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 altercellular uptake of dopamine, nor adrenaline, or serotonin.

Although Its precise mechanism of action is not yet known, g abapentin is known to bind with high affinity to binding sites in the brain wh ch are associated with a pha2 delte subunits of voltage sensitive ca cium channels. In vitro, gabapentin modu ates the act vity of GABA synthesizing enzyme GAD as well as the activity of glutamate s ynthesizing enz yme. In various animal models, gabapentin showed anticonvulsive, analgesic, anxiolytic and neuoprotective properties.

Indications

■ **Epilepsy**

- Monotherapy (including patients with newly d agnosed seizures) or add-on therapy in adults and children over 12 ye ars of age w th simp e and comp lexpart al seizures with and w thout secondary generalization.
- Add-on therapy in adults and children aged 3 years and above w th partial seizures with and without secondar y generaliz ation

■ **Neuropathic** pa inin adults

For the treatmentof Neuropathic pain in diabetic polyneuropathy and postherpeticneuralgia in adults.

Dosage & Administration

- Nurona® Capsules should be sw allowed whole with sufficient fluid regardless of meals.
- The interval between 2 singledoses 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 usu a ly long term therapy isrequired.
- In neuropathic pain no clin cal studies were conducted for more than 5 months.
- Discontinuation (f c inically required) should be gradu al 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 followingdose 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 dose is divided into three doses.
Neuropathic pain in adults	300mg X 1	300mg X 2	300mg X 3	300mg tid can be given Ini tially then increased to 1800mg tid (according to pain intensity), but a daily dose of 3600mg should not be exceeded.

Use in renal impairment

NuronaÛ dos age should be adjusted according to the following table:

(ml/min)	Gabapentin Total da ly 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	Dosing given following each 4 hours of hemodialysis (No treatment in dialysis free days)

Use in pediatrics

No sufficient experience for monother apy 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 teratogeniceffects (malformations) so gabapentin should beusedduring pregnancy only ifthe potential benefit justifies the potential riskto 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 forthe 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 pancrealitis 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, especiallyupon treatment initiation, dose titration, changing medication, alsoin 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 maybe obtained in the detennination of total urine protein by dipsticktests, so it is advised to verify results or to use alternativemethods.
- 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
- Aswith other Antiepileptics, gabapentin should notbe abruptly discontinued because ofthe 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 andhyperactivity).

Drug interactions

- Gabapentin is not appreciably metabolized nor does it interfere with the metabolism of commonly coadministered antiepileptics such as carbamazepine, phenytoin, valproicacid, 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 antacidintake.
- 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 contentof lactose.
- Acute pancreatitis
- Not effective againstprimarily 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® 100mg capsules: Gabapentin 100mg (available in different pack sizes).
Nurona® 300mg capsules: Gabapentin 300mg (available in different pack sizes).
Nurona® 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 instructionsis dangerous for you.**
- **Follow strictly the doctor's proscription, method for use and the instructions of the pharmacist who sold themedicament .**
- **The doctor and the pharmacist are experts in medicine, its benefits and risks .**
- **Do not by yourselfinterrupt the period of treatment prescribed for you.**
- **Do not repeat the same prescription without consulting your doctor.**

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