Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product
Pregared MDS

2. Qualitative and quantitative composition
Each Hard Gelatin capsule contains;
Pregabalin .....75 mg
Mecobalamin.....1500 mcg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form
Capsules
Yellow / Yellow colour hard gelatin capsule size "2" Containing to white colour powder.

4. Clinical particulars
4.1 Therapeutic indications
Management of neuropathic pain associated with diabetic peripheral neuropathy. Management of post herpetic Neuralgia.
Adjunct therapy for adult patient with partial onset of seizures. Management of Fibromyalgia.

4.2 Posology and method of administration
Route of administration: Oral use
Pregabalin and Mecobalamin capsules can be taken with or without food. Dose may be increased up to 300 mg Pregabalin/day within one week based on efficacy and tolerabillty. Dose need not to be adjusted in case of renal dysfunction.

4.3 Contraindications
Pregabalin and Mecobalamin capsules are contra-indicated in patients with known hypersensitivity to Pregabalin or Mecobalamin or any of Its components. Angioedema and hypersensitivity reactions have occurred in patients receiving Pregabalin therapy.

4.4 Special warnings and precautions for use
Pregabalin
Insomnia, nausea, headache, and diarrhea. Taper gradually over a minimum of 1 week. High incidence of hemangiosarcoma was identified in two different strains of mice when administered pregabalin. Clinical significance of this finding is unknown. Inform patients to notfy their physician if changes in vision occur. Discontinue treatment with pregabalin if myopathy is diagnosed or suspected or if markedly elevated creatine kinase levels occur. May cause decrease in platelet count and PR interval prolongation.
Mecobalamin
Should not be used for > 1 month in patients if no clinically therapeutic outcome is observed. Susceptible to photolysis, hence caution should betaken so as not to expose

the capsules to direct light.

4.5 Interaction with other medicinal products and other forms of interaction

Pregabalin

Since Pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans (<2% of a dose recovered in urine as metabolltes), does not inhibit drug metabolism in vitro, and is not bound to plasma proteins, It is unlikely to produce, or be subject to, pharmacokinetic interactions.

4.6 Fertility, pregnancy and lactation

Pregnancy

Anti-epileptic drugs (AEDs) have the potential to affect fetal development throughout pregnancy. Considering the broad therapeutic indications of pregabalin (PGB) and Its potential teratogenic effects, it's advisable to avoid this drug during pregnancy.

Lactation

It is not known n 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.

4.7 Effects on ability to drive and use machines

It can impair the driving ability as you may experience side effects like dizziness, sleepiness after taking this medicine. Thus, be cautious while on this medicine

4.8 Undesirable effects

Pregabalin:

The common adverse effects of pregabalin are dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, and 'thinking abnormal" (primarily difficulty with concentratiorv attention).

Mecobalamin

Mecobalamin is relatively safe and devoid of side effects. Could infrequently cause pulmonary oedema, CHF, peripheral vascular thrombosis, polycythemia vera, mild transient diarrhea, itching, transitory exanthema, feeling of swelling of entire body.

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

Pregabalin seems to be relatively benign in overdose. There is a report of an overdose where 8 grams of Pregabalin were taken with no clinically unexpected effects arising, and a report of an 11.5 gram overdose with more serious consequences. General supportive care of the patient is indicated, and in overdose side effects such as agitation, coma, seizures, haemopoetic suppression, sinus tachycardia, and urinary retention are possible.

Treatment or Management of Overdose

There is no specific antidote for overdose with pregabalin. H 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 hemodialysis 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 signmcant renal impairment. Standard hemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours).

5. **Pharmacological** properties

5.1 Pharmacodynamic properties

Pharmacological Group: Antiepileptic **ATC code:**
Pregabalin: N03AX16 Mecobalamin: B03BA05 Mechanism of Action:
Pregabalin binds with high affinity to the alpha,-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-delta subunit may be involved in pregabalin's antinociceptive and antiseizure effects in animal models. In vitro, pregabalin reduces the calcium dependent release of several neurotransmitters, possibly by modulation of calcium channel function. While pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), It does not bind direcfly to GABA (A) & GABA (B), or benzo-diazepine receptors, does not augment GABA(A) 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 does not block sodium channels, is not active at opiate receptors, and does not alter cyclo-oxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline re uptake.
Mecobalamin
Mecobalamin is the neurologically active form of vitamin B,,, which increases myelin sheath formation and regenerates neurons. Mecobalamin (Methyl-B,,) is one of the two forms of biologically active vitamin Bl. Methyl-B. is the principal form of circulating vitamin Bu, hence the form which is transported into peripheral tissue. Methyl-B,, is absorbed by the intestine by a specific mechanism which uses the intinsic factor and by a diffusion process in which approximately 1 % of the ingested dose is absorbed. Cyanocobalamin and hydroxy-cobalamin are forms of the vitamin that require conversion to mecobalamin.

5.2 Pharmacokinetic properties

Pregabalin is well absorbed after oral administration. It is eliminated largely by renal excretion.
It has elimination half-life of about 6 hours. Absorption and Distribution:
Administration, maximum plasma concentration (Cmax) and area under plasma concentration time curve (AUG) values increase lineariy. Following repeated administration, steady state is achieved within 24 to 48 hours. Multiple doses pharmacokinetic can be predicted from single dose data.
The rate of pregabalin absorption is decreased when given with food, resulting in decrease in Cmax of approximately 25% to 30% and increase in Tmax to approximately 3 hours. However, administration of pregabalin with food has no clinically relevant effect on total absorption of Pregabalin. Therefore, pregabalin can be taken with or wlthoutfood.
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 transpoter which is responsible for the transport of large amino acid across the brain barrier. Although there are no data in humans, pregabalin has been shown to cross the placenta in rats and is present in milk of lactating rats.
Metabollsm and Ellmlnatlon:
Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 90% of the administered dose was recovered in urine as unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of dose. In preclinical studies, pregabalin (S-enantiomer) did not undergo racemization to the R-enantiomer in mice, rats, rabbits or monkey.
Pregabalin is eliminated from systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half Ine of 6.3 hours in subject 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 neariy proportional to creatinine clearance.

5.3 Preclinical safety data
In vivo studies and population pharmaco/cineticana/ysis
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. Co-administration of pregabalin with the oral contraceptives norethisterone and/or ethinyl oestradiol does not influence the steady-state pharmacokinetics of either substance.
Pregabalin may potentiate the effects of ethanol and lorazepam. In controlled clinical trials, multiple oral doses of pregabalin co-administered with oxycodone, lorazepam, or ethanol did not result in clinically important effects on respiration. In the postmarketing experience, there are reports of respiratory failure and coma in patients taking pregabalin and other CNS depressant medicinal products. Pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.
Mecobalamin
These may cause side effects, but many people have no, or minor, side effects. Check with your doctor n any of these most COMMON side effects persist or become bothersome:
Bloated feeling; headache; Itching; mild diarrhea; mild fever; nausea; vomiting. Seek medical attention right away if any of these SEVERE side effects occur:
Severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); lower back or side pain.

6. Pharmaceutical particulars
6.1 List of excipients
Lactose Talc
Dibasic calcium Phosphate EHG Capsules Size “2”

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 Months

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

6.5 Nature and contents of container
Alu - Alu Blister Pack
10 Capsules are blister packed with Aluminum - Aluminum foil; such 1 blister packed in one carton pack.
Pack size: 1 x 10 Capsules in one carton box along with packing leaflet.

6.6 Special precautions for disposal and other handling
No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Name:	Redefine Healthcare LTD
Address:	P.O Box 1907-00606Westland Nairobi
Country:	Kenya

manufacturing site addresses

Name:	Mars Remedies Pvt Ltd
Address:	635, GIDC Estate, Waghodia-391760, Vadodara, GUJARAT
Country:	India

8. Marketing authorization number
CTD10604

9. Date of first registration
H2024/CTD10604/22045

10. Date of revision of the text
November 2024