Pregabalin and Methylcobalamin

Precob

POM

Composition:

Each hard gelatin capsule contains:

Pregabalin	75mg
Methylcobalin	750mcg

Mechanism of action of pregabalin

Pregabalin binds with high affinity to the alpha$_2$-delta site (an auxiliary subunit of voltage-gated calcium channels) inn central nervous system tissues. Although the mechanism of action of pregabalin is unknown, results with genetically modified mice and with compounds structurally related to pregabalin(such as gabapentin) suggest that binding to the alpha$_2$-delta subunit may be involved in pregabalin's antinociceptive and antiseizure effects in animal models. *In vitro,* pregabalin reducues calcium-dependent release of several neurotransmitters, possibly by modulation of calcium channel function. While pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), it does not bind directly to GABA(A) & GABA(B), or benzodiazepine receptors, does not augment GABA(A) responses in cultured neurons, does not alter rat brain GABA or have or have acute effects on GABA uptake or degradation. However, in cultured neurons prolonged application of Pregabalin increases the density of GABA transporter protein and increases the rate of functional GABA transport. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine,serotonin,or noradrenaline reuptake.

Methylcobalamin:

Methylcobalamin is the neurologically active form if vitamin B_{12},which increases myelin sheath formation and regenerates neurons. Methylcobalamin (methyl-B_{12}) is one of the two forms of biologically active vitamin B_{12}. Methyl-B_{12} is the principal of circulating vitamin B_{12}; hence the form which is transported into peripheral tissue.methyl-B_{12} is absorbed by the intestine by a specific mechanism which uses the intrinsic factor and by a diffusion process in which approximately 1% of the ingested dose is absorbed. Cyanocobalamin, and hydroxycobamin are forms of the vitamin that require conversion to methylcobalamin.

Pharmacokinetics

Pregabalin is well absorbed after oral administration.

It is eliminated largely by renal excretion.

It has elimination half-life of about 6 hours.

Absorption and Distribution

Following oral administration of Pregabalin capsules under fasting conditions, peak plasma concentration occur within 1.5 hours. Pregabalin oral bioavailability is=90% and is independent of dose. Following single (25 to 300 mg) and multiple-dose (75 to 900 mg/day) administration, maximum plasma concentrations (Cmax) and area under the plasma concentration-time curve (AUC) value increases linearly. Following repeated administration, steady state is achieved with 24 to 48 hours; multiple-dose pharmacokinetics can be predicted from single-dose data.

The rate of Pregabalin absorption is decreased when given with food, resulting in a decrease in Cmax of approximately 25% to 30% and an increase in Tmax to approximately 3 hours. However, administration

of Pregabalin with food has no clinically relevant effect on the total absorption of Pregabalin. Therefore, Pregabalin can be taken with or without food.
Pregabalin does not bind to plasma proteins. The apparent volume of distribution of Pregabalin following oral administration is approximately 0.5L/kg. Pregabalin is a substitute for system L transporter which is responsible for the transport of large amino acids across the blood brain barrier. Although there are no data in humans, Pregabalin has been shown to cross the blood brain in mice, rats, and monkeys. In addition, Pregabalin has been shown to cross the placenta in rats and is present in the milk of lactating rats.

Metabolism and elimination

Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 90% 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 0.9% of the dose. In pre-clinical studies, Pregabalin (S-enantiomer) did not undergo racemization to R-enantiomer in mice, rats, rabbits or monkeys.
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half-life of 6.3 hours in subjects with normal renal function. Mean renal clearance was estimated to be 67.0 to 80.9 mL/min in young healthy subjects. Because pregabalin is not bound to plasma proteins this clearance rate indicates that renal tubular reabsorption is involved.
Pregabalin elimination is nearly proportional to creatinine clearance (clcr)

Indications

PRECOB is indicated for:
Management of neuropathic pain associated with diabetic peripheral neuropathy
Management of post herpetic neuralgia
Adjunctive therapy for adult patients with partial onset of seizures
Management of fibromyalgia

DOSAGE & ADMINISTRATION

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

Neuropathic pain associated with diabetic peripheral neuropathy

The maximum recommended dose of PRECOB is 150 mg two times a day (300 mg/day) in patients with creatinine clearance of at least 60 mL/min. begin 150 mg/day. The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Because PRECOB is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function.
Although PRECOB was also studied at 600 mg/day, there is no evidence that this dose confers additional significant benefit and this dose was less well tolerated. In view of dose-dependent adverse reactions, treatment with doses above 300 mg/day is not recommended.

Post Herpetic Neuralgia

The recommended dose of PRECOB is 75 mg to 150 mg two times a day. The dose may be increased to 300 mg/day within 1 week based on efficacy & tolerability.
Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300 mg/day & who are able to tolerate PRECOB, may be treated with a dose of 300mg two times a day. In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation due to adverse reactions, reverse dosing above 300 mg/day for those patients who have on-going pain and are tolerating 300 mg daily.
In patients with creatinine clearance of at least 60 ml/min, begin dosing at 75 mg two times a day. Because PRECOB is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function.

Management of Fibromyalgia

The recommended dose of PRECOB for fibromyalgia is 300 to 400 mg/day. Begin dosing at 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 benefit with 300 mg/day may be further increased to 225 mg two times a day (450 mg/day). Although PRECOB was also studied at 600 mg/day, there is no evidence that this dose confers additional significant benefit and this dose was less well tolerated. In view of dose-dependent adverse reactions, treatment with doses above 450 mg/day is not recommended.

Side effects

Blurry vision, dizziness, dry mouth, sleepiness, swelling of hands and feet, trouble concentrating, weight gain

Seek medical attention right away if any of these SEVERE side effects occur: severe allergic reactions(rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); bloating or swelling of the hands, feet or ankles; changes in vision; confusion; fast or irregular heartbeat; fever; inability to control urination; loss of coordination; mental or mood changes; muscle aches, pain ,tenderness, or weakness (especially if this occurs with a fever or general feeling or discomfort); speaking problems; sudden, unexplained weight gain; suicidal thoughts or actions; unusual tiredness or weakness.

CONTRAINDICATIONS

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

Storage

Store in a dry place below 30^0C (82^0F)

Protect from light

Keep all the medicine out of reach of children.

Packing

3 strips in a box. Each Alu-Alu strip contains 10 capsules.

Manufactured for & Distributed by:

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