SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE FINISHED PRODUCT

Neuran 300 mg Capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ACTIVE INGREDIENTS	PER TABLET (MG)
Gabapentin	300 mg

For excipients, see 6.1

3. PHARMACEUTICAL FORM

Capsule

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

- Epilepsy: Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 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.

4.2 Posology and Method of administration

For oral use. Gabapentin can be given with or without food. When in the judgement 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

Epilepsy typically requires long-term therapy. Dosage is determined by the treating physician according to individual tolerance and efficacy.

Adults and Pediatric Patients Over 12 Years of Age:

In clinical trials, the effective dosing range was 900 to 3600 mg/day. Therapy may be initiated by titrating the dose as described in Table 1 or by administering 300 mg three times a day (TID) on Day 1. Thereafter, based on individual patient response and tolerability, the dose can be further increased in 300 mg/day increments every 2-3 days up to a maximum dose of 3600 mg/day. Slower titration of gabapentin dosage may be appropriate for individual patients. The minimum time to reach a dose of 1800 mg/day is one week, to reach 2400 mg/day is a total of 2 weeks, and to reach 3600 mg/day is a total of 3 weeks. Dosages up to 4800 mg/day have been well tolerated in long-term open-label clinical

studies. 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.

Table 1 - DOSING CHART - INITIAL TITRATION		
Day 1	**Day 2**	**Day 3**
300 mg once a day	300 mg two times a day	300 mg three times a day

Pediatric Patients Aged 3-12 Years:
The starting dose should range from 10 to 15 mg/kg/day and the effective dose is reached by upward titration over a period of approximately three days. The effective dose of gabapentin in children aged 6 years and older is 25 to 35 mg/kg/day. Dosages up to 50 mg/kg/day have been well tolerated in a long-term clinical study. The total daily dose should be divided in three single doses, 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 medicinal products without concern for alteration of the plasma concentrations of gabapentin or serum concentrations of other antiepileptic.

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 three divided doses. Reduced dosages are for patients with renal impairment (creatinine clearance < 79 ml/min).
b. To be administered as 300 mg every other day.

Dosage Adjustments in Patients Undergoing Haemodialysis
For patients undergoing haemodialysis who have never received gabapentin, a loading dose of 300 to 400 mg, then 200 to 300 mg of gabapentin following each 4 hours of haemodialysis.

Note: The information given here is limited. For further information consult your doctor or pharmacist.

4.3 Contraindication

Gabapentin is contraindicated in patients who are hypersensitive to gabapentin or the product's components.

4.4 Special warnings and precautions for use

- General: Although there is no evidence of rebound seizures with gabapentin abrupt withdrawal of anticonvulsants in epileptic patients may precipitate status epilepticus.
- 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.
- Inform your physician about any prescription or nonprescription medications, alcohol, or drugs you are now taking or plan to take during your treatment with gabapentin.
- Gabapentin may impair your ability to drive a car or operate potentially dangerous machinery. Until it is known that this medication does not affect your ability to engage in these activities, do not drive a car or operate potentially dangerous machinery.
- Gabapentin has potential for an increase of suicidal thoughts or behaviours.

4.5 Interaction with other medicinal products and other forms of 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 anti-epileptic agents.
- Coadministration of gabapentin with oral contraceptives containing norethindrone and/or ethinyl estradiol, does not influence the steady-state pharmacokinetics of either component.
- Coadministration of gabapentin with antacids containing aluminium and magnesium, reduces gabapentin bioavailability up to 24%. It is recommended that gabapentin be taken at the earliest two hours following antacid administration.
- Renal excretion of gabapentin is unaltered by probenecid.
- A slight decrease in renal excretion of gabapentin that is observed when it is coadministered with cimetidine is not expected to be of clinical importance.

4.6 Pregnancy and lactation

Use During Pregnancy

- There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.
- You should inform your physician if you are pregnant, or if you are planning to become pregnant, or if you become pregnant while you are taking gabapentin.

Use During 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. You should inform your physician if you are breast feeding an infant.

- Gabapentin should be used in nursing mothers only if the benefits clearly out-weigh the risks.

4.7 Effects on ability to drive and use machines

Not Applicable

4.8 Undesirable Effects

- Adverse effects from gabapentin therapy are generally mild to moderate in severity, and tend to diminish with continued use.
- **Those indicating need for medical attention**

  Incidence more frequent: Alaxia (Clumsiness and unsteadiness) - may be dose-related; nystagmus (continuous, uncontrolled, back-and-forth and /or rolling eye movements).

  Incidence less frequent: Amnesia (loss of memory); depression, irritability, or other mood or mental changes.

  Incidence rare: Leukopenia (usually asymptomatic; rarely, fever or chills; cough or hoarseness; lower back or side pain; painful or difficult urination).
- **Those indicating need for medical attention only if they continue or are bothersome**

  Incidence more frequent: Dizziness; fatigue (unusual tiredness or weakness); myalgia (muscle ache or pain); peripheral edema (swelling of hands, feet, or lower legs); somnolence (drowsiness) - may be dose-related; tremor (trembling or shaking); vision abnormalities, including blurred vision and diplopia (double vision).

  Incidence less frequent or rare: Asthenia (weakness or loss of strength); back pain; dryness of mouth or throat; dysarthria (slurred speech); frequent urination; gastrointestinal effects, including constipation, diarrhea, dyspepsia (indigestion); nausea, and vomiting; headache; hypotension (low blood pressure); impotence (decrease in sexual desire or ability); insomnia (trouble in sleeping); rhinitis (runny nose); tinnitus (noise in ears); trouble in thinking; twitching; weight gain.

4.9 Overdose

Acute, life-threatening toxicity has not been observed with gabapentin overdoses of up to 49 grams. Symptoms of the overdoses included dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhoea. 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 haemodialysis, based on prior experience it is not usually required. However, in patients with severe renal impairment, haemodialysis may be indicated.

An oral lethal dose of gabapentin was not identified in mice and rats given doses as high as 8000 mg/kg. Signs of acute toxicity in animals included ataxia, laboured breathing, ptosis, hypoactivity, or excitation.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The mechanism of action is unknown. Gabapentin does not react with GABA receptors, is not metabolized to a GABA agonist or to GABA, and does not inhibit GABA uptake or degradation. In rats, gabapentin interacts with a novel binding site on cortical neurons that may be associated with the L-system amino acid transporter of brain cell membranes.

5.2 Pharmacokinetic properties

Absorption
Rapid. Gabapentin is absorbed in part by the L-amino acid transport system, which is a carrier-mediated, saturable transport system; as the dose increases, bioavailability decreases. Bioavailability ranges from approximately 60% for a 300mg dose to approximately 35% for a 1600mg dose. Absorption is unaffected by food.

Distribution
Volume of distribution (VolD) is approximately 50 to 60 L. Gabapentin penetrates the blood-brain barrier, yielding cerebrospinal fluid (CSF) concentrations approximately equal to 20% of corresponding steady-state plasma through concentrations in patients with epilepsy. Brain tissue concentrations in one patient undergoing temporal lobectomy were approximately 80% of corresponding plasma concentrations.

Protein Binding
Very low (< 5%)

Biotransformation
Gabapentin is not metabolized.

Elimination
Renal Entire absorbed dose, as unchanged drug. Gabapentin clearance is directly proportional to creatinine clearance. In dialysis Gabapentin can be removed from plasma by hemodialysis. The elimination half-life of Gabapentin is independent of dose and averages 5 to 7 hours.

5.3 Preclinical Safety Data

NOT APPLICABLE

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipeints

In-Active Constituents
Partial pregelatinized starch
Talc
Magnesium stearate

6.2 Incompatibilities

NOT APPLICABLE

6.3 Shelf life

3 years from date of manufacture

6.4 Special precaution for storage

Store below 30˚C. Protect from moisture.

6.5 Nature and contents of container

Blister Pack

Type	:	Push-through blister pack; the package consists of a transparent themoformable plastic material and a heat-sealable lacquered backing material.
Material	:	Thermoformable plastic material : Polyvinylidene Chloride (PVDC) Backing Material : Aluminium Foil

6.6 Special precautions for disposal and other handling

NOT APPLICABLE

7. MARKETING AUTHORISATION HOLDER ADDRESS

Name	:	HOVID Bhd.
Address	:	121, Jalan Tunku Abdul Rahman, (Jalan Kuala Kangsar) 30010 Ipoh, Perak, Malaysia

Manufacturer Name :

Name	:	HOVID Bhd.
Address	:	Lot 56442, 7 ½ Miles, Jalan Ipoh / Chemor, 31200 Chemor, Perak., Malaysia.

8. MARKETING AUTHORISATION NUMBER

HOV/MAL/022

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE AUTHORISATION

April 2018

10. DATE OF REVISION OF THE TEXT

February 2019