VULTIN 600

ANTIEPILEPTIC/ NEUROPATHIC PAIN

Each film coated tablet contains:
Gabapentin 600 mg

✧ **PRODUCT DESCRIPTION:**
White, oval, biconvex, film coated tablet with engraved GBP 600 on one side and scored on the other.

✧ **MECHANISM OF ACTION:**
Pharmacology
Gabapentin is structurally related to the neurotransmitter GABA; however, Gabapentin and its metabolites do not bind to GABA (A) or GABA (B) receptors or influence the degradation or uptake of GABA. The analgesic action of Gabapentin has been demonstrated in animal models of analgesia where Gabapentin prevented allodynia and hyperalgesia. Pain related responses in neuropathic pain models and in peripheral inflammation models were prevented or decreased by Gabapentin. Immediate pain-related behaviors were not altered.
The mechanism by which Gabapentin exerts its analgesic effects is unknown. It has been suggested the mechanism of action may be by Gabapentin preventing thrombospondin from binding to alpha-2 delta-1 (a receptor involved in excitatory synapse formation). The anticonvulsant action of Gabapentin has been demonstrated in animal test systems; however, the mechanism by which Gabapentin prevents seizure activity is unknown.
Pharmacokinetics
Absorption
Gabapentin bioavailability is not dose-proportional. That is, as the dose is increased, bioavailability decreases.
Gabapentin is absorbed from the gastrointestinal tract by means of a saturable mechanism. After multiple dosing peak plasma concentrations usually occur within 2 to 3 hours of a dose and a steady state within 1 to 2 days.
Absolute bioavailability of Gabapentin capsules is approximately 60%.
Distribution
Gabapentin is distributed into breast milk.
It is widely distributed throughout the body but binding to plasma proteins is minimal. It has a volume of distribution equal to 57.7 liters.
Metabolism
Gabapentin is excreted unchanged in the urine, and is not appreciably metabolized.
Excretion
The elimination half-life of Gabapentin is independent of dose and averages 5 to 7 hours.
The renal clearance of Gabapentin was 150 mL/min.
Fecal: 10% to 23%
Renal: 76% to 81%
In elderly patients, and in patients with impaired renal function, Gabapentin plasma clearance is reduced. Gabapentin elimination-rate constant, plasma clearance, and renal clearance are directly proportional to creatinine clearance.

✧ **INDICATION:**
Epilepsy - Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children age 3 years and above. Safety and effectiveness for adjunctive therapy in pediatric patients below the age of 3 years have not been established.
Neuropathic pain - Gabapentin is indicated for the treatment of neuropathic pain which includes diabetic neuropathy, post-herpetic neuralgia and trigeminal neuralgia in adults age 18 years and above. Safety and effectiveness in patients below the age of 18 years have not been established.

✧ **DOSAGE AND ADMINISTRATION:**
Oral
General
Gabapentin is given orally with or without food.
When in the judgment of the clinician there is a need for dose reduction, discontinuation, or substitution with an alternative medication, this should be done gradually over a minimum of one week.
Epilepsy
Adults and pediatric patients over 12 years of age
The effective dosing range was 900 to 3600 mg/day. Therapy may be initiated by administering 300 mg three times a day (TID) on Day 1, or by titrating the dose as described in Table 1. Thereafter, the dose can be increased in three equally divided doses up to a maximum dose of 3600 mg/day. Dosages up to 4800 mg/day have been well tolerated in long-term open-label clinical studies. The maximum time between doses in the three times a day (TID) schedule should not exceed 12 hours to prevent breakthrough convulsions.

Table 1. Dosing Chart – Initial Titration

Dose	Day 1	Day 2	Day 3
900 mg	300 mg QD[a]	300 mg BID[b]	300 mg TID[c]

[a]QD = once a day
[b]BID = two times a day
[c]TID = three times a day

Pediatric patients age 3-12 years
The starting dose should range from 10 to 15 mg/Kg/day given in equally divided doses (three times a day), and the effective dose reached by upward titration over a period of approximately three days. The effective dose of Gabapentin in pediatric patients age 5 years and older is 25 to 35 mg/Kg/day given in equally divided doses (three times a day). The effective dose in pediatric patients ages 3 to less than 5 years is 40 mg/Kg/day given in equally divided doses (three times a day). Dosages up to 50 mg/Kg/day have been well tolerated in a long-term clinical study. The maximum time interval between doses should not exceed 12 hours.
It is not necessary to monitor Gabapentin plasma concentrations to optimize Gabapentin therapy. Further, Gabapentin may be used in combination with other antiepileptic drugs without concern for alteration of the plasma concentrations of Gabapentin or serum concentrations of other antiepileptic drugs.
Neuropathic pain in adults
The starting dose is 900 mg/day given as three equally divided doses, and increased if necessary, based on response, up to a maximum dose of 3600 mg/day. Therapy should be initiated by titrating the dose as described in Table 1.
Dosage adjustment in impaired renal function for patients with neuropathic pain or epilepsy
Dosage adjustment is recommended in patients with compromised renal function as described in Table 2 and/or those undergoing hemodialysis.

Table 2. Dosage of Gabapentin in Adults Based on Renal Function

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	150[b]-300

[a] Total daily dose should be administered as a TID regimen. Doses used to treat patients with normal renal function (creatinine clearance > 80 mL/min) range from 900 to 3600 mg/day. Reduced dosages are for patients with renal impairment (creatinine clearance < 79 mL/min).
[b] To be administered as 300 mg every other day.

Dosage adjustment in patients undergoing hemodialysis
For patients undergoing hemodialysis who have never received Gabapentin, a loading dose of 300 to 400 mg is recommended, then 200 to 300 mg of Gabapentin following each 4 hours of hemodialysis.

FRONT
17.0 cm.
28.5 cm.

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Kapook_Job Print: 19-08-24 Scale 100%

Product	Code No.	Dimension	Packaging Type	Thickness
VULTIN 600	IVMY 0052	W 17.0 x L 28.5 cm.	Wood Free Paper (กระดาษปอนด์)	60 g (0.08 mm.)

Designed by: (PDM, PDC-M, PDC-A, PDO-M, PDO-A)
Checked by: (PDM/ASPD)
Approved by: (MD (Only Pattern and Colors))
LRA: (Date)
IRA: (Date)
QCC-PM: (Date)
CUSTOMER/SALES DEPT: (Date)
PM Specification
Approved by: PLC: (Date)

BACK

17.0 cm.

28.5 cm.

WARNING AND PRECAUTION:

Abrupt discontinuation; may increase seizure frequency or precipitate status epilepticus; discontinue gradually over a minimum of 1 week
Gabapentin is not generally considered effective in the treatment of absence seizures.
Patients who require concomitant treatment with morphine may experience increases in Gabapentin concentrations. Patients should be carefully observed for signs of CNS depression, such as somnolence, and the dose of Gabapentin or morphine should be reduced appropriately.
There is potential for an increase in risk for suicidal thoughts or behavior.
It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Gabapentin should be discontinued if an alternative etiology for the signs or symptoms cannot be established.
Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)/multiorgan hypersensitivity, including fatal cases, has been reported; evaluate early signs/symptoms and discontinue Gabapentin if confirmed.
Respiratory depression: Gabapentin has been associated with severe respiratory depression. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of Central Nervous System (CNS) depressants and the elderly might be at higher risk of experiencing this severe adverse reaction. Dose adjustments might be necessary in these patients.
Pediatric patients (age 3 to 12 years): neuropsychiatric adverse events, including emotional lability, hostility, thought disorder, and hyperkinesia, have been reported.
Renal impairment or hemodialysis; dose adjustment of Gabapentin is necessary.
Monitoring recommended for suicidality, worsening depression, and/or any unusual behavioral or mood changes (eg, anxiety, agitation, hostility, mania, and hypomania).
Effects on the ability to drive and use machines
Gabapentin may impair the ability to drive a car or operate potentially dangerous machinery. Patients are advised not to drive or operate potentially dangerous machinery, until it is known that this medication does not affect their ability to engage in these activities.
Sodium metabisulfite: This preparation contains Sodium metabisulfite that may cause serious allergic type reactions in certain susceptible patients. Do not use if known to be hypersensitive to bisulfites.

PREGNANCY AND LACTATION:

Pregnancy
There is insufficient clinical experience with Gabapentin in pregnancy to confirm its safety in this patient population. Since Gabapentin is frequently prescribed with other anticonvulsants, a clear association between maternal Gabapentin use and fetal adverse effects cannot be determined. Due to lack of adequate, well-controlled studies, hence it is recommended that Gabapentin should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.
Lactation
Gabapentin is excreted in human milk. Because the effect on the nursing infant is unknown, caution should be exercised when Gabapentin is administered to a nursing mother. Gabapentin should be used in nursing mothers only if the benefits clearly outweigh the risks.

SIDE EFFECT:

The most commonly reported adverse effects associated with Gabapentin are somnolence, dizziness, ataxia, and fatigue.
Nystagmus, tremor, diplopia, amblyopia, pharyngitis, rhinitis, dysarthria, nausea and vomiting, weight gain, edema, dyspepsia, amnesia, weakness, paraesthesia, arthralgia, myalgia, headache, purpura, leucopenia, anxiety, and urinary-tract infection may occur less frequently.
Rarely, pancreatitis, altered liver function tests, erythema multiforme, Stevens-Johnson syndrome, and blood glucose fluctuations in diabetics have been reported.
Common psychiatric effects include confusion, depression, and nervousness, and, more rarely, hallucinations and psychoses.
Other adverse effects include acute renal failure, allergic reactions, alopecia, angioedema, chest pain, hepatitis, jaundice, movement disorders such as choreoathetosis, dyskinesia and dystonia, palpitations, thrombocytopenia, and tinnitus.
An antiepileptic hypersensitivity syndrome, comprising fever, rash, eosinophilia, and lymphadenopathy, along with other organ involvement such as hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis, has been associated with some antiepileptic drugs including Gabapentin. Early manifestations, such as fever and/or lymphadenopathy, may be present without evident rash; patients with such signs or symptoms should be evaluated immediately and therapy stopped in the absence of a clear etiology.
Respiratory, thoracic and mediastinal disorders
Frequency 'rare': Respiratory depression
Post-marketing experience*
Dysphagia

CONTRAINDICATION:

Hypersensitivity to Gabapentin or any component of the product.

DRUG INTERACTION:

No interaction between Gabapentin and Phenobarbital, Phenytoin, Valproic acid, or Carbamazepine has been observed. Gabapentin steady-state pharmacokinetics are similar for healthy subjects and patients with epilepsy receiving these antiepileptic agents.
Coadministration of Gabapentin with oral contraceptives containing Norethindrone and/or Ethinyl estradiol, does not influence the steady-state pharmacokinetics of either component.
Renal excretion of Gabapentin is unaltered by Probenecid.
The absorption of Gabapentin from the gastrointestinal tract is reduced by antacids containing Aluminium with magnesium; it is recommended that Gabapentin is taken at least 2 hours after any such antacid. Morphine has been reported to reduce the clearance of Gabapentin; patients receiving both drugs should be monitored for signs of CNS depression and doses should be reduced accordingly. Cimetidine has also been reported to reduce the renal clearance of Gabapentin but licensed product information does not consider this to be of clinical importance.
Concurrent use of Gabapentin and the following may result in reduced anticonvulsant effectiveness:

- Ginkgo
- Evening Primrose
- Ketorolac

Concurrent use of Gabapentin and Hydrocodone may result in decreased bioavailability of Hydrocodone.

OVERDOSE AND TREATMENT:

Symptoms
In mild to moderate overdose, patients may present with sedation, ataxia, slurred speech, nystagmus, movement disorders, and gastrointestinal upset. In more severe cases, patients may present with mild hypotension and profound central nervous system depression requiring intubation.
Treatment
Treatment of Gabapentin exposure is largely supportive in nature with careful attention to airway protection in severe cases.
Although Gabapentin can be removed by hemodialysis, based on prior experience it is usually not required. However, in patients with severe renal impairment, hemodialysis may be indicated.

STORAGE:

Store at temperature of not more than 30°C.

DOSAGE FORM AND PACKAGING AVAILABLE:

600 mg Tablet, Blister 10x10's

DATE OF REVISION:

August 19, 2024

Manufactured by:
UNISON LABORATORIES CO., LTD.
39 Moo 4, Klong Udomcholjorn, Muang Chachoengsao,
Chachoengsao 24000 Thailand

C-MY/190824-04 (AR)
(DRGD_MY as per email dated 22/12/15);*Directive_May 2020

IVMY 0052

PM Specification

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