Nervax®

Pregabalin Capsules

Composition:

Nervax 75 mg: Each capsule contains: Pregabalin 75 mg.
Nervax 150 mg: Each capsule contains: Pregabalin 150 mg.
Nervax 300 mg: Each capsule contains: Pregabalin 300 mg.
Excipients: Mannitol, sodium starch glycolate, talc and colloidal silicon dioxide.

Properties:

Absorption: Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentrations occurring within 1 hour following both single and multiple dose administration. Pregabalin oral bioavailability is estimated to be ≥90 % and is independent of dose. Following repeated administration, steady state is achieved within 24 to 48 hours. The rate of pregabalin absorption is decreased when given with food resulting in a decrease in C_{max} by approximately 25-30 % and a delay in t_{max} to approximately 2.5 hours. However, administration of pregabalin with food has no clinically significant effect on the extent of pregabalin absorption.
Distribution: The apparent volume of distribution of pregabalin following oral administration is approximately 0.56 l/kg. Pregabalin is not bound to plasma proteins.
Elimination: Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Pregabalin mean elimination half-life is 6.3 hours. Pregabalin plasma clearance and renal clearance are directly proportional to creatinine clearance.
Dosage adjustment in patients with reduced renal function or undergoing haemodialysis is necessary.

Indications:

Neuropathic pain:
Nervax is indicated for the treatment of peripheral and central neuropathic pain in adults.
Epilepsy:
Nervax is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization.
Generalised Anxiety Disorder:
Nervax is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.

Contraindications:

Nervax is contraindicated for patients with known hypersensitivity to any of its components.

Precautions and warnings:

Nervax treatment may cause weight gain.
Some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycaemic medicinal products.
There have been reports in the post-marketing experience of hypersensitivity reactions, including cases of angioedema. Pregabalin should be discontinued immediately if symptoms of angioedema, such as facial, perioral, or upper airway swelling occur.
Nervax may cause dizziness and somnolence and impair patients ability to drive or operate machinery.
In the post-marketing experience, visual adverse reactions have also been reported, including loss of vision, visual blurring or other changes of visual acuity, many of which were transient. Discontinuation of pregabalin may result in resolution or improvement of these visual symptoms.
Cases of renal failure have been reported and in some cases discontinuation of pregabalin did show reversibility of this adverse reaction.
There are insufficient data for the withdrawal of concomitant antiepileptic medicinal products, once seizure control with pregabalin in the add-on situation has been reached, in order to reach monotherapy on pregabalin.
After discontinuation of short-term and long-term treatment with pregabalin withdrawal symptoms have been observed in some patients. The following events have been mentioned: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, pain, convulsion, hyperhidrosis and dizziness. The patient should be informed about this at the start of the treatment.
Convulsions, including status epilepticus and grand mal convulsions, may occur during pregabalin use or shortly after discontinuing pregabalin.
Increased seizure frequency may occur in patients with seizure disorders if **Nervax** is rapidly discontinued. Withdraw **Nervax** gradually over a minimum of 1 week.
There have been post-marketing reports of congestive heart failure in some patients receiving pregabalin. These reactions are mostly seen in elderly cardiovascular compromised patients during pregabalin treatment for a neuropathic indication. Pregabalin should be used with caution in these patients. Discontinuation of pregabalin may resolve the reaction.
In the treatment of central neuropathic pain due to spinal cord injury the incidence of adverse reactions in general, central nervous system adverse reactions and especially somnolence was increased. This may be attributed to an additive effect due to concomitant medicinal products (e.g. anti-spasticity agents) needed for this condition. This should be considered when prescribing pregabalin in this condition.
Antiepileptic drugs, including **Nervax**, increase the risk of suicidal thoughts or behavior .
There are post-marketing reports of events related to reduced lower gastrointestinal tract function (e.g., intestinal obstruction, paralytic ileus, constipation) when pregabalin was co-administered with medications that have the potential to produce constipation, such as opioid analgesics. When pregabalin and opioids will be used in combination, measures to prevent constipation may be considered (especially in female patients and elderly).
Cases of abuse and encephalopathy have been reported

Pregnancy and Lactation:

There are no adequate data on the use of pregabalin in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk to humans is unknown. Therefore, **Nervax** should not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. Effective contraception must be used in women of child bearing potential.
It is not known if pregabalin is excreted in the breast milk of humans; however, it is present in the milk of rats. Therefore, breast-feeding is not recommended during treatment with pregabalin.

Interactions with other drugs:

In vivo studies no clinically relevant pharmacokinetic interactions were observed between pregabalin and phenytoin, carbamazepine, valproic acid, lamotrigine, gabapentin, lorazepam, oxycodone or ethanol. Population pharmacokinetic analysis indicated that oral antidiabetics, diuretics, insulin, phenobarbital, tiagabine and topiramate had no clinically significant effect on pregabalin clearance.
Co-administration of pregabalin with the oral contraceptives norethisterone and/or ethinyl oestradiol does not influence the steady-state pharmacokinetics of either substance.

Dosage and administration:

The dose range is 150 to 600 mg per day given in either two or three divided doses. **Nervax** may be taken with or without food.
Neuropathic pain
Pregabalin treatment can be started at a dose of 150 mg per day. Based on individual patient response and tolerability, the dosage may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval.
Epilepsy
Pregabalin treatment can be started with a dose of 150 mg per day. Based on individual patient response and tolerability, the dosage may be increased to 300 mg per day after 1 week. The maximum dosage of 600 mg per day may be achieved after an additional week.
Generalised Anxiety Disorder
The dose range is 150 to 600 mg per day given as two or three divided doses. The need for treatment should be reassessed regularly.
Discontinuation of pregabalin
In accordance with current clinical practice, if pregabalin has to be discontinued either in neuropathic pain or epilepsy, it is recommended this should be done gradually over a minimum of 1 week.
Patients with renal impairment
As pregabalin clearance is directly proportional to creatinine clearance, dosage reduction in patients with compromised renal function must be individualised according to creatinine clearance (CL_{cr}).
Pregabalin is removed effectively from plasma by haemodialysis (50 % of drug in 4 hours). For patients receiving haemodialysis, the pregabalin

daily dose should be adjusted based on renal function. In addition to the daily dose, a supplementary dose should be given immediately following every 4-hour haemodialysis treatment.

Creatinine Clearance (CL_{cr}) (ml/min)	Total Pregabalin Daily dose *		Dose Regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
≥60	150	600	BID or TID
≥30 - <60	75	300	BID or TID
≥15 - <30	25-50	150	QD or BID
<15	25	75	QD
Supplementary dosage following haemodialysis (mg)			
	25	100	Single dose +

TID = Three divided doses
BID = Two divided doses
QD = Single daily dose
* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose
+ Supplementary dose is a single additional dose

Use in patients with hepatic impairment
No dosage adjustment is required for patients with hepatic impairment.
Use in children and adolescents (12 to 17 years of age)
The safety and effectiveness of pregabalin in pediatric patients below the age of 12 years and adolescents has not been established.
The use in children is not recommended.
Use in the elderly (over 65 years of age)
Elderly patients may require a dose reduction of pregabalin due to a decreased renal function.

Overdosage:
In overdoses up to 15 g, no unexpected adverse reactions were reported. Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary.

Side Effects:
The most commonly reported adverse reactions were dizziness and somnolence. Adverse reactions were usually mild to moderate in intensity. In all controlled studies, the discontinuation rate due to adverse reactions was 13 % for patients receiving pregabalin and 7 % for patients receiving placebo. The most common adverse reactions resulting in discontinuation from pregabalin treatment groups were dizziness and somnolence.
Mentioned below all the side effects listed by class and frequency
(Very common >1/10, common > 1/100, < 1/10) , rare <1/100)
Blood and lymphatic system disorders
Rare, Neutropenia.
Metabolism and nutrition disorders
Common: Appetite increased, Uncommon: Anorexia, Rare: Hypoglycaemia
Psychiatric disorders
Common: Euphoric mood, confusion, libido decreased, irritability, Uncommon: Depersonalisation, anorgasmia, restlessness, depression, agitation, mood swings, insomnia exacerbated, depressed mood, word finding difficulty, hallucination, abnormal dreams, libido increased, panic attack, apathy, Rare: Disinhibition, elevated mood
Nervous system disorders
Very Common: Dizziness, somnolence, Common: Ataxia, disturbance in attention, coordination abnormal, memory impairment, tremor, dysarthria, paraesthesia, Uncommon: Cognitive disorder, hypoaesthesia,visual field defect, nystagmus, speech disorder, myoclonus, hyporeflexia, dyskinesia, psychomotor hyperactivity, dizziness postural, hyperaesthesia, ageusia, burning sensation, intention tremor, stupor, syncope.
Rare: Hypokinesia,parosmia,dysgraphia
Eye disorders
Common: Vision blurred, diplopia, Uncommon: Visual disturbance, dry eye, eye swelling, visual acuity reduced, eye pain, asthenopia, lacrimation increased, Rare: Photopsia, eye irritation, mydriasis, oscillopsia, altered visual depth perception, peripheral vision loss, strabismus, visual brightness
Ear and labyrinth disorders
Common: Vertigo, Rare: Hyperacusis
Cardiac disorders
Uncommon: Tachycardia, Rare: Atrioventricular block first degree, sinus tachycardia, sinus arrhythmia, sinus bradycardia.
Vascular disorders
Uncommon: Flushing, hot flushes, Rare: Hypotension, peripheral coldness, hypertension
Respiratory ,thoracic and mediastinal disorders
Uncommon: Dyspnoea, nasal dryness. Rare: Nasopharyngitis, cough, nasal congestion, epistaxis, rhinitis, snoring, throat tightness
Gastrointestinal disorders
Common: Dry mouth, constipation, vomiting, flatulence, Uncommon: Abdominal distension, salivary hypersecretion, gastrooesophageal reflux disease, hypoaesthesia oral. Rare: Ascites, dysphagia, pancreatitis.
Skin and subcutaneous tissue disorders
Uncommon: Sweating, rash popular, Rare: Cold sweat, urticaria
Musculoskeletal and connective tissue disorders
Uncommon: Muscle twitching, joint swelling, muscle cramp, myalgia, arthralgia, back pain, pain in limb, muscle stiffness,
Rare: Cervical spasm, neck pain, rhabdomyolysis.
Renal and urinary disorders
Uncommon: Dysuria, urinary incontinence, Rare: Oliguria, renal failure
Reproductive system and breast disorders
Common: Erectile dysfunction, Uncommon: Ejaculation delayed, sexual dysfunction, Rare: Amenorrhoea, breast pain, breast discharge, dysmenorrhoea, hypertrophy breast.
General disorders and administration site conditions
Common : Fatigue, oedema peripheral, feeling drunk, oedema, gait abnormal, Uncommon: Asthenia, fall, thirst, chest tightness,
Rare: Pain exacerbated anasarca, pyrexia, rigors.
Investigations
Common: Weight increased, Uncommon: Alanine aminotransferase increased, blood creatine phosphokinase increased, aspartate aminotransferase increased, platelet count decreased, Rare: Blood glucose increased, blood creatinine increased, blood potassium decreased, weight decreased, white blood cell count decreased.
Consult your Pharmacist or Physician if any side effect is observed.

Pharmaceutical Precautions:
Keep at room temperature (15-30°C).
Do not use beyond the expiry date or if the product shows any sign of deterioration.

Presentations:
Nervax 75 mg: Pack of 20 capsules.
Nervax 150 mg: Pack of 60 capsules.
Nervax 300 mg: Pack of 60 capsules.
Hospital packs are available.

THIS IS A MEDICAMENT
- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Strictly follow the doctor's prescription, the method of use and the instruction 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.

Keep medicament out of reach of children.

Council of Arab Health Ministers & Union of Arab Pharmacists.

Manufactured by:
TABUK PHARMACEUTICAL MANUFACTURING CO.,
P.O. Box 3633, Tabuk-Saudi Arabia.

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