

Paper 35-45 gsm  
Carton size: 90 x 30 x 145 mm

Front side

Size: 320 (L) x 480 (H) mm  
Final folding size: 30 x 170 mm  
Drg. No.: W0990002999Z-000



## PREGABALIN + METHYLCOBALAMIN (VITAMIN B<sub>12</sub>)

### NEURICA-M 75/150

75 mg / 750 mcg Capsule  
150 mg / 750 mcg Capsule

ANTIEPILEPTICS

#### PRODUCT NAME:

Neurica-M 75/150

#### DOSAGE FORM AND STRENGTH:

Pregabalin 75/150 mg and Methylcobalamin 750 mcg

#### PHARMACOLOGIC CATEGORY:

Antiepileptics

#### PRODUCT DESCRIPTION:

Capsules

Neurica-M 75: Red/White Colored "2" size hard gelatin capsule containing light pink colored powder

Neurica-M 150: Blue/Light Blue Colored "2" size hard gelatin capsule containing light pink colored powder

#### FORMULATION/COMPOSITION:

Neurica-M 75:

Each capsule contains:

Pregabalin .....75 mg  
Methylcobalamin JP....750 mcg

Neurica-M 150:

Each capsule contains:

Pregabalin .....150 mg  
Methylcobalamin JP....750 mcg

#### PHARMACODYNAMICS/PHARMACOKINETICS:

##### Pregabalin

Pregabalin is a structural derivative of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). Pregabalin does not bind directly to GABA<sub>A</sub>, GABA<sub>B</sub>, or benzodiazepine receptors, does not augment GABA<sub>A</sub> responses in cultured neurons, does not alter rat brain GABA concentration or have acute effects on GABA uptake or degradation. However, in cultured neurons, prolonged application of pregabalin increases the density of GABA transporter protein and increases the rate of functional GABA transport.

Pregabalin binds with high affinity to the alpha<sub>1</sub>-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues. Although the mechanism of action of pregabalin is unknown, results with genetically modified mice and with compounds structurally related to pregabalin (such as gabapentin) suggest that binding to the alpha<sub>1</sub>-delta subunit may be involved in pregabalin's anticonvulsive and antiseizure effects in animal models. *In vitro*, pregabalin reduces the calcium dependent release of several neurotransmitters, possibly by modulation of calcium channel function.

Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or norepinephrine reuptake.

##### Methylcobalamin

Methylcobalamin (Mecobalamin, MeCbl), is one of the two biologically active vitamin B12. Mecobalamin acts as an important cofactor in the reaction of one class of the B12 enzymes, the methyltransferases. The B12-dependent methyltransferases play an important role in amino acid metabolism in many organisms as well as in one-carbon metabolism and CO<sub>2</sub> fixation in anaerobic microbes. Among them, methionine synthase is the most extensively studied B12-dependent methyltransferase in humans. As the cofactor of the enzyme methionine synthase, mecobalamin functions to catalyse the transfer of the methyl group from methylene tetrahydrofolate to homocysteine (Hcy) to form methionine and tetrahydrofolate.

Because mecobalamin acts as an important cofactor of methionine synthesis, supplements of mecobalamin enhance the efficiency of the remethylation pathway, consequently accelerating Hcy consumption and reducing its concentration. Thus, lowering homocysteine concentrations to the normal range (4–15 μmol/l) seems to be an effective therapeutic method in decreasing the risks of the diseases mentioned above.

In an animal study, intragastric administration of mecobalamin was also found to improve the arterial baroreflex function, which is a new target for the prevention of stroke in stroke-prone, spontaneously hypertensive rats. It was also postulated that the reduction of homocysteine concentration might contribute to the baroreflex sensitivity, thus improving the effect of mecobalamin.

Deficiency of vitamin B12 results in the lack of mecobalamin and has been associated with significant neurological pathology, especially peripheral neuropathy. In an *in vitro* study, chronic administration of mecobalamin protected cultured retinal neurons against NMDA-receptor-mediated glutamate neurotoxicity, probably by altering the membrane properties through SAM-mediated methylation. It was also suggested that altered membrane properties induced by SAM-mediated methylation is the major route of the neuroprotective effect of mecobalamin in several types of CNS insults.

##### Pharmacokinetics:

##### Pregabalin

Pregabalin is well absorbed after oral administration, is eliminated largely by renal excretion and has an elimination half-life of about 6 hours.

##### Absorption

Following oral administration of pregabalin capsules under fasting conditions, peak plasma concentrations occur within 1.5 hours. Pregabalin oral bioavailability is ≥ 90% and is independent of dose. Following single - (25 to 300 mg) and multiple- dose (75 to 900 mg/day) administration, maximum plasma concentrations (C<sub>max</sub>) and area under the plasma concentration-time curve (AUC) values increase linearly. 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<sub>max</sub> of approximately 25% to 30% and an increase in T<sub>max</sub> to approximately 3 hours. However, administration of pregabalin with food has no clinically relevant effect on the total absorption of pregabalin. Therefore, pregabalin can be taken with or without food.

##### Distribution

Pregabalin does not bind to plasma proteins. The apparent volume of distribution of pregabalin following oral administration is approximately 0.5 L/kg. Pregabalin is a substrate for system L transporter which is responsible for the transport of large amino acids across the blood brain barrier. Although there are no data in humans, pregabalin has been shown to cross the blood brain barrier in mice, rats, and monkeys.

##### Metabolism

Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 90% of the administered dose was recovered in the urine as unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of the dose. In preclinical studies, pregabalin (S-enantiomer) did not undergo racemization to the R-enantiomer in mice, rats, rabbits, or monkeys.

##### Excretion

Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half-life of 6.3 hours in subjects with normal renal function. Mean renal clearance was estimated to be 67.0 to 80.9 mL/min in young healthy subjects. Because pregabalin is not bound to plasma proteins this clearance rate indicates that renal tubular reabsorption is involved. Pregabalin elimination is nearly proportional to creatinine clearance (CLcr).

##### Special populations

##### Geriatrics

Pregabalin oral clearance tended to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with age-related decreases in CLcr. Reduction of pregabalin dose may be required in patients who have age-related compromised renal function.

##### Gender

Population pharmacokinetic analyses of the clinical studies showed that the relationship between daily dose and pregabalin drug exposure is similar between genders.

##### Renal impairment and haemodialysis

Pregabalin clearance is nearly proportional to creatinine clearance (CLcr). Dosage reduction in patients with renal dysfunction is necessary. Pregabalin is effectively removed from plasma by haemodialysis. Following a 4-hour haemodialysis treatment, plasma pregabalin concentrations are reduced by approximately 50%. For patients on haemodialysis, dosing must be modified.

##### Paediatric Pharmacokinetics

Pharmacokinetics of pregabalin has not been adequately studied in paediatric patients.

##### Methylcobalamin

##### Absorption

Evidence indicates methylcobalamin is utilized more efficiently than cyanocobalamin to increase levels of one of the coenzyme forms of vitamin B12. Experiments have demonstrated similar absorption of methylcobalamin following oral administration. The quantity of cobalamin detected following a small oral dose of mecobalamin is similar to the amount detected following the administration of cyanocobalamin, but significantly more cobalamin accumulates in liver tissue, which is associated with mecobalamin intake.

##### Distribution and Metabolism

Cobalamin circulates in plasma bound to two carrier proteins: transcobalamin (TC) and haptocorrin. TC is a 43-kDa non-glycoprotein that transfers cobalamin from the intestine into the blood stream and then into all the cells of the body. Cobalamin-saturated transcobalamin (holoTC) constitutes 6–20% of total plasma cobalamin. The unsaturated TC is called apotranscobalamin, which constitutes the major part of TC. Additionally, total homocysteine (tHcy) and methylmalonic acid are considered to be two functional markers of vitamin B12 status in adults.

##### Excretion

Human urinary excretion of methylcobalamin is about one third of that of a similar dose of cyanocobalamin, indicating substantially greater tissue retention.

##### INDICATIONS:

Pregabalin and Methylcobalamin Capsules are indicated for the treatment of peripheral neuropathic pain in adults.

#### DOSAGE AND MODE ROUTE OF ADMINISTRATION:

Pregabalin and Methylcobalamin Capsules is given orally with or without food.

The dose range for pregabalin is 150 to 300 mg per day given in two or three divided doses. The dosage range for methylcobalamin for clinical effectiveness is 0.5–6 mg/day, and no significant therapeutic advantage is observed beyond this range. However, the most commonly used dose was 0.5–1.5 mg/day administered orally.

Pregabalin and Methylcobalamin Capsules treatment can be started at a dose of two capsules b.i.d. Based on individual patient response and tolerability, the dosage may be increased to 4 capsules in two divided doses after an interval of 3 to 7 days.

##### Discontinuation of pregabalin

If Pregabalin and Methylcobalamin capsules has to be discontinued, it is recommended this should be done gradually over a minimum of 1 week.

##### Patients with renal impairment

In view of dose-dependent adverse events and since pregabalin is eliminated primarily by renal excretion, the dose should be adjusted in patients with reduced renal function. Dosage adjustment in patients with renal impairment should be based on creatinine clearance (CLcr), as indicated in Table 1, determined by the following formula:

$$CL_{Cr} (\text{ml/min}) = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dL)}} \times (0.85 \text{ for female patients})$$

Table 1: Pregabalin Dosage Adjustment Based on Renal Function

Creatinine Clearance (CLcr) (mL/min)	Total Pregabalin Daily Dose (mg/day)*				Dose Regimen
≥ 60	150	300	450	600	BID or TID
30-60	75	150	225	300	BID or TID
15-30	25-50	75	100-150	150	QD or BID
<15	25	25-50	50-75	75	QD

##### Supplementary dosage following hemodialysis (mg)

Patients on the 25 mg QD regimen: take one supplemental dose of 25 mg or 50 mg  
Patients on the 25–50 mg QD regimen: take one supplemental dose of 50 mg or 75 mg  
Patients on the 50–75 mg QD regimen: take one supplemental dose of 75 mg or 100 mg  
Patients on the 75 mg QD regimen: take one supplemental dose of 100 mg or 150 mg

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.

For patients undergoing hemodialysis, pregabalin daily dose should be adjusted based on renal function. In addition to the daily dose adjustment, a supplemental dose should be given immediately following every 4-hour hemodialysis treatment as mentioned in Table 1.

#### CONTRAINDICATIONS & PRECAUTION(S), WARNING(S):

Pregabalin and Methylcobalamin Capsules is contraindicated in patients who are hypersensitive to pregabalin or Methylcobalamin or any of the components of this product.

#### PRECAUTIONS & WARNINGS:

##### Pregabalin

##### General

##### Angioedema

There have been postmarketing reports of angioedema in patients during initial and chronic treatment with pregabalin. Specific symptoms included swelling of the face, mouth (tongue, lips, and gums), and neck (throat and larynx). There were reports of life-threatening angioedema with respiratory compromise requiring emergency treatment. Pregabalin should be discontinued immediately in patients with these symptoms.

Caution should be exercised when prescribing pregabalin to patients who have had a previous episode of angioedema. In addition, patients who are taking other drugs associated with angioedema (e.g., angiotensin converting enzyme inhibitors) may be at increased risk of developing angioedema.

##### Hypersensitivity

There have been postmarketing reports of hypersensitivity in patients shortly after initiation of treatment with pregabalin. Undesirable effects include skin redness, blisters, hives, rash, dyspnea, and wheezing. Pregabalin should be discontinued immediately in patients with these symptoms.

##### Suicidal behavior and ideation

Antiepileptic drugs (AEDs), including pregabalin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Anytime considering prescribing pregabalin or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

##### Tumorigenic Potential

In standard preclinical *in vivo* lifetime carcinogenicity studies of pregabalin, an unexpectedly high incidence of hemangiosarcoma was identified in two different strains of mice. The clinical significance of this finding is unknown. Clinical experience during pregabalin's premarketing development provides no direct means to assess its potential for inducing tumors in humans.

In clinical studies across various patient populations, comprising 6396 patient-years of exposure in patients >12 years of age, new or worsening-preexisting tumors were reported in 57 patients. Without knowledge of the background incidence and recurrence in similar populations not treated with pregabalin, it is impossible to know whether the incidence seen in these cohorts is or is not affected by treatment.

##### Treatment of central neuropathic pain due to spinal cord injury

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.

##### Dizziness and Somnolence

320 mm

170 mm

150 mm

**Oxycodone**  
Multiple-dose administration of pregabalin (300 mg twice a day) in healthy subjects had no effect on the rate and extent of oxycodone single-dose pharmacokinetics. Single-dose administration of oxycodone (10 mg) had no effect on the steady-state pharmacokinetics of pregabalin.

**Ethanol**  
Multiple-dose administration of pregabalin (300 mg twice a day) in healthy subjects had no effect on the rate and extent of ethanol single-dose pharmacokinetics and single-dose administration of ethanol (0.7 g/kg) had no effect on the steady-state pharmacokinetics of pregabalin.

**Antiepileptic Drugs**  
Steady-state trough plasma concentrations of phenytoin, phenobarbital, topiramate, carbamazepine and carbamazepine 10, 11 epoxide, valproic acid, and lamotrigine were not affected by concomitant pregabalin (200 mg three times a day) administration. These drugs have no effect on the pharmacokinetics of pregabalin and pregabalin has no effect on the pharmacokinetics of the mentioned drugs. Tiagabine also had no effect on the pharmacokinetics of pregabalin. As with all AEDs, pregabalin should be withdrawn gradually to minimize the potential of increased seizure frequency in patients with seizure disorders. If pregabalin is discontinued this should be done gradually over a minimum of 1 week.

**Oral hypoglycemics**  
Concomitant administration of glyburide, insulin or metformin with pregabalin did not affect the pharmacokinetics of pregabalin.

**Furosemide**  
Concomitant administration of furosemide with pregabalin did not affect the pharmacokinetics of pregabalin.

**CNS Depressants**  
Patients who require concomitant treatment with CNS depressants such as opiates or benzodiazepines should be informed that they may experience additive CNS side effects, such as somnolence.

**Alcohol**  
Patients should be told to avoid consuming alcohol while taking pregabalin, as pregabalin may potentiate the impairment of motor skills and sedating effects of alcohol.

**Antibiotics**  
May alter the intestinal microflora and may decrease the absorption of methylcobalamin.

**Cholestyramine, colestipol**  
May decrease the enteropathic re-absorption of methylcobalamin.

**Metformin, para-aminosalicylic acid and potassium chloride**  
May decrease the absorption of methylcobalamin.

**Nitrous oxide**  
Can produce a functional methylcobalamin deficiency.

**Patient with Renal Impairment**  
Pregabalin dosage adjustment should be considered in cases of renal impairment. (Refer Dosage and Administration, Patients with renal impairment)

**ADVERSE EFFECTS:**

**Pregabalin**  
The most common side effects events seen with pregabalin treatment are dizziness, somnolence, headache, ataxia, asthenia, dry mouth, constipation, edema, blurred vision, weight gain, and "thinking abnormal" (primarily difficulty with concentration/attention). Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In all controlled and uncontrolled trials across various patient populations during the premarketing development of pregabalin, more than 10,000 patients have received pregabalin. Approximately 5000 patients were treated for 6 months or more, over 3100 patients were treated for 1 year or longer, and over 1400 patients were treated for at least 2 years.

**Controlled Studies with Neuropathic Pain Associated with Diabetic Peripheral Neuropathy**  
In clinical trials in patients with neuropathic pain associated with diabetic peripheral neuropathy, 9% of patients treated with pregabalin and 4% of patients treated with placebo discontinued prematurely due to undesirable effects. In the pregabalin treatment group, the most common reasons for discontinuation due to undesirable effects were dizziness (3%) and somnolence (2%). In comparison, <1% of placebo patients withdrew due to dizziness and somnolence. Other reasons for discontinuation from the trials, occurring with greater frequency in the pregabalin group than in the placebo group, were asthenia, confusion, and peripheral edema. Each of these events led to withdrawal in approximately 1% of patients.

**Most Common Undesirable Effects**  
Table 2 lists all undesirable effects, regardless of causality, occurring in ≥1% of patients with neuropathic pain associated with diabetic neuropathy in the combined pregabalin group for which the incidence was greater in this combined pregabalin group than in the placebo group. A majority of pregabalin-treated patients in clinical studies had undesirable effects with a maximum intensity of "mild" or "moderate".

**Table 2: Treatment-emergent adverse reaction incidence in controlled trials in Neuropathic Pain Associated with Diabetic Peripheral Neuropathy (Events in at least 1% of all pregabalin -treated patients and at least numerically more in all pregabalin than in the placebo group)**

Body system - Preferred term	75 mg/day %	150 mg/day %	300 mg/day %	600 mg/day %	All PGB* %	Placebo %
Body as a whole						
Asthenia	4	2	4	7	5	2
Accidental injury	5	2	2	6	4	3
Back pain	0	2	1	2	2	0
Chest pain	4	1	1	2	2	1
Face edema	0	1	1	2	1	0
Digestive system						
Dry mouth	3	2	5	7	5	1
Constipation	0	2	4	6	4	2
Flatulence	3	0	2	3	2	1
Metabolic and nutritional disorders						
Peripheral edema	4	6	9	12	9	2
Weight gain	0	4	4	6	4	0
Edema	0	2	4	2	2	0
Hypoglycemia	1	3	2	1	2	1
Nervous system						
Somnolence	4	6	13	16	12	3
Neuropathy	9	2	2	5	4	3
Ataxia	6	1	2	4	3	1
Vertigo	1	2	2	4	3	1
Confusion	0	1	2	3	2	1
Euphoria	0	0	3	2	2	0
Incoordination	1	0	2	2	2	0
Thinking abnormal <sup>†</sup>	1	0	1	3	2	0
Tremor	1	1	1	2	1	0
Abnormal gait	1	0	1	3	1	0
Amnesia	3	1	0	2	1	0
Nervousness	0	1	1	1	1	0
Respiratory system						
Dyspnea	3	0	2	2	2	1
Special senses						
Blurry vision <sup>‡</sup>	3	1	3	6	4	2
Abnormal vision	1	0	1	1	1	0

\* PGB: pregabalin  
† Thinking abnormal primarily consists of events related to difficulty with concentration/attention but also includes events related to cognition and language problems and slowed thinking.  
‡ Investigator term; summary level term is amblyopia.

**Controlled Studies in Postherpetic Neuralgia**  
**Undesirable Effects Leading to Discontinuation**  
In clinical trials in patients with postherpetic neuralgia, 14% of patients treated with pregabalin and 7% of patients treated with placebo discontinued prematurely due to undesirable effects. In the pregabalin treatment group, the most common reasons for discontinuation due to undesirable effects were dizziness (4%) and somnolence (3%). In comparison, less than 1% of placebo patients withdrew due to dizziness and somnolence. Other reasons for discontinuation from the trials, occurring in greater frequency in the pregabalin group than in the placebo group, were confusion (2%), as well as peripheral edema, asthenia, ataxia, and abnormal gait (1% each).

**Most Common Undesirable Effects**  
Table 3 lists all undesirable effects, regardless of causality, occurring in ≥1% of patients with neuropathic pain associated with postherpetic neuralgia in the combined pregabalin group for which the incidence was greater in this combined pregabalin group than in the placebo group. In addition, an event is included, even if the incidence in the all pregabalin group is not greater than in the placebo group, if the incidence of the event in the 600 mg/day group is more than twice that in the placebo group. A majority of pregabalin-treated patients in clinical studies had undesirable effects with a maximum intensity of "mild" or "moderate". Overall, 12.4% of all pregabalin-treated patients and 9.0% of all placebo-treated patients had at least one severe event while 8% of pregabalin-treated patients and 4.3% of placebo-treated patients had at least one severe treatment-related adverse event.

**Table 3: Treatment-emergent adverse reaction incidence in controlled trials in Neuropathic Pain Associated with Postherpetic Neuralgia (Events in at least 1% of all pregabalin -treated patients and at least numerically more in all pregabalin than in the placebo group)**

Body system - Preferred term	75 mg/d %	150 mg/d %	300 mg/d %	600 mg/d %	All PGB* %	Placebo %
Body as a whole						
Infection	14	8	6	3	7	4
Headache	5	9	5	8	7	5
Pain	5	4	5	5	5	4
Accidental injury	4	3	3	5	3	2
Flu syndrome	1	2	2	1	2	1
Face edema	0	2	1	3	2	1
Digestive system						
Dry mouth	7	7	6	15	8	3
Constipation	4	5	5	5	5	2
Flatulence	2	1	2	3	2	1
Vomiting	1	1	3	3	2	1
Metabolic and nutritional disorders						
Peripheral edema	0	8	16	16	12	4
Weight gain	1	2	5	7	4	0
Edema	0	1	2	6	2	1

**Musculoskeletal system**

	1	1	1	1	1	0
Myasthenia	1	1	1	1	1	0
Nervous system						
Dizziness	11	18	31	37	26	9
Somnolence	8	12	18	25	16	5
Ataxia	1	2	5	9	5	1
Abnormal gait	0	2	4	8	4	1
Confusion	1	2	3	7	3	0
Thinking abnormal <sup>†</sup>	0	2	1	6	2	2
Incoordination	2	2	1	3	2	0
Amnesia	0	1	1	4	2	0
Speech disorder	0	0	1	3	1	0
Respiratory system						
Bronchitis	0	1	1	3	1	1
Special senses						
Blurry vision <sup>‡</sup>	1	5	5	9	5	3
Diplopia	0	2	2	4	2	0
Abnormal vision	0	1	2	5	2	0
Eye Disorder	0	1	1	2	1	0
Urogenital System						
Urinary Incontinence	0	1	1	2	1	0

\* PGB: pregabalin  
† Thinking abnormal primarily consists of events related to difficulty with concentration/attention but also includes events related to cognition and language problems and slowed thinking.  
‡ Investigator term; summary level term is amblyopia.

**Controlled Studies with Fibromyalgia**  
**Undesirable Effects Leading to Discontinuation**  
In clinical trials in patients with fibromyalgia, 19% of patients treated with pregabalin (150–600 mg/day) and 10% of patients treated with placebo discontinued prematurely due to undesirable effects. In the pregabalin treatment group, the most common reasons for discontinuation due to undesirable effects were dizziness (6%) and somnolence (3%). In comparison, <1% of placebo-treated patients withdrew due to dizziness and somnolence. Other reasons for discontinuation from the trials, occurring with greater frequency in the pregabalin treatment group than in the placebo treatment group, were fatigue, headache, balance disorder, and weight increased. Each of these undesirable effects led to withdrawal in approximately 1% of patients.

**Most Common Undesirable Effects**  
Table 4 lists all undesirable effects, regardless of causality, occurring in ≥2% of patients with fibromyalgia in the "all pregabalin" treatment group for which the incidence was greater in the all pregabalin treatment group than in the placebo treatment group.

**Table 4: Treatment-emergent adverse reaction incidence in controlled trials in Fibromyalgia (Events in at least 2% of all pregabalin -treated patients and occurring more frequently in the all pregabalin-group than in the placebo treatment group)**

System organ Class - Preferred term	150 mg/d %	300 mg/d %	450 mg/d %	600 mg/d %	All PGB* %	Placebo %
Ear and Labyrinth Disorders						
Vertigo	2	2	2	1	2	0
Eye Disorders						
Vision blurred	8	7	7	12	8	1
Gastrointestinal Disorders						
Dry mouth	7	6	9	9	8	2
Constipation	4	4	7	10	7	2
Vomiting	2	3	3	2	3	2
Flatulence	1	1	2	2	2	1
Abdominal distention	2	2	2	2	2	1
General Disorders and Administrative Site Conditions						
Fatigue	5	7	6	8	7	4
Edema peripheral	5	5	6	9	6	2
Chest pain	2	1	1	2	2	1
Feeling abnormal	1	3	2	2	2	0
Edema	1	2	1	2	2	1
Feeling drunk	1	2	1	2	2	0

**Methylcobalamin**  
Methylcobalamin has no known toxicity at the dosage for clinical effects and it appears to be well tolerated, with a safety and tolerability profile similar to that of the placebo. Mild transient diarrhea, polycythemia vera, itching, transitory exanthema and the feeling of swelling of the entire body has been associated with methylcobalamin.

**OVERDOSAGE AND TREATMENT:**  
**Signs, Symptoms and Laboratory Findings of Acute Overdosage in Humans**  
There is limited experience with overdose of pregabalin. The highest reported accidental overdose of pregabalin during the clinical development program was 8000 mg, and there were no notable clinical consequences. In clinical studies, some patients took as much as 2400 mg/day. The types of adverse events experienced by patients exposed to higher doses (≥900 mg) were not clinically different from those of patients administered recommended doses of pregabalin.  
**Treatment or Management of Overdose**  
There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; usual precautions should be observed to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient.  
Although haemodialysis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal impairment. Standard hemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours).

**STORAGE CONDITION:**  
STORE AT TEMPERATURES NOT EXCEEDING 30°C.

**DOSAGE FORMS AND PACKAGING AVAILABLE:**  
Capsules  
Alu/Alu Blister Pack of 10 capsules (Box of 30's).

**INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):**  
Not Applicable

**NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:**  
**Marketing Authorization Holder**  
Brown & Burk Philippines Inc  
U-501, 5/F, SEDCCO I Bldg., 120 Rada cor., Legaspi Sts., Legaspi Village, Makati City, Philippines

**NAME AND ADDRESS OF MANUFACTURER:**  
**MICRO LABS LIMITED**  
92, Sipcot Industrial Complex,  
Hosur-635 126 (T.N), INDIA.

**CAUTION STATEMENT:**  
FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION .

**ADR REPORTING STATEMENT:**  
FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: [www.fda.gov.ph](http://www.fda.gov.ph)  
Seek medical attention immediately at the first sign of Adverse Drug Reaction.

**REGISTRATION NUMBER:**  
NEURICA-M 75: DR-XY 48072  
NEURICA-M 150: DR-XY 48071

**DATE OF FIRST AUTHORIZATION:**  
31 MAY 2022

**DATE OF REVISION OF PACKAGE INSERT:**  
Aug. 2022

EXG-ML01I-1793

PHARMACODE  
READING  
DIRECTION

<b>MICRO LABS LIMITED, BANGALORE, INDIA</b>					
1	Product Name	Neurica-M 75/150		Colours Used	
2	Strength	75 mg/750 mcg and 150 mg/750 mcg		<input checked="" type="checkbox"/> BLACK	
3	Component	Leaflet			
4	Category	Export - Philippines			
5	Dimension	320 (L) x 480 (H) mm			
6	Artwork Code	EXG-ML01I-1793			
7	Pharma Code	153 (Front Side) and 154 (Back Side)			
8	Reason for Change	New Artwork			
		Prepared by (DTP)	Checked by (PD)	Approved by	
Sign				Head CQA	Head Production/ Packing (Site)
Date		Kantharaju L.		Head QC (Site)	Head QA (Site)
27-10-2022					