reduced in proportion to creatinine clearance (e.g., patients with a creatinine clearance of 7.5mL/min should receive one-half the daily dose that patients with a creatinine clearance (CL_{cr}) of 15mL/min receive).

Patients undergoing Hemodialysis
The recommended loading dose of GABIX (Gabapentin) is 300mg to 400mg then 200mg to 300mg following each 4 hours of hemodialysis. For renally impaired patients undergoing hemodialysis, the maintenance dose of gabapentin should be based on the dosing recommendations found in Table above. In addition to the maintenance dose, an additional 200mg to 300mg dose following each 4 hour hemodialysis treatment is recommended.

ADVERSE REACTIONS
Very common
Viral infection, somnolence, dizziness, ataxia, fatigue and fever.

Common
Pneumonia, respiratory infection, urinary tract infection, otitis media, leucopenia, anorexia, increased appetite, hostility, confusion, emotional lability, depression, anxiety, nervousness, thinking abnormal, convulsions, hyperkinesias, dysarthria, amnesia, tremor, insomnia, headache, sensations such as paresthesia, hypaesthesia, coordination abnormal, nystagmus, increased, decreased, or absent reflexes, visual disturbances such as amblyopia, diplopia, vertigo, hypertension, vasodilatation, dyspnea, bronchitis, pharyngitis, cough, rhinitis, vomiting, nausea, dental abnor malities, gingivitis, diarrhea, abdominal pain, dyspepsia, constipation, dry mouth or throat, flatulence, facial edema, purpura most often described as bruises resulting from physical trauma, rash, pruritus, acne, arthralgia, myalgia, back pain, twitching, impotence, peripheral edema, abnormal gait, asthenia, pain, malaise, flu syndrome, WBC (white blood cell count) decreased, weight gain, accidental injury, fracture and abrasion.

Uncommon
Allergic reactions (e.g., urticaria), hypokinesia, palpitations, generalized edema, elevated liver function tests SGOT (AST) and SGPT (ALT) and bilirubin.

CONTRAINDICATIONS
Gabapentin is contraindicated in patients with known hypersensitivity to gabapentin or any of the excipients of the product.

PRECAUTIONS
- Antiepileptic drugs (AEDs), including gabapentin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Gabapentin should not be abruptly discontinued because of the possibility of increasing seizure frequency.
- If a patient develops acute pancreatitis under treatment with gabapentin, discontinuation of gabapentin should be considered.
- Gabapentin should not be considered a treatment of absence seizures and may exacerbate these seizures in some patients. Consequently, gabapentin should be used with caution in patients who have mixed seizure disorders that include absence seizures.
- Patients should be advised neither to drive a car nor to operate complex machinery until they have gained sufficient experience on gabapentin.

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

Nursing Mother
Gabapentin is secreted into breast milk following oral administration. The effect on the nursing infant is unknown. Therefore, gabapentin should be used in nursing women only if the potential benefits clearly out weigh the risks.

Drug Interactions
Phenytoin, Valproic acid, Carbamazepine or Phenobarbitone
There is no interaction during the concomitant administration of gabapentin with these drugs. Gabapentin steady-state pharmacokinetics is similar for healthy subjects and patients with epilepsy receiving anti-epileptic agents.

Morphine
Patients who require concomitant treatment with morphine may experience increase in gabapentin AUC by 44% compared to gabapentin administered without morphine. Patients should be carefully observed for signs of CNS depression such as somnolence and the dose of gabapentin or morphine should be reduced appropriately.

Antacid
Gabapentin's bioavailability was reduced up to 24% when co-administered at the same time with an aluminium and magnesium containing antacid. It is recommended that gabapentin be taken about two hours following any such antacid administration.

Naproxen: Co-administration of naproxen sodium (250mg) with gabapentin (125mg) appears to increase the amount of gabapentin absorbed by 12% to 15%. These doses are lower than the therapeutic doses for both drugs. The magnitude of interaction within the recommended dose is not known.

Hydrocodone
Co-administration of gabapentin decreases hydrocodone C_{max} and AUC values in a dose-dependent manner relative to administration of hydrocodone alone. Hydrocodone increases gabapentin AUC values by 14%.

OVERDOSAGE
Acute, life-threatening toxicity has not been observed with gabapentin overdoses of up to 49g. Symptoms of the overdoses included dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhea. All patients recovered fully with supportive care. Reduced absorption of gabapentin at higher doses may limit drug absorption at the time of overdosing and, hence, minimise toxicity from overdoses. Overdoses of gabapentin, particularly in combination with other CNS depressant medications, may result in coma. Although gabapentin can be removed by hemodialysis, based on prior experience it is not usually required. However, in patients with severe renal insufficiency hemodialysis may be indicated.

STORAGE
Store at 25°C (Excursions permitted between 15°C to 30°C). Protect from sunlight & moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
GABIX (Gabapentin) Capsules 100mg is available in blister pack of 10's.

GABIX (Gabapentin) Capsules 300mg is available in blister pack of 10'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.

Manufactured by:
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