

# Nurona®

## (Gabapentin)

### Pharmacological Properties

Gabapentin is a lipophilic analogue related in structure to the neurotransmitter GABA, but it is not biotransformed into GABA, not a GABA agonist or antagonist, and doesn't alter cellular uptake of dopamine, nor adrenaline, or serotonin.

Although its precise mechanism of action is not yet known, gabapentin is known to bind with high affinity to binding sites in the brain which are associated with a  $\alpha 2\delta$  subunit of voltage sensitive calcium channels. In vitro, gabapentin modulates the activity of GABA synthesizing enzyme GAD as well as the activity of glutamate synthesizing enzyme. In various animal models, gabapentin showed anticonvulsive, analgesic, anxiolytic and neuroprotective properties.

### Indications

#### ■ Epilepsy

- Monotherapy (including patients with newly diagnosed seizures) or add-on therapy in adults and children over 12 years of age with simple and complex partial seizures with and without secondary generalization.
- Add-on therapy in adults and children aged 3 years and above with partial seizures with and without secondary generalization

#### ■ Neuropathic pain in adults

For the treatment of Neuropathic pain in diabetic polyneuropathy and postherpetic neuralgia in adults.

### Dosage & Administration

- Nurona® Capsules should be swallowed whole with sufficient fluid regardless of meals.
- The interval between 2 single doses should not exceed 12 hours.
- Nurona® dose is determined depending on individual tolerance and effect.
- Duration of treatment in epilepsy is determined according to physician judgment and usually long term therapy is required.
- In neuropathic pain no clinical studies were conducted for more than 5 months.
- Discontinuation (if clinically required) should be gradual over a period of one week
- Dose should be increased in 100mg steps in patients with poor condition, low BW or after transplantation
- The dose may be titrated according to the following dose scheme:

Epilepsy	Day 1	Day 2	Day 3	
Monotherapy & Add-on therapy in Patients over 12 years of age	300mg X 1	300mg X 2		300 mg T.I.D. can be given initially then can be increased to 1200mg/day. A dose of 2400mg should not be exceeded, as insufficient efficacy and safety data are available.
Add-on therapy in Patients 3-12 years of	10mg /kg BW	20mg /kg BW	30mg /kg BW	Dose may be increased to 40-50mg/kg BW/day if required and the maintenance doses divided into three doses. 300mg tid can be given initially then increased to 1800mg tid (according to pain intensity), but a daily dose of 3600mg should not be exceeded.
Neuropathic pain in adults	300mg X 1	300mg X 2	300mg X 3	

### Use in renal impairment

Nurona® dosage should be adjusted according to the following table:

(ml/min)	Gabapentin Total daily dose range (mg/day)	
		Three times daily 100mg x 3 every other day
Hemodialysis patients (Not previously treated with gabapentin)	Loading dose: 300-400 Maintenance: 200-300	Doses given following each 4 hours of hemodialysis (No treatment in dialysis free days)

### Use in pediatrics

No sufficient experience for monotherapy in children <12 years or for add-on therapy in children <3 years.

## Use in pregnancy & lactation

- Pregnancy Category C, There are no adequate and well-controlled studies in pregnant women. Animal experiments have not shown evidence of teratogenic effects (malformations) so gabapentin should be used during pregnancy only if the potential benefit justifies the potential risk to the infant.
- Gabapentin is secreted into human milk, so an assessment should be done concerning its potential to cause serious side effects in the fetus and its importance as antiepileptic treatment for the mother.

## Side effects

Usually mild to moderate in intensity. Most frequently, dizziness, headache, fatigue, somnolence, anorexia, nausea vomiting, weight increase, nervousness, insomnia, ataxia, nystagmus, and paresthesia. Occasionally asthenia, tremor, back pain, myalgia, fracture, edema in face, extremities or the whole body, pruritus, visual disturbances (amblyopia and diplopia), rhinitis, pharyngitis, coughing, dental abnormalities, gingivitis, thinking abnormal, dysarthria, amnesia, depression, emotional lability, increased appetite, dyspepsia, dry mouth, constipation, abdominal pain, leukopenia, urinary incontinence, impotence, vasodilatation and hypertension occurred. Rarely hemorrhagic pancreatitis and allergic reactions (Stevens-Johnson syndrome, erythema multiforme) have been reported. Aggressive behaviour and hyperkinesia were reported in pediatric patients less than 12 years.

## Driving and operating machines

The ability to work in exposed places, drive and operate complex machines is impaired since gabapentin may slow down reactions through its action on the CNS causing sedation and dizziness, especially upon treatment initiation, dose titration, changing medication, also in conjunction with alcohol.

## Precautions

- Blood glucose should be monitored in patients with diabetes mellitus since fluctuations in blood glucose were detected in clinical trials
- False positive results may be obtained in the determination of total urine protein by dipstick tests, so it is advised to verify results or to use alternative methods.
- Since hemorrhagic pancreatitis was reported, clinical examination should proceed to ensure early diagnosis (persisting abdominal pain, nausea and repeated vomiting), and accordingly therapy with gabapentin is to be stopped immediately
- As with other Antiepileptics, gabapentin should not be abruptly discontinued because of the possibility of increasing seizure frequency.
- Neuropsychiatric manifestations occurred in pediatrics aged 3-12 years, these events were mild to moderate and included, emotional lability (behavioral problems), hostility (aggressive behaviors), thought disorder (concentration problems and change in school performance), and hyperkinesia (primarily restlessness and hyperactivity).

## Drug interactions

- Gabapentin is not appreciably metabolized nor does it interfere with the metabolism of commonly coadministered antiepileptics such as carbamazepine, phenytoin, valproic acid, or Phenobarbital
- Gabapentin doesn't impair the effect of oral contraceptives containing norethindrone &/or ethinyl estradiol, but coadministration with other antiepileptics known to have that effect may lead to contraceptive failure
- Antacids containing magnesium or aluminum may reduce gabapentin bioavailability therefore it should be administered at least 2 hours after the antacid intake.
- Cimetidine slightly decreases renal elimination of gabapentin when it is coadministered with
- Alcohol or centrally acting drugs of abuse may exaggerate some gabapentin CNS side effects (e.g. somnolence and ataxia)

## Contraindications

- Known hypersensitivity to any of the ingredients
- Galactosemia (galactose intolerance) due to capsules content of lactose.
- Acute pancreatitis
- Not effective against primarily generalized seizures, such as absences

## Overdose

Dizziness, diplopia, dysarthria, sedation, and mild diarrhea are among the symptoms of overdose, but acute, life-threatening toxicity has not been observed with doses up to 49 gm/day. Gabapentin is removable by hemodialysis, but experience indicates that this is unnecessary except in renal impairment.

## Presentations

- Nurona<sup>®</sup> 100mg capsules: Gabapentin 100mg (available in different pack sizes).
- Nurona<sup>®</sup> 300mg capsules: Gabapentin 300mg (available in different pack sizes).
- Nurona<sup>®</sup> 400mg capsules: Gabapentin 400mg (available in different pack sizes)

( This is a medicament - keep medicaments out of reach of children )

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, method for use and the instructions of the pharmacist who sold the medicament .
- The doctor and the pharmacist are experts in medicine, its benefits and risks .
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Pharma International