Volar®

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Gabapentin

DESCRIPTION:
Volar® contains gabapentin, a lipophilic analogue structurally related to GABA.
Inactive Ingredients: Maize starch, lactose monohydrate, talc.

PHARMACOLOGY:
Its' precise mechanism of action is not yet known. Gabapentin is not active at GABAA and GABAB receptors nor at GABA uptake carriers in the brain. Gabapentin binds with high affinity to binding sites in the brain which are associated with alpha2delta-subunits of voltage sensitive calcium channels. In vitro, gabapentin modulates the activity of the GABA synthesizing enzyme GAD as the well as the activity of the glutamate synthesizing enzyme. NMR investigations revealed that gabapentin increases GABA synthesis in rat and human brain. The release of various monoamine neurotransmitters is being reduced. In various animals' models, gabapentin showed anticonvulsive, analgesic, anxiolytic and neuroprotective properties.
Mean c-max plasma gabapentin concentrations occurred approximately 3 hours (t-max) following single oral doses of gabapentin regardless of dose size or formulation. Mean t-max values following multiple dose administration were approximately 1 hour shorter than values following single dose administration.
Mean c-max and AUC values increased with increasing dose; however, the increase was less than dose proportional. Plasma gabapentin concentrations found in children are similar to those in adults. Following repeated, three times daily gabapentin administration, steady-state was achieved within 1 to 2 days and was maintained throughout the dosing regime.

INDICATIONS:
Volar® is indicated for the treatment of the following cases:
- Epilepsy: Monotherapy (including treatment of patients with newly diagnosed seizures) 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: For the treatment of neuropathic pain in adults.

CONTRAINDICATIONS:
Volar® is contraindicated in patients with known hypersensitivity to the product or any of its ingredients, in patients with acute pancreatitis, in patients with galactosemia (galactose intolerance) due to their lactose content, and it is not effective against primarily generalized seizures, such as absences.
Notes: No systemic studies in patients 65 years or older have been conducted with gabapentin. However, clinical investigations in this age group do not indicate an adverse event profile different from that observed in younger patients.
Epilepsy: There is not yet sufficient experience for monotherapy with gabapentin in children below 12 years of age nor as add-on therapy in children below 3 years of age.

SIDE EFFECTS:
The most frequent adverse effects are: Somnolence, fatigue, dizziness, headache, nausea, vomiting, weight increase, nervousness, insomnia, unsteady gait (ataxia), ocular tremors (nystagmus), unpleasant sensations, such as tickling (paresthesias) and loss of appetite (anorexia).
The following occur frequently (1 to <10%): Feeling of weakness, visual disturbances (amblyopia, dilopia), trembling of the hands (tremor), twitching, arthralgia, pain, increased, decreased or absent reflexes, diarrhea, slurred speech (dysarthria), thinking abnormal, loss of memory (amnesia), dry mouth, depression, confusion and emotional lability.
Rarely (0.01 to <0.1%): Thrombopenia, palpitations, tinnitus, pancreatitis, side effects upon abrupt discontinuation of therapy (in most cases anxiety, insomnia, nausea, pain, sweating, chest pain), allergic reactions (e.g urticaria), increased hepatic values, motility disorders (e.g choreoathetosis, dyskinesia, dystonia), hallucinations, alopecia, angioedema, acute renal failure, urinary incontinence.
The following adverse effects also occurred frequently (1 to <10%) during clinical trials: impaired digestion (dyspepsia), constipation, abdominal pain, urinary incontinence, increased appetite, runny nose (rhinitis), throat inflammation (pharyngitis), coughing, muscle pain (myalgia), back pain, edema in face, extremities or the whole body, impotence, dental abnormalities, inflammation of the gums, itching (pruritus), reduction in white blood cells (leucopenia), fractures, vasodilatation and hypertension, dry throat, fever, acne, rash, flatulence, hypesthesia and dyspnea. In addition, aggressive behaviour, respiratory tract infections, bronchitis, and excessive, partly uncontrolled movements (hyperkinesia) have been frequently (1 to <10%) observed in clinicals trials in children from 3 to 12 years of age.
The occurrence of hemorrhagic pancreatitis has been reported under treatment with gabapentin.
Allergic reactions (Stevens-Johnson syndrome and erythema multiforme) have been reported in single cases under treatment with gabapentin.
Elevated liver function tests have been reported in combination with other antiepileptic drugs.

WARNINGS AND PRECAUTIONS:
- For patients with impaired renal function, the gabapentin dosage must be reduced.
- Hemorrhagic pancreatitis has been reported under treatment with gabapentin. For this reason, treatment with gabapentin must be stopped at the first sign of clinical symptoms of pancreatitis (persistent upper abdominal complaints, nausea and recurrent vomiting). In addition to thorough clinical examination, appropriate laboratory tests should also be performed for early recognition of pancreatitis.
- Experience with the use of gabapentin in chronic pancreatitis is not adequate. The treating physician must decide in such cases whether treatment with **Volar®** should be continued or withdrawn.
- This product contains:
  Lactose monohydrate: If the patient has been told by the doctor that he has intolerance to some sugars, he should contact his doctor before taking this medicinal product.
- Pregnancy and lactation: **Volar®** should be taken during pregnancy only after careful benefit-risk assessment, since no experience has been made with the safety of use during pregnancy. Gabapentin is excreted in human milk. Since it cannot be ruled out that gabapentin may cause side effects in the infant, gabapentin treatment of the mother should only be continued if the benefits clearly outweigh the risks.
- Effects on ability to drive and use of machines: Gabapentin acts on the CNS and may cause individually sedation, dizziness or other signs of CNS depression. Therefore, **Volar®** even if administered as prescribed-may slow down reactions to such a degree that the capability to drive a car, to operate complex machinery or to work in exposed places is impaired. This applies particularly at the start of treatment, if the dose is increased, or if the medication is changed as well as in conjunction with alcohol.
- Drug/laboratory test interactions: False positive readings may be obtained in the semi-quantitative determination of total urine protein by dipstick tests. It is therefore recommended to verify such a positive dipstick test result by methods based on a different analytical principle such the Biuret method, turbidimetric or dye-binding methods- or to use these alternative methods from the beginning.

DRUG INTERACTIONS:
- Pharmacokinetic interaction studies have been performed on interactions between gabapentin and phenytoin, valproic acid, carbamazepine, or phenobarbital. During the clinical trails, no significant changes in plasma concentration levels of these drugs were observed after additional administration of gabapentin to patients receiving these antiepileptic drugs as standard therapy.
- Gabapentin does not influence the effect of oral contraceptives containing norethisterone and/or ethinylestradiol. However, in combination with other antiepileptics known to disrupt the effect of oral contraceptives, failure of the contraceptive effect must be expected.
- Concurrent administration of **Volar®** with magnesium or aluminium containing antacids may reduce the bioavailability of gabapentin by up to 24%. **Volar®** Should not be administered earlier than at least 2 hours after the antacid intake.
- The renal elimination of gabapentin is slightly decreased when coadministered with cimetidine.
- Alcohol or centrally acting drugs of abuse may exaggerate some gabapentin CNS side effects (e.g. somnolence and ataxia).

DOSAGE AND ADMINISTRATION:
Volar® capsules should be swallowed whole with suffuicient fluid intake. Administration may be made during or between meals. In three-time daily administration, care should be taken that the interval between two single doses does not exceed 12 hours. Whether a missed dose of **Volar®** (this means more than 12 hours passed since the last administration) should be made up for by taking an additional dose of **Volar®** later or not is at the physician's discretion. In concurrent treatment with magnesium or aluminum containing antacids, **Volar®** should be taken at least 2 hours after administration of the antacid. This largely avoids a reduction in gabapentin bioavailability. The duration of administration depends on the clinical requirements. In the treatment of epilepsy, usually, long-term therapy is required. If therapy with **Volar®** capsules should be discontinued, the dose is reduced, or switched to another drug, this should be done gradually over a minimum of one week, although there is no evidence of a rebound phenomenon (increased occurrence of epileptic seizures following abrupt withdrawal of therapy). In the treatment of neuropathic pain, efficacy and safety has not been examined in clinical studies for treatment periods longer than 5 months.

- Epilepsy

Monotherapy and add-on therapy in patients over 12 years of age
Initial and maintenance dose: Treatment with **Volar®** is started with 300 mg capsules. The dose may be titrated gradually within the first 3 days of treatment to 900 mg gabapentin/day according to the following dose scheme:

	Morning	Noon	Evening
Day 1 (300 mg gabapentin/day)	---	---	1 **Volar®** 300 mg capsule
Day 2 (600 mg gabapentin/day)	1 **Volar®** 300 mg capsule	---	1 **Volar®** 300 mg capsule
Day 3 (900 mg gabapentin/day)	1 **Volar®** 300 mg capsule	1 **Volar®** 300 mg capsule	1 **Volar®** 300 mg capsule

Alternatively, starting with Day 1, three times daily 1 **Volar®** 300 mg capsule can be administered (corresponding to 900 mg gabapentin/day). Then the daily dose may be increased within a week to 1800 mg gabapentin, thereafter to maximally 3600 mg gabapentin, if necessary. The total daily dose may not exceed 3600 mg gabapentin. Total daily dosages up to 4800 mg/day have been well tolerated in long-term open-label clinical studies. The total daily dose should be divided into three equal single doses.
Add-on therapy in children between 3 and 12 years of age
Initial and maintenance dose: For the add-on-therapy in children aged 3 to 12 years, lower strengths with 300 mg (**Volar®** 300 mg capsules) and 400 mg (**Volar®** 400 mg capsules) gabapentin are available. A stepwise titration to a maintenance dose of 30 mg gabapentin/kg BW/day takes place over the first 3 days of treatment.
On Day 1, the dose is 10 mg gabapentin/kg BW, on Day 2, 20 mg gabapentin/kg BW, and on Day 3, the dose is 30 mg gabapentin/kg BW. Thereafter, the dose may be increased to maximally 35 mg gabapentin/kg BW/day, if required (See Tables Below). Total dosages up to 40-50 mg/Kg BW per day have been well tolerated in a clinical long-term study.

- Dosage of gabapentin in pediatric patients age 3-12 years:

Body weight of child (kg)	Dosage (mg/day)
17-25	600
26-36	900
37-50	1200
51-72	1800

- Pediatric dosing chart:

Body weight of child (kg)	Dosage/day 1	Dosage/day 2	Dosage/day 3
17-25	200 mg	400 mg	600 mg
26-36	300 mg	600 mg	900 mg

The total daily dose should be divided into three equal single doses. The time between two consecutive doses should not exceed 12 hours.

- Neuropathic pain

Initial and maintenance dose
On the first 3 days of treatment, step-wise dose increase may be made to 900 mg gabapentin/day according to the following dosing scheme:

	Morning	Noon	Evening
Day 1 (300 mg gabapentin/day)	---	---	1 **Volar®** 300 mg capsule
Day 2 (600 mg gabapentin/day)	1 **Volar®** 300 mg capsule	---	1 **Volar®** 300 mg capsule
Day 3 (900 mg gabapentin/day)	1 **Volar®** 300 mg capsule	1 **Volar®** 300 mg capsule	1 **Volar®** 300 mg capsule

As an alternative, if the pain intensity requires, 3x daily 1 **Volar®** 300 mg capsule (corresponding to 900 mg gabapentin/day) may be taken starting on Day 1. Then the daily dose may be increased within a week to 1800 mg gabapentin, thereafter to maximally 3600 mg gabapentin, if necessary. The total daily dose may not exceed 3600 mg gabapentin. The total daily dose should be divided into three equal single doses.
Note for all indications: For patients with impaired renal function (creatinine clearance less than 80 ml/min), and patients undergoing hemodialysis, the dosage should be adjusted according to the below table. In these patients, **Volar®** should be administered in capsule form (300 mg or 400 mg):

- Dosage in reduced renal function

Renal function Creatinine clearance (ml/min)	Gabapentin total daily dose* (range in mg/day)
≥ 80	900 - 3600 mg
50 – 79	600 – 1800 mg
30 – 49	300 – 900 mg
15 – 29	150** - 600 mg
< 15	150** - 300 mg

* divided into three single doses daily.
** 300 mg gabapentin every other day.

- Dosage in hemodialysis

For patients undergoing hemodialysis who have never received **Volar®**, a loading dose of 300 mg to 400 mg gabapentin is recommended, then 300 mg gabapentin following each 4 hours of hemodialysis. On dialysis-free days there should be no treatment with **Volar®**.

OVERDOSAGE:
Symptoms of overdoses included dizziness, diplopia, dysarthria, sedation, and mild diarrhea. Acute, life- threatening to icity has not been observed with gabapentin overdoses of up to 49 g per day. Gabapentin can be removed from the circulating blood by means of hemodialysis. Experience has shown that this is not usually necessary. Hemodialysis may be indicated in patients with impaired renal function.

PRESENTATIONS:
Volar® 300 Capsules: Packs of 30 capsules. Each capsule contains 300 mg Gabapentin.
Volar® 400 Capsules: Packs of 30 capsules. Each capsule contains 400 mg Gabapentin.

STORAGE CONDITIONS:
Store below 30°C.

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

Keep medicament out of reach of children

Manufactured by Dar Al Dawa, Na'ur - Jordan

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