

PREGALIN M

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for **PREGALIN M** (Pregabalin 75/150 mg & Methylcobalamin 750 mcg Capsules)

[Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Pregabalin:* Pregabalin binds to an auxiliary subunit ($\alpha_2\delta$ protein) of voltage-gated calcium channels in the central nervous system. *Methylcobalamin:* Methylcobalamin is involved in the synthesis of thymidine from deoxyuridine and promotes the synthesis of DNA and RNA by acting as a coenzyme in the formation of methionine from homocysteine. Methylcobalamin is reported to accelerate the synthesis of nucleic acids in bone marrow, as well as the maturation and division of erythroblasts, resulting in an increase in the production of erythrocytes. It is also reported to maintain axonal function by promoting nucleic acid and protein synthesis.

INDICATIONS: Combination of pregabalin and Methylcobalamin is indicated for management of neuropathic pain.

DOSAGE AND ADMINISTRATION: Treatment will be started with a capsule containing pregabalin 150mg with methylcobalamin 750mcg once daily or a capsule containing pregabalin 75mg with methylcobalamin 750mcg twice daily. The dose may be increased after an interval of 3 to 7 days. Based on individual patient response and tolerability, the maximum recommended dose is four capsules of pregabalin 150mg with Methylcobalamin 750mcg per day in divided doses.

CONTRAINDICATION: Hypersensitivity to the active substance or to any of the excipients.

WARNINGS & PRECAUTIONS: *Pregabalin: Diabetic patients:* Some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycaemic medicinal products. *Hypersensitivity reactions:* Pregabalin should be discontinued immediately if symptoms of angioedema, such as facial, perioral, or upper airway swelling occur. *Dizziness, somnolence, loss of consciousness, confusion and mental impairment:* Pregabalin treatment has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall) in the elderly population. There have also been postmarketing reports of loss of consciousness, confusion and mental impairment. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicinal product. *Vision-related effects:* Patients treated with pregabalin may experience blurred vision, which typically resolves with continued dosing. Some patients may also develop visual acuity changes or other eye issues. *Renal failure:* Cases of renal failure have been reported and in some cases discontinuation of pregabalin did show reversibility of this adverse reaction. *Withdrawal of concomitant anti-epileptic medicinal products:* 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, suggestive of physical dependence. *Congestive heart failure:* Post-marketing reports have linked pregabalin use with congestive heart failure, particularly in elderly patients with cardiovascular issues. *Treatment of central neuropathic pain due to spinal cord injury:* Pregabalin use for central neuropathic pain due to spinal cord injury may increase the incidence of central nervous system adverse reactions like somnolence, possibly due to interactions with other medications. *Suicidal Ideation and Behaviour:* There is a potential risk of suicidal ideation and behaviour associated with pregabalin use, necessitating monitoring and appropriate treatment considerations, especially in patients with psychiatric history. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge. *Reduced lower gastrointestinal tract function:* When pregabalin and opioids will be used in combination, measures to prevent constipation may be considered (especially in female patients and

elderly). **Misuse, abuse potential or dependence:** Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of pregabalin misuse, abuse or dependence. **Encephalopathy:** Cases of encephalopathy have been reported, mostly in patients with underlying conditions that may precipitate encephalopathy.

Methylcobalamin: Should be given with caution in patients suffering from folate deficiency. The following warnings and precautions suggested with parent form vitamin B12 .The treatment of vitamin B12 deficiency can unmask the symptoms of polycythemia vera. Megaloblastic anemia is sometimes corrected by treatment with vitamin B12. But this can have very serious side effects. Don't attempt vitamin B12 therapy without close supervision by your healthcare provider. Do not take vitamin B12 if Leber's disease, a hereditary eye disease. It can seriously harm the optic nerve, which might lead to blindness.

DRUG INTERACTIONS: Pregabalin: In vivo studies and population pharmacokinetic analysis: Accordingly, in *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. **Oral contraceptives, norethisterone and/or ethinyl oestradiol:** Co-administration of pregabalin with the oral contraceptives norethisterone and/or ethinyl oestradiol does not influence the steady-state pharmacokinetics of either substance. **Central nervous system influencing medical products:** Pregabalin may enhance effects of ethanol and lorazepam. While co-administration with oxycodone or ethanol in clinical trials did not affect respiration, post-marketing reports suggest potential for respiratory depression and coma with CNS depressants. **Interactions and the elderly** No specific pharmacodynamic interaction studies were conducted in elderly volunteers. Interaction studies have only been performed in adults. **Methylcobalamin:-**Serum concentrations may be decreased by use of oral contraceptives. Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations. Parenteral chloramphenicol may attenuate the effect of vitamin B12 in anaemia. Folic acid, particularly in large doses, can cover up vitamin B12 deficiency, and cause serious health effects. Early research suggests that vitamin C supplements can destroy dietary vitamin B12. It isn't known whether this interaction is important, but to stay on the safe side, take vitamin C supplements at least 2 hours after meals.

ADVERSE REACTIONS:Pregabalin: Nasopharyngitis, appetite increased, euphoric mood, confusion, irritability, disorientation, insomnia, libido decreased, dizziness, somnolence, headache, ataxia, coordination abnormal, tremor, dysarthria, amnesia, memory impairment, disturbance in attention, paraesthesia, hypoaesthesia, sedation, balance disorder, lethargy, vision blurred, diplopia, vertigo, vomiting, nausea, constipation, diarrhoea, flatulence, abdominal distension, dry mouth, muscle cramp, arthralgia, back pain, pain in limb, cervical spasm, erectile dysfunction, oedema peripheral, oedema, gait abnormal, fall, feeling drunk, feeling abnormal, fatigue, weight increased. **Methylcobalamin:** Methylcobalamin is relatively safe and devoid of side effects. However, it could infrequently cause the following reactions. Cardiovascular: pulmonary edema and congestive heart failure early in treatment; peripheral vascular thrombosis. Hematological: polycythemia vera Gastrointestinal: mild transient diarrhea Dermatological: itching; transitory exanthema Miscellaneous: feeling of swelling of entire body.

MARKETED BY:



TORRENT PHARMACEUTICALS LTD.

IN/PREGALIN M 75,150mg/MAY-17/01/ABPI

(Additional information is available on request)