Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Pregabin® 50 (Pregabalin Capsules 50 mg)

2. Qualitative and quantitative composition

Each hard gelatin capsule contains:

Pregabalin BP	50 mg
Excipient	Q.S

Approved colors used in empty capsule shell (for a full list of excipients, see section 6.1)

3. Pharmaceutical form:

Capsules

Pregabin® 50 - Red/White Size "4" hard gelatin capsule contains white color powder.

4. Clinical particulars

4.1 Therapeutic indications

Neuropathic pain: It is indicated for the treatment of peripheral and central neuropathic pain in adults.
Epilepsy: It is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization.
Generalized Anxiety Disorder: It is indicated for the treatment of Generalized Anxiety Disorder (GAD) in adults.

4.2 Posology and method of administration

Posology: The dose range is 150 to 600 mg per day given in either two or three divided doses.
Method of administration: Oral

4.3 Contraindications

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

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 reactions: There have been reports in the post-marketing experience of hypersensitivity reactions, including cases of angioedema. 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 post-marketing 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: In controlled trials, a higher proportion of patients treated with Pregabalin reported blurred vision than did patients treated with placebo which resolved in a majority of cases with continued dosing. In the clinical studies where ophthalmologic testing was conducted, the incidence of visual acuity reduction and visual field changes was greater in Pregabalin-

treated patients than in placebo-treated patients; the incidence of fundoscopic changes was greater in placebo-treated patients.
Renal failure: Cases of renal failure have been reported and in some cases discontinuation of Pregabalin did show reversibility of this adverse reaction. **Congestive heart failure:** There have been post-marketing reports of congestive heart failure in some patients receiving Pregabalin. These reactions are mostly seen in elderly cardiovascular compromised patients during Pregabalin treatment for a neuropathic indication. Pregabalin should be used with caution in these patients. Discontinuation of Pregabalin may resolve the reaction.
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.
Encephalopathy: Cases of encephalopathy have been reported, mostly in patients with underlying conditions that may precipitate encephalopathy.

4.5 Interaction with other medicinal products and other forms of interaction
Since Pregabalin is predominantly 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 interactions.

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 ethinylestradiol
Co-administration of Pregabalin with the oral contraceptives norethisterone and/or ethinyloestradiol does not influence the steady-state pharmacokinetics of either Substance.

Central nervous system influencing medical products

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 post-marketing experience, there are reports of respiratory failure and coma in patients taking Pregabalin and other central nervous system (CNS) depressant medicinal products. Pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.

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

4.6Pregnancy and lactation
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 Capsules should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the fetus).

Lactation: Pregabalin is excreted into human milk. The effect of Pregabalin on newborns/infants is unknown. A decision must be made whether to discontinue breast-feeding or to discontinue Pregabalin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7Effects on ability to drive and use machines.
This drug can cause dizziness, drowsiness, and blurry vision. It may affect your ability to think, see, or move. You shouldn't drive, use machinery, or do other tasks that require alertness until you know how this drug affects you.

4.8Undesirable effects
Nasopharyngitis, Neutropenia, Hypersensitivity, Angioedema, allergic reaction, Appetite increased, euphoric mood, confusion, irritability, disorientation, insomnia.
Gastro-intestinal disorders: Vomiting, nausea, constipation, diarrhea, flatulence, abdominal distension, dry mouth.
Nervous system disorders: Dizziness, somnolence, headache.
Blood disorders: Hypotension, hypertension, hot flushes, flushing, peripheral coldness.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse to the relevant National Regulatory Authority.
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 hemodialysis if necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-epileptics, other anti-epileptics
ATC code: N03AX16
The active substance, Pregabalin, is a gamma-amino butyric acid analogue [(S)-3-(aminomethyl)-5-methylhexanoic acid].
Mechanism of action: Pregabalin binds to an auxiliary subunit (α2-δ protein) of voltage-gated calcium channels in the central nervous system.

5.2 Pharmacokinetic properties

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 concentrations 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 Tmax to approximately 2.5 hours. However, administration of Pregabalin with food has no clinically significant effect 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 l/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. Dose adjustment in patients with reduced renal function or undergoing hemodialysis is necessary.

Linearity / non-linearity: Pregabalin pharmacokinetics are linear over the recommended daily dose range. Inter-subject pharmacokinetic variability for Pregabalin is low (< 20%). Multiple dose pharmacokinetics are predictable from single-dose data. Therefore, there is no need for routine monitoring of plasma concentrations of Pregabalin.

Gender: Clinical trials indicate that gender does not have a clinically significant influence on the plasma concentrations of Pregabalin.

Renal impairment: Pregabalin clearance is directly proportional to creatinine clearance. In addition, Pregabalin is effectively removed from plasma by hemodialysis (following 4-hour hemodialysis treatment plasma Pregabalin concentrations are reduced by approximately 50%). Because renal elimination is the major elimination pathway, dose reduction in patients with renal impairment and dose supplementation following hemodialysis is necessary.

Hepatic impairment: No specific pharmacokinetic studies were carried out in patients with impaired liver function. Since Pregabalin does not undergo significant metabolism and is excreted predominantly as unchanged drug in the urine, impaired liver function would not be expected to significantly alter Pregabalin plasma concentrations.

Elderly (over 65 years of age): Pregabalin clearance tends to decrease with increasing age. This decrease in Pregabalin oral clearance is consistent with decreases in creatinine clearance associated with increasing age. Reduction of Pregabalin dose may be required in patients who have age related compromised renal function.

Breast-feeding mothers: The pharmacokinetics of Pregabalin given every 12 hours (300 mg daily dose) was evaluated in 10 lactating women who were at least 12 weeks postpartum. Lactation had little to no influence on Pregabalin pharmacokinetics. Pregabalin was excreted into breast milk with average steady-state concentrations approximately 76% of those in maternal plasma. The estimated infant dose from breast milk (assuming mean milk consumption of 150 ml/kg/day) of women receiving 300 mg/day or the maximum dose of 600 mg/day would be 0.31 or 0.62 mg/kg/day, respectively. These estimated doses are approximately 7% of the total daily maternal dose on mg/kg basis.

5.3 Preclinical safety data

In animal studies, pregabalin was well tolerated at clinically relevant exposures. CNS effects (e.g. hypoactivity, hyperactivity, ataxia) were

observed in repeated-dose studies in rats and monkeys. Retinal atrophy, commonly seen in aged albino rats, occurred following long-term exposure at ≥5 times the human exposure.

Pregabalin was not teratogenic in mice, rats, or rabbits. Developmental toxicity occurred in rats and rabbits only at exposures above those achieved clinically. In prenatal/postnatal studies, developmental effects were noted in rats at exposures more than 2 times human exposure.
Fertility and male reproductive effects were observed only at exposures well above therapeutic levels and were reversible or considered of limited clinical relevance.
Pregabalin was not genotoxic. In carcinogenicity studies, no tumors were seen in rats (up to 24 times human exposure). In mice, hemangiosarcoma occurred at high exposures via a non-genotoxic mechanism not considered relevant to humans.
In juvenile rats, toxicity was qualitatively similar to that in adults, though with greater sensitivity. Effects included CNS signs, transient body weight suppression, and reversible changes in startle response.

6. Pharmaceutical particulars

6.1 List of Excipients:

Supertab
21AN
Maize Starch
Purified Talc
E.H.G Capsule Size '4' (Red/White)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C, protect from direct sunlight, heat and moisture.

6.5 Nature and contents of container

Pregabin® 50 Capsules are each available in the pack of 3 x 10's

6.6 Special precautions for disposal and other

Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder

KRISHNA CHEMISTS LTD.
P.O. BOX 3328-
00506 NAIROBI,
KENYA.

8. Marketing Authorization Number

H2021/CTD6928/2055ER

9. Date of first authorization/renewal of the authorization

16/09/2021

10. Date of revision of the text

11/02/2025