Plenica

Pregabalin

Oral use

25, 75, 150 and 300 mg capsules

Formulae
Plenica 25 Capsules: Each capsule contains Pregabalin 25 mg. Excipients: Lactose anhydrous; Pregelatinized corn starch; Sodium lauryl sulphate; Colloidal silicon dioxide; Talc.
Plenica 75 Capsules: Each capsule contains Pregabalin 75 mg. Excipients: Lactose anhydrous; Pregelatinized corn starch; Sodium lauryl sulphate; Colloidal silicon dioxide; Talc.
Plenica 150 Capsules: Each capsule contains Pregabalin 150 mg. Excipients: Lactose anhydrous; Pregelatinized corn starch; Sodium lauryl sulphate; Colloidal silicon dioxide; Talc.
Plenica 300 Capsules: Each capsule contains Pregabalin 300 mg. Excipients: Lactose anhydrous; Pregelatinized corn starch; Sodium lauryl sulphate; Colloidal silicon dioxide; Talc.

Therapeutic action
Antiepileptic. Antineuralgic. Anxiolytic.

Indications
Adjunctive therapy for adult patients with partial onset seizures, with or without secondary generalization, in co-administration with other antiepileptic drugs.
Management of peripheral and central neuropathic pain in adults.
Management of generalized anxiety disorders in adults.
Management of fibromyalgia.

Pharmacological action
While Pregabalin is a structural derivative of gamma-aminobutyric acid (GABA), it does not bind directly to GABA or benzodiazepine receptors and does not alter GABA concentration or its effects in the central nervous system. Although the mechanism of action of Pregabalin is unknown, it reduces the calcium-dependent release of several neurotransmitters, possibly by modulation of calcium channel function.

Pharmacokinetics:
Following oral administration of Pregabalin under fasting conditions, the substance is rapidly absorbed and peak plasma concentrations occur within 90 minutes after single or multiple-dose administration. Pregabalin oral bioavailability is ≥ 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, however, there is no clinically relevant effect on the total absorption of Pregabalin.

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Pregabalin does not bind to plasma proteins. In laboratory animals it has been shown to cross the blood brain barrier and the placenta and it is present in the milk of lactating animals. The apparent volume of distribution of Pregabalin following oral administration to humans is approximately 0.5 l/kg.
Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled Pregabalin, approximately 98% of the administered dose was recovered in the urine as unchanged Pregabalin. The N-methylated derivative of Pregabalin, the major metabolite of Pregabalin found in urine, accounted for less than 1% of the dose. Pregabalin is eliminated primarily by renal excretion with a mean elimination half-life of 6.3 hours. Pregabalin elimination is directly proportional to creatinine clearance.
Renal impairment: Pregabalin clearance is directly proportional to creatinine clearance. Additionally, Pregabalin is effectively removed from plasma by hemodialysis (following a 4-hour hemodialysis treatment, plasma Pregabalin concentrations are reduced by approximately 50%). Since Pregabalin is eliminated primarily by renal excretion, the dose should be reduced in patients with renal impairment and a supplemental dose should be given immediately following every hemodialysis treatment.
Hepatic impairment: As Pregabalin is not significantly metabolized and is excreted nearly unchanged in the urine, an impairment in hepatic function should not significantly alter Pregabalin plasma levels.
Elderly: Creatinine clearance tends to decrease with increasing age and can therefore result in a decrease of Pregabalin clearance. Patients with age-related decrease in renal function may require a reduction in Pregabalin dose.

Dosage and administration
Plenica can be given with or without food.
Total dose is of 150 to 600 mg per day, divided and administered either two or three times daily.
Epilepsy:
Initial dose: It is recommended that patients be started on a total daily dose of 150 mg/day (75 mg two times a day).
Based on individual patient response and tolerability, the dose may be increased to 300 mg/day after one week. Maximum recommended dose is of 600 mg/day, and it can be achieved after one additional week of treatment.
Neuropathic pain:
Initial dose: Dosing should begin at 150 mg/day (75 mg two times a day).
Based on efficacy and tolerability, dose may be increased to 300 mg/day after 3 to 7 days. Maximum recommended dose is of 600 mg/day which can be achieved after one additional week of treatment.
Generalized anxiety disorder:
Initial dose: Dosing should begin at 150 mg/day (75 mg two times a day).
Based on efficacy and tolerability, dose may be increased to
300 mg/day after one week of treatment. After one additional week dose can be increased to 450 mg/day. Maximum recommended dose is of 600 mg/day which can be achieved after one additional week of treatment.
Necessity of treatment continuation should be evaluated periodically.
Fibromyalgia:
The recommended dose is 300 to 450 mg/day.
Initial dose: Dosing should begin at 150 mg/day (75 mg two times a day) and may be increased to 300 mg/day (150 mg two times a day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 450 mg/day (225 mg two times a day) during the following week. Maximum recommended dose is 450 mg/day.
Treatment discontinuation:
When discontinuing treatment, taper gradually over a minimum of 1 week, irrespectively from indication.
Patients with renal impairment:
Pregabalin is eliminated practically unchanged, primarily by renal excretion and proportionally to creatinine clearance. Therefore in patients with renal impairment dosage should be adjusted based on creatinine clearance, as indicated below:

Creatinine Clearance (ml/minute)	Total Pregabalin daily dose		Dose Regimen
	Initial dose (mg/day)	Maximum dose (mg/day)	
≥ 60	150	600	Two or three times daily
30 - 60	75	300	Two or three times daily
15 - 30	25 - 50	150	Once or two times daily
> 15	25	75	Once daily

Creatinine clearance may be estimated from serum creatinine (mg/dl) determination using following equation:

$$\text{Creatinine clearance} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}}$$

In female patients the results must be adjusted by multiplying with 0.85.

Supplementary dose following hemodialysis:
Pregabalin is effectively eliminated from plasma through hemodialysis (50% of the dose after 4 hours). In addition to the daily dose a single supplemental dose of 25 to 100 mg should be given immediately following every 4-hour hemodialysis treatment.
Patients with hepatic impairment:
No dose adjustment needed.
Elderly patients:
Elderly patients may show age-related compromised renal function which may require dose adjustment.

Contraindications
Known hypersensitivity to Pregabalin or any other component of the product. Nursing. Pediatric patients.

Warnings
As with other antiepileptic drugs, in case of being necessary to discontinue treatment with **Plenica**, it should be tapered gradually over a minimum of one week.
Patients with rare familial galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not be administered this product.
According to actual medical practice, certain diabetic patients showing weight gain during treatment with Pregabalin, may require adjustment of the hypoglycemic medication.
There is no sufficient information regarding the possibility of discontinuing concomitant antiepileptic medication in associated treatments, once the epileptic crisis was effectively controlled with Pregabalin.

Precautions
Pregabalin may cause dizziness and somnolence thus affecting the capacity of car driving and operating machines. It is recommended that patients under Pregabalin therapy should not drive cars, operate machines or perform risky activities until not having determined if this medication affects their capacity to perform these activities.
An increase of the incidence of blurred vision was reported in patients treated with Pregabalin which resolved in a majority of cases with continued dosing. Patients should be informed that if changes in vision occur, they should notify their physician. If visual disturbance persists, further assessment should be considered.

Following abrupt or rapid discontinuation of treatment, some patients reported symptoms including insomnia, nausea, headache, and diarrhea.
Pregabalin associated weight gain was related to dose and duration of exposure. The long-term cardiovascular effects of Pregabalin associated weight gain are unknown.
Pregabalin treatment may cause peripheral edema with no apparent association between peripheral edema and cardiovascular complications such as hypertension or congestive heart failure nor with deterioration in renal or hepatic function.
Higher frequencies of weight gain and peripheral edema were observed in diabetic patients taking both Pregabalin and thiazolidinediones. As the thiazolidinedione class of antidiabetic drugs can exacerbate or lead to heart failure, care should be taken when co-administering **Plenica** and these agents.
Plenica should be used with caution in patients with congestive heart failure with Class III or IV N4HA cardiac status.
Pregabalin treatment was associated with creatinine kinase elevations and isolated cases of rhabdomyolysis were also reported. Patients must promptly report unexplained muscle pain, tenderness, or weakness, particularly if these muscle symptoms are accompanied by malaise or fever. **Plenica** treatment should be discontinued immediately if myopathy is diagnosed or suspected or if markedly elevated creatinine kinase levels occur.
Pregabalin treatment was associated with a decrease in platelet count. However, it was not associated with an increase in bleeding-related adverse reactions.
Pregabalin treatment was associated with PR interval prolongation in the electrocardiogram. Nevertheless there was no increased risk of PR prolongation in patients with baseline PR prolongation or in patients taking other PR prolonging medications.
Pregnancy: Studies performed in laboratory animals showed reproduction toxicity when treated with Pregabalin. There are no adequate and well-controlled studies in pregnant women. Therefore **Plenica** should not be administered during pregnancy unless, according to physician's criteria, the potential benefit to the mother justifies the potential risk to the fetus. Women of childbearing age must use an effective contraceptive method before initiating treatment with **Plenica** and during the complete treatment period.
Nursing: It is not known if Pregabalin is excreted in human milk. Treatment with **Plenica** is therefore contraindicated in nursing mothers.
Pediatric use: The safety and efficacy of Pregabalin in pediatric patients have not been established.
Geriatric use: No overall differences in safety and efficacy were observed between elderly patients and younger patients. Elderly patients may show age-related renal impairment and therefore the Pregabalin dose needs to be adjusted.

Drug interactions
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 alter metabolism of other drugs and does not bind to plasma proteins, it will very unlikely produce or be altered by pharmacokinetic interactions. Specifically, there are no pharmacokinetic interactions between Pregabalin and the following antiepileptic drugs; phenytoin, carbamazepine, valproic acid, lamotrigine, gabapentine, phenobarbital and topiramate. Additive effects on cognitive and gross motor functioning may appear when co-administering Pregabalin with oxycodone, lorazepam and ethanol. No clinically important effects on respiration were seen. Caution should be excercised when co-administering Pregabalin and thiazolidinediones.
Drug abuse and dependence: Pregabalin is not known to be active at receptor sites associated with drugs of abuse. As with any Central Nervous System active drug, physicians should carefully evaluate patients for history of drug abuse and observe them for signs of misuse or abuse (e.g., development of tolerance, dose escalation, drug seeking behavior).

Adverse reactions
Most frequently reported adverse events were: dizziness, somnolence, dry mouth, edema, blurred vision, weight gain and "thinking abnormal" (primarily difficulty with concentration / attention). The adverse reactions most frequently leading to discontinuation were dizziness and somnolence.
Following is a list of all treatment-emergent adverse reactions occurring more frequently than within the placebo group, categorized by body system and frequency. These reactions may also be related to the underlying pathology and/or the co-administered drugs.
Body as a whole: Frequent: Weight gain, fatigue, peripheral edema, feeling drunk, edema, abnormal gait. Infrequent: Asthenia, falling, thirst, chest pain. Rare: Exacerbated pain, anasarca, pyrexia, shiver, weight loss.
Hematological: Rare: Neutropenia.
Metabolism and nutrition disorders: Frequent: Increased appetite, fluid retention. Infrequent: Anorexia. Rare: Hypoglycemia.
Psychiatric: Frequent: Euphoria, confusion, anxiety, libido decreased, irritability, disorientation, depression. Infrequent: Depersonalization, anorgasmy, restlessness, agitation, balance disorder, exacerbated insomnia, depressive mood, speech disorder, hallucinations, abnormal dreams, libido increased, panic attacks, apathy. Rare: Disinhibition.
Nervous system: Very frequent: Dizziness, somnolence, headache. Frequent: Ataxia, disturbances in concentration, disturbances in attention, coordination abnormal, memory impairment, tremor, dysarthria, hypoesthesia, lethargy, paresthesia. Infrequent: Cognition disorders, abnormality of accommodation, nystagmus, speech disorder, myoclonus, hyporeflexia, dyskinesia, psychomotor hyperactivity, abnormal coordination, hyperesthesia, ageusia, burning sensation, intentional tremor, stupor, syncope. Rare: Hypokinesia, parosmia, dysgraphia.
Eye disorders: Frequent: Blurred vision, diplopia. Infrequent: Abnormal vision, dry eyes, blepharitis, reduced vision, pain in or around the eyes, asthenopia, increase in lacrimation. Rare: Photopsia, eye irritation, mydriasis, oscillopsia, visual depth disorders, peripheral vision loss, strabismus, visual brightness.
Ear and labyrinth disorders: Frequent: Vertigo, balance disorders. Rare: Hyperacusia.
Cardiovascular system: Infrequent: Tachycardia, rubor, suffocation. Rare: First degree atrioventricular block, sinus tachycardia, sinus arrhythmia, sinus bradycardia, hypotension, peripheral coldness, hypertension.
Respiratory system: Frequent: Sinusitis, pharyngolaryngeal pain. Infrequent: Dyspnea, nasal dryness. Rare: Rhinopharyngitis, cough, nasal congestion, epistaxis, rhinitis, snores, throat pain.
Digestive system: Frequent: Dry mouth, constipation, vomiting, flatulence, abdominal distension. Infrequent: Sialorrhea, gastroesophageal reflux, oral hypoesthesia. Rare: Ascites, dysphagia, pancreatitis.
Skin and appendages: Infrequent: Sweating, papular rash. Rare: Cold sweat, rash.
Musculoskeletal system: Frequent: Arthralgia, muscle spasms, back pain. Infrequent: Joint swelling, muscle cramps, myalgia, pain in extremities, muscle rigidity. Rare: Cervical spasm, neck pain, rhabdomyolysis.
Urinary system: Infrequent: Dysuria, urinary incontinence. Rare: Oliguria, renal failure.
Genital system: Frequent: Erectile dysfunction. Infrequent: Abnormal ejaculation, sexual dysfunction. Rare: Amenorrhea, mastalgia, galactorrhea, dysmenorrhea, mammary hypertrophy.
Laboratory: Infrequent: Increase in alanine aminotransferase (ALAT or GPT), increase in aspartate aminotransferase (ASAT or GOT), increase in plasma creatinine phosphokinase (CPK), decrease in platelets. Rare: Increase of glycemia, increase of plasma creatinine, decrease of kalemia, decrease of leucocytes.

Overdosage
Overdosages up to 15 grams did not show unexpected adverse events. Treatment of Pregabalin overdosage should include general supportive treatment and may include hemodialysis if necessary.

How supplied
Plenica 25 Capsules: Packages containing 30 capsules.
Plenica 75 Capsules: Packages containing 30 capsules.
Plenica 150 Capsules: Packages containing 30 capsules.
Plenica 300 Capsules: Packages containing 30 capsules.

Sold under prescription.
Made in Argentina.
Product authorized by the Ministry of Health.
Certificate N° 53,241.
Technical Director: Jorgelina D'Angelo, Pharmacist.
Revised: October 2007.

Medicinal product.
Keep out of the reach of children.
Keep in a dry place at a temperature below 30°C.

Manufactured by:
Roemmers S.A.I.C.F.
Fray Justo Sarmiento 2350,
B1636AKJ Olivos, Buenos Aires, Argentina.

Distributed by:
Droguerie Phenicia.

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ROEMMERS
CONCERN FOR LIFE

Colores: Negro 20% Negro
Producto: Plenica 25/75/150/300 mg - Exp. Líbano (en inglés)
Presentación: Cápsulas
Material: Prospecto en taco
Plano N°: RO/4/5/0160/1
Dirección de fibra: Paralela al texto
Gramaje: 50 grs/m²

Medidas: 270 x 160 mm
Código de material: 2054401843
Película: 13178
Fecha: 02/18 **Cód. óptico N°:** 3
Observaciones: Reemplaza a las Pel. Nº 11687 y 13132
Insumo para utilizar en Plenica 25 y 75.