SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE PRODUCT: PBREN 75 (Pregabalin Capsules BP 75 mg)

Strength: 75 mg

Pharmaceutical form: Capsule

White to off white granular powder filled in hard gelatin capsule "Size 2" having pink cap and white body.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Qualitative Composition:

Composition:
Each Hard Gelatin Capsule Contains:

Pregabalin BP	75 mg
Excipients	q. s.

Colour: Approved colours used in capsule shells.

3. PHARMACEUTICAL FORM: Capsule

White to off white granular powder filled in hard gelatin capsule "Size 2" having pink cap and white body.

4. CLINICAL DATA:

4.1 Therapeutic indications:

For the treatment of diabetic peripheral neuropathy (DPN). Post herpetic neuralgia (PHN), as adjunctive therapy for adult patients with partial onset seizures and Fibromyalgia.

4.2 Posology and method of administration:

Pregabalin is given orally with or without food. When discontinuing pregabalin, taper gradually over a minimum of 1 week.

Neuropathic Pain Associated with Diabetic Peripheral Neuropathy
The maximum recommended dose is 100 mg three times a day (300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Because pregabalin is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function.

Postherpetic Neuralgia
The recommended dose is 75 to 150 mg two times a day, or 50 to 100 mg three times a day (150 to 300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 75 mg two times a day, or 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability.

Adjunctive Therapy for Adult Patients with Partial Onset Seizures
Pregabalin at doses of 150 to 600 mg/day has been shown to be effective as adjunctive therapy in the treatment of partial onset seizures in adults. Both the efficacy and adverse event profiles of pregabalin have been shown to be dose-related. Administer the total daily dose in two or three divided doses. In general, it is recommended that patients be started on a total daily dose no greater than 150 mg/day (75 mg two times a day, or 50 mg three times a day). Based on individual patient response and tolerability, the dose may be increased to a maximum dose of 600 mg/day. Because pregabalin is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function.

Management of Fibromyalgia
The recommended dose for fibromyalgia is 300 to 450 mg/day. Begin dosing at75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability.

Neuropathic Pain Associated with Spinal Cord Injury
The recommended dose range of pregabalin for the treatment of neuropathic pain associated with spinal cord injury is 150 to 600 mg/day. The recommended starting dose is 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief after 2 to 3 weeks of treatment with 150 mg two times a day and who tolerate may be treated with up to 300 mg two times a day.

4.3 Contraindications:

Pregabalin is contraindicated in patients with known hypersensitivity to pregabalin or any of its components. Angioedema and hypersensitivity reactions have occurred in patients receiving pregabalin therapy.

4.4 Special warnings and precautions for use:

Angioedema
Postmarketing reports of angioedema in patients during initial and chronic treatment. Specific symptoms included swelling of the face, mouth (tongue, lips and gums), and neck (throat and larynx). There were reports of life-threatening

angioedema with respiratory compromise requiring emergency treatment. Discontinue immediately in patients with these symptoms.
Exercise caution when prescribing pregabalin to patients who have had a previous episode of angioedema. In addition, patients who are taking other drugs associated with angioedema (e.g., angiotensin converting enzyme inhibitors [ACE-inhibitors]) may be at increased risk of developing angioedema.

Hypersensitivity
Adverse reactions included skin redness, blisters, hives, rash, dyspnea, and wheezing. Discontinue pregabalin immediately in patients with these symptoms.

Withdrawal of Antiepileptic Drugs (AEDs)
As with all AEDs, withdraw pregabalin gradually to minimize the potential of increased seizure frequency in patients with seizure disorders. If pregabalin is discontinued, taper the drug gradually over a minimum of 1 week.

Dizziness and Somnolence
Pregabalin may cause dizziness and somnolence. Inform patients that pregabalin-related dizziness and somnolence may impair their ability to perform tasks such as driving or operating machinery.

Abrupt or Rapid Discontinuation
Following abrupt or rapid discontinuation of pregabalin, some patients reported symptoms including insomnia, nausea, headache, anxiety, hyperhidrosis, and diarrhea. Taper pregabalin gradually over a minimum of 1 week rather than discontinuing the drug abruptly.

4.5 Interaction with other medicinal products and other forms of interactions:

Since pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans (<2% of a dose recovered in urine as metabolites), and does not bind to plasma proteins, its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions or protein binding displacement. In vitro and in vivo studies showed that pregabalin is unlikely to be involved in significant pharmacokinetic drug interactions. Specifically, there are no pharmacokinetic interactions between pregabalin and the following antiepileptic drugs: carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital, and topiramate. Important pharmacokinetic interactions would also not be expected to occur between pregabalin and commonly used antiepileptic drugs.

Multiple oral doses of pregabalin were co-administered with oxycodone,

lorazepam, or ethanol. Although no pharmacokinetic interactions were seen, additive effects on cognitive and gross motor functioning were seen when pregabalin was co-administered with these drugs. No clinically important effects on respiration were seen.

4.6 Pregnancy and lactation:

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Use pregabalin during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Paediatric Use
The safety and efficacy of pregabalin in paediatric patients have not been established.

Geriatric Use
Pregabalin is known to be substantially excreted by the kidney, and the risk of toxic reactions to pregabalin may be greater in patients with impaired renal function. Because pregabalin is eliminated primarily by renal excretion, adjust the dose for elderly patients with renal impairment.

4.7 Effects on ability to drive and use machines:

Pregabalin may have minor or moderate influence on the ability to drive and use machines. Pregabalin 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.

4.8 Undesirable effects

The following adverse reactions have been identified during post-approval use of pregabalin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Nervous System Disorders- Headache
Gastrointestinal Disorders-Nausea, Diarrhoea
Reproductive System and Breast Disorders-Gynecomastia, Breast Enlargement

Reporting of suspected adverse reactions
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. Healthcare professionals are asked to report

any suspected adverse reactions to the National Regulatory Authority via the national reporting system (https://pv.pharmacyboardkenya.org/). By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

The highest reported accidental overdose of pregabalin during the clinical development program was 8000 mg, and there were no notable clinical consequences.
Treatment or Management of Overdose
There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; observe usual precautions 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.
Standard hemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pregabalin binds to the α2-δ subunit of the voltage-gated calcium channels in central nervous system tissues. In vitro, pregabalin reduces calcium influx at nerve terminals, which may inhibit the release of excitatory neurotransmitters such as glutamate. Through this mechanism, pregabalin may modulate nerve impulses involved in the transmission of pain.
Pregabalin does not mimic GABA at GABAA or GABAB receptors, nor does it augment GABAA responses like benzodiazepines or barbiturates. In contrast to vascular calcium channel blockers, pregabalin does not alter systemic blood pressure or cardiac function. Various in vitro and in vivo results differentiate pregabalin from GABA uptake inhibitors or GABA transaminase inhibitors. In addition, pregabalin does not block sodium channels, it is not active at opiate receptors, it does not alter cyclooxygenase enzyme activity, it is not a serotonin agonist, it is not a dopamine antagonist, and it is not an inhibitor of dopamine, serotonin or noradrenaline reuptake.

5.2 Pharmacokinetic properties

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 radiolabelled 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 racemisation 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.

5.3 Preclinical safety data:

1 Pharmacol Biochem Behav. 2015 Aug; 135:31-9. doi: 10.1016/j.pbb.2015.05.007. Epub 2015 May 16.

Antinociceptive and hypnotic activities of pregabalin in a neuropathic pain-like model in mice.

Wang TX, Yin D, Guo W, Liu YY, Li YD, Qu WM, Han WJ, Hong ZY, Huang ZL.

Author information

Abstract

To evaluate the antinociceptive and hypnotic effects of pregabalin, we established a neuropathic pain-like model in mice using partial sciatic nerve ligation (PSNL), and examined thermal hyperalgesia, mechanical allodynia, electroencephalogram, rota-rod testing, and c-Fos expression in the anterior cingulate cortex. Gabapentin was used as a reference drug in the study. Pregabalin administered i.g. at 12.5 and 25mg/kg prolonged the duration of thermal latencies by 1.4- and 1.6-fold and increased the mechanical

threshold by 2.2- and 3.1-fold 3h after administration, respectively, but did not affect motor coordination in PSNL mice, compared with vehicle control. Pregabalin (12.5 and 25mg/kg) given at 6:30 increased the amount of non-rapid eye movement sleep in a 4-h period by 1.3- and 1.4-fold, respectively, in PSNL mice. However, pregabalin (25mg/kg) given at 20:30 did not alter the sleep pattern in normal mice. Immunohistochemical study showed that PSNL increased c-Fos expression in the neurons of anterior cingulate cortex by 2.1-fold, which could be reversed by pregabalin. These results indicate that pregabalin is an effective treatment for both neuropathic pain and sleep disturbance in PSNL mice.

KEYWORDS:
Anterior cingulate cortex; Neuropathic pain; Pregabalin; Sleep disturbance; c-Fos

2 Anat Rec (Hoboken). 2013 Dec;296(12):1907-12. doi: 10.1002/ar.22816. Epub 2013 Oct 17.

Pregabalin alters nociceptive behavior and expression level of P2X3 receptor in the spinal dorsal horn in a rat model induced by chronic compression of the dorsal root ganglion.

Yu J[1], Fu P, Zhang Y, Liu S, Cui D.

Author information

Abstract

P2X3 receptors are present in the spinal dorsal horn (SDH) and play an essential role in the regulation of nociception and pain. Pregabalin (PGB) has been used as a new antiepileptic drug in the treatment of neuropathic pain. However, it is unclear whether PGB-induced analgesia was associated with the P2X3 receptor in SDH. Here, rats were randomly divided into four groups (n = 12 per group), including 2 sham operation groups, which was treated by normal saline (Sham + NS group) or PGB (Sham + PGB group), other 2 groups with chronic compression of the dorsal root ganglion, a normal saline-treated CCD group (CCD+NS group), and a PGB-treated CCD group (CCD + PGB group). A rat model ofneuropathic pain was used by compressing the right L4 and L5 dorsal root ganglia. Each group was evaluated using the mechanical withdrawal threshold (MWT). The mRNA and protein levels of the P2X3 receptor in the ipsilateral SDH were measured by RT-PCR, western blot, and immunofluorescence on 14 day after CCD operation. CCD rats showed the highest mechanical hyperalgesia and the lowest pain threshold in the four groups. Simultaneously, CCD rats showed higher P2X3 mRNA and protein expression in ipsilateral side of the SDH than the sham operation rats. However, the MWT was increased and expression of P2X3 mRNA and protein in the ipsilateral SDH in CCD rats was decreased 3 days after PGB treatment. Thus, PGB may partially reverse mechanical hyperalgesia in CCD rats by inhibiting P2X3 receptor expression

in the ipsilateral SDH.

KEYWORDS:
P2X3 receptor; Pregabalin; dorsal root ganglion; neuropathic pain; spinal dorsal horn

3 J Pain. 2007 May;8(5):422-9. Epub 2007 Feb 9.
Pregabalin reduces muscle and cutaneous hyperalgesia in two models of chronic muscle pain in rats.
Yokoyama T[1], Maeda Y, Audette KM, Sluka KA.
Author information
Abstract:
Pregabalin is used for treatment of neuropathic pain conditions. The present study evaluated effects of pregabalin in 2 rat models of muscle-induced hyperalgesia: Inflammatory and noninflammatory. Muscle hyperalgesia (withdrawal threshold to compression of the muscle) and cutaneous hyperalgesia of the paw (withdrawal threshold to von Frey filaments) were measured before and after induction of hyperalgesia and after treatment with pregabalin (saline, 10 to 100 mg/kg i.p.). In the inflammatory model, 3% carrageenan injected into 1 gastrocnemius muscle decreased the mechanical withdrawal threshold of the paw bilaterally and the compression withdrawal threshold of the muscle ipsilaterally 2 weeks later. Pregabalin (10 to 100 mg/kg) increased the compression withdrawal threshold of the inflamed muscle when compared with vehicle controls. Pregabalin also increased the mechanical withdrawal threshold of the paw bilaterally, but only with 100 mg/kg. In the noninflammatory model, 2 unilateral injections of acidic saline into the gastrocnemius muscle produced bilateral cutaneous and muscle hyperalgesia 24 hours after the second injection. Pregabalin (10 to 100 mg/kg i.p.) significantly increased the compression withdrawal thresholds of the muscle and the mechanical withdrawal threshold of the paw bilaterally when compared with vehicle. However, pregabalin also has significant motor effects at the higher doses (60 to 100 mg/kg). Therefore, pregabalin reduces both muscle and cutaneous hyperalgesia that occurs after muscle insult in 2 animal models of muscle pain at doses that do not produce ataxia. **PERSPECTIVE:** This study shows that pregabalin reduces both cutaneous and muscle hyperalgesia in inflammatory and noninflammatory models of muscle pain. Thus, pregabalin may be an effective treatment for people with chronic muscle pain.

4 Eur J Pharmacol. 2006 Dec 28;553(1-3):82-8. Epub 2006 Sep 23.
Pregabalin action at a model synapse: binding to presynaptic calcium channel alpha2-delta subunit reduces neurotransmission in mice.
Joshi I, Taylor CP.
Author information

Department CNS Biology, Pfizer Global R&D, 2800 Plymouth Road, Ann Arbor, MI 48105, USA.

Abstract

Pregabalin, ((S)-3-(aminomethyl)-5-methylhexanoic acid, also known as (S)-3-isobutyl GABA, Lyricatrade mark) is approved for treatment of certain types of peripheral neuropathic pain and as an adjunctive therapy for partial seizures of epilepsy both the EU and the USA and also for generalized anxiety disorder in the EU. Though pregabalin binds selectively to the alpha(2)-delta (alpha(2)-delta) auxiliary subunit of voltage-gated calcium channels, the cellular details of pregabalin action are unclear. The high density of alpha(2)-delta in skeletal muscle fibers raises the question of whether pregabalin alters excitation-contraction coupling. We used the mouse soleus neuromuscular junction from mice containing an artificially mutated alpha(2)-delta Type 1 protein (R217A) as a model to examine the effect of pregabalin. Pregabalin reduced nerve-evoked muscle contractions by 16% at a clinically relevant concentration of 10 muM in wildtype mice. When acetylcholine receptors were blocked with curare,pregabalin had no effect on contraction from direct stimulation of muscle, suggesting a lack of drug effects on contraction coupling. Our data are consistent with pregabalin having no effect on striated muscle L-type calcium channel function. However, in mice expressing mutant (R217A) alpha(2)-delta Type 1, there was no significant effect of pregabalin on nerve-evoked muscle contraction. We propose that pregabalin reduces presynaptic neurotransmitter release without altering postsynaptic receptors or contraction coupling and that these effects require high affinity binding to alpha(2)-delta Type 1 auxiliary subunit of presynaptic voltage-gated calcium channels

6. PHARMACEUTICAL DATA:

6.1 List of excipients:

Sr. No.	Name of Excipients
1.	Mannitol BP
2.	Size"2" Hard Gelatin Capsules Shell having pink caps and white body IH

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light and moisture.

6.5 Nature and contents of the container:

Pbren 75 is available as an Alu-PVC blister of 10 capsules. Such 3 blisters are packed in a primary carton along with the package leaflet.

6.6 Special precautions for disposal and other handling

Not applicable

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

MARKETING AUTHORIZATION HOLDER
La Renon Healthcare Pvt. Ltd.
207-208, ISCON Elegance, Circle-P, Prahlad Nagar Cross Roads, S.G. Highway, Ahmedabad-380015, Gujarat, India.

Manufactured By:
Stanford Laboratories Pvt. Ltd.
(A subsidiary company of La Renon Healthcare Pvt. Ltd.)
8, Industrial Area, Mehatpur, Distt. Una, (H.P.) 174315, India.

8. MARKETING AUTHORIZATION NUMBER

H2021/CTD6187/2014ER

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION

DATE OF FIRST REGISTRATION: **23/May/2021**

DATE OF LATEST RENEWAL OF THE REGISTRATION: **17/June/2026**

10. DATE OF REVISION OF THE TEXT

17.05.2026