Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

SEREMAX FORTE (Pregabalin 75 mg, Methylcobalamin 750 mcg & Alpha lipoic acid 100 mg capsules)

2. Qualitative and quantitative composition

COMPOSITION:
Each hard gelatin
capsule contains:
Pregabalin..... 75 mg
Methylcobalamin.....750 mcg
Alpha lipoic acid USP..... 100 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Hard gelatin Capsule for Oral Administration.

4. Clinical particulars

4.1 Therapeutic indications

Seremax Forte is indicated for Painful Diabetic Neuropathy.

4.2 Posology and method of administration

The dose range is 150-600 mg per day given in either two or three divided doses.

Neuropathic pain
Pregabalin:

Pregabalin treatment can be started at a dose of 150mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose 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.

Methylcobalamin:

Oral administration of Methylcobalamin (500 mcg three times daily for four month) resulted in subjective improvement in burning sensation, numbness, loss of sensation, and muscle cramps.

Alpha Lipoic Acid:

In diabetic neuropathy dose is 300 milligrams daily of the oral preparation, should be taken in divided doses.

Method of administration:

SEREMAX FORTE is for oral use only, may be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipient.

4.4 Special warnings and precautions for use

Diabetic patients

In accordance with current clinical practice, some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycemic medicinal products.

Hypersensitivity reaction

There have been reports in the post marketing experience of hypersensitivity reaction, including cases of angioedema. Pregabalin should be discontinued immediately if symptom 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 an 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.

Renal failure

Cases of renal failure have been reported and in some cases discontinuation of Pregabalin did Show reversibility of this adverse reaction.

4.5 Interaction with other medicinal products and other forms of interaction

Since pregabalin is predominately excreted unchanged in the urine, undergoes negligible metabolism in humans (<2% of a dose recovered in urine as metabolites), does not inhibit drug metabolism in vitro, and is not bound to plasma proteins, it is unlikely to produce, or be subject to, pharmacokinetic interaction.

In vivo studies and population pharmacokinetic analysis:

Accordingly, in vivo studies no clinically relevant pharmacokinetic interaction was observed between Pregabalin and phenytoin, carbamazepine, Valproic acid, lamotrigine, gabapentin, lorazepam, oxycodone or ethanol. Population pharmacokinetic analysis indicated that oral anti diabetics, diuretics, insulin, phenobarbital, tiagabine and topiramate had no clinically significant effect on pregabalin clearance.

Oral contraceptives, norethisterone and/or ethinyl estradiol:

Co-administration of Pregabalin with the oral contraceptives norethisterone and/or ethinyl estradiol does not influence the steady state pharmacokinetics of either substance.

Ethanol, lorazepam, oxycodone:

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 additives in the impairment of cognitive and gross motor function caused by oxycodone.

Interaction and the elderly:

No specific pharmacodynamic interaction studies were conducted in elderly volunteers. Interaction studies have only been performed in adults.

Methylcobalamin: There is no known adverse reaction when taken in conjugation with medications.

Alpha Lipoic Acid: Supplemental alpha-lipoic acid may lower blood glucose levels.

4.6 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.

SEREMAX FORTE should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweigh the potential risk to the fetus).

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.

Methylcobalamin:

Pregnancy and Breastfeeding

Methylcobalamin is generally considered safe for pregnant and breastfeeding women.

Fertility

Methylcobalamin is believed to positively influence male fertility by potentially improving sperm parameters like count, motility, and morphology.

Alpha Lipoic Acid:

Pregnancy and Breastfeeding

Alpha-lipoic acid (ALA) has shown potential benefits in pregnancy, particularly for high-risk pregnancies, but there's limited information on its safety during breastfeeding. While some studies suggest ALA may be safe in pregnancy when taken orally in moderate doses (up to 600mg daily for 4 weeks), it's crucial to consult with a healthcare professional before using it during pregnancy or breastfeeding .

Fertility

Alpha-lipoic acid (ALA) is a powerful antioxidant that may improve fertility in both men and women by reducing oxidative stress and improving sperm quality and egg health.

4.7 Effects on ability to drive and use machines

Pregabalin
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

Pregabalin

The most commonly reported adverse reaction were dizziness and somnolence. Adverse reactions were usually mild to moderate in intensity. In all controlled studies, the discontinuation rate due to adverse reaction was 12 % for patients receiving pregabalin and 5% for patients receiving placebo. The most common adverse reaction resulting in discontinuation from pregabalin treatment group were dizziness and somnolence. The following reaction have been mentioned: insomnia, headache, nausea, anxiety, diarrhea, flu syndrome, convulsions, nervousness, depression, pain, hyperhidrosis and dizziness. The patient should be informed about this at the start of the treatment. In case of unexpected effects consult your doctor.

Methylcobalamin:

Methylcobalamin has excellent tolerability and no known toxicity.

Alpha Lipoic Acid:

Alpha Lipoic Acid in doses up to 600 milligrams daily has been well tolerated.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the relevant national regulatory authority pharmacovigilance.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product

4.9 Overdose

In overdoses up to 15g, no unexpected adverse reactions were reported. In the post-marketing experience, the most commonly reported adverse reaction observed when Pregabalin was taken in overdose included somnolence, confusional state, agitation, and restlessness. Treatment of Pregabalin overdose should include general supportive measures and may include hemodialysis if necessary.

Alpha-lipoic acid

A reported dose of 6 g caused death in a pediatric patient as well as our patient, but others survived doses of 6 g and 18 g.

Methylcobalamin

Since Methylcobalamin is a water-soluble vitamin, it's generally considered safe, even at high doses.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pregabalin:
Pharmacotherapeutic group: Antiepileptics, other antiepileptics

ATC code: N03AX16

Mechanism of action:

Pregabalin binds to an auxiliary subunit (α2-δ protein) of voltage-gated calcium channels in the central nervous system.

Methylcobalamin

Mechanism of action:
The exact mechanism of action is not yet, elucidated, it is possible that Methylcobalamin is needed for the synthesis of melatonin, since the biosynthesis formation of melatonin requires the donation of a methyl group.

ATC Code: B03BA05.

Alpha Lipoic Acid:

Mechanism of action:

Alpha Lipoic Acid and its reduced metabolite, dihydrolipoic acid (DHLA), form a redox couple and may scavenge a wide range of reactive oxygen species. Alpha-lipoic acid has biological antioxidant activity, antioxidant recycling activity and activity in enhancing biological energy production.

ATC Code: A16AX01.

5.2 Pharmacokinetic properties

Pregabalin
Pregabalin steady-state pharmacokinetics are similar in healthy volunteers, patients with epilepsy receiving anti-epileptic drugs and patients with chronic pain.

Absorption:

Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentration 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 Cmax 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 effects on the extent of pregabalin absorption.

Distribution:

In preclinical studies, 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 apparent volume of distribution of pregabalin following oral administration is approximately 0.56 1/kg. Pregabalin is not bound to plasma proteins.

Biotransformation:

Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 98% of the radioactivity recovered in the urine was 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, there was no indication of racemization of pregabalin S-enantiomer to the R-enantiomer.

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.

Methylcobalamin:

Absorption of Methylcobalamin following oral administration. The quantity of Methylcobalamin detected following a small oral dose of Methylcobalamin but significantly more Methylcobalamin accumulates in liver tissue following administration of Methylcobalamin. Human urinary excretion of Methylcobalamin is about one-third, indicating substantially greater tissue retention.

Alpha Lipoic Acid:

Alpha Lipoic Acid is absorbed from the small intestine and distributed to the liver via the portal circulation and to various tissues in the body via the systemic circulation. Alpha-lipoic acid readily crosses the blood-brain barrier. It is found, after its distribution to the various body tissues, intracellularly, intramitochondrial and extracellularly.

5.3 Preclinical safety data

Not Applicable

6. Pharmaceutical Particulars

6.1 List of Excipients

List of Excipients:
Maize Starch, Sodium Starch Glycolate, Microcrystalline Cellulose, Purified

Talcum, Colloidal Anhydrous Silica , Magnesium Stearate, Purified water , EHG Caps “1” Scarlet/Scarlet.

6.2 Incompatibilities

None

6.3 Shelf-Life

24 months

6.4 Special Precautions for storage

Store below 30°C in a dry place. Protect from light and moisture. Keep the medicine out of reach of children.

6.5 Nature and Content of container

One Alu-Alu blister of 10 capsules packed in a primary carton along with the Pack Insert.

6.6 Special precautions for disposal and other handling

None

7. Marketing Authorization Holder

Company Name: THEON PHARMACEUTICALS LTD

Address: 400, Industrial Area, Phase-I,
Panchkula-134113, Haryana

Country: India
Telephone: +91 172 5210200, 5011077, 5033850
Telefax: +91 172 5033851

8. Marketing Authorization Number

3550

9. Date of first authorization/renewal of the authorization

18TH MARCH 2016

10. Date of revision of the text

16/06/2026