Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Gabamed- M
(Pregabalin and Methylcobalamin Capsules)

2. Qualitative and quantitative composition

Each Hard gelatin capsule contains:
Pregabalin B.P.....75 mg
Methylcobalamin U.S.P.....1500 mcg

Excipient(s) with known effect: Each capsule contains lactose monohydrate 93.50 mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Capsules

Scarlet/Scarlet coloured capsule containing off white colour powder.

4. Clinical particulars

4.1 Therapeutic indications

Pregabalin and Methylcobalamin capsules are prescribed for the treatment of

- Possesses anxiolytic, analgesic and anticonvulsant activity.
- Possess high bioavailability (90% vs 33-66%) compared to gabapentin.
- Highly effective in relieving the neuropathic pain.
- Improves mood and reduces sleep disturbance.
- Acts as neuroprotective, promotes myelination in neurons.
- Relieves burning sensation, numbness, and loss of sensation & muscle
- cramps in diabetic neuropathy.
- Peripheral Neuropathy.
- Diabetic Neuropathy.
- Drug Induced Neuropathy

4.2 Posology and method of administration

For adults one capsule two or three times daily or as directed by physician Pregabalin and Methylcobalamin Capsules should be taken before food intake.

4.3 Contraindications

Hypersensitivity. Pregnancy, lactation. Driving or working with machines, or do other dangerous activities

4.4 Special warnings and precautions for use

- May cause peripheral oedema.

- Regular vision check is recommended.
- May decrease platelet count and prolong PR interval.
- Discontinue treatment if patients develop severe angioedema.
- Withdraw treatment gradually over at least 1 week.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent use with oxycodone, lorazepam and ethanol may increase the CNS effects.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

As the potential risk for humans is unknown, effective contraception must be used in women of child bearing potential.

Pregnancy

There are no adequate data from the use of pregabalin in pregnant women.

Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Pregabalin and Methylcobalamin Capsules should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus).

Breast-feeding

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.

Fertility

There are no clinical data on the effects of pregabalin on female fertility.

In a clinical trial to assess the effect of pregabalin on sperm motility, healthy male subjects were exposed to pregabalin at a dose of 600 mg/day. After 3 months of treatment, there were no effects on sperm motility.

Methylcobalamin

Methylcobalamin should not be used for the treatment of megaloblastic anaemia of pregnancy.

4.7 Effects on ability to drive and use machines:

Pregabalin and Methylcobalamin Capsules may have minor or moderate influence on the ability to drive and use machines. It may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether this medicinal product affects their ability to perform these activities.

Methylcobalamin: No effect.

4.8 Undesirable effects

In the post-marketing experience, the most commonly reported adverse reactions observed when pregabalin was taken in overdose included somnolence, confusional state, agitation, and restlessness.In rare occasions, cases of coma have been reported.

Treatment of pregabalin overdose should include general supportive measures

and may include haemodialysis if necessary.

Methylcobalamin
No any serious effect due to overdose.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

In the post-marketing experience, the most commonly reported adverse reactions observed when pregabalin was taken in overdose included somnolence, confusional state, agitation, and restlessness.
In rare occasions, cases of coma have been reported.
Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary.
Methylcobalamin
No any serious effect due to overdose.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiepileptics, other antiepileptics ATC code: N03AX16
The active substance, pregabalin, is a gamma-aminobutyric acid analogue ((S)-3-(aminomethyl)-5- methylhexanoic acid).
Pregabalin is an oral medication that is chemically related to gabapentin (Neurontin, Gabarone). It is used for treating pain caused by neurologic diseases such as post herpetic neuralgia as well as seizures. It also is used for treating fibromyalgia. The mechanism of action of pregabalin is unknown. Pregabalin binds to calcium channels on nerves and may modify the release of neurotransmitters (chemicals that nerves use to communicate with each other). Reducing communication between nerves may contribute to pregabalin's effect on pain and seizures.
Methylcobalamin
Vitamin B12 normally plays a significant role in the metabolism of every cell of the body, especially affecting the DNA synthesis and regulation but also fatty acid synthesis and energy production.[40] However, many (though not all) of the effects of functions of B12 can be replaced by sufficient quantities of folic acid (vitamin B9), since B12 is used to regenerate folate in the body. Most vitamin B12 deficiency symptoms are actually folate deficiency symptoms, since they include all the effects
of pernicious anemia and megaloblastosis, which are due to poor synthesis of DNA when the body does not have a proper supply of folic acid for the production of thymine.[41] When sufficient folic acid is available, all known B12 related deficiency syndromes normalize, save those narrowly connected with the vitamin B12-dependent enzymes Methylmalonyl Coenzyme A mutase, and 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR), also known as

methionine synthase; and the buildup of their respective substrates (methylmalonic acid, MMA) and homocysteine.

5.2 Pharmacokinetic properties

Pregabalin:

Absorption: Pregabalin is rapidly absorbed when administered on an empty stomach, with peak plasma concentrations occurring within one hour. Pregabalin oral bioavailability is estimated to be greater than or equal to 90% and is independent of dose. The rate of pregabalin absorption is decreased when given with food resulting in a decrease in Cmax by approximately 25 to 30% and a delay in Tmax to approximately 2.5 hours. Administration with food, however, has no clinically significant effect on the extent of absorption.

Distribution: Pregabalin has been shown to cross the blood–brain barrier in mice, rats, and monkeys. Pregabalin has been shown to cross the placenta in rats and is present in the milk of lactating rats. In humans, the volume of distribution of pregabalin for an orally administered dose is approximately 0.56 L/kg and is not bound to plasma proteins.

Metabolism: Pregabalin undergoes negligible metabolism in humans. Approximately 98% of the radioactivity recovered in the urine was unchanged pregabalin. The major metabolite is N-methyl pregabalin.

Excretion: Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Renal clearance of pregabalin is 73 mL/minute

Methylcobalamin:

Methylcobalamin as adenosylcobalamin and hydroxocobalamin. These act as co-enzymes in the trans methylation of homocysteine to methionine; in the isomerisation of methylmalonyl co-enzyme to succinyl co-enzyme and with folate in several metabolic pathways respectively. Deficiency of Vitamin B12 interferes with haemopoiesis and produces megaloblastic anaemia.

5.3 Preclinical safety data

In conventional safety pharmacology studies in animals, pregabalin was well-tolerated at clinically

relevant doses. In repeated dose toxicity studies in rats and monkeys CNS effects were observed, including hypo activity, hyperactivity and ataxia. An increased incidence of retinal atrophy commonly observed in aged albino rats was seen after long term exposure to pregabalin at exposures≥ 5 times the mean human exposure at the maximum recommended clinical dose.

Pregabalin was not teratogenic in mice, rats or rabbits. Foetal toxicity in rats and rabbits occurred only at exposures sufficiently above human exposure. In prenatal/postnatal toxicity studies, pregabalin induced offspring developmental toxicity in rats at exposures >2 times the maximum recommended human exposure.

Adverse effects on fertility in male and female rats were only observed at exposures sufficiently in excess of therapeutic exposure. Adverse effects on male reproductive organs and sperm parameters were reversible and occurred only at exposures sufficiently in excess of therapeutic exposure or were associated with spontaneous degenerative processes in male reproductive organs in the

rat. Therefore, the effects were considered of little or no clinical relevance.

Pregabalin is not genotoxic based on results of a battery of in vitro and in vivo tests.
Two-year carcinogenicity studies with pregabalin were conducted in rats and mice. No tumours were observed in rats at exposures up to 24 times the mean human exposure at the maximum recommended clinical dose of 600 mg/day. In mice, no increased incidence of tumour was found at exposures similar to the mean human exposure, but an increased incidence of haemangiosarcoma was observed at higher exposures. The non-genotoxic mechanism of pregabalin-induced tumour formation in mice involves platelet changes and associated endothelial cell proliferation. These platelet changes were not present in rats or in humans based on short term and limited long term clinical data. There is no evidence to suggest an associated risk to humans.
In juvenile rats the types of toxicity do not differ qualitatively from those observed in adult rats. However, juvenile rats are more sensitive. At therapeutic exposures, there was evidence of CNS clinical signs of hyperactivity and bruxism and some changes in growth (transient body weight gain suppression). Effects on the oestrus cycle were observed at 5-fold the human therapeutic exposure. Reduced acoustic startle response was observed in juvenile rats 1-2 weeks after exposure at >2 times the human therapeutic exposure. Nine weeks after exposure, this effect was no longer observable.
Methylcobalamin
Not available.

6. Pharmaceutical particulars

6.1 List of excipients
Lactose Monohydrate
Maize Starch
Colloidal Silicon Dioxide (Aerosil)
Purified Talc
Magnesium Stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life

36 months from date of manufacturing.

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
10 tablets are packed in one Alu-Alu blister such 3 blister are packed in a carton with insert.

6.6 Special precautions for disposal and other handling

This medicinal product does not require any special storage conditions.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Name: Pro med pharmaceuticals ltd,
Address: P.O BOX 22953 – 00100, Nairobi
Country: Kenya.

Manufacturing site address:

Name: Brussels laboratories pvt. Ltd
Address: 33, changodar ind. Estate, Sarkhej –bavla road, Changodar -382210, ahmedabad, gujarat
Country: India.

8. Marketing authorization number

H2024/CTD10016/22294

9. Date of first registration

22/03/2024

10. Date of revision of the text

November 2024