28-04-2020

PREGY® Capsules
(Pregabalin)

DESCRIPTION:

PREGY® contains the active ingredient pregabalin. Pregabalin is an analogue of the neurotransmitter gamma-aminobutyric acid (GABA). lt has analgesic and anticonvulsant activity. lts chemical name is (S)-3-(aminomethyl)-5-methylhexanoic acid

Molecular formula : $C_8H_{17}NO_2$
Molecular weight : 159.23

COMPOSITION:

PREGY® 25mg Capsules	**PREGY**® 50mg Capsules	**PREGY**® 75mg Capsules	**PREGY**® 100mg Capsules	**PREGY**® 150mg Capsules
Each capsule contain:	Each capsule contain:	Each capsule contain:	Each capsule contain:	Each capsule contain:
Pregabalin MS 25mg	Pregabalin MS 50mg	Pregabalin MS 75mg	Pregabalin MS 100mg	Pregabalin MS 150mg

PHARMACOLOGY:
Mechanism of Action

PREGY®(pregabalin) binds to the •2-• subunit of the voltage-gated calcium channels in central nervous system tissues. Pregabalin reduces calcium influx at nerve terminals, which may inhibit the release of excitatory neurotransmitters such as glutamate. Through this mechanism, **PREGY**® may modulate nerve impulses involved in the transmission of pain. However, the clinical relevance of these findings in man is unknown

Pregabalin reduces the release of several neurotransmitters, including glutamate, noradrenaline and substance P

Pregabalin does not show affinity for receptor sites or alter responses associated with the action of several common drugs for treating seizures or pain. Pregabalin does not interact with either $GABA_A$ or $GABA_B$ receptors; it is not converted metabolically into GABA or a GABA agonist; it is not an inhibitor of acute GABA uptake or degradation

PHARMACOKINETICS:
Pregabalin steady-state pharmacokinetics is 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 C_{max} 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 effect on the extent of pregabalin bioavailability
Distribution
In humans, the apparent volume of distribution of pregabalin following oral administration is approximately 0.56L/kg. Pregabalin is not bound to plasma proteins. At clinical doses of 150 to 600mg/day, the average steady-state plasma pregabalin concentrations were approximately 1.5 and 6.0µg/ml, respectively
Metabolism
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. Renal clearance (CLcr) derived from Phase l studies was 73ml/min. Pregabalin mean elimination half-life is 6.3 hours. Pregabalin plasma clearance and renal clearance are directly proportional to creatinine clearance

Pregabalin clearance is reduced in patients with impaired renal function

INDICATIONS:

PREGY®(Pregabalin) is indicated for the management of neuropathic pain associated with:

- Diabetic peripheral neuropathy
- Postherpetic neuralgia
- Spinal cord injury
- Fibromyalgia
- **PREGY**® is also indicated adjunctive therapy for adult patients with partial onset seizures

CONTRAINDICATIONS:

PREGY® is contraindicated in patients who have demonstrated hypersensitivity to pregabalin or to any of the excipients

PRECAUTIONS:
Hereditary Problems of Galactose Metabolism
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine
Weight Gain
In the controlled studies, weight gain occurred more frequently in patients treated with pregabalin than in patients treated with placebo
Hypersensitivity Reactions
There have been reports in the post-marketing experience of hypersensitivity reactions, including cases of angioedema
Dizziness and Somnolence
Pregabalin causes dizziness and somnolence. In the controlled studies, dizziness and somnolence generally began shortly after initiation of pregabalin and occurred more frequently at higher doses
Suicidal Behaviour and Ideation
Antiepileptic drugs (AED), including pregabalin, increase the risk of suicidal thoughts or behaviour in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviour and/or any unusual changes in mood or behaviour

USE IN PREGNANCY: Category C
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

Patient should be instructed to notify their physician if they become pregnant or intend to become pregnant during their therapy

USE IN LACTATION:
It is not known if pregabalin is excreted in the breast milk of humans; however, it is present in the milk of rats. Therefore, breastfeeding is not recommended in women taking pregabalin

INTERACTIONS WITH OTHER MEDICINES
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, pregabalin is unlikely to produce, or be subject to, pharmacokinetic interactions

ADVERSE EFFECTS
The most commonly reported adverse effects were dizziness and somnolence. Adverse effects were usually mild to moderate in intensity. Other adverse effects includes fatigue, weight increased, dry mouth, headache, ataxia, oedema, diplopia, tremor, constipation, nausea, disturbance in attention, vertigo and peripheral swelling

- Psychiatric disorders: Euphoric mood, libido decreased, irritability, disorientation, insomnia
- Nervous system disorders: Paraesthesia, amnesia, sedation
- Gastrointestinal disorders: Vomiting, flatulence, abdominal distension
- Reproductive system and breast disorders: Erectile dysfunction
- General disorders and administration site disorders: Feeling drunk, feeling abnormal

DOSAGE AND ADMINISTRATION:
The dose range is 150 to 600mg per day given in two divided doses
Pregabalin may be taken with or without food

210 mm

120 mm

ADULTS:
Neuropathic Pain Associated with Diabetic Peripheral Neuropathy

The recommended starting dose for **PREGY**® is 150mg/day, given in two or three divided doses (75mg BID or 50mg TID), with or without food in patients with a creatinine clearance rate of at least 60ml/min. Efficacy of **PREGY**® has been demonstrated within the first week. Based on individual patient response and tolerability, the dose may be increased to 150mg BID (300mg/day) after one week

For patients who experience significant and ongoing pain and can tolerate pregabalin 300mg/day well, maximum daily dose of 600mg (300mg twice a day, BID) can be used
Neuropathic Pain Associated with Postherpetic Neuralgia

The recommended starting dose for **PREGY**® is 150mg/day, given in two or three divided doses (75mg BID or 50mg TID), with or without food in patients with a creatinine clearance rate of at least 60ml/min. Efficacy of pregabalin has been demonstrated within the first week. Based on individual patient response and tolerability, the dose may be increased to 150mg BID (300mg/day) after one week

For patients who experience significant and ongoing pain and can tolerate pregabalin 300mg/day well, maximum daily dose of 600mg (300mg twice a day, BID) can be used
Neuropathic Pain Associated with Spinal Cord Injury

The recommended starting dose for **PREGY**® is 150mg/day, given in two divided doses (75mg BID), with or without food in patients with a creatinine clearance rate of at least 60ml/min. Efficacy of **PREGY**® has been demonstrated within the first week. Based on individual patient response and tolerability, the dose may be increased to 150mg BID (300mg/day) after one week

For patients who experience significant and ongoing pain and can tolerate pregabalin 300mg/day well, a maximum daily dose of 600mg (300mg twice a day, BID) may be considered
Pain Associated with Fibromyalgia

The recommended dosage is 300 to 450mg/day, given in two divided doses. The recommended starting dose for **PREGY**® is 150mg/day, given in two divided doses (75mg BID), with or without food in patients with a creatinine clearance rate of at least 60ml/min. Based on individual response and tolerability, the dose may be increased to 150mg BID (300mg/day) after one week

Patients who do not experience sufficient benefit with 300mg/day may be further increased to 225mg BID (450mg/day). In some patients, efficacy of **PREGY**® has been demonstrated within the first week

For patients who experience significant and ongoing pain and can tolerate pregabalin 300mg/day well, maximum daily dose of 600mg (300mg twice a day, BID) can be used
Adjunctive therapy for adult patients with partial onset seizures

PREGY® at doses of 150 to 600mg/day has been shown to be effective as adjunctive therapy in the treatment of partial onset seizures in adults. 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 150mg/day (75mg two times a day, or 50mg three times a day). Based on individual patient response and tolerability, the dose may be increased to a maximum dose of 600mg/day
Use in Renal Impairment

Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. As pregabalin clearance is directly proportional to creatinine clearance dosage reduction in patients with compromised renal function must be individualised according to creatinine clearance (CLcr), as indicated in table below:

Pregabalin Dosage Adjustment Based on Renal Function

Creatinine Clearance (CLcr) (ml/min)	Total Pregabalin Daily Dose*		Dose Regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
• 60	150	600	Two divided doses
30 - 60	75	300	Single daily dose or two divided doses
15 - 30	25 - 50	150	Single daily dose or two divided doses
<15	25	75	Single daily dose
	Supplementary dosage following haemodialysis (mg)		
	25	75	Single dose+
* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose			
+ Supplementary dose is a single additional dose			

Use in Hepatic Impairment:
No dosage adjustment is required for patients with hepatic impairment
Geriatrics (> 65 years):
Pregabalin oral clearance tends to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with age-related decreases in creatinine clearance. Reduction of pregabalin dose may be required in patients who have age-related compromised renal function
Paediatrics (<18 years of age):
The safety and efficacy of pregabalin in paediatric patients (<18 years of age) have not been established and its use in this patient population is not recommended

OR
As directed by the physician

DOSING CONSIDERATIONS:

In accordance with current clinical practice, if **PREGY**® (pregabalin) has to be discontinued, it is recommended this should be done gradually over a minimum of 1 week

OVERDOSAGE:
Symptoms
In overdoses up to 15g, no unexpected adverse effects were reported
Commonly reported adverse events observed when pregabalin was taken in overdose included affective disorder, somnolence, confusional state, depression, agitation and restlessness
Management
There is no specific antidote for pregabalin. Treatment of pregabalin overdose should be symptomatic and supportive

STABILITY:
See expiry on the pack

PRESENTATION:
PREGY® 25mg capsules in a pack of 14's
PREGY® 50mg capsules in a pack of 14's
PREGY® 75mg capsules in a pack of 14's
PREGY® 100mg capsules in a pack of 14's
PREGY® 150mg capsules in a pack of 14's

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity. Store between 15 to 30°C
Improper storage may deteriorate the medicine

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

پریگی® کیپسول
(پریگیبالن)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

R.N-10/HA/04/2020

210 mm

120 mm